

**Research on the mechanisms of  
temperature-dependent sex determination in  
American alligator (*Alligator mississippiensis*)**

**Yatsu, Ryohei**

**SOKENDAI**  
**(The Graduate University for Advanced Studies)**

**School of Life Science**

**Department of Basic Biology**

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## **General introduction**

Two main modes of sex determination exist among gonochoristic vertebrates; genotypic sex determination (GSD) and environmental sex determination (ESD). Among the ESD systems, wide varieties of environmental factors have been displayed to influence sex determination. However, most prominent is the temperature-dependent sex determination (TSD), which is prevalent among the reptiles and is found in all studied crocodilians, tuataras, and in many of turtles and lizard species as well (Bull 1980, Kohno, Parrott et al. 2014). Although the main difference between the two lies in the initial activation trigger, temperature-dependent disruption of GSD and sex reversal can also take place in some lizard and fish species as well (Nakamura 2010). Incubation temperature of the developing embryo during specific temperatures sensitive period (TSP) is able to direct the individual's sexual fate, and initiate gonadal sex differentiation to either ovary or testis. Ever since the initial discovery of TSD, its mechanism of action has been questioned and although multiple theories have been suggested, it remains elusive.

Vertebrate gonadal sexual development follows a conserved pattern (Yao and Capel 2005), in which the onset of bipotential genital ridge formation during embryonic period is accompanied by sex determination period shortly after. During this period the aforementioned systems (GSD/ESD) are activated in various ways, and determine the gonadal sex of the individual by initiating specific gene cascade associated with ovary- or testis-differentiation. While the specific upstream ovarian- or testis-determining trigger may widely vary depending on species, the downstream genetic action and its

complex networks are fairly conserved in each cascade and utilize mostly similar gene sets, which result in similar sex-specific cell differentiation and regulation of sex steroid hormones (Sinclair, Smith et al. 2002). These gonadal transformations later influence the sex of the individual on the endocrine, behavioral and physiological level. Several sex-determining factors have been uniquely identified in many of the organisms with GSD. In contrast, the TSD mechanism still remains unclear and the identification of the initial activation mechanism in TSD system are being widely sought after.

Research for elucidation of TSD has undergone considerable history and progress since its first discovery. In 1966, while studying African lizards species, Charnier first documented TSD in reptiles (Charnier 1966), and which led to the foundation of modern vertebrate TSD studies. During the initial discovery, TSD was met with harsh skepticism and were suspected to be due to temperature-dependent differential mortality, which later were proven untrue and subsequent discovery and proof of TSD naturally taking place in other reptiles, such as turtles and crocodilians, further cemented validity of TSD in wildlife (Bull 1980, Ferguson and Joanen 1982). Single- and double-temperature shift experiments at various developmental stages established TSD temperature range, patterns and TSP in many of the species.

Although no clear model organism is established for reptiles, gonadogenesis has been extensively studied in only a very few reptile species, including the American alligator *Alligator mississippiensis*, and red-eared sliders *Trachemys scripta* (Smith and Joss 1993, Kohno, Parrott et al. 2014). Much of the early works focused on the sex steroid hormone effect upon the sex determination. Sex steroid hormone levels were

manipulated via administration of pharmacological reagents directly onto the eggshell, and the developing embryos successfully displayed altered sexual development (Crews 1994, Lance 2009). As more genes-related to sexual development was identified in model organisms, later studies focused on expressions of key genes related to sex differentiation, such as *SOX9*, *AMH*, and *CYP19A1*. Although these comparative studies were able to characterize the key gene expression movement in the downstream cascade, much of the upstream gene cascade still remained a mystery. Species that display TSD are commonly thought to lack heteromorphic sex chromosomes (Wang, Pascual-Anaya et al. 2013, Green, Braun et al. 2014). Instead, TSD is believed to be triggered by thermosensitive factor in the gonad, as turtle gonad organ culture experiments were able to demonstrate endogenous thermosensitivity (Moreno-Mendoza, Harley et al. 2001, Shoemaker-Daly, Jackson et al. 2010). These major findings provided the foundation for the current research presented, and now, using *Alligator mississippiensis* as experimental organism, further insights on TSD mechanisms have been achieved. In this thesis, several new findings in TSD research using *Alligator mississippiensis* is documented, including identification of potential thermosensitive trigger (Chapter 1) and comprehensive characterization of transcriptome during initial phases of sex determination (Chapter 2), and I provide a novel model for TSD mechanism based on obtained results.

## **Chapter 1.**

**TRPV4 associates environmental temperature and  
sex determination in the American alligator**

## **Introduction**

Highly diverse modes of sex determination have been observed among vertebrates. In most cases, sex is determined genetically (genotypic sex determination; GSD), which has been characterized by the presence of a key sex-determining gene. In contrast, in many reptiles including crocodilians, select chelonians and squamates, differential sexual outcomes have been identified under varying incubation temperatures during a critical temperature sensitive period (TSP) in the developing embryo (temperature-dependent sex determination; TSD) (Charnier 1966, Bull 1980, Rhen and Schroeder 2010). As an alternative to the GSD system, in which the heritable traits dictate subsequent gonadal differentiation, all species studied to date that exhibit TSD appear to lack sexually heteromorphic chromosomes (Wang, Pascual-Anaya et al. 2013, Green, Braun et al. 2014), and sexual development is assumed to be initiated mostly by environmental cues, independent of the individual's genetic background. However, genetic researches in reptiles are particularly hindered by lack of available genetic manipulation techniques, compared to other vertebrate species, and much of the sex determination mechanism in this pivotal vertebrate clade is yet to be understood.

American alligators, *Alligator mississippiensis*, display TSD, and the developing embryo detects a thermal stimulus that apparently directs the sexual fate of the bipotential gonad; this critical range of incubation temperatures is shared among all other crocodilians studied to date (Ferguson and Joanen 1982, Lang and Andrews 1994, Deeming 2004). Eggs incubated at a constant temperature of 33°C yields 100% male offspring, whereas incubation temperatures below 30°C lead to female biased offspring sex ratio during TSP (Ferguson stages 21 to 24) (Ferguson 1985). Downstream sexual differentiation processes in alligators follows a fairly similar pattern often shared among

vertebrates. Male producing temperatures (MPT) facilitates the medullary supporting cells to enlarge and proliferate, which in turn initiates their arrangement into distinct seminiferous cords by hatching (stage 27), and eventual testicular morphogenesis (Smith and Joss 1993). Dynamic anti-Müllerian hormone (*AMH*) upregulation and ensuing SRY-box 9 (*SOX9*) upregulation are observed during the sex determination phase (Urushitani, Katsu et al. 2011). At female producing temperatures (FPT), however, primordial germ cell proliferation occurs in the thickened cortex while the medulla undergoes extensive fragmentation (Smith and Joss 1993, Moore, Uribe-Aranzábal et al. 2008). By developmental stage 27, irreversible female commitment occurs with the eventual onset of estradiol-17 $\beta$  synthesis by aromatase (*CYP19A1*), thus completing ovarian morphogenesis (Moore, Uribe-Aranzábal et al. 2008).

However, it remains elusive how incubation temperature during the TSP triggers TSD and the subsequent differentiation cascade. Transformation of the initial environmental temperature signal to a biochemical signaling in TSD is not understood in any species, including species with temperature-dependent sex reversal (Nakamura 2010). Isolated gonads from a TSD reptile, *Trachemys scripta*, have been demonstrated to be directly receptive to thermal stimuli, suggesting that the initial reception of environmental cues can be triggered through an endogenous sensory mechanism (Shoemaker-Daly, Jackson et al. 2010). This mechanism hypothesized to be shared among TSD reptiles, including in the alligator as well.

Various mechanisms of thermal detection have been reported in the past, these include protein conformational changes, structural shifts in nucleic acid, and membrane property changes. In eukaryotes especially, several multi-pass

transmembrane ion channels have been the focus for thermal sensing (Cho, Yang et al. 2012, Sengupta and Garrity 2013), most prominent of which is the transient receptor potential (TRP) cation channel superfamily. The channels in this superfamily have been the most extensively characterized among vertebrates. The TRP channels in this superfamily mostly function as environmental sensors primarily through  $\text{Ca}^{2+}$  signaling, uniquely activated by various internal or external cues including osmolarity, pH, pressure, and temperature (Gees, Owsianik et al. 2012). At present, 10 thermosensitive TRP channels have been identified in humans and rodents: TRPV1, TRPV2, TRPV3, TRPV4, TRPM2, TRPM3, TRPM4, TRPM5, TRPM8, and TRPA1. Many of the thermosensitive TRP channels possess well-defined ranges of activation as well as wide diversification in physiological and functional properties (Vay, Gu et al. 2012), and are an ideal candidate as potential thermosensor within TSD mechanism, particularly the TRPV4 since the mammalian TRPV4 channel is known to be activated by moderate heat (33-34°C) (Guler, Lee et al. 2002, Heller and O'Neil 2007).

Here, we report the involvement of *A. mississippiensis* TRPV4 (AmTRPV4) ortholog in temperature-dependent sex determination. Electrophysiological analysis reveals AmTRPV4 functions as a molecular thermal sensor at a threshold near the range observed in TSD for this species, and pharmacological manipulation of channel activity affects the sexual differentiation processes in spite of incubation temperature during development. This is the first demonstration of a link between a well-described thermo-sensory mechanism, TRP channel, and regulation of TSD, shedding light on the elusive TSD molecular mechanism.

## Results

### *Expression and cloning of AmTRPV4*

To examine the presence of thermosensitive TRP channels in the gonad during the sex determination period in the American alligator, expression for orthologs of the mammalian thermosensitive TRP channels was screened at the onset of TSP and sex determination (Ferguson stage 21) using RT-PCR. Gene expression was limited to 5 TRP ion channels: *TRPV2*, *TRPV4*, *TRPM3*, and faintly from *TRPA1* and *TRPM8* (Figure 1-1A). Of the 5 confirmed TRP channels expressed in the gonad, *TRPV4* expression was of particular interest due to ideal predicted activation temperature. Thus, AmTRPV4 was deemed noteworthy for further investigation. Quantitative RT-PCR analysis for *TRPV4* was conducted during various developmental stages; at the bipotential stage (stage 19), onset of TSP and sex determination (stage 21), end of TSP and onset of sexual differentiation (stage 24), and latent stages of sex differentiation (stage 27) at both MPT and FPT. The time series revealed a sexually dimorphic expression patterns in the gonad, with suppression at the FPT (Figure 1-1B). *AmTRPV4* expression was also examined in the chorioallantoic membrane, as well as in the epidermal tissues, and its expression was confirmed, although a sexually dimorphic pattern was not observed (Figure 1-2A and B).

AmTRPV4 clone (857 aa) was amplified, slightly shorter in comparison to other reported reptilian TRPV4 orthologs, and phylogenetic analysis showed the AmTRPV4 to be more closely related to birds and other reptilian TRPV4 orthologs, when compared to mammalian TRPV4s (Figure 1-3). An evolutionary comparison of various TRPV4 orthologs seemingly points toward overall sequence conservation among the higher vertebrates (Figure 1-4). Overall similarity in amino acid sequences were observed between alligator TRPV4 and mouse (*Mus musculus*; 86%), human

(*Homo sapiens*; 85%), chicken (*Gallus gallus*; 87%), lizard (*Takydromous tachydromoides*; 88%), and snake (*Elaphe quadrivirgata*; 88%) (Liedtke, Choe et al. 2000, Nagai, Saitoh et al. 2012, Saito and Tominaga 2014). Aside from the proline rich domain (PRD), major domains in the TRPV4 channel structure shared high amino acid sequence identity among higher vertebrate orthologs, and hence, we expected a similar temperature-induced channel activation pattern in AmTRPV4 as observed from mammalian TRPV4 channel activation.

#### *AmTRPV4 is a potential candidate in TSD initiation*

At present, very little of the TRPV4 channel thermosensitivity properties have been well characterized in non-mammalian vertebrate species, and hence, characterization of AmTRPV4 was essential before further investigation. Following AmTRPV4 isolation, ion channel functional properties and activation threshold against thermal stimulus were assessed using the *Xenopus laevis* oocyte expression system (Saito, Banzawa et al. 2014). Administration of mammalian TRPV4-specific agonist elicited a clear response in cRNA-injected oocytes, and not in negative control (water injected oocyte), indicating successful expression in the oocyte. Furthermore, thermal sensitivity was also confirmed and heat stimulation successfully elicited clear inward current (Figure 1-5A and B). *Xenopus* oocytes subjected to water (mock) injection showed no heat-induced current, suggesting specific heat activity by AmTRPV4. An Arrhenius plot analysis indicated an average temperature threshold as  $37.30 \pm 0.54^\circ\text{C}$  ( $n=17$ ), revealing a warm temperature threshold (Figure 1-5C).

Chemical responsiveness to mammalian TRPV4-specific agonists and antagonist administration was examined. AmTRPV4-expressing oocytes displayed

current flow with perfusion of GSK1016790A, a potent TRPV4 specific agonist (Thorneloe, Sulpizio et al. 2008, Vincent and Duncton 2011), at a dose of 50 nM (Figure 1-5D). In addition, RN1734, a known TRPV4-specific antagonist (Vincent and Duncton 2011), was able to partially and reversibly inhibit AmTRPV4 activated by GSK1016790A (Figure 1-5E). Furthermore, RN1734 also was able to inhibit temperature-induced currents in AmTRPV4-expressing oocytes in a reversible manner (Figure 1-5F).

AmTRPV4 was next expressed in HEK293 cells and Ca<sup>2+</sup> imaging experiments were performed to examine whether activation of AmTRPV4 is capable of increasing intracellular Ca<sup>2+</sup> concentration ([Ca<sup>2+</sup>]<sub>i</sub>). [Ca<sup>2+</sup>]<sub>i</sub> increased during a heat stimulation above room temperature, as well as after administration of GSK1016790A (Figure 1-5G). In contrast, mock-transfected HEK293 cells showed only faint responses to both stimuli (Figure 1-5H), suggesting that the Ca<sup>2+</sup> influx was specifically mediated by the AmTRPV4 channel activation. These results confirmed the sensitivity of AmTRPV4 to warm temperatures, and its responses to chemicals (an agonist and antagonist) were found to be similar to that described for mammalian TRPV4.

*Inhibition of AmTRPV4 during sex determination alter male determination and differentiation-related gene expression*

Marked expression of AmTRPV4 in the gonad during TSP, as well as heat-dependent channel activation at a temperature proximate to temperature range involved with alligator TSD provide strong evidence for a possible role of AmTRPV4 in TSD. In order to assess the role of AmTRPV4 during TSD, the channel was evaluated via pharmacological manipulation. Alligator eggs were given a single

administration of the chemical agonist GSK1016790A or antagonist RN1734 *in ovo* at stage 19 (bipotential gonad stage), using two different concentrations (0.005 µg/g/egg, and 0.5 µg/g/egg). These doses should be considered as nominal, as we lack information concerning the chemicals' permeation of the eggshell and half-life *in vivo*. Also, by dosing AmTRPV4 agonist and antagonist to the whole embryo via *in ovo* exposure, we were able to observe potential full body effects following activation or inhibition of AmTRPV4, replicating an elevated or low thermal effect. The eggs were incubated under MPT (33.5°C) or FPT (30.0°C) conditions and subsequent effects were examined at stage 27 (stage prior to hatching), focusing on various sex differentiation related genes, and specifically on *AMH*, *SOX9*, and *CYP19A1* gonadal gene expression as sexual markers (Figure 1-6*A*, *B* and *C*, Figure 1-7*A* and *B*).

Quantitative RT-PCR analysis revealed that two genes (*AMH* and *SOX9*) related to testicular differentiation were significantly down-regulated by administration of the AmTRPV4 antagonist RN1734 at MPT conditions in a dose-dependent manner (Figure 1-6*A* and *B*). Recorded body weights of the embryos were similar among all experimental groups, and the differential expressions were not due to delayed embryonic development (Smith and Joss 1993) (Figure 1-8). Similarly, expression levels assessed by *in situ* hybridization on the differentiated gonads also reflected the results from quantitative RT-PCR, and the lowered gene expression level of *AMH* was confirmed (Figure 1-6*D*). Administration of an AmTRPV4 agonist, GSK1016790A, at FPT did not result in a significant change in gene expression levels based on quantitative RT-PCR, possibly due to sexually dimorphic *AmTRPV4* expression (reduced expression at female generating temperatures) as reported above (Figure 1-1*B*, 1-6*A*, *B*, and *C*). Interestingly, upon closer inspection, the immunohistochemistry

revealed an ectopic upregulation of *SOX9* in agonist-treated FPT gonads, indicating that AmTRPV4 activation initiated expression of one of the genes required for male sex differentiation (Figure 1-6E). It should be noted, however, that administration of GSK1016790A at the higher dosage induced high mortality; necropsy data indicated premature embryo death that occurred shortly after drug administration. Hence, only low dosage results were available for analysis of the TRPV4 agonist exposure group. In contrast to the genes primarily associated with testicular differentiation, expression levels for *CYP19A1* was unaffected regardless of altered AmTRPV4 channel activity with differing thermal environments (Figure 1-6C). As a result, due to a lack of significantly altered *CYP19A1* expression, feminization of RN1734-treated embryos incubated at MPT was very limited: that is, we were not able to induce a feminized gene expression pattern in the gonad following inhibition of AmTRPV4 suggesting that this channel is not effective in the ovarian pathway.

Histological analysis (Figure 1-9A and B) revealed that while there were instances of complete feminization following exposure to RN1734, over all both RN1734- and GSK10016790A-treated samples were histologically and morphologically similar to their respective control groups despite significantly lowered *AMH* and *SOX9* gene expression levels in the RN1734-treated groups. However, RN1734-treated groups displayed an increase in prominent Müllerian ducts in a dosage-dependent manner, consistent with lowered *AMH* expression (Figure 1-9A and D). In some of these individuals, the ducts showed remarkable signs of regression, namely the reduction in the mesosalpinx (Austin 1989). Although the AmTRPV4 targeted treatment did not yield statistically significant phenotypic changes, it did result in a rise of individuals

with an abnormal sexual phenotype, with both male-like (testis-like gonad) and female-like (developed Müllerian duct) characteristics.

In summary, manipulation of AmTRPV4 activity impeded induction of the testicular differentiation cascade on a molecular level, but had little effect on the ovarian differentiation cascade, suggesting that TRPV4 does not solely account for thermosensitive trigger mechanism in TSD, but rather, may be part of a larger, more complex mechanism in place.

## Discussion

Here, we demonstrate an active involvement of TRPV4 channel during TSD in *A. mississippiensis*, and its possible role for promoting male development in a temperature-dependent manner. This is the first experimental demonstration of a link between a well-described thermo-sensory mechanism, TRPV4 channel, and regulation of TSD. In many of the environmentally sex determination (ESD) models, it is widely accepted that a presence of an environmental sensor-like element is responsible for the initiation of sex determination cascade. Similarly, several candidate factors have been investigated in TSD species in the past, including epigenetic influences (Matsumoto, Buemio et al. 2013, Parrott, Kohno et al. 2014), heat shock proteins (Kohno, Katsu et al. 2010), cold inducible RNA binding protein (Kohno, Katsu et al. 2010, Rhen and Schroeder 2010), and enzymes related to endocrine signaling such as estrogenic (Lance 2009, Cruze, Kohno et al. 2012) and/or glucocorticoid (Hayashi, Kobira et al. 2010, Yamaguchi and Kitano 2012). However, no link between sex determination pathway and temperature sensation could be experimentally demonstrated through these factors

and they remained mostly speculations based on correlative data. Our findings serve as a first step toward shedding a new light on the underlying thermosensitive mechanism.

Our results indicate that while AmTRPV4 channel activity may significantly influence male gonadal sex determination pathway at a molecular level, it alone does not account for the initiation of gonadal sex determination mechanism, as evidenced by lack of significant gonadal sex reversal due to unaltered *CYP19A1* expression, and seemingly independent female gonad sex determination pathway. Rather, TRPV4 is expected to be a component of the much larger framework governing the initiation of TSD. Ambient temperature can broadly influence multiple targets at once and most likely several elements are involved in the TSD mechanism one way or the other, including the potential factors investigated previously. Furthermore, co-regulation of Ca<sup>2+</sup> signaling by multiple TRP channels has been well described before (Cheng, Sun et al. 2010), and other TRP channels observed could also be involved. Although current study employs pharmacological manipulation as a first step to study AmTRPV4's role in TSD, more sophisticated methodology is desired in order to evaluate the relational extent between TRPV4 and TSD in the near future.

Our results also indicate that alligator TRPV4 channel activates at 37.3°C, higher than we had originally anticipated, that is, artificial incubation at a constant temperature of 35°C or higher have been associated with embryonic death in the past studies (Ferguson and Joanen 1982, Lang and Andrews 1994). In the wild however, we regularly recorded nest temperatures in that range from nests that produce viable hatchlings (Figure 1-10). We observed that nest temperature fluctuates daily and during incubation in natural alligator nest, and many nests exhibited elevated temperatures, suggesting thermal patterns during incubation may be critical as well.

Although mammalian TRPV4 activates at 27-34°C, AmTRPV4 showed activation at a relatively higher temperature, near 37°C, based on our results. Evolutionary shift in temperature sensitivity has been observed among thermosensitive TRP channel orthologs from various vertebrate species and would most likely account for the difference observed in AmTRPV4. How much of our results from the *Xenopus* oocyte *in vitro* experiment translates to the actual embryonic environment during TSP are up to debate. Although MPT (33.5°C) is relatively lower than supposed activation temperature, *in ovo* administration experiment showed that inhibiting AmTRPV4 activity was still able to induce significant differential gene expression. Activation temperatures of TRP channels have been reported to shift depending on the cellular environment (Heller and O'Neil 2007). In the case of TRPV4, membrane properties greatly influence thermal sensitivity (Heller and O'Neil 2007, Garcia-Elias, Mrkonjic et al. 2013), and a delicate difference in the membrane environment may account for the 4°C margin of difference in this case.

A relatively small degree of sexual dimorphism in *AmTRPV4* gene expression helps explain why the molecular mechanisms behind TSD are so difficult to identify; unlike GSD, in which dynamic sexually dimorphic gene expression (e.g., mammalian *Sry*, galline *DMRT1*) determines sexual fate, the TSD may not necessarily be initiated by dimorphic gene expression alone, as implied from our results with TRPV4 channel activity in alligators. Overdependence on comparative analysis between TSD and GSD models may restrict further discoveries; an independent approach will be required for constructing TSD models in the future. It has been suggested that ‘cumulative discrepancy’ underlies TSD, as implied in many of the TSD reptiles (Quinn, Georges et

al. 2007), and activation of AmTRPV4 during the lengthy TSP may contribute to such cumulative mechanism.

Multiple functions have been attributed to the mammalian TRPV4, a polymodal  $\text{Ca}^{2+}$ -permeable channel, including cell-death induction, alteration of gene expression, channel trafficking, and protein interactions by careful maintenance of  $\text{Ca}^{2+}$  levels (Nilius and Voets 2013). This highly flexible and adaptable nature is suitable for regulating cell fate; TRPV4 plays a crucial role in various cellular differentiations, such as chondrocyte (Muramatsu, Wakabayashi et al. 2007), myofibroblast (Rahaman, Grove et al. 2014), osteoclast (Masuyama, Vriens et al. 2008), and keratinocyte (Sokabe, Fukumi-Tominaga et al. 2010). TRPV4-assisted steady influx of  $\text{Ca}^{2+}$  allows for  $\text{Ca}^{2+}$ /calmodulin (CaM) complex-mediated molecular cascades to take place, such as *Sox9* upregulation in chondrocyte differentiation (Muramatsu, Wakabayashi et al. 2007, Nilius and Voets 2013). Consistent with previous reports, AmTRPV4-mediated  $\text{Ca}^{2+}$  influx through channel activation was confirmed, and the positive relationship observed between AmTRPV4 channel activity and *SOX9* expression from our results resembled the regulatory relationship reported during chondrocyte differentiation. TRPV4's role in gonad morphogenesis is less studied, though  $\text{Ca}^{2+}$  influx is an essential component in mammalian male sex determination (Argentaro, Sim et al. 2003, Hanover, Love et al. 2009). Indeed, CaM is crucial for the nuclear import of SOX9 and its subsequent transcriptional activity in mammals, and the loss of a SOX9-CaM interaction is associated with autosomal sex reversal (SRA) disease in humans (Argentaro, Sim et al. 2003). Additionally, innate male biased sexual dimorphism in TRPV4 channel activity has been reported in several studies involving TRPV4-deficient mouse (Clark, Votta et

al. 2010, van der Eerden, Oei et al. 2013). Interestingly, van der Eerden *et al.* (2013) speculated TRPV4 as a male-specific regulator of osteal cell differentiation.

Crocodilians represent an interesting presence among the reptiles. *Alligator mississippiensis* is believed to display a type II TSD pattern (Lang and Andrews 1994, Deeming 2004), in which the embryo feminization is attained at both low and extreme high temperatures, although 100% male productions at incubation temperatures as high as 36°C have also been previously reported (Ferguson and Joanen 1982). Based on our results, this may even imply a presence of a secondary thermosensitive mechanism, though molecular data concerning high temperature female are scarce, and require more investigation before making further insights. While that, in and of itself, already indicates a complex TSD-triggering mechanism among crocodilians, their sex determination threshold temperature is also substantially higher than majority of TSD reptiles (Lang and Andrews 1994), and the sexual developmental pattern are distinct from other reptile species (e.g., *AMH* expression precedes *SOX9* during testis differentiation) (Western, Harry et al. 1999). Variation in the TSD pattern, as well as inconsistency in the gene expression patterns early on in the sex determination even among other TSD reptiles (Yao and Capel 2005, Shoemaker and Crews 2009, Valenzuela, Neuwald et al. 2013), questions the extent of homogeneity and diversity within TSD mechanisms and potential role of TRPV4 in TSD. Non-mammalian vertebrate TRP channels are only starting to be analyzed, including those in reptiles (Saito, Nakatsuka et al. 2012, Di-Poï and Milinkovitch 2013), and further insight is expected in the near future.

## Materials and Methods

### *Animals, tissue collection and chemicals*

Alligator eggs were collected at Lake Woodruff National Wildlife Refuge, Volusia County, FL, were approved by and under permits from the Florida Fish and Wildlife Conservation Commission and the U.S. Fish and Wildlife Service (Permit #: SPGS-10-44). Alligator eggs were collected in June of 2011 to 2013. All works involving alligators were approved by and was performed under the guidelines specified by the Institutional Animal Care and Use Committee at Medical University of South Carolina (Permit #: AR3036). Once the eggs were collected, they were transported to Hollings Marine Laboratory (Medical University of South Carolina; Charleston, SC, USA) where they were incubated in damp sphagnum moss.

Embryonic developmental stage of each clutch was determined using criteria described by Ferguson (1985) (Ferguson 1985). Until embryonic stage 19, the eggs were incubated under FPT (30.0°C), at which point they each underwent random treatments and were separated into two groups, incubated under MPT (33.5°C) or FPT (30.0°C). GSK1016790A, (Sigma-Aldrich, St. Louis, MO, USA) and RN1734 (Tocris Bioscience, Bristol, UK) were dissolved in ethanol for embryonic exposure experiment. 0.005, 0.5 µg/g egg of agonist (GSK1016790A) and antagonist (RN1734) were administered once at stage 19 *in ovo*. Ethanol was administrated as vehicle in control group. The alligator embryonic GAM (gonad adrenal mesonephros complex), chorioallantoic membrane, and epidermal tissues were sampled at stages 19, 21, 24 and 27, and subsequently preserved in either RNAlater (Life Technologies, Carlsbad, CA, USA) or 4% paraformaldehyde until further analysis.

### *Molecular cloning of AmTRPV4 and sequence analysis*

Total RNA was extracted from female neonatal gonad, using RNeasy kit (Qiagen, Valencia, CA, USA). Full coding region of the AmTRPV4 was determined by standard procedure using SmartRACE kit (Takara, Ohtsu, Japan), and finally full-length AmTRPV4 was cloned with KOD+ polymerase (Toyobo, Osaka, Japan). The amplified full-length AmTRPV4 cDNA product was then subcloned into pOX+ vector (Saito, Banzawa et al. 2014) for electrophysiological analysis. Primer information is reported in Table 1-1.

Multiple sequence alignment for vertebrate TRPV4 homologues was performed using the CLUSTAL W (Thompson, Higgins et al. 1994). Phylogenetic relationships of TRPV4 were then examined using TRPV4 amino acid sequences derived from GenBank/EMBL database. The TRPV4 genes and species used are summarized in Table 1-2. Based on TRPV4 conserved sites, which include the ankyrin repeat domains and transmembrane domains (652 residues in AmTRPV4), with all the alignment gap sites were eliminated, minimum-evolution methods (Rzhetsky and Nei 1993) was applied to construct an evolutionary tree, using MEGA 5 software (Tamura, Peterson et al. 2011). The statistical confidence was then computed by bootstrap method with 1000 replications.

### *Oocyte electrophysiology*

The alligator TRPV4 channel was expressed in the oocytes of the African clawed frog *Xenopus laevis*, and ionic currents were recorded using the two-electrode voltage-clamp method as described previously (Saito, Banzawa et al. 2014). cRNA of the full length AmTRPV4 channel clone inserted between *X. laevis* β-globin 5' and 3' UTR in the pOX+ vector was synthesized using mMessage mMachine kit (Life

Technologies) according to the manufacturer's protocol, and was injected into *Xenopus* oocytes (4, 10 ng/μl) and ionic currents were recorded 2-5 days post-injection using a heat perfusion system. ND96 solution, which consists of 96 mM NaCl, 2 mM KCl, 1.8 mM CaCl<sub>2</sub>, 1 mM MgCl<sub>2</sub>, and 5 mM 2-[4-(2-Hydroxyethyl)-1-piperazinyl] ethanesulfonic acid (HEPES), was used as bath solution after adjusted to pH 7.4. The oocytes were voltage-clamped at -60 mV. All chemicals used for assay were diluted into ND96 bath solution, and applied to the AmTRPV4 expressing oocytes through perfusion. Likewise, heated thermal stimulations were applied to the oocytes by heated ND96 bath solution perfusion. Temperature threshold for activation was determined by Arrhenius plot, using Origin software (OriginLab, Northhampton, MA, USA). All procedures involving the care and use of the frogs were approved by Institutional Animal Care and Use Committee of National Institutes of Natural Sciences, Japan.

#### *Ca<sup>2+</sup>-imaging experiments*

Alligator TRPV4 was expressed in HEK293 cells, and Ca<sup>2+</sup>-imaging experiments were performed using methods previously described (Saito, Banzawa et al. 2014). HEK293 was cotransfected with AmTRPV4 recombinant pcDNA3.1+ vector and DsRed containing pCMV vector using Effectene Transfection Reagent (QIAGEN) following manufacturer's protocol. The transfected cells were incubated at 33 °C and then used for Ca<sup>2+</sup>- imaging experiments after incubation lasting ~24 h. Fura-2 was loaded into cells by incubating at 33°C for 1h with fura-2 acetoxyethyl ester. During recording, the fura-2-loaded cells were placed in a recording chamber filled with bath solution (140 mM NaCl, 5 mM KCl, 10 mM HEPES, 2 mM MgCl<sup>2</sup>, 2 mM CaCl<sup>2</sup>, 10 mM glucose, pH 7.4). Heated bath solution was perfused for thermal stimulation. For

chemical stimulation, GSK1016790A (50 nM) or ionomycin (2.5  $\mu$ M) were dissolved in bath solution and perfused.  $[Ca^{2+}]_i$  in transfected cells were measured under light at 340 nm and 380 nm, while fluorescent signals at 500 nm were recorded and their ratios (F340/F380) were calculated. The cells expressing DsRed were used for analysis as AmTRPV4 expressing cells. For negative control experiments, HEK293 cells were cotransfected with pcDNA3.1 and DsRed containing pCMV vectors.

#### *Nest Temperature data*

One hundred and eighty TidbiT v2 programmable temperature data loggers (Onset Computer, Bourne, MA, USA) were deployed in 48 alligator nests during the 2010-2014 nesting seasons to determine actual nest temperatures within wild American alligator nests. The loggers were placed within the nest touching eggs at the bottom, middle and top of the nest throughout the incubation process. A fourth temperature logger was also placed on the outside of the nest hanging in the air above to collect ambient air temperature. The thermistors were programmed to record the temperature every five min and were picked up either when the nest hatched, or after 75 days of deployment time (whichever came first). Once retrieved, data from the thermistors were downloaded to examine temperature profiles throughout the incubation period as well as during the period of sexual determination.

For thermister deployment, a vertical 25 cm channel next to the nest chamber was dug out on one side of the eggs within the nest. A rebar or wooden stake with all of the thermistors tied to it was inserted into the thermistor chamber farthest away from the eggs as possible to keep the thermistors at the nest site during the removal of the neonates. Starting from the bottom of the eggs in the nest a thermister would be placed

touching the bottom egg, with the serial number and depth of placement noted on the data sheet. The nesting material would then be placed on that thermister until the middle of the egg chamber where the second thermister would be placed touching an egg. This process was replicated with the third and/or top thermister. The top of the nest was covered with the natural nesting material and left alone until thermistors were recovered. To verify temperature accuracy, the loggers were placed into an incubator with set temperature shifts to verify the accuracy of all loggers. The last calibration had variability within all of the sensors of 0.16 of a degree of true calibration. Out of the 48 nests in which thermistors were deployed, 32 nests hatched, 10 nests were dead, and 6 were depredated (3 hogs, 1 raccoon and 2 fire ants).

#### *Expression profiling and statistical methods*

Gonadal tissues were carefully dissected from the GAM samples stored in RNAlater. Total RNAs were then extracted from gonadal, chorioallantoic membrane, and epidermal tissues, using SV Total RNA Isolation System (Promega, Madison, WI, USA). Template cDNA was synthesized from purified total RNA with iScript cDNA synthesis kit (Bio-Rad, Hercules, CA, USA). Primers used for TRP expression profiling was validated by confirming TRP expression in various tissues with 35 PCR reaction cycles. Real-time quantitative PCR reactions were performed using ABI Prism 7000 (Life Technologies) using the SYBR-Green PCR core reagents kit (Life Technologies), in the presence of appropriate primers, with *RPL8* as a housekeeping gene. Primers used were constructed based on previously reported sequences (Mochizuki, Sokabe et al. 2009, Parrott, Kohno et al. 2014). Primer information is reported in Table 1-1. Each gene was assayed in triplicate samples with relative standard curve method under the

following conditions: 2 min at 50 °C and 10 min at 95 °C, followed by 40 two-temperature cycles (15 sec at 95 °C and 1 min at 60 °C). Data acquisition and analyses were performed by ABI Prism 7000 SDS software ver 1.1 (Life Technologies). The average individual gene expressions were normalized to each average *RPL8* mRNA expression level. The quantitative RT-PCR results are presented as mean ± SEM. Two-way ANOVA was performed for comparisons among temperature responses at different developmental stages in TRPV4 channel expression profiling. Multigroup comparisons between MPT experimental groups were performed using one-way ANOVA, followed by stepwise Tukey-Kramer post hoc adjustments. Comparison between FPT experimental groups was performed using Student's *t*-test. Statistical analyses were performed using GraphPad Prism (Version 5.0b; GraphPad Software, Inc., San Diego, CA, USA) software. *P*-value lower than 0.05 was considered to be statistically significant.

#### *Histological analysis*

After fixation of GAM tissues in 4% paraformaldehyde, they were dehydrated and embedded in paraffin. GAMs were cross-sectioned at 6 µm, re-hydrated using reverse ethanol gradient, and stained with hematoxylin and eosin for standard HE staining. Morphological changes were assessed using Pearson's chi-square test of independence. For *in situ* hybridization analysis, Alligator *AMH* riboprobe, using design by Western *et al.* (1999), was hybridized *in situ* to sections following standard protocols using species-specific digoxigenin-labeled antisense riboprobes at 65°C. Primer information is reported in Table 1-1. For immunohistochemistry, sections of deparaffinized GAMs were washed twice in PBS, microwaved in citrate buffer for 10

min. Samples were then incubated with blocking solution consisting of 0.5% Boehringer Blocking reagent (Roche), 10% heat-inactivated fetal bovine serum (FBS), 3% bovine serum albumin (BSA), and 0.2% Triton-X-100 in PBS for 30 min. Sections were incubated with anti-SOX9 antibody (Chemicon AB5535) which was reportedly compatible with turtle SOX9 (Barske and Capel 2010) as primary antibody in fresh blocking solution overnight at 4 °C at 1:1000. The samples were then washed three times in fresh blocking solution (as described above, with the exception of using 1% FBS instead) for 30 min, and then blocked for an additional hour with anti-rabbit secondary antibody label Alexa Fluor 488 (Life Technologies) at 1:200 at room temperature. The DNA was stained with Hoechst at 1:1000.

### **Figure legends**

**Figure 1-1.** Developmental expression profile of American alligator TRP channels in gonad during sexual development. (A) The mRNA levels of various thermosensitive TRP channels were assessed in gonads at the onset of TSP (stage 21) incubated under MPT and FPT conditions. Gene expressions of 5 AmTRP ion channels (AmTRPV2, AmTRPV4, AmTRPA1, AmTRPM3, AmTRPM8) were observed in varying expression levels. (B) Quantitative RT-PCR analysis was performed for AmTRPV4 at various key sexual developmental stages including bipotential (stage 19; n=13), sex determination (stage 21; n=14, 14), sex differentiation (stage 24; n=14, 15), and pre-hatching (stage 27; n=14, 15) stages at both FPT and MPT temperature conditions respectively; ± SEM. Temperature sensitive period is indicated in gray.

**Figure 1-2.** TRPV4 channels expression in chorioallantoic membrane and epidermal tissues during sexual development. Quantitative RT-PCR analysis was performed for AmTRPV4 at various key sexual developmental stages including bipotential (stage 19), sex determination (stage 21), sex differentiation (stage 24), and pre-hatching (stage 27) stages at both temperature conditions, in (A) chorioallantoic membrane tissue and (B) abdominal epidermal tissues;  $\pm$  SEM. Temperature sensitive period is indicated in gray.

**Figure 1-3.** Phylogenetic tree of vertebrate TRPV4. Phylogenetic relationship among TRPV4 amino acid sequences for selected higher vertebrate species is shown. Phylogenetic tree was constructed based on conservative domains including ankyrin repeat and transmembrane domain, using minimum evolution method with Jones-Taylor-Thornton model. Bootstrap value is indicated beside the respective branch (Bootstrap values below 70 percent not shown). Database accession numbers of genes used is tabulated in Table 1-2. Zebrafish TRPV4 was used as outgroup, and Western clawed frog TRPV4b, c, d, e, f is omitted for simplicity.

**Figure 1-4.** Vertebrate TRPV4 amino acid alignment and identity. (A) Alignment of TRPV4 amino acid sequences from various vertebrates TRPV4; overall similarity in amino acid sequences were observed between alligator TRPV4 and mouse (*Mus musculus*; 86%), human (*Homo sapiens*; 85%), chicken (*Gallus gallus*; 87%), lizard (*Takydromous tachydromoides*; 88%), and snake (*Elaphe quadrivirgata*; 88%) TRPV4. Major channel structures are indicated with a bar, including proline-rich domain (PRD), ankyrin repeat domain (ARD), transmembrane region (TM), pore loop (PL), TRP domain (TRP), and calmodulin binding domain (CaMBD). Numbers indicate amino

acid residue position. The alignment was created using ClustalW. (B) Schematic for the major functional structure, and amino acid identity (%) for each of the selected vertebrate TRPV4, in comparison to AmTRPV4.

**Figure 1-5.** AmTRPV4 is a thermosensitive TRP channel that activates near alligator TSD temperature range. (A) A representative trace of the current (upper) activated in response to corresponding changes in bath solution temperature (lower) in the *Xenopus* oocytes expressing AmTRPV4 using a two-electrode voltage-clamp method. (B) A representative temperature-response profile for AmTRPV4 activation by heat. (C) A representative Arrhenius plot for heat-induced AmTRPV4 activation. The average threshold for activation was  $37.30 \pm 0.54^\circ\text{C}$ ; n=17. (D) A representative trace of the AmTRPV4 current in the oocyte activated by a TRPV4 agonist (GSK1016790A indicated in a black bar); n=4. (E) A representative trace of AmTRPV4 current in the oocyte activated by administration of a specific TRPV4 agonist (GSK1016790A indicated by a black bar) and subsequently inhibited by TRPV4 specific antagonist (RN1734 indicated by a gray bar); n=4. (F) A representative current trace of AmTRPV4 expressing oocyte activated by heat stimulus and subsequently inhibited by a specific TRPV4 antagonist (RN1734 indicated by a gray bar); n=4. (G) A representative averaged changes of  $[\text{Ca}^{2+}]_i$  in AmTRPV4-expressing HEK293 cells (n= 75) under both heat and chemical stimulation.  $[\text{Ca}^{2+}]_i$  changes in AmTRPV4-expressing cells (indicated as an average trace  $\pm$  SE; left y-axis) were observed along with temperatures (indicated by open circle trace; right y-axis). Applications of a TRPV4 agonist (GSK1016790) and ionomycin are shown with a black and gray bars, respectively. (H) Representative  $[\text{Ca}^{2+}]_i$  and temperature changes in mock transfected HEK293 cells (n =36).

**Figure 1-6.** Pharmaceutical activation and inhibition of AmTRPV4 during sex determination alters male differentiation. Stage 19 embryos were administered AmTRPV4 antagonist RN1734 (0.5, 0.005 µg/g egg) or agonist GSK1016790A (0.5, 0.005 µg/g egg) *in ovo* and incubated under MPT and FPT conditions, respectively, until stage 27. (A-E) The mRNA levels of major sex differentiation genes, (A) *AMH*, (B) *SOX9*, and (C) *CYP19A1* in the gonad at stage 27 were examined using quantitative RT-PCR analysis for each treatment: MPT control (n=12), 0.005 RN (n=13), 0.5 RN (n=12), FPT control (n=13), 0.005 GSK (n=15). Asterisks indicate statistically significant change in expression; ± SEM; \*  $P \leq 0.05$ ; \*\*  $P \leq 0.01$ . Markedly lower mRNA expression was observed for *AMH* and *SOX9*, both involved with male differentiation cascade. (D) *In situ* hybridization was performed on gonadal cross sections using *AMH* antisense riboprobe. White bar indicates 100 µm. (E) Immunohistochemistry for SOX9 and Hoechst was performed on gonad cross sections. White bar indicates 100 µm.

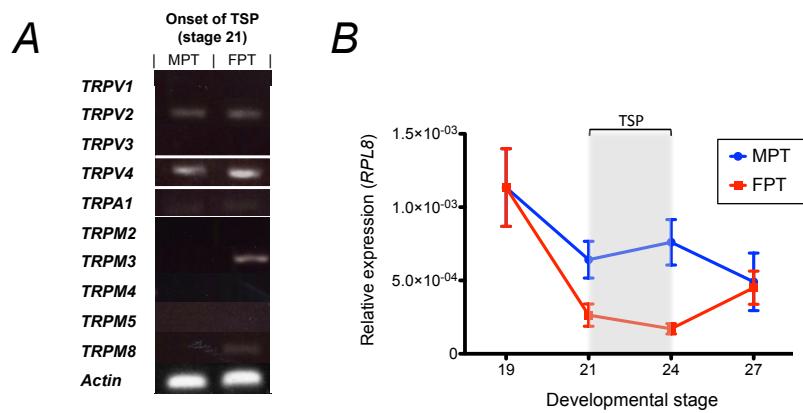
**Figure 1-7.** Expression levels of major sexually differentiation genes, DMRT1 and FOXL2. The mRNA levels of major genes related to sexual development, (A) Doublesex and mab-3 related transcription factor 1 (*DMRT1*), and (B) Forkhead box protein L2 (*FOXL2*), were also examined using quantitative RT-PCR analysis. Trend similar to dosage-dependent down regulation was observed for *DMRT1*, gene involved with male differentiation.

**Figure 1-8.** Comparison of embryo body weights. Embryonic body weight at the time of sampling (Ferguson stage 27) was recorded for all experimental groups. Treatment of RN1734, TRPV4 antagonist, or GSK1016790A, TRPV4 agonist, on the embryo at MPT and FPT, respectively, did not alter the final body weight, and the no delay in development rate was observed.

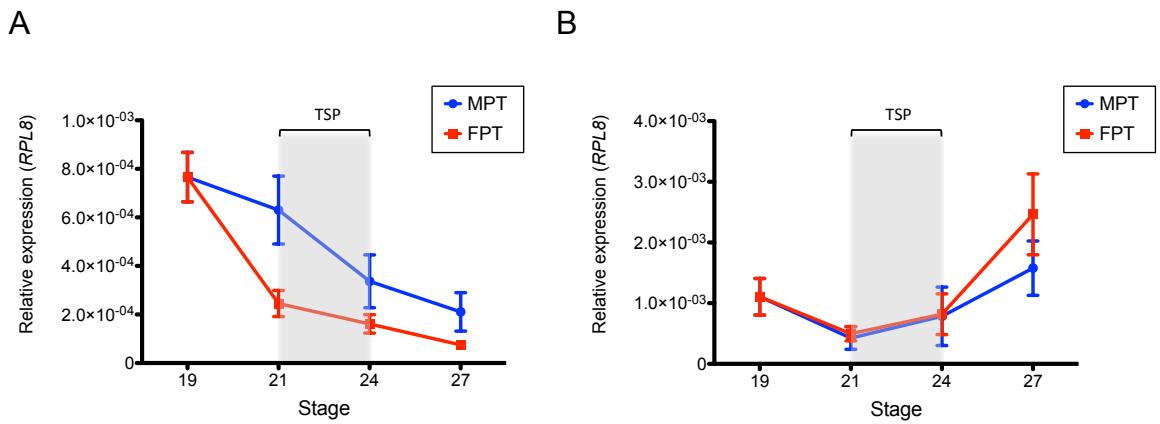
**Figure 1-9.** AmTRPV4 inhibition causes rise in Müllerian duct development in MPT.  
(A) Histological analysis of sexual development was performed. Cross-sections of HE stained gonad and Müllerian duct at stage 27 for FPT control (n=11), 0.005 GSK (n=15), MPT control (n=13), 0.005 RN (n=11), and 0.5 RN (n=11). Instances of ovarian development were observed in RN1734-treated groups. (B) Graph showing number of individuals with ovarian, testicular, or ambiguous morphology in each treatment groups. (C) Graph showing number of individuals with prominent Müllerian duct in each treatment groups. White bar indicates 100  $\mu$ m.

**Figure 1-10.** Representative alligator nest temperature data from the wild. The thermisters were placed within the nest touching eggs at the bottom, middle and top of the nest throughout the entire incubation process. Many nests exhibited elevated temperatures throughout the course of incubation, and a relatively hot nest temperature of 35°C or higher was regularly recorded, with viable hatchlings.

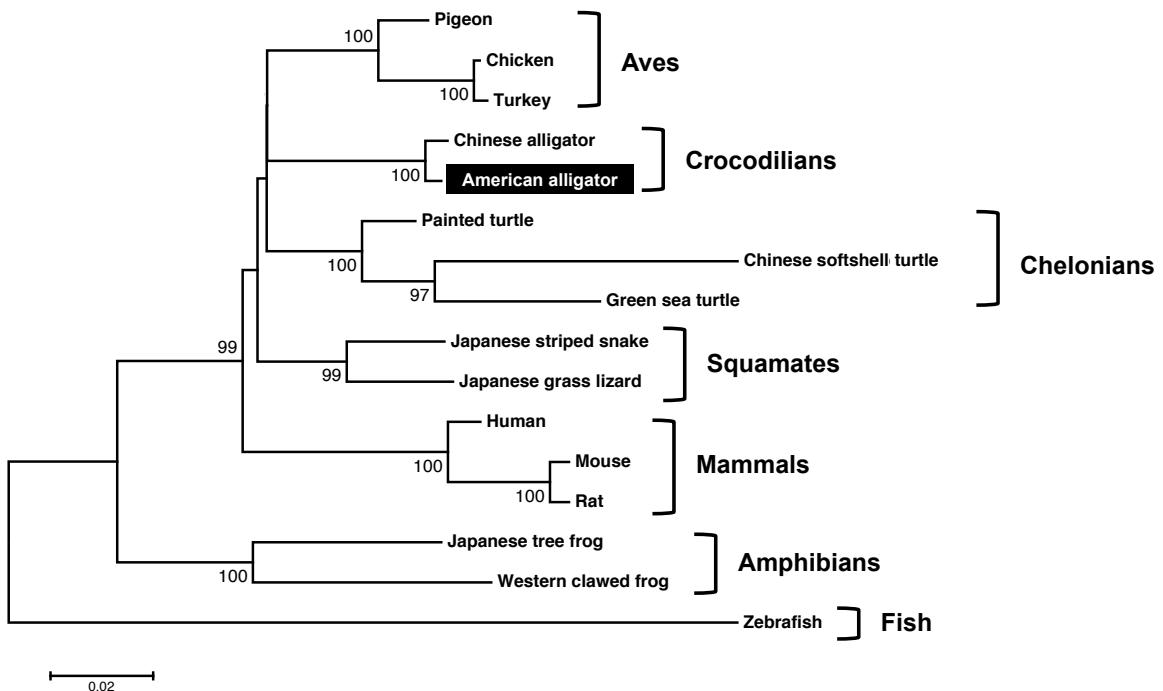
**Figure 1-1**



**Figure 1-2**



**Figure 1-3**

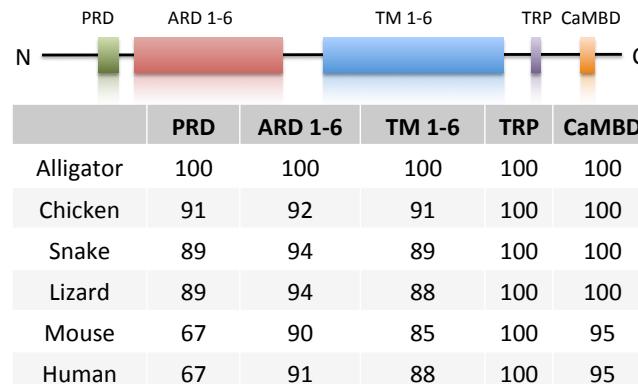


**Figure 1-4**

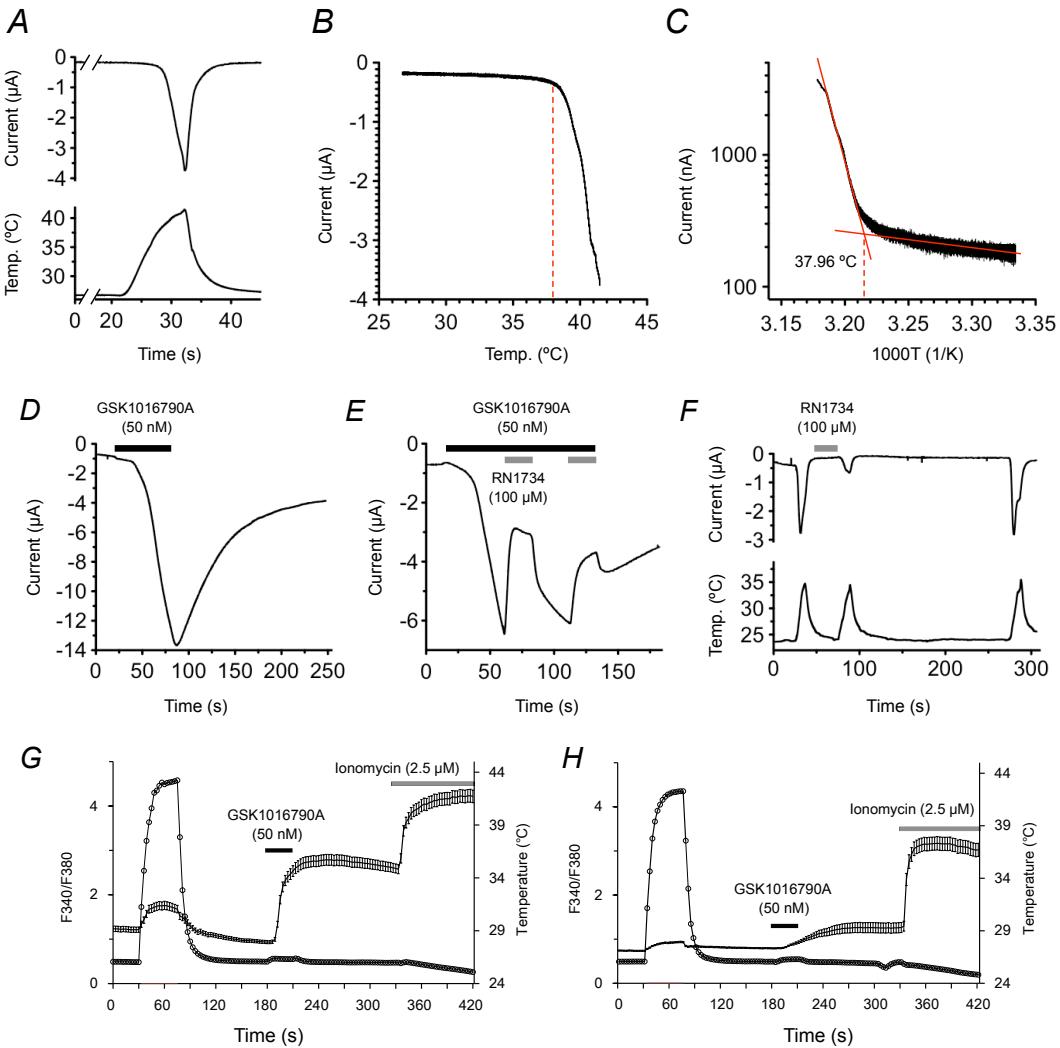
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Alligator TRPV4	MTDPEEPQPQVGEPSGQGD-----DAFPILSSLANLNFSEEG-----VSPPAEARSTPASPGDSKQNLRLMKFGQAFRGRGPMPNPMQDLESTIYESSIONVPAPKAPMDSLFDYCTYHHPSD 110														
Chicken TRPV4	HADPDP-----RDAGCWLGD-----DFPILSSLANLFLEVEDT-----PSAEPGRCPGACDGKQNLRLMKFHGAFRRCGPCKPMELLESTIYESSVVPAPKAPMDSLFDYCTYHHPSD 105														
Snake TRPV4	MANLEDAAAHASPSESTESPSEEL-SPONDSFPLSSLANLFENEDG----APAEEAARTPPGAGDKQNLRLMKFHGAFRRCGPCKPMELLESTIYESSVVPAPKAPMDSLFDYCTYHHPSD 116														
Lizard TRPV4	MANLEDAAAHASPSESTESPSEEL-SPONDSFPLSSLANLFENEDG----APAEEAARTPPGAGDKQNLRLMKFHGAFRRCGPCKPMELLESTIYESSVVPAPKAPMDSLFDYCTYHHPSD 116														
Human TRPV4	MADSSEGPRAGPGEVAELPDESGTGGEAFPLSSLANLFEGEDGSLSPSPADS-R-PAGPDGDRPNLRLMKFGQAFRGRGVNPMLLESTIYESSVVPAPKAPMDSLFDYCTYHHPSD 119														
Mouse TRPV4	MADPDGGPRAAPGEVAEPPGDESGTSGEAFPLSSLANLFEGEGSSSLSPVDSR-PAGPDGDRPNLRLMKFGQAFRGRGVNPMLLESTIYESSVVPAPKAPMDSLFDYCTYHHPSD 119														
Alligator TRPV4	NKRRRKRVVEKQPGSKGPAPNPPILKFVNPRILFDIVSRGSTADLDGLLPFLLSHKVRLTDDEFREPSTGKTCPLKALLNLAGKNTDITPLLLDIAERTGNLRFLNSPFRDVYXRGQ 230														
Chicken TRPV4	NKRRRKRVVEKPVAGTKGPAPNPPILKFVNPRILFDIVSRGSTADLDGLLPFLLSHKVRLTDDEFREPSTGKTCPLKALLNLAGKNTDITPLLLDIAERTGNMRREFINSPFRDVYXRGQ 235														
Snake TRPV4	NKRRRKALEKPKPSTKGPAPNPPILKFVNPRILFDIVSRGSTADLDGLLPFLLTBKRLTDDEFREPSTGKTCPLKALLNLNGKNTDITPLLDIAERTKGS TREFINSPFRDVYXRGQ 236														
Lizard TRPV4	NKRRRKALEKPKPSTKGPAPNPPILKFVNPRILFDIVSRGSTADLDGLLPFLLTBKRLTDDEFREPSTGKTCPLKALLNLNGKNTDITPLLDIAERTKGS TREFINSPFRDVYXRGQ 236														
Human TRPV4	NKRRWKKIIEKQPSKPKAPAPOPPPILKFVNPRILFDIVSRGSTADLDGLLPFLLTBKRLTDDEFREPSTGKTCPLKALLNLNGKNTDITPLLDIAERTGNMRREFINSPFRDVYXRGQ 239														
Mouse TRPV4	NKRRWKKIIEKQPSKPKAPAPOPPPILKFVNPRILFDIVSRGSTADLDGLLPFLLTBKRLTDDEFREPSTGKTCPLKALLNLNGKNTDITPLLDIAERTGNMRREFINSPFRDVYXRGQ 239														
PRD	ARD 1	ARD 2	ARD 3	ARD 4	ARD 5	ARD 6	TM 1	TM 2	TM 3	TM 4	TM 5	TM 6	CaMBD		
Alligator TRPV4	TALHIAIERRCKHVYVELVEKGADEVHAQARHGRFOPKDEGGYFYFGELPLSLACTNQPHIVHVLHALVIAADMTRENTKFVTKMYDLLLIKCALKLPD 350	TALHIAIERRCKHVYVELVEKGADEVHAQARHGRFOPKDEGGYFYFGELPLSLACTNQPHIVHVLHALVIAADMTRENTKFVTKMYDLLLIKCALKLPD 345	TALHIAIERRCKHVYVELVEKGADEVHAQARHGRFOPKDEGGYFYFGELPLSLACTNQPHIVHVLHALVIAADMTRENTKFVTKMYDLLLIKCALKLPD 356	TALHIAIERRCKHVYVELVEKGADEVHAQARHGRFOPKDEGGYFYFGELPLSLACTNQPHIVHVLTEAHKAJADLRDOSRGNFTVHALVIAADMTRENTKFVTKMYDLLLIKCALKLPD 356	TALHIAIERRCKHVYVELVEKGADEVHAQARHGRFOPKDEGGYFYFGELPLSLACTNQPHIVHVLTEAHKAJADLRDOSRGNFTVHALVIAADMTRENTKFVTKMYDLLLIKCALKLPD 356	TALHIAIERRCKHVYVELVEKGADEVHAQARHGRFOPKDEGGYFYFGELPLSLACTNQPHIVHVLTEAHKAJADLRDOSRGNFTVHALVIAADMTRENTKFVTKMYDLLLIKCALKLPD 359	TALHIAIERRCKHVYVELVEKGADEVHAQARHGRFOPKDEGGYFYFGELPLSLACTNQPHIVHVLTEAHKAJADLRDOSRGNFTVHALVIAADMTRENTKFVTKMYDLLLIKCALKLPD 359	TSLHIAIERRCKHVYVELVEKGADEVHAQARHGRFOPKDEGGYFYFGELPLSLACTNQPHIVHVLTEAHKAJADLRDOSRGNFTVHALVIAADMTRENTKFVTKMYDLLLIKCSRLPD 359							
Alligator TRPV4	TNLLEALLNNDGLSPLMQAATKTKGIGIFQHIIIREVRVDEDARHLSRKFKDNQAYGPVYSSLYDLSLDTGCEEVSVLEILVYNSKINRNHMLAEVPINELLDKWRKPFGAWSFYIVNVSYL 470	TNLLEALLNNDGLSPLMQAATKTKGIGIFQHIIIREVRVDEDARHLSRKFKDNQAYGPVYSSLYDLSLDTGCEEVSVLEILVYNSKINRNHMLAEVPINELLDKWRKPFGAWSFYIVNVSYL 470	TNLLEALLNNDGLSPLMQAATKTKGIGIFQHIIIREVHDEVRHLSRKFKDNQAYGPVYSSLYDLSLDTGCEEVSVLEILVYNSKINRNHMLAEVPINELLDKWRKPFGAWSFYIVNVSYL 465	TNLLEALLNNDGLSPLMQAATKTKGIGIFQHIIIREVHDEVRHLSRKFKDNQAYGPVYSSLYDLSLDTGCEEVSVLEILVYNSKINRNHMLAEVPINELLDKWRKPFGAWSFYIVNVSYL 476	TNLLEALLNNDGLSPLMQAATKTKGIGIFQHIIIREVHDEVRHLSRKFKDNQAYGPVYSSLYDLSLDTGCEEVSVLEILVYNSKINRNHMLAEVPINELLDKWRKPFGAWSFYIVNVSYL 476	TNLLEALLNNDGLSPLMQAATKTKGIGIFQHIIIREVHDEVRHLSRKFKDNQAYGPVYSSLYDLSLDTGCEEVSVLEILVYNSKINRNHMLAEVPINELLDKWRKPFGAWSFYIVNVSYL 476	TNLLEALLNNDGLSPLMQAATKTKGIGIFQHIIIREVHDEVRHLSRKFKDNQAYGPVYSSLYDLSLDTGCEEVSVLEILVYNSKINRNHMLAEVPINELLDKWRKPFGAWSFYIVNVSYL 479	TNLLEALLNNDGLSPLMQAATKTKGIGIFQHIIIREVHDEVRHLSRKFKDNQAYGPVYSSLYDLSLDTGCEEVSVLEILVYNSKINRNHMLAEVPINELLDKWRKPFGAWSFYIVNVSYL 479							
Alligator TRPV4	CAMIIFTLIAJYYPVPEGICPAPVTTTIDYLRLAGEVITLFTGVLFFFTNVDLPLMKKCPGVNSPFDIDGSFOLLYFIYSLVVLVETGCLYAGIEAYLAJVNVFALVJLGHMNALYFTRLGLK 590	CAMIIFTLIAJYYPVPEGICPAPVTTTIDYLRLAGEVITLFTGVLFFFTNVDLPLMKKCPGVNSPFDIDGSFOLLYFIYSLVVLVETGCLYAGIEAYLAJVNVFALVJLGHMNALYFTRLGLK 585	CAMIIFTLIAJYYPVPEGICPAPVTTTIDYLRLAGEVITLFTGVLFFFTNVDLPLMKKCPGVNSPFDIDGSFOLLYFIYSLVVLVETGCLYAGIEAYLAJVNVFALVJLGHMNALYFTRLGLK 596	CAMIIFTMWAYYPLPECTPPVPPYTTTIDYLRLAGEVITLFTGVLFFFTNVDLPLMKKCPGVNSPFDIDGSFOLLYFIYSLVVLVAAALYLAGIEAYLAJVNVFALVJLGHMNALYFTRLGLK 596	CAMIIFTMWAYYPLPECTPPVPPYRTTVYRLAGEVITLFTGVLFFFTNVDLPLMKKCPGVNSPFDIDGSFOLLYFIYSLVVLVAAALYLAGIEAYLAJVNVFALVJLGHMNALYFTRLGLK 596	CAMIIFTMWAYYPLPECTPPVPPYRTTVYRLAGEVITLFTGVLFFFTNVDLPLMKKCPGVNSPFDIDGSFOLLYFIYSLVVLVAAALYLAGIEAYLAJVNVFALVJLGHMNALYFTRLGLK 599	CAMIIFTMWAYYPLPECTPPVPPYRTTVYRLAGEVITLFTGVLFFFTNVDLPLMKKCPGVNSPFDIDGSFOLLYFIYSLVVLVAAALYLAGIEAYLAJVNVFALVJLGHMNALYFTRLGLK 599	CAMIIFTMWAYYPLPECTPPVPPYRTTVYRLAGEVITLFTGVLFFFTNVDLPLMKKCPGVNSPFDIDGSFOLLYFIYSLVVLVAAALYLAGIEAYLAJVNVFALVJLGHMNALYFTRLGLK 599							
Alligator TRPV4	GTYSIMIQKLFLPDLFPLFLVYLLPMIGYASRILVSLNLPCT-----SCGKDQSNCTDMPAYPSCRSDQSFSTFLDLPFLKT1GMQDLEMIESAKYGVFILLVITYIILTFVILLNLNLIALMG 706	GTYSIMIQKLFLPDLFPLFLVYLLPMIGYASRILVSLNLPCT-----SCGKDQSNCTDMPAYPSCRSDQSFSTFLDLPFLKT1GMQDLEMIESAKYGVFILLVITYIILTFVILLNLNLIALMG 706	GTYSIMIQKLFLPDLFPLFLVYLLPMIGYASRILVSLNLPCT-----SCGKDQSNCTDMPAYPSCRSDQSFSTFLDLPFLKT1GMQDLEMIESAKYGVFILLVITYIILTFVILLNLNLIALMG 705	GTYSIMIQKLFLPDLFPLFLVYLLPMIGYASRILVSLNLPCT-----SCGKDQSNCTDMPAYPSCRSDQSFSTFLDLPFLKT1GMQDLEMIESAKYGVFILLVITYIILTFVILLNLNLIALMG 716	GTYSIMIQKLFLPDLFPLFLVYLLPMIGYASRILVSLNLPCT-----SCGKDQSNCTDMPAYPSCRSDQSFSTFLDLPFLKT1GMQDLEMIESAKYGVFILLVITYIILTFVILLNLNLIALMG 716	GTYSIMIQKLFLPDLFPLFLVYLLPMIGYASRILVSLNLPCT-----SCGKDQSNCTDMPAYPSCRSDQSFSTFLDLPFLKT1GMQDLEMIESAKYGVFILLVITYIILTFVILLNLNLIALMG 716	GTYSIMIQKLFLPDLFPLFLVYLLPMIGYASRILVSLNLPCT-----SCGKDQSNCTDMPAYPSCRSDQSFSTFLDLPFLKT1GMQDLEMIESAKYGVFILLVITYIILTFVILLNLNLIALMG 719	GTYSIMIQKLFLPDLFPLFLVYLLPMIGYASRILVSLNLPCT-----SCGKDQSNCTDMPAYPSCRSDQSFSTFLDLPFLKT1GMQDLEMIESAKYGVFILLVITYIILTFVILLNLNLIALMG 719							
Alligator TRPV4	ETVGQVSKEKSQIKWKLQWATTILDIDERSFPVVKRKAFLRSGEMVTVGKGIDGTPDRWCFRDEVNWSHWQNQLGII1NEDPDKGNETTYQYGSFHTVGRLLRDRNSTVPPRVVUELNKNSQPD 826	ETVGQVSKEKSQIKWKLQWATTILDIDERSFPVVKRKAFLRSGEMVTVGKGIDGTPDRWCFRDEVNWSHWQNQLGII1NEDPDKGNETTYQYGSFHTVGRLLRDRNSTVPPRVVUELNKNSQPD 825	ETVGQVSKEKSQIKWKLQWATTILDIDERSFPVVKRKAFLRSGEMVTVGKGIDGTPDRWCFRDEVNWSHWQNQLGII1NEDPDKGNETTYQYGSFHTVGRLLRDRNSTVPPRVVUELNKNSQPD 836	ETVGQVSKEKSQIKWKLQWATTILDIDERSFPVVKRKAFLRSGEMVTVGKGIDGTPDRWCFRDEVNWSHWQNQLGII1NEDPDKGNETTYQYGSFHTVGRLLRDRNSTVPPRVVUELNKNSQPD 836	ETVGQVSKEKSQIKWKLQWATTILDIDERSFPVVKRKAFLRSGEMVTVGKGIDGTPDRWCFRDEVNWSHWQNQLGII1NEDPDKGNETTYQYGSFHTVGRLLRDRNSTVPPRVVUELNKNSQPD 839	ETVGQVSKEKSQIKWKLQWATTILDIDERSFPVVKRKAFLRSGEMVTVGKGIDGTPDRWCFRDEVNWSHWQNQLGII1NEDPDKGNETTYQYGSFHTVGRLLRDRNSTVPPRVVUELNKNSQPD 839	ETVGQVSKEKSQIKWKLQWATTILDIDERSFPVVKRKAFLRSGEMVTVGKGIDGTPDRWCFRDEVNWSHWQNQLGII1NEDPDKGNETTYQYGSFHTVGRLLRDRNSTVPPRVVUELNKNSQPD 839								
Alligator TRPV4	EVVVPPLCQHGASNOQIDDRPQH-LNGKKECHI* 857	EVVVPPLCQHGASNOQIDDRPQH-LNGKKECHI* 857	DVVPVPLGTMGTAERAR---HGQTSPSP* 852	DVVPVPLGTMGTAERAR---HGQTSPSP* 852	SNAKE TRPV4	EVVVPPLDSMCAGANAHKPSPYHSWSRKDEAQI* 868	Lizard TRPV4	EVVVPPLDSMRSPANNEHKPSPYHSWSRKDESH* 868	Human TRPV4	EVVVPPLDSMGNPRCDGHQQGYPRKWRTDDAPL* 871	Mouse TRPV4	EVVVPPLDSMGNPRCDGHQQGYPRKWRTDDAPL* 871			

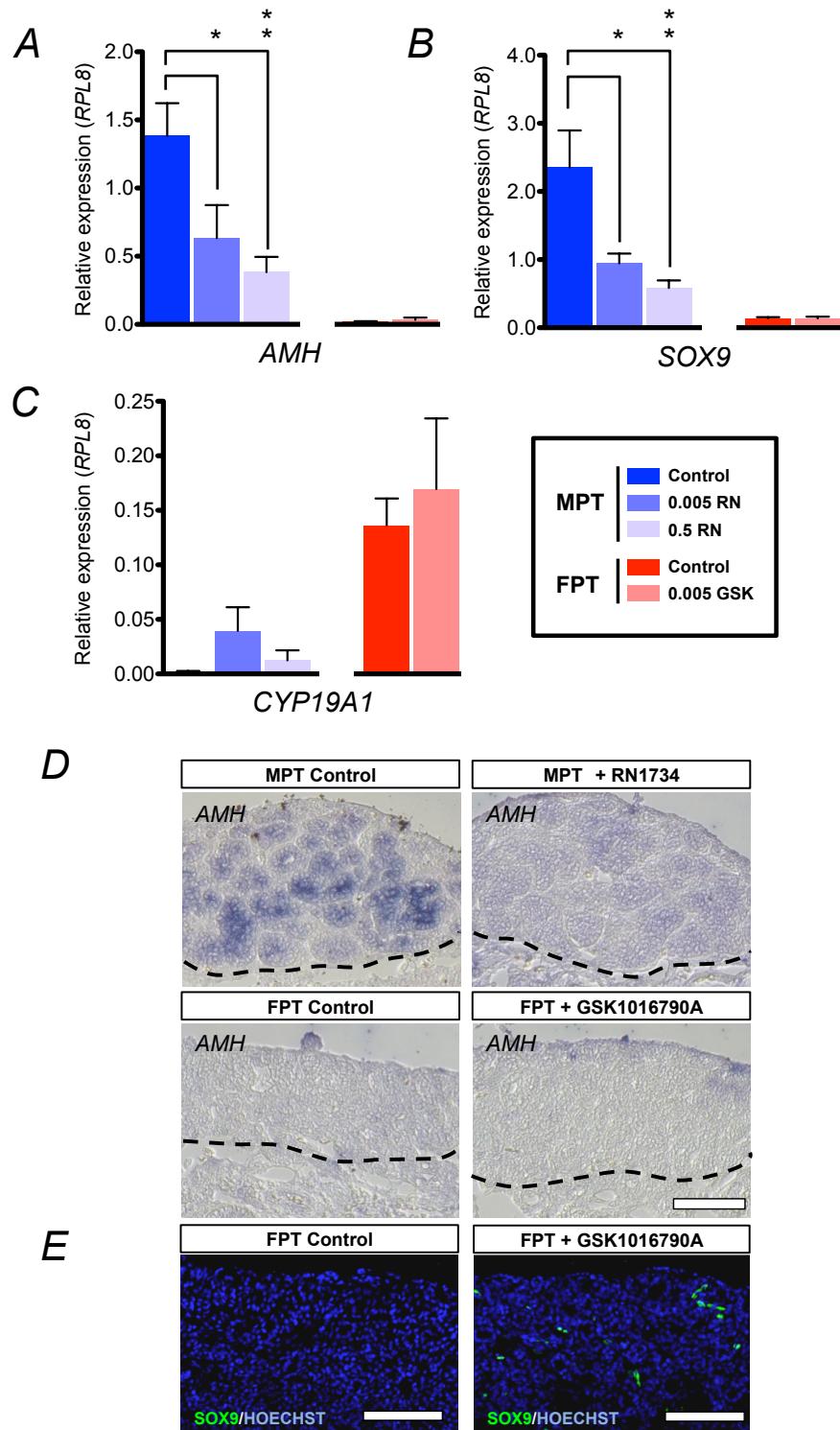
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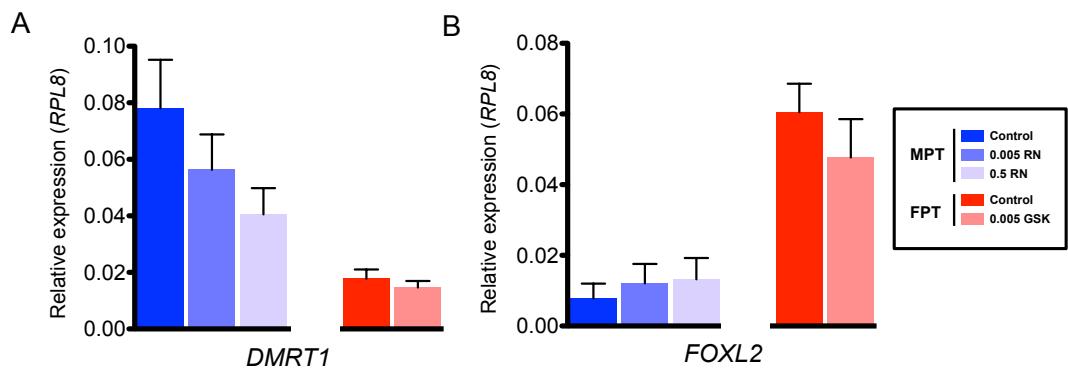
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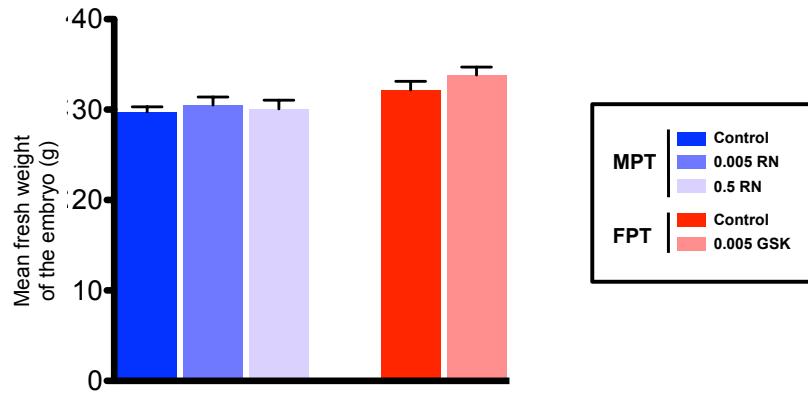
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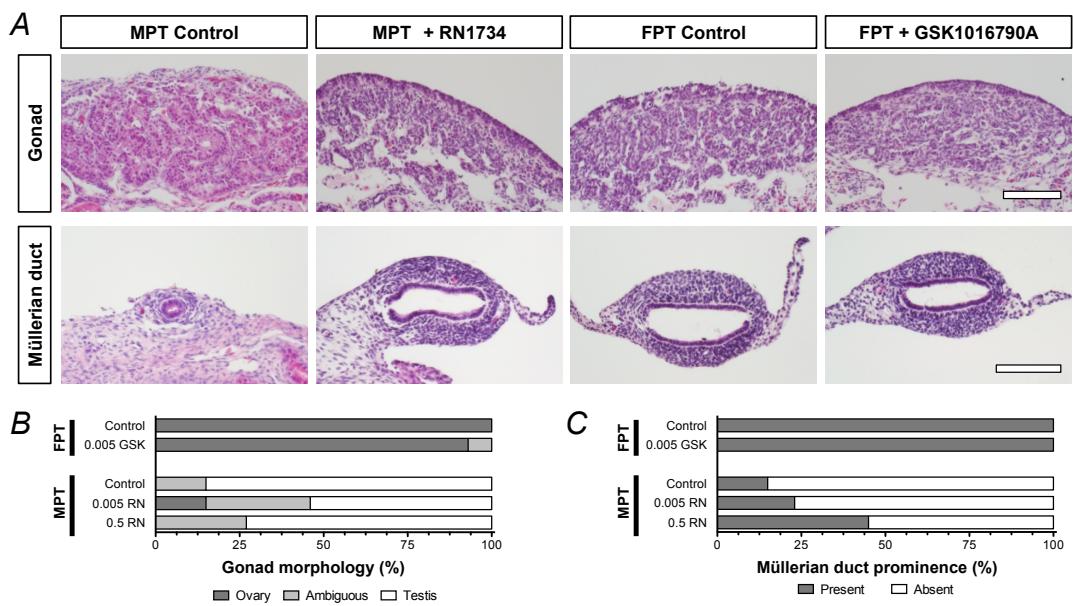
**Figure 1-7**



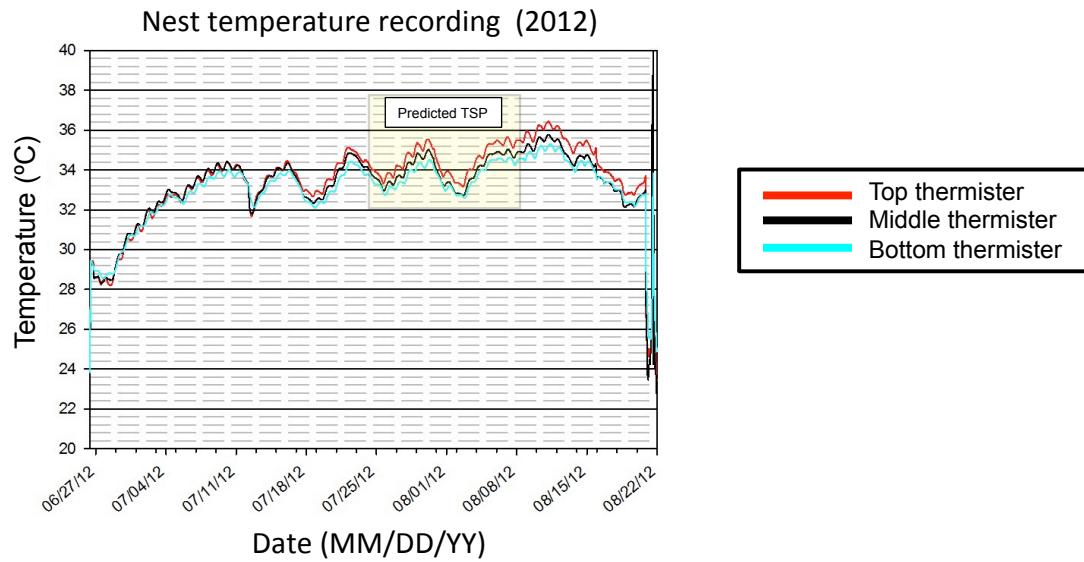
**Figure 1-8**



**Figure 1-9**



**Figure 1-10**



**Table 1-1**

Name	Sequence	
<b>TRPV4 cloning and isolation</b>		
aTRPV4-A:	5'-TTYTTYCARRCCNAARGAYGARGGN-3'	
aTRPV4-B:	5'-GGNGGNTAYTTYTAYTTYGGNGAR-3'	
aTRPV4-C:	5'-ACYTGNNCNACNGTYTCNCCCAT-3'	
aTRPV4-D:	5'-GCCCATGNARYTTCCADATRTGYTT-3'	
5'RACE-1	5'-TCCCAGGTGTTGCGCCGGAGTCCTGG-3'	
5'RACE-2	5'-AGCACCGGTGGGGCAGGTGTCCAAGGAG-3'	
3'RACE-1	5'-GAGACGGTGGGGCAGGTGTCCAAGGAG-3'	
3'RACE-2	5'-ATCTGGAAGCTGCAGTGGGCCACCACC-3'	
Cloning	5'-TGTGTGCTGACCCATAACCGTGCCAG-3'	5'-CCCGGGAGAGGAGAAACATGGTCAAG-3'
<b>TRP subtype gene expression RT-PCR</b>		
TRPV1	5'-GAATCTGAAGTCACCGACGAGCA-3'	5'-AAAGATCCTCCTGCGATCATAGTACTTG-3'
TRPV2	5'-CTCAGTCTTGCCTACCATTGTC-3'	5'-AGACCATCAACGGGGTAGTATT-3'
TRPV3	5'-GCTTATGGCAAGAACCAAATCCA-3'	5'-CCCTCAGATACTGCCCTGAACAAATA-3'
TRPV4	5'-GAGTCCACCATCTACGAGTCCTCC-3'	5'-CAGGTTCAAGCAGTGCCTTGGG-3'
TRPM2	5'-CTTTCCGGGACACCTATGAGTTCTT-3'	5'-TCACGAACTCAGGCTTGTGAAAT-3'
TRPM3	5'-GTCATTCGGCATGTTGGAGATGC-3'	5'-GTGCTTTCCAGTTGTACGGAGT-3'
TRPM4	5'-TGCGACTCATCCACATCTCGC-3'	5'-CGAGGAGGAAGACAACAAGGAGAAC-3'
TRPM5	5'-ATGATGCCTGCAAAGGTTCTACCA-3'	5'-CGGTCTCGCTGTTGTGATAACATTC-3'
TRPM8	5'-GAAACACACAAAGGAACCTCCTACTAATG-3'	5'-ACATTCTCCTCGGAAGTCCTACTGA-3'
TRPA1	5'-ACAGAAAACGTATAGCAGTCCACTCC-3'	5'-CAATATGGCAGCTTCTCTAAGTTGT-3'
<b>Quantitative RT-PCR primer</b>		
RPL8	5'-GGTGTGGCTATGAATCCTGT-3'	5'-ACGACGAGCAGCAATAAGAC-3'
TRPV4	5'-TCACCTTCGTGCTGCTGCTT-3'	5'-AGATCTGCTTGTCTCCTTG-3'
SOX9	5'-AGTACCCCCATCTGCACAAC-3'	5'-CCCGTTCTCACCGACTTT-3'
AMH	5'-AGCAGCTAACCTCTTGAGGA-3'	5'-TAGCAGAAAGCCAGAAGGTGC-3'
CYP19A1	5'-CAGCCAGTTGGACTTGATCA-3'	5'-TTGTCCCTTTACAGGATAG-3'
DMRT1	5'-AGCCCAACTCACTCAACAAG-3'	5'-GATGGAAGGAACATCCTGAA-3'
FOXL2	5'-CATCAGCAAGTCCCCCTC-3'	5'-GGGCACCTTGATGAAACAC-3'
<b>In situ probe primer</b>		
amh	5'- GTGTTTCAACCAGGATGACGCCGGTGCT -3'	5'- GGCTCCTCCGACTGCACCAAGGCGCTCC -3'

**Table 1-2**

**Transient Receptor Potential Vanilloid Receptor subtype 4 homologs in various vertebrates.**

Common name	Scientific name	Accession number
American alligator	<i>Alligator mississippiensis</i>	LC12707
Chinese alligator	<i>Alligator sinensis</i>	XM_006015214.1
Chicken	<i>Gallus gallus</i>	NM_204692.1
Turkey	<i>Meleagris gallopavo</i>	XM_003210979.1
Pigeon	<i>Columba livia</i>	XM_005498200.1
Painted turtle	<i>Chrysemys picta</i>	XM_005298531.1
Chinese softshell turtle	<i>Pelodiscus sinensis</i>	XM_006130238.1
Green sea turtle	<i>Chelonia mydas</i>	XM_007058340.1
Japanese striped snake	<i>Elaphe quadrivirgata</i>	AB_666090.1
Japanese grass lizard	<i>Takydromus tachydromoides</i>	AB_666089.1
Human	<i>Homo sapiens</i>	NM_021625.4
Mouse	<i>Mus musculus</i>	NM_022017.3
Rat	<i>Rattus norvegicus</i>	NM_023970.1
Japanese treefrog	<i>Hyla japonica</i>	AB809362.1
Western clawed frog	<i>Xenopus tropicalis</i>	ENSXETT00000040300 (TRPV4a)
Zebrafish	<i>Danio rerio</i>	NM_001042730.1

## **Chapter 2.**

**RNA-seq analysis of the gonadal transcriptome during *Alligator mississippiensis*  
temperature-dependent sex determination and differentiation**

## **Introduction**

The intimate interaction between the environment and the organism can be profound; ambient environmental stimuli, such as temperature, are powerful catalysts for biomolecular movement and development that manifest as permanent biological changes. Such is the case for temperature-dependent sex determination (TSD), in which the sexual fates of organisms are seemingly determined not by genotypic factors, but by environmental temperature during a specific embryonic period known as the temperature sensitive period (TSP). In vertebrates, TSD has been observed primarily in reptiles, and the bipotential gonad itself is thought to be receptive to thermal signals (Bull 1980, Bull 1985, Shoemaker-Daly, Jackson et al. 2010). However, mechanistic details of this interaction between environmental temperature and TSD transcriptional profile cascade have remained unclear. While many past reports have focused on conserved genes with known function in sexual differentiation across vertebrates, such as *AMH*, *CYP19A1*, and *SOX9* (*Morrish and Sinclair 2002, Valenzuela, Neuwald et al. 2013, Kohno, Parrott et al. 2014*), very few other genes have been closely investigated, leading to a limited understanding of overall gene expression throughout TSD. Critical questions, such as how the developing gonad translates temperature cues into specific biochemical signals, remain unanswered.

Several hypotheses accounting for the molecular mechanism underlying TSD have been proposed. Steroid hormone involvement has long been suspected to play a role in TSD, as these molecules are known to play a critical role in sex differentiation in non-mammalian vertebrates (Lance 2009). Furthermore, glucocorticoid has been demonstrated to induce sex reversal in various vertebrate species including reptiles (Warner, Radder et al. 2009, Nakamura 2010), though how the syntheses of steroid

hormones are regulated by temperature remain unanswered. Another major mode of biological response to temperature is epigenetic modification; mounting evidence points toward an involvement of epigenetic modifications in sexual development (Piferrer 2013). Past studies reported sexually dimorphic DNA methylation patterns in promoter regions of major sexual development genes in a temperature specific manner, including TSD organisms (Navarro-Martin, Vinas et al. 2011, Matsumoto, Buemio et al. 2013, Parrott, Kohno et al. 2014). Other factors often associated with temperature stress, such as heat shock proteins (*HSPs*) and cold inducible RNA binding proteins (*CIRBPs*), have also been suggested to play a role in TSD (Kohno, Katsu et al. 2010, Rhen and Schroeder 2010). These varying responses to thermal influences at multiple levels ultimately result in a highly receptive regulatory network that underlies multitudes of cellular processes. Thus, the effect of temperature on the molecular environment can be profound and far-reaching, and consequently, there is crucial need to gain a comprehensive picture in order to fully understand the molecular mechanisms underlying TSD.

Crocodilians are thought to be entirely composed of TSD species (Lang and Andrews 1994), which includes the American alligator, *Alligator mississippiensis* (Ferguson and Joanen 1982). In *A. mississippiensis* TSD, the sexual fates of bipotential gonads are directed in a temperature-dependent manner to differentiate into either testes at a male producing temperature (MPT) at 33.5°C, or into ovaries at female producing temperature (FPT) at 30°C or 34.5°C (Ferguson and Joanen 1983, Lang and Andrews 1994). A recent report shows that sex determination in alligator embryo is thermosensitive as early as stage 15 (Ferguson developmental stage), approximately 18-20 days after oviposition (Ferguson 1985, McCoy, Parrott et al. 2015). Prior to this

report, however, the TSP was defined as occurring during stages 21-24, roughly between 31-46 days after oviposition. It is during this later period (stages 21-24) that temperature effects are reflected in the gonadal development, and many of the key sex determination/differentiation genes acquire sexually dimorphic expression patterns (Lang and Andrews 1994, Morrish and Sinclair 2002, Valenzuela, Neuwald et al. 2013, Kohno, Parrott et al. 2014, McCoy, Parrott et al. 2015). The timing of developmental stages and whole-body morphological growth is also greatly influenced by temperature during embryogenesis in the long term (Deeming and Ferguson 1989). Unfortunately, an effective method to perform gene manipulation is not currently feasible in alligators, and options are limited for detailed studies. This holds true with many of other reptiles and hence, much of the sex determination mechanisms studies in this evolutionary pivotal clade has been primarily resolved through comparative analyses with mammalian or avian sex determination mechanisms.

With rapidly emerging next generation sequencing technologies, global transcriptome studies such as high-throughput RNA sequencing (RNA-seq) is becoming readily available for non-model organisms (Smith, Bernatchez et al. 2013, Sun, Liu et al. 2013). In addition, a number of reptilian genomes have become publicly available (St John, Braun et al. 2012, Shaffer, Minx et al. 2013, Wan, Pan et al. 2013), and comprehensive annotated crocodilian genome assemblies have been released on the National Center for Biotechnology Information (NCBI) (Wan, Pan et al. 2013, Green, Braun et al. 2014). As one of the first TSD species with a published genome, the alligator *A. mississippiensis* is an ideal species for studying molecular signaling cascades and gene expression networks during sex determination in TSD species.

In this study, RNA-seq analyses were performed on developing alligator embryonic gonads incubated under MPT or FPT conditions and sampled at various time points to assess transcriptome changes related to each temperature condition during gonadal differentiation. We present an initial investigation into the sexual development cascade within the alligator TSD system, and provide descriptive data on expression patterns during early sexual development, with the emphasis on the identification of novel candidate genes that might account for alligator sex determination. To our knowledge, this is the first whole transcriptome analysis performed on a TSD organism. These results should allow for insights into the early progression of testis and ovarian fate, and provide a foundation for better understanding the genetic programs driving vertebrate TSD.

## Results and discussion

### *Experimental design and sequence assembly*

For sample preparation for transcriptome analyses, field collected *A. mississippiensis* eggs were transported to the laboratory and incubated under FPT (30°C) until Ferguson developmental stage 19 (Ferguson 1985), a period in which the gonads are still bipotential and morphologically indistinguishable. At stage 19, a subset of eggs was shifted to MPT (33.5°C) while the remaining eggs were maintained at FPT for the subsequent incubation period (Figure 2-1). Incubations at high FPT (34.5 °C) were not performed in the current study. Tissues comprising the developing gonad were carefully dissected at multiple time points after stage 19; at Day 0, 3, 6, and 12 post-stage 19 for analysis on sex determination cascade. The samples represent the bipotential gonad prior to incubation temperature shift (Day 0), post temperature shift (Day 3), and during

sexual fate commitment and differentiation (Day 6, 12). Although the embryos are incubated under different temperatures, the embryonic staging indicate that at least until Day 12 the embryos at respective time points are at within same developmental stage, and confounding variables by differential temperature effects are minimized (Kohno and Guillette 2013). In addition to Day 0-12 (sex determination phase), gonads from Day 18, 24, 30, and 36 post-stage 19 were also sampled (sex differentiation phase), although Day 36 was sampled in FPT only (Figure 2-2). Illumina HiSeq2500 sequencing produced a total of 375.2 million paired-end reads (2 x 101 bp) and were assessed for quality. The reads were mapped to the alligator genome assembly (allMis0.2), using the latest NCBI annotation available at the time (NCBI *Alligator mississippiensis* Annotation Release 100). The average mapping rates was 88.3%, among which 94.8% of the mapped reads were single hits, indicating an overall relatively good quality of reads.

#### *Transcriptome characterization of alligator gonadal development*

Differentially expressed gene (DEG) analysis was performed using Cuffdiff workflow (ver 2.2.1) (Trapnell, Williams et al. 2010, Trapnell, Roberts et al. 2012) to screen DEGs with false discovery rate (FDR) adjusted *p*-value <0.01. To evaluate differential expression across development for embryos incubated at the same temperature, multiple comparisons of the fold differences were conducted between temporally adjacent time points under each incubation condition (MPT/FPT). Development-dependent DEG analysis revealed extensive gene expression kinetics during the course of gonadal morphogenesis, and were profiled (Figure 2-3a, b; Figure 2-4a, Table 2-1). Overall, at MPT, Day 0-12 showed 788 DEGs, of which 158 (20.1%)

displayed expression movement at multiple occasions. At FPT, Day 0-12 showed 555 total DEGs, of which 113 DEGs (20.3%) also displayed expression movement at multiple occasions. Several noteworthy gene expression patterns were observed; under both MPT and FPT conditions, the transition from Day 3 to 6 accounted for the majority of DEGs, and nearly half of the total DEGs (460 and 250, respectively) were specific to Day 3-6. This timing corresponds to the onset of morphological differentiation in which the enlargement of presumptive Sertoli cells are observed in the medulla at MPT (Stage 21), and might be an indication of the activation of male and female cascade and gonadal fate commitment (Smith and Joss 1993).

Increases in the magnitude of sexually dimorphic gene expression profiles were then examined in detail. Sex-dependent DEG analysis between MPT and FPT samples were conducted at each corresponding time points in respective groups for intergroup comparisons (Figure 2-3c, Figure 2-4b, Table 2-2). Day 0-12 intersex comparisons revealed a total of 457 DEGs. MPT biased gene expression in each time point gradually increased with the progression of sexual development (68, 97, and 137 DEGs at Day 3, 6, and 12, respectively). However, similar to intrasexual development-dependent DEGs, a majority of sexually dimorphic gene expression was time point specific. Ten genes were consistently sexually dimorphic at all 3 time points (*AMH, EIF4A2, IFRD1, JARID2, KDM6B, KRT10, LOC102561378, LOC102574081, UCP2*).

#### *Identification of immediate temperature-responsive genes*

Cross-comparisons between Day 0 FPT embryos and Day 3 at MPT and FPT were performed to evaluate for the MPT-specific immediate temperature-responsive

gene expression (Figure 2-5). In order to assess the impact of the temperature shift between Day 0 FPT and Day 3 MPT on gene expression, as well as to account for the shared gene expression movement between Day 0-3 FPT and Day 0-3 MPT, significant male-specific differential expressions between Day 0 FPT and Day 3 MPT with resulting sexual dimorphism between Day 3 embryos were identified. The analysis generated 131 MPT specific DEGs (Figure 2-5a), of which 41 were also found to be sexually dimorphic between Day 3 MPT and Day 3 FPT as well (Figure 2-5b). Seventeen genes with significant upregulation at MPT (*UCP2*, *GALNT5*, *EIF4A2*, etc.) and 24 with significant downregulation (*KDM6B*, *LOC102562106*, *CSRP2*, etc.) were detected, and are likely candidates for immediate temperature-responsive genes (Table 3). While the current study focused upon FPT-to-MPT shift, a complementary MPT-to-FPT study would be ideal to fully identify potential upstream temperature-responsive genes in both male and female sex determination cascades.

Oxidative stress responsive-gene uncoupling protein-2 (*UCP2*) displayed the most prominent up-regulation, and suggests the presence of oxidative stress signaling in gonads incubated at MPT (Chan, Wu et al. 2009). Oxidative stress can be induced by number of factors including the thermosensitive cation channel *TRPV4*, which incidentally is also tightly co-localized with *UCP2* in mammals (Guler, Lee et al. 2002, Cohen, Brown et al. 2011, Bubolz, Mendoza et al. 2012). Interestingly, *TRPV4* has also recently been observed to potentially be involved with alligator TSD (Yatsu, Miyagawa et al. 2015) and may partially account for the immediate temperature-responsive DEGs identified in the current study. Interestingly, other DEGs identified in this study (e.g. *UPK3A*, *C/EBPA*, *ESPN*, etc.) are also co-expressed with *TRPV4* in other mammalian tissues, and may share a functional pathway (Homma, Nomiya et al. 2013, Ovrevik,

Refsnes et al. 2015). However, the relationship shared between these genes and *TRPV4* during the alligator gonadal sex determination is yet to be elucidated.

Gene ontology (GO) analysis was performed on the temperature-responsive transcripts. Interestingly, ‘Regulation of transcription, DNA-dependent’ was one of the highest biological process terms highlighted, and several transcriptional regulators were detected (Figure 2-5c). Most were downregulated by the temperature shift to MPT, such as *KDM6B* and *JARID2*. The roles of chromatin remodelers such as *Cbx2* and *Jmjc1* have been well documented in mammalian sex determination (Katoh-Fukui, Tsuchiya et al. 1998, Kuroki, Matoba et al. 2013), which prompt us to speculate that similar chromatin modification might occur during alligator TSD. Further analysis using Chromatin Immunoprecipitation (ChIP) techniques may help elucidate the chromatin state in alligator gonads during TSD. *WNT11*, which is expressed in mammalian granulosa cells, was also downregulated by shifts to MPT (Harwood et al., 2008). Transcription factor CCAAT/enhancer binding protein  $\alpha$  (*C/EBPA*) was upregulated by shifting incubation temperature to MPT. *C/EBPA* is observed to be active in a wide array of cell differentiation cascades, including mammalian germ cell sex differentiation (Ewen, Jackson et al. 2010). Because the current study did not distinguish between cell types, gene expression specific to somatic and primordial germ cell sex development is unclear. Vertebrate somatic and germ cell sex determination cascades are distinct. Thus, resolving the spatial expression patterns for these genes in alligators will further aid in characterizing their roles and functions during TSD.

#### *Characterization of known sexual development genes*

Although vertebrate upstream sex determination mechanisms differ by species, downstream sex differentiation genes appear to be highly conserved by comparison (Morrish and Sinclair 2002), and expression pattern of genes that have been well characterized in alligator sex differentiation were investigated (Figure 2-6). Overall, our RNA-seq data was in accordance with the previous reports, based mostly on studies utilizing RT-PCR and *in situ* hybridization techniques. Although, a few surprising discrepancies were revealed by the precise transcript level measurements afforded by RNA-seq analysis (Western, Harry et al. 1999, Western, Harry et al. 2000, Parrott, Kohno et al. 2014). For example, the timing of sexual dimorphism in *AMH* expression was earlier than previously thought, and was observed as early as Day 3. There was a significant upregulation of *AMH* under both MPT and FPT conditions between Day 0 and Day 3; however, the degree of upregulation was far greater at MPT (approximately a 7-fold increase) and continued upregulation was observed at later time points, whereas up-regulation in FPT diminished (Figure 2-6). Expression of *AD4BP/SF1*, a nuclear receptor involved in gonadogenesis and steroidogenic cell differentiation, was reportedly dynamic in alligator during and after sex determination, though depending on the literature, contradicting expression patterns were also reported (Western, Harry et al. 2000, Valenzuela, Neuwald et al. 2013). Here, our results indicate that *AD4BP/SF1* is initially fairly stable at both temperatures and only later shows an increase in expression, but does not show significant sexual dimorphism at any time point examined. Expression patterns of *FOXL2*, *FGF9*, *LHX9*, *WNT4*, and *RSPO1* were also characterized, last of which was not sexually dimorphic at any time point during Day 0-12. Species differences in the expression pattern of *RSPO1* during ovarian differentiation have been noted in the past (Smith, Shoemaker et al. 2008, Matsumoto,

Hannigan et al. 2014), and similar to the pattern observed during *Trachemys scripta* gonad sex differentiation (Matsumoto, Hannigan et al. 2014), there may be a brief female-biased expression between Day 12 and 18 in the alligator.

#### *Characterization of candidate sexual development genes*

Next, we investigated expression patterns that might provide insight into those genes with central roles in alligator sex determination. Cross-comparative analyses of development-dependent DEGs and sex-dependent DEGs were performed. Differentially expressed genes between sequential time points that also showed sexually dimorphic expression were considered to be potentially critical for gonadal sex determination. This criterion was employed to screen out significant gene expression movement in each MPT and FPT cascades that resulted in sexual dimorphism. With this criterion, 74 female and 172 male upregulated gene candidates (230 genes total) for sexual development were identified (Figure 2-7, Table 2-4), including *SOX9*, *AMH*, and *FOXL2*. Genes screened for Day 3 MPT were overall identical to the genes categorized as immediate temperature-responsive genes, with 4 additional genes identified (*AMH*, *FAP*, *COL8A2*, and *COL11A1*). The number of candidate genes increased greatly between Day 3 and Day 6 at MPT, corresponding with the expression of genes involved in testis determination, while only a few candidate genes were identified between Day 3 and Day 6 at FPT.

At MPT, candidate genes identified between Day 3 and Day 6 contained many of the genes with known roles in vertebrate male sexual development, and were profiled for the first time in alligators. These include upregulation of *DMRT3*, *TEX11*, in addition to previously reported *SOX9*, *PIWIL1* and *TDK*, which are essential for

mammalian spermatogenesis (Saxe, Chen et al. 2013), were also observed to be up-regulated at MPT during this time. These observations provide details into the transcriptional pathway underlying male fate commitment in alligator, and also reveal genes with potentially crucial roles in somatic and germ cell sex determination/differentiation.

In both the MPT and FPT cascade, several DEG involved with steroid biosynthesis and metabolism were identified, including *HSD17B1*, *STAR*, and *HSD3B2*. Also, some genes expression patterns appeared to have reversed sexually dimorphism between alligator and model organisms. For example, *HEMGN*, a gene critical for male chicken testis development (Nakata, Ishiguro et al. 2013), was up-regulated at FPT. *ARX*, a gene involved in mammalian testis development (Kitamura, Yanazawa et al. 2002) was downregulated on Day 12 at MPT and remained so at later time points. The implications of these gene expression patterns in alligator sex determination are yet to be determined. Finally, 7 uncharacterized transcripts were found to be differentially expressed at various time points. Interestingly, six of these transcripts were identified as ncRNAs (e.g., *LOC102575456*, *LOC102563416*, *LOC102573435*), though their functions and roles during alligator sexual development are yet to be defined. The presence of these ncRNAs may have significant consequences on alligator sex determination as ncRNA (*MHM*) regulation of *DMRT1* plays a pivotal role in *Gallus gallus* sex determination (Teranishi, Shimada et al. 2001). These observations during the early stages of alligator sexual development highlight both conserved elements and divergences from sex determining mechanisms found in other vertebrates.

#### *Inference of regulatory network*

Gene ontology analyses of the candidate genes for sexual development recognized 25 genes with putative transcriptional regulatory functions, among which 9 were transcription factors (Table 2-5, Figure 2-8). The gene expression patterns were further characterized as long-term, short-term, or ambiguous depending on the duration of continuous sexual dimorphism during Day 0-12 and Day 18-36. Network modeling of genes from both male and female cascades were performed using the NetGenerator tool (Weber, Henkel et al. 2013) (see Materials and Methods) (Figure 2-9). The predicted expression patterns based on the modeling overall fit the interpolated expression pattern (Figure 2-9a,b), and more than half of the total modeled interactions satisfied the robustness test. The regulatory network model at MPT consisted of 33 edges, 12 robust putative gene-to-gene interactions, and 7 robust putative influences from MPT (Figure 2-9c). At FPT, 10 putative edges were constructed with 5 robust putative influences of FPT and 3 robust gene-to-gene interactions (Figure 2-9d). As expected, the temperature influences on the regulatory genes were predicted to be widespread in both conditions. In the MPT cascade, *SOX9*, and *ARX* were predicted to be responsible for regulating a number of genes while in the FPT cascade, *FOXL2* was predicted to regulate the phosphatase, *EYA1*, and *FABP4*. Currently, these inferred networks are based on gene expression correlation and generic gene interactions. *In vitro* techniques such as reporter assays will be useful to evaluate such interactions and provide greater insight into the functional relationships between genes in this putative network.

## Conclusion

Here, we present the first RNA-seq analysis of gonadal sex determination in a TSD organism. Our analysis clearly shows the dynamic influence of incubation temperature on gene expression, providing insights regarding the state of the gonad at MPT. Differential expression of *UCP2*, *WNT11*, and *KDM6B* highlight the presence of oxidative stress, regulation of Wnt signaling pathway, and chromatin modification on testis development. Furthermore, the global view of gene expression patterns in the gonad during sex determination identified candidate genes that may be integral for the alligator sex determination cascade. Use of network modeling allowed further prediction of the underlying TSD genetic pathway and provides a conceptual framework for empirical tests probing the function of these pathways. These findings, along with the gene expression profiles, will aid future researches on TSD species, and in turn contribute toward further understanding of the vertebrate sex determination mechanisms.

## Methods

### *Tissue collection and experimental design*

Alligator eggs were collected from five clutches in June of 2010 at Lake Woodruff National Wildlife Refuge, Volusia County, FL, USA under permits from Florida Fish and Wildlife Conservation Commission and the U.S. Fish and Wildlife Service (Permit #: SPGS-10-44). All work involving alligators was performed under the guidelines specified by the Institutional Animal Care and Use Committee at the Medical University of South Carolina (Permit #: 3069). After the eggs were collected from nests, they were transported to the Medical University of South Carolina (Charleston, SC, USA) and incubated under previously established conditions (Milnes, Bermudez et al.

2005, Urushitani, Katsu et al. 2011). Rate of embryonic development was predicted based on previous data, and staged according to criteria described by Ferguson (Ferguson 1985, Kohno and Guillette 2013). All eggs were incubated under FPT (30°C) conditions until embryonic stage 19, at which point eggs were split into two incubating temperatures, MPT (33.5°C) and FPT, and sampled over the course of 36 days. This design was adopted to account for any potential sexual dimorphism present prior to stage 19, and to differentiate between temperature-responsive and developmental genes during the alligator TSD mechanism. The alligator embryos were sampled at various time points starting at stage 19, and 3rd, 6th, 12th, 18th, 24th, and 30th days post-stage 19. Additionally, FPT embryos at 36 days post-stage 19 were also sampled.

#### *RNA extraction and Illumina library preparation*

Gonad-adrenal mesonephros (GAM) complex was first sampled from the alligator embryos and preserved in RNAlater (Ambion/Thermo Fisher Scientific, Waltham, MA, USA) at -20°C, and later, the gonadal tissue was further dissected from the GAM complex under a dissecting microscope. Total RNA from each individual gonad was extracted using ISOGEN reagent (Nippon Gene, Toyama, Japan) and was purified with Promega SV Total RNA Isolation system (Promega, Madison, WI, USA) according to the manufacturer's instructions. Qubit RNA assay kit (Life Technologies, Carlsbad, CA, USA), dsDNA HS assay kit (Life Technologies), and Agilent 2100 Bioanalyzer RNA pico kit assay (Agilent Technologies, Santa Clara, CA, USA) was used to assess concentration, DNA contamination, and overall quality. Triplicates were selected from each time point and temperature condition between Day 0 to Day 12 (total of 21 individuals), and single samples were selected from each time point and

temperature between Day 18 and Day 36 (total of 7 individuals). Our primary analyses were conducted on the initial phases of sexual determination/differentiation, while single samples taken from Day 18-36 were used to provide an overview for general gene expression kinetics in latter stages. 500 ng of total RNA from each gonad samples was then used for library preparation with Illumina TruSeq RNA sample preparation v2 kit (Illumina, San Diego, CA, USA), following the manufacturer's instructions. The libraries were then evaluated by using KAPA library quantification kit (Kapa Biosystems, Woburn, MA USA) and 2100 Bioanalyzer High Sensitivity DNA assay (Agilent Technologies). Finally, the multiplexed libraries were pooled into three groups, and sequenced using Illumina HiSeq2500 instrument (Illumina) at National Institute for Basic Biology in Okazaki, Japan. Sequencing was performed as 101 bp, paired-end reads in three lanes. The RNA-seq reads are available through DRA under the accession number: DRA004128-41.

#### *Differential gene expression analysis*

Initial FASTQ files were subjected to quality assessment using FastQC tool (<http://www.bioinformatics.bbsrc.ac.uk/projects/fastqc/>). Raw reads were then mapped and assembled using the Tuxedo pipeline (Tophat software: ver. 2.0.12; Cufflinks software: ver.2.2.1) (Trapnell, Pachter et al. 2009, Trapnell, Williams et al. 2010, Trapnell, Roberts et al. 2012). Individual paired-end sequence reads from each sample were aligned to publicly available alligator genome assembly (NCBI database; Assembly name: allMis0.2; Assembly accession: GCF\_000281125.1) with supplement gene model annotation (NCBI *Alligator mississippiensis* Annotation Release 100), and directed to report best possible alignment found with '-read-realign-edit-dist' option.

The mapping rates for each experimental group were assessed using Samtools ‘flagstat’ command (Li, Handsaker et al. 2009). Differential expression between each condition was tested following the Cufflinks workflow (ver. 2.2.1), and Cuffdiff software. The significance of initial differential expression was tested at significance level  $\alpha = 0.05$ , adjusted with allowed FDR at 0.05 following Benjamini-Hochberg correction. DEGs were further screened by FDR at 0.01.

#### *Gene ontology mapping*

Contigs were blasted against the NCBI nr database using blastx program, with a minimum E-value score set to 1.0E-06. Successful blast hit results were then imported to Blast2GO program (ver. 3.1.3) where they were functionally mapped and annotated (Conesa, Gotz et al. 2005). Cut-off threshold was set to 55 and the GO level weighting set to 5. Additionally, InterPro IDs from InterProScan were merged to the annotation for further accuracy. ‘Make combined graph’ analysis was performed to score and evaluate the GO distribution in defined gene sets, and top 10 GO terms with highest node scores were selected.

#### *Statistical analysis and network inference*

Basic statistical analysis and graph constructions were conducted using Microsoft Excel, R, and GraphPad Prism software (Version 5.0b; GraphPad Software, Inc., San Diego, CA, USA). Log<sub>2</sub> transformed FPKM+1 values were used for both the MA plot and hierarchical clustering heatmap. The NetGenerator tool (ver. 2.4) (Weber, Henkel et al. 2013) was used to perform network inference analysis with time-series log<sub>2</sub> fold change from select candidate DEGs (Table 2-5) under each incubation

temperature condition. NetGenerator offers modeling gene regulatory network from time series data, based on linear differential expression intensities with consideration of influences from external stepwise input signals. Network analysis and robustness analysis was conducted using modified protocol from Schulze et al (2015). In current analysis, input signal was defined as the environmental temperature (MPT or FPT). Prior-knowledge gene-to-gene coexpression data was based on *Mus musculus* (confidence score=0.25) as obtained from Genemania (<http://genemania.org/data/>) and was implemented in the analysis (Moggs, Tinwell et al. 2004, Gallardo, John et al. 2007, Hernandez-Novoa, Bishop et al. 2008, Lattin, Schroder et al. 2008, Thorrez, Van Deun et al. 2008, Schreiner, Bell et al. 2009)(Jacobs et al., 2010; Zapala et al., 2005; Akerblad et al., 2005). Several parameters were tested and ‘allowedError’ was adjusted at 0.01. Robustness of the network was tested using two methods. In the first test, the inference analysis was repeated 1000 times with artificial Gaussian noise (mean=0; standard deviation=0.05) distributed to the expression data to test for susceptibility to perturbations. In second test, the inference analysis was repeated 1000 times with 10% of the total prior knowledge randomly omitted to test for dependency of the interactions on prior knowledge. Interactions that were predicted more than 50% of the time in both tests were considered robust.

### Figure legends

**Figure 2-1.** Experimental design. Experimental design of the RNA-seq analysis is illustrated. Bipotential, sex fate commitment and sex differentiation period are indicated, with temperature sensitive period (TSP; indicated in light brown). The dotted line represents the end of the TSP. Eggs were first incubated under female producing

temperature (FPT; indicated in red) until just prior to the onset of sexual differentiation (stage 19; Day 0), which were then either shifted to male producing temperature (MPT; indicated in blue) or kept at FPT. Gonadal regions were sampled from individuals at several subsequent time points (Day 3, 6, 12) with corresponding approximate developmental stage (Ferguson) displayed in the bottom table. Day 0-12 represents the timing of sexual differentiation, and three individuals per temperature condition per time points are used.

**Figure 2-2.** Additional experimental design. Experimental design of the additional RNA-seq analysis during sex differentiation period is illustrated. The dotted line represents the close of the TSP. The eggs were first incubated at female producing temperature (FPT; indicated in red) until just prior to sexual differentiation (stage 19; Day 0), at which point groups of eggs were either shifted to male producing temperature (MPT; indicated in blue) or kept at FPT. Gonadal regions were sampled from individuals at several subsequent time points (Day 18, 24, 30, 36) with corresponding approximate developmental stage (Ferguson) displayed in the bottom table. Day 18-36 represents sex differentiation group, and one individual per temperature condition per time points are used.

**Figure 2-3.** Overlap of development-dependent and sex-dependent differentially expressed genes. Venn diagram of differentially expressed genes (DEGs) in (a) Day 0 to Day 12 MPT (indicated in blue) conditions and (b) Day 0 to Day 12 FPT (indicated in red) conditions based on genome mappings of Tophat. (c) Venn diagram for number of DEGs between Day 0 to Day 12 MPT and FPT conditions at respective time points,

based on genome mapping using Tophat. Number values in blue indicate the number of genes with MPT-biased expression, while values in red indicate the number of genes with FPT-biased expression. All DEGs were determined based on statistical significance (FDR < 0.01) using Cuffdiff software. Further details are available in Table 2-1 and 2-2.

**Figure 2-4.** Development-dependent DEGs and Sex-dependent DEGs in alligator transcriptomic profiles. (a) MA plot, with gene expression values expressed as  $\log_2\text{FPKM}$  and fold change expressed as  $\text{Log}_2\text{FC}$ , is constructed using differential expression analysis between each time point (Day 0-3, Day 3-6, Day 6-12). (b) MA plot, with gene expression values expressed as  $\log_2\text{FPKM}$  and fold change expressed as  $\text{Log}_2\text{FC}$ , is constructed using differential expression analysis results between FPT and MPT ( $30^\circ\text{C}$  vs  $33.5^\circ\text{C}$ ) for Day 3 FPT vs Day 3 MPT, Day 6 FPT vs Day 6 MPT, and Day 12 FPT vs Day 12 MPT. For both MA plot, 20,181 genes, based on NCBI genome annotation, were examined for differential expression. Red dots indicate significantly up- or down-regulated genes at FDR < 0.01.

**Figure 2-5.** Candidate temperature-responsive differential gene expression.

(a) Venn diagrams show the number of DEGs between Day 0 and Day 3 incubated either under MPT (indicated in blue) or FPT (indicated in red). 131 genes (indicated in bold) were found to have MPT-specific gene expression movement, possibly in response to changes in incubation temperature. (b) 41 out of 131 genes were found to have been up- or down-regulated significantly enough to be sexually dimorphic. 17 genes displayed MPT-biased expression and 24 genes displayed FPT-biased expression.

Red, blue, and grey indicate FPT-, MPT- or non-bias, respectively. (c) Top 10 biological process gene ontology terms mapped to the candidate temperature-responsive genes with highest node score, based on Blast2GO program.

**Figure 2-6.** Expression profiles of major genes involved in sex differentiation.

Expression profiles of various major genes involved in gonadal sex determination in model organisms are displayed based on FPKM values from RNA-seq analysis under FPT conditions (indicated in red) and MPT conditions (indicated in blue). Predicted onset of sexual differentiation is indicated in orange background; \* FDR  $\leq 0.01$ .

**Figure 2-7.** Candidate potential critical genes central for sex determination. (a) Cross comparison between development- and sex-dependent DEGs (FDR  $< 0.01$ ; Fig. 2) was performed among Day 0 to Day 12, and a total of 230 genes were identified as candidate genes for *A. mississippiensis* sex determination. Green and orange arrows indicate up- and down-regulation, respectively, with number of corresponding genes indicated. The majority of gene expression dynamics associated with development was observed to be MPT-specific. Further information is available in Table 4 (b) Hierarchical clustering analysis of sexual dimorphism (M-F log<sub>2</sub>FC) in the candidate genes at Day 3, 6, and 12. Red color indicates high *z*-score (female biased expression) while blue indicates a low *z*-score (male biased expression).

**Figure 2-8.** Expression profiles of candidate transcription factors involved in sex differentiation. Expression profiles of candidate transcription factors involved in gonadal sex determination are displayed based on FPKM values from RNA-seq analysis

under FPT conditions (indicated in red) and MPT conditions (indicated in blue).

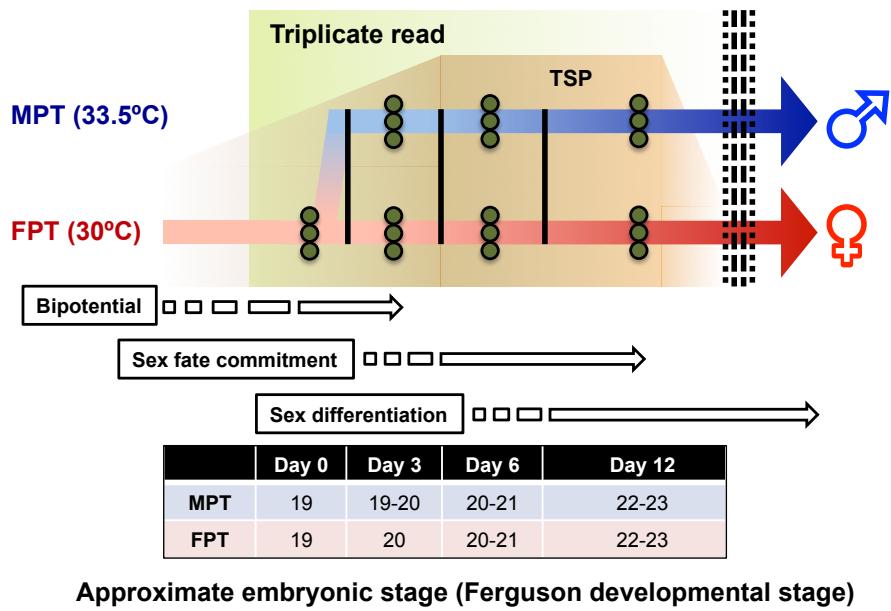
Predicted onset of sexual differentiation is indicated in orange background; \* FDR

$\leq 0.01$ .

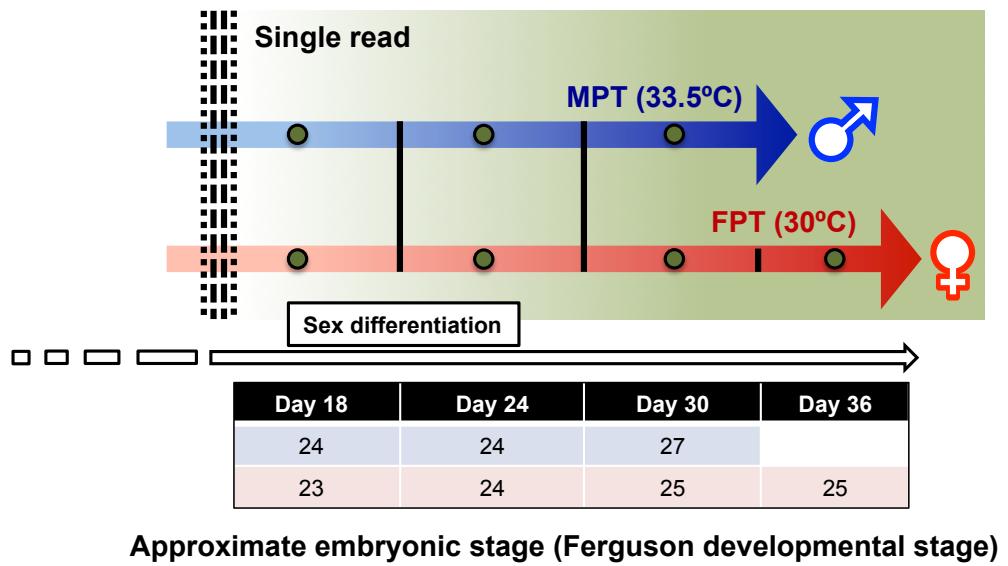
**Figure 2-9.** NetGenerator derived model prediction of MPT and FPT cascade.

(a-b) Interpolated expression (dotted line; dots indicate actual recorded fold change) and inferred patterns derived from the predicted NetGenerator model (solid line) of putative transcriptional regulatory genes over the course of sex differentiation at both (a) MPT and (b) FPT. (c-d) Inferred network model at both (c) MPT and (d) FPT. Robust (solid line) and non-robust (dotted line) predicted interactions are displayed as gene-gene interactions (black), and temperature-gene interactions (MPT:blue; FPT:red). Thickened lines indicate interaction with high robustness (80% or above). Following genes names were modified for inference network: LOC102562106 (*JARID2-1*), LOC102561337 (*JARID2-2*), LOC102569158 (*WNT11*), LOC102560544 (*EEF1A1*), LOC102577358 (*DMRT3*), LOC102573123 (*SOX9*), LOC102576325 (*PAKI*), LOC102559361 (*EDNRB*), LOC102563625 (*PDE2A*), and LOC102577040 (*FOXL2*)

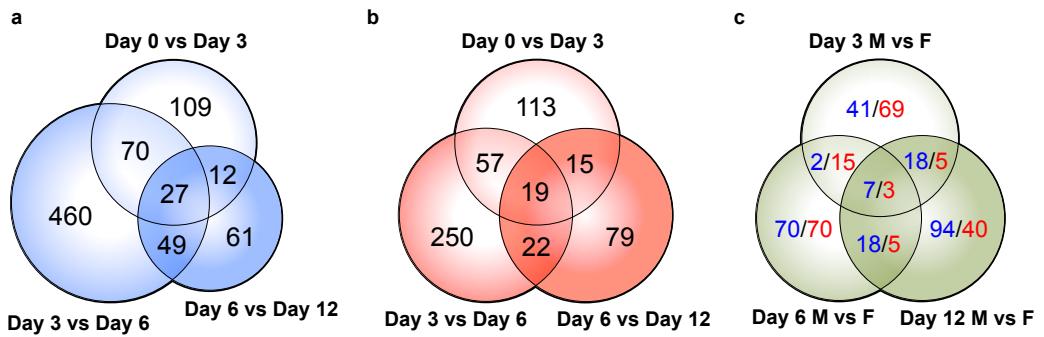
**Figure 2-1**



**Figure 2-2**

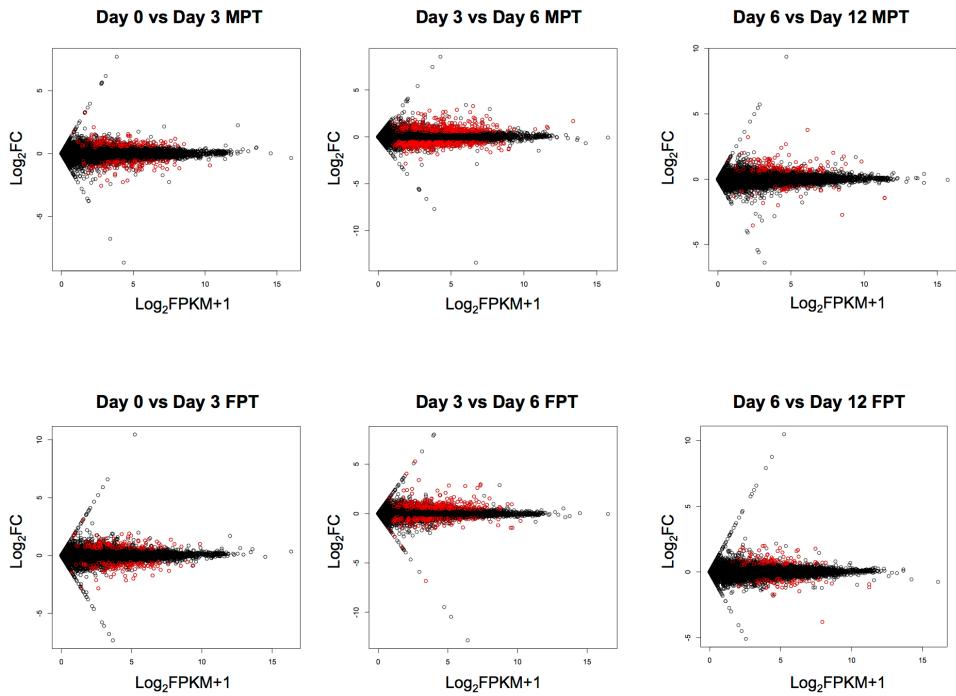


**Figure 2-3**

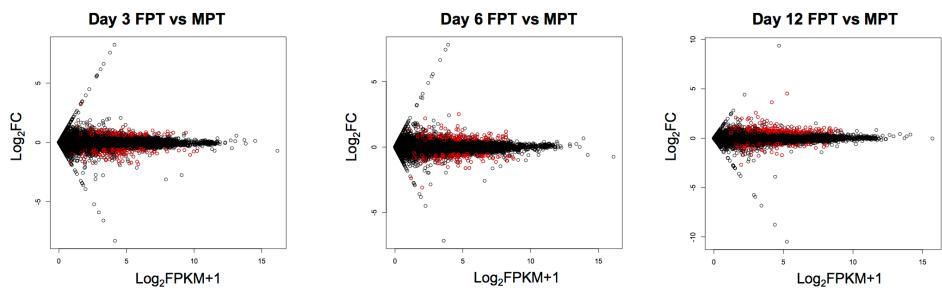


**Figure 2-4**

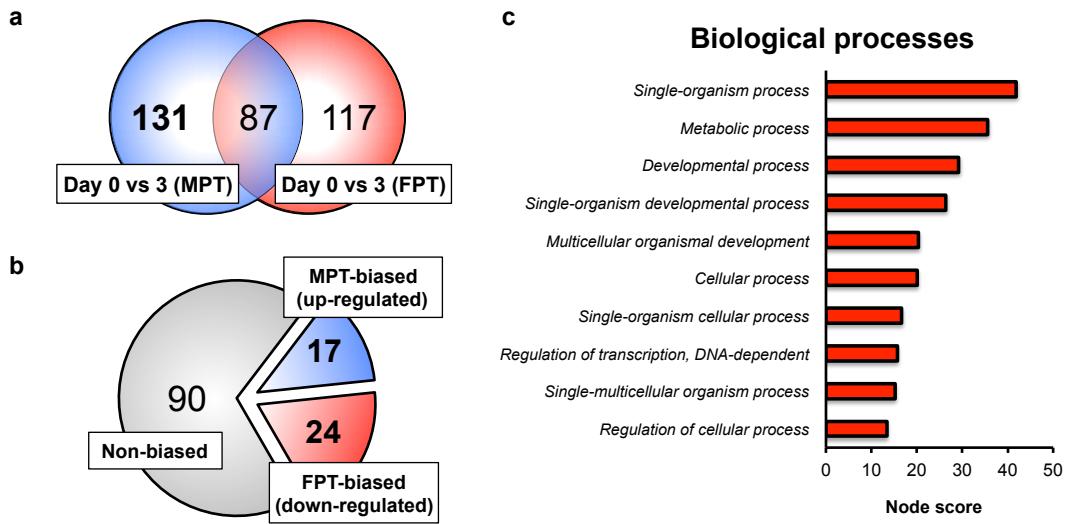
**a**



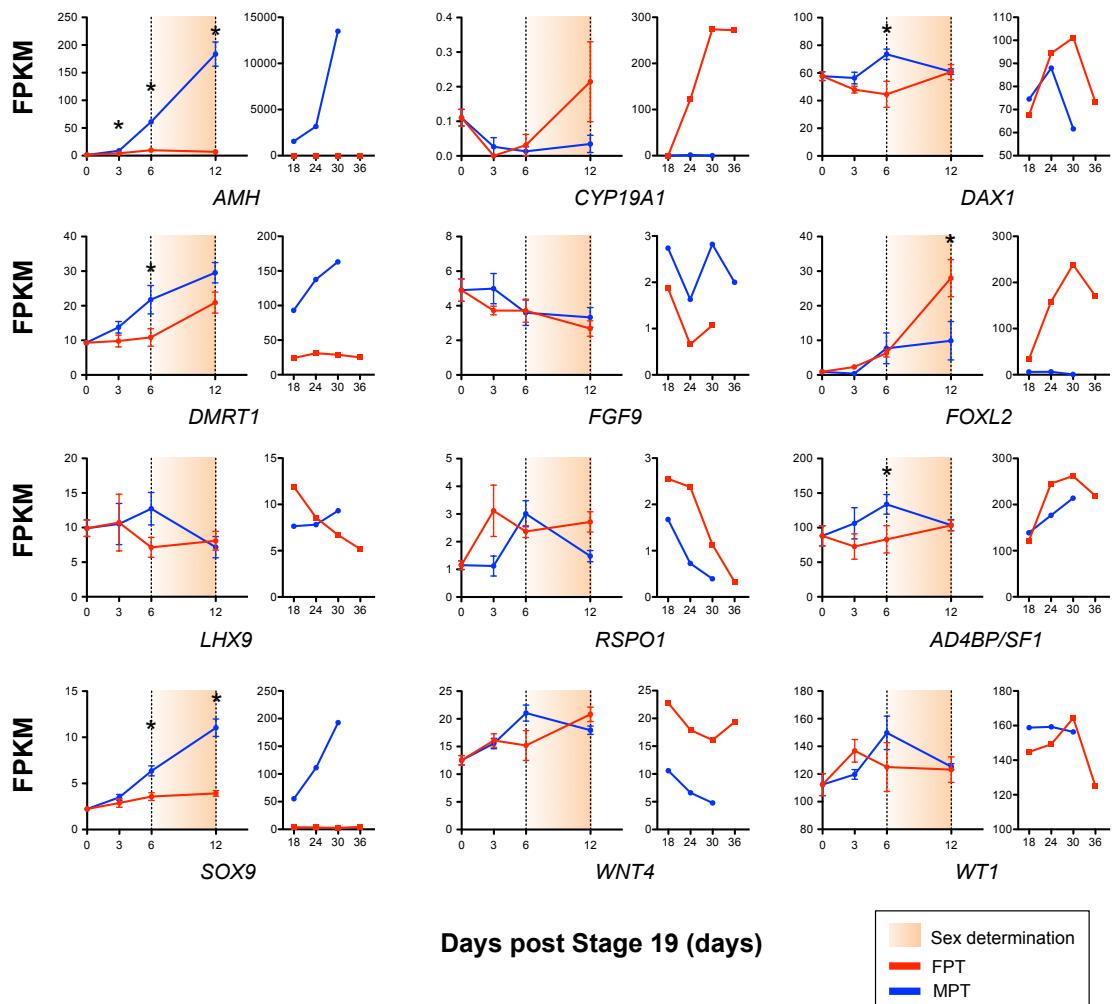
**b**



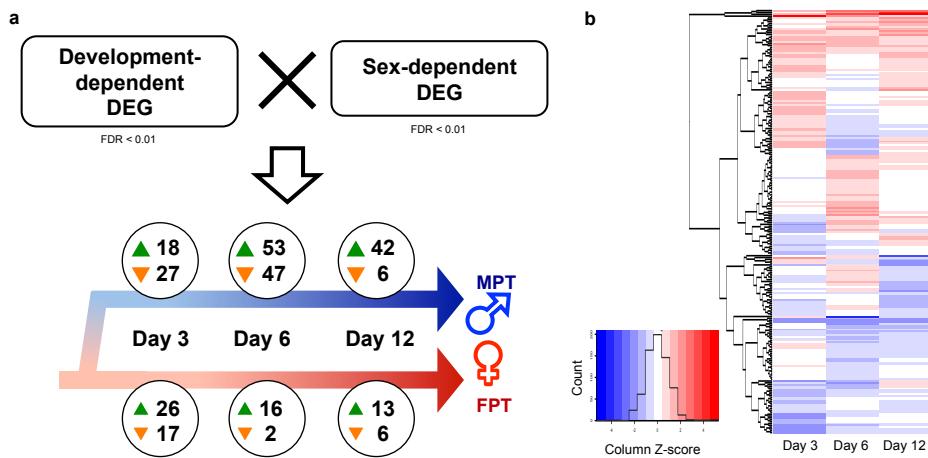
**Figure 2-5**



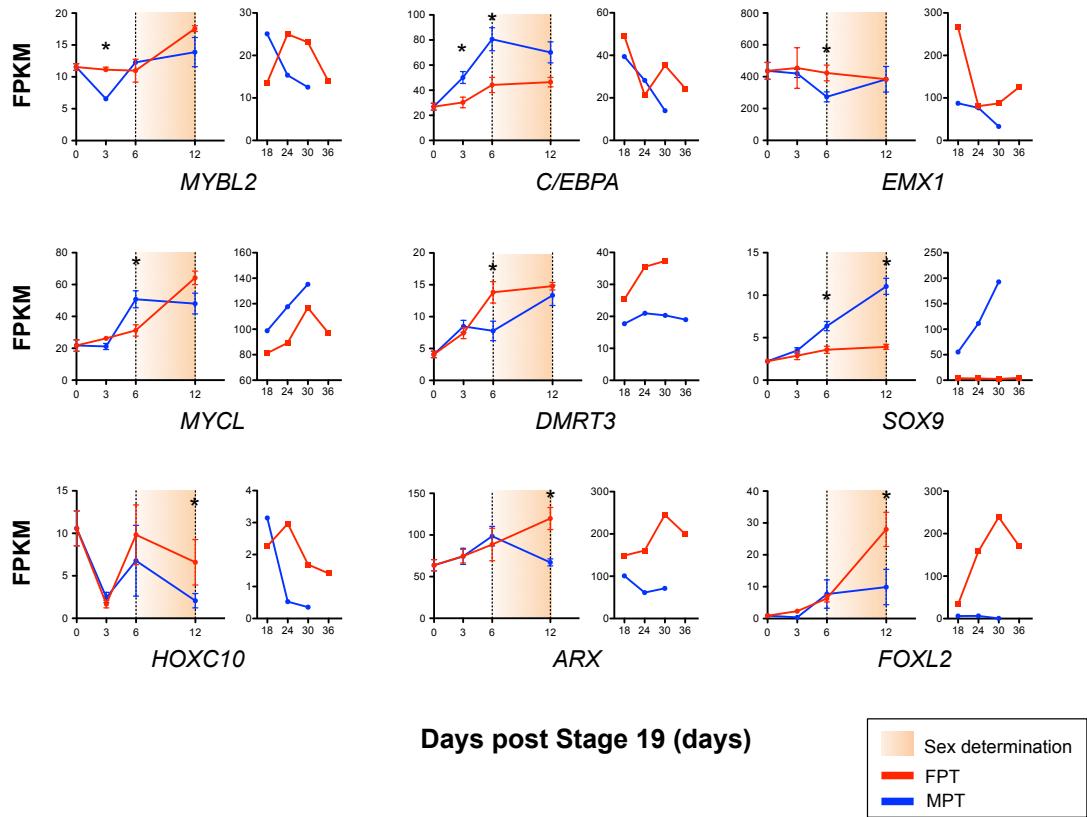
**Figure 2-6**



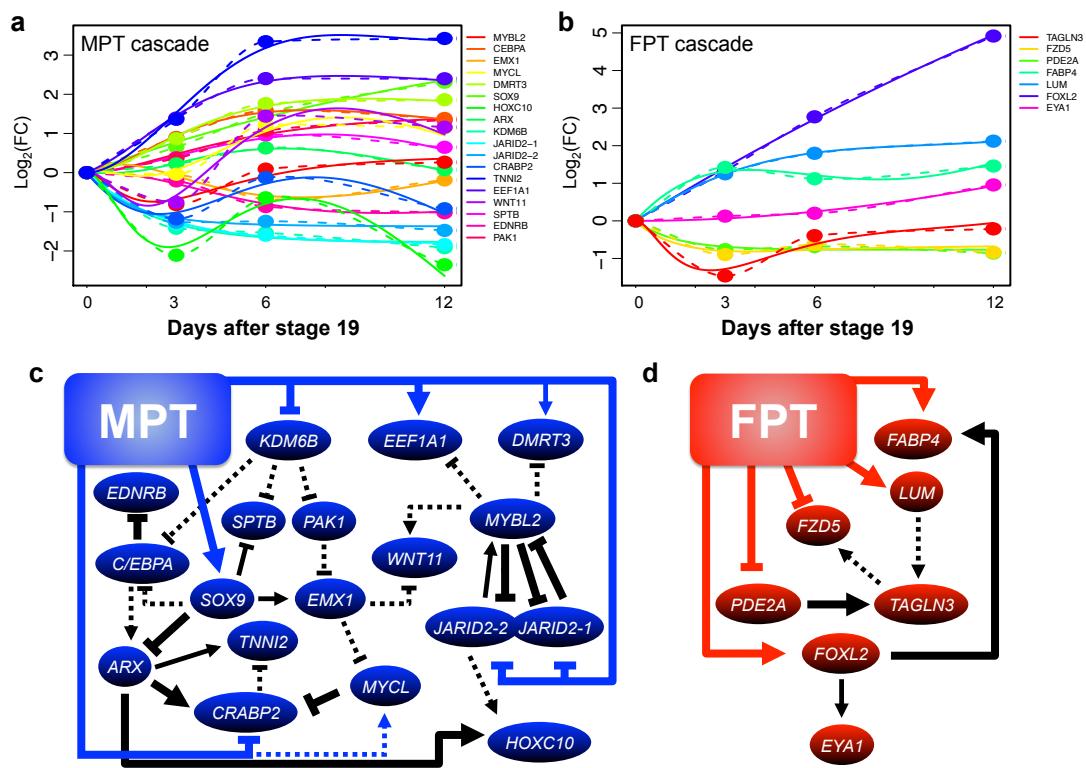
**Figure 2-7**



**Figure 2-8**



**Figure 2-9**



**Table 2-1.** Annotation of development-dependent dimorphic genes in gonad during Day 0-12

Day 0 (FPT) vs Day 3 (MPT)											
Up-regulated						Down-regulated					
Gene ID	Gene Symbol	LOG2(FC)	FDR	RefSeq Accession	Description	Gene ID	Gene Symbol	LOG2(FC)	FDR	RefSeq Accession	Description
XLOC_003593	AMH	2.76	2.63E-03	XM_006261559.1	anti-Mullerian hormone	XLOC_007791	LOC102569784	-3.11	2.63E-03	XM_006266039.1	collagen alpha-1(VIII) chain-like
XLOC_012454	LOC102565224	2.02	2.63E-03	XM_006270968.1	neuroblast differentiation-associated protein AHNAK-like	XLOC_011459	COL8A2	-2.43	2.63E-03	XM_006269879.1	collagen, type VIII, alpha 2
XLOC_011989	LOC102574848	1.93	2.63E-03	XM_006270435.1	mast cell protease 1A-like	XLOC_005250	NOV	-2.42	2.63E-03	XM_006263555.1	nephroblastoma overexpressed
XLOC_000735	TNRC6B	1.91	2.63E-03	XM_006258541.1	trinucleotide repeat containing 6B, transcript variant X1	XLOC_010405	OSTN	-2.25	2.63E-03	XM_006267889.1	osteocrin
XLOC_014000	SLC15A1	1.65	2.63E-03	XM_006272640.1	solute carrier family 15 (oligopeptide transporter), member 1	XLOC_012148	CDCD3	-2.22	9.85E-03	XM_006270625.1	coiled-coil domain containing 3
XLOC_011915	FAT2	1.65	2.63E-03	XM_006270390.1	FAT atypical cadherin 2	XLOC_019721	HOXC10	-2.11	2.63E-03	XM_006278447.1	homeobox C10
XLOC_012722	TTR	1.61	2.63E-03	XM_006271257.1	transthyretin	XLOC_001548	SMOC2	-1.89	2.63E-03	XM_006259389.1	SPARC related modular calcium binding 2
XLOC_011963	LPP	1.61	4.73E-03	XM_006278489.1	LIM domain containing preferred translocation partner in lipoma	XLOC_002977	LOC102566431	-1.76	8.24E-03	XM_006260896.1	chromosome unknown open reading frame, human C9orf96
XLOC_006327	LOC102570551	1.56	4.73E-03	XM_006264538.1	keratin, type I cytoskeletal 14-like	XLOC_012549	FSTL5	-1.67	2.63E-03	XM_006271075.1	folistatin-like 5
XLOC_007754	TNMD	1.52	2.63E-03	XM_006265998.1	tenomodulin	XLOC_016580	LOC102558436	-1.66	2.63E-03	XM_006275267.1	zinc finger protein 184-like
XLOC_000204	UCP2	1.47	2.63E-03	XM_006257947.1	uncoupling protein 2 (mitochondrial, proton carrier)	XLOC_005656	GYS2	-1.58	2.63E-03	XM_006263801.1	glycogen synthase 2 (liver)
XLOC_004390	LOC102558761	1.47	2.63E-03	XM_006262430.1	cathelicidin-OH antimicrobial peptide-like	XLOC_000062	ADAM19	-1.57	2.63E-03	XM_006257806.1	ADAM metallopeptidase domain 19
XLOC_004741	GALNT5	1.46	2.63E-03	XM_006262802.1	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase	XLOC_007790	HDXA10	-1.53	2.63E-03	XM_006265365.1	homeobox A10
XLOC_009466	SLC26A9	1.45	2.63E-03	XM_006267811.1	solute carrier family 26 (anion exchanger), member 9	XLOC_013275	KDM6B	-1.42	2.63E-03	XM_006271864.1	lysine (K)-specific demethylase 6B
XLOC_004389	LOC102558544	1.44	2.63E-03	XM_006262429.1	cathelicidin-2-like	XLOC_019258	FAP	-1.41	2.63E-03	XM_006277995.1	fibroblast activation protein, alpha
XLOC_013303	OSGIN1	1.40	2.63E-03	XM_006271885.1	oxidative stress induced growth inhibitor 1	XLOC_004684	COL11A1	-1.41	2.63E-03	XM_006262736.1	collagen, type XI, alpha 1, transcript variant X3
XLOC_006593	LOC102560544	1.39	8.24E-03	XM_006264808.1	elongation factor 1-alpha-like	XLOC_020025	ACTG2	-1.36	2.63E-03	XM_006278736.1	actin, gamma 2, smooth muscle, enteric, transcript variant X2
XLOC_020119	TNNI2	1.36	2.63E-03	XM_006278383.1	troponin I type 2 (skeletal, fast)	XLOC_014642	FABP7	-1.35	8.24E-03	XM_006273821.1	fatty acid binding protein 7, brain
XLOC_016502	HIPK2	1.33	2.63E-03	XM_006275178.1	homeodomain interacting protein kinase 2, transcript variant X2	XLOC_013166	APCD11	-1.34	2.63E-03	XM_006271755.1	adenomatous polyposis coli down-regulated 1-like
XLOC_015166	ITGB6	1.32	2.63E-03	XM_006273817.1	integrin, beta 6, transcript variant X2	XLOC_012145	LOC102562106	-1.32	2.63E-03	XM_006270621.1	protein Jumonji-like
XLOC_010819	CYGB	1.31	2.63E-03	XM_006269221.1	cystoglobin, transcript variant X1	XLOC_011463	CSRP2	-1.31	2.63E-03	XM_006269901.1	cysteine and glycine-rich protein 2
XLOC_012453	LOC102564995	1.28	2.63E-03	XM_006270967.1	neuroblast differentiation-associated protein AHNAK-like	XLOC_019126	VIPR2	-1.31	9.85E-03	XM_006277863.1	vasoactive intestinal peptide receptor 2
XLOC_001313	LOC102575660	1.23	2.63E-03	XM_006259135.1	dimeethylamine monoxygenase [N-oxide-forming] 1-like, transcript variant X3	XLOC_006235	PRDM6	-1.31	8.24E-03	XM_006264455.1	PR domain containing 6
XLOC_003595	JSRP1	1.21	2.63E-03	XM_006261560.1	junctional sarcoplasmic reticulum protein 1	XLOC_010400	LOC102566853	-1.30	2.63E-03	XM_006267866.1	receptor-type tyrosine-protein phosphatase N2-like
XLOC_016865	LOC102569893	1.20	2.63E-03	XM_006275549.1	dermatopontin-like	XLOC_017214	LOC102557978	-1.29	2.63E-03	XM_006275887.1	myeloid protein 1-like
XLOC_016506	NFIC	1.18	2.63E-03	XM_006275182.1	nuclear factor I/C (CCAAT-binding transcription factor), transcript variant X1	XLOC_016496	FBLN2	-1.29	2.63E-03	XM_006275174.1	fibulin 2
XLOC_004035	EIF4A2	1.18	2.63E-03	XM_006262029.1	eukaryotic translation initiation factor 4A2	XLOC_012144	LOC102561337	-1.27	2.63E-03	XM_006270617.1	protein Jumonji-like
XLOC_015961	ADAM28	1.17	2.63E-03	XM_006274644.1	ADAM metallopeptidase domain 28	XLOC_010746	ACTA2	-1.25	2.63E-03	XM_006269140.1	actin, alpha 2, smooth muscle, aorta
XLOC_020066	LOC102565712	1.16	8.24E-03	XM_006278787.1	flucocytolytic protein FL011-like, transcript variant X1	XLOC_006201	PLAC9	-1.24	2.63E-03	XM_006264408.1	placenta-specific 9, transcript variant X2
XLOC_010743	LOC102576768	1.10	2.63E-03	XM_006269137.1	lysosomal acid lipase/cholesteryl ester hydrolase-like	XLOC_000614	PRSS35	-1.24	2.63E-03	XM_006258407.1	protease, serine, 35
XLOC_019417	LOC102560584	1.10	4.73E-03	XM_006278134.1	macrophage-expressed gene 1 protein-like	XLOC_004098	ADAMTS15	-1.24	2.63E-03	XM_006262089.1	ADAM metallopeptidase with thrombospondin type 1 motif, 15
XLOC_007107	UPK3A	1.09	2.63E-03	XM_006265339.1	uroplakin 3A	XLOC_009984	LMOD1	-1.23	2.63E-03	XM_006258800.1	leiomodin 1 (smooth muscle)
XLOC_01273	LOC102573334	1.09	2.63E-03	XM_006265415.1	low-density lipoprotein receptor-related protein 1-like	XLOC_017186	CRABP2	-1.18	2.63E-03	XM_006275867.1	cellular retinoic acid binding protein 2
XLOC_018940	LOC102559753	1.09	2.63E-03	XM_006277671.1	inactive serine/threonine-protein kinase TEX14-like	XLOC_008932	ANGPTL1	-1.18	2.63E-03	XM_006267260.1	angiopoietin-like 1, transcript variant X2
XLOC_014317	LOC102559961	1.06	2.63E-03	XM_006272668.1	vassopressin V1a receptor-like	XLOC_001140	SOX10	-1.17	2.63E-03	XM_006258955.1	SRY (sex determining region Y)-box 10
XLOC_013332	MDGA1	1.04	2.63E-03	XM_006271918.1	MAM domain containing glycosylphosphatidylinositol anchor 1	XLOC_019338	TAGLN	-1.14	2.63E-03	XM_006278069.1	transgelin
XLOC_001024	ZFHX3	1.02	2.63E-03	XM_006258819.1	zinc finger homeobox 3	XLOC_018105	LOC102567885	-1.11	2.63E-03	XM_006276825.1	ADAMTS-like protein 2-like
XLOC_011601	RANBP3L	1.02	2.63E-03	XM_006270043.1	RAN binding protein 3-like	XLOC_012067	CTGF	-1.06	2.63E-03	XM_006270533.1	connective tissue growth factor
XLOC_019823	LOC102564018	1.01	2.63E-03	XM_006278540.1	cysteine-rich venom protein helothermine-like	XLOC_001309	LOC102576189	-1.06	2.63E-03	XM_006259136.1	dimethylallylamine monooxygenase [N-oxide-forming] 3-like
XLOC_011273	LOC102574050	1.01	4.73E-03	XM_006269699.1	SH3 and multiple ankyrin repeat domains 3-like	XLOC_001896	LOC102567354	-1.06	2.63E-03	XM_006259759.1	twist-related protein 1-like
XLOC_015057	LOC102568110	1.01	2.63E-03	XM_006273705.1	acyl-coenzyme A synthetase ACSM4, mitochondrial-like	XLOC_008171	ARG2	-1.06	2.63E-03	XM_006266445.1	arginase 2
XLOC_009391	LOC102566850	0.99	2.63E-03	XM_006267730.1	FRAS1-related extracellular matrix protein 2-like	XLOC_009566	ELN	-1.05	2.63E-03	XM_006267934.1	elastin
XLOC_003859	CERC2	0.99	2.63E-03	XM_006261831.1	cat eye syndrome chromosome region, candidate 2	XLOC_019573	LOC102561818	-1.03	2.63E-03	XM_006278306.1	class I histocompatibility antigen, Gogo-C'0203 alpha chain-like
XLOC_019268	LAMA3	0.98	2.63E-03	XM_006278007.1	laminin, alpha 3	XLOC_009568	LOC102575456	-1.03	2.63E-03	XM_0363216.1	uncharacterized LOC102575456, transcript variant X1
XLOC_006694	SLC14A	0.97	2.63E-03	XM_006264916.1	solute carrier family 1 (glutamate/neuronal amino acid transporter), member 4	XLOC_015332	LOC102560570	-1.02	2.63E-03	XM_006273996.1	disintegrin and metalloproteinase domain-containing protein 19-like
XLOC_013428	LOC102566162	0.96	2.63E-03	XM_006272019.1	uncharacterized LOC102566162	XLOC_007033	HPGDS	-1.01	4.73E-03	XM_006265263.1	hematopoietic prostaglandin D synthase
XLOC_014454	LOC102573200	0.93	2.63E-03	XM_006273095.1	neuin-4-like, transcript variant X1	XLOC_017258	TBX18	-1.00	2.63E-03	XM_006275946.1	T-box 18
XLOC_000587	TRPC4AP	0.91	2.63E-03	XM_006258376.1	transient receptor potential cation channel, subfamily C, member 4 associated protein	XLOC_002973	DBH	-1.00	2.63E-03	XM_006260879.1	dopamine beta-hydroxylase (dopamine beta-monoxygenase)
XLOC_009560	TEC13	0.91	2.63E-03	XM_006267920.1	transcription elongation factor A (SII), 3	XLOC_008541	CNDP1	-0.99	2.63E-03	XM_006266824.1	camosine dipeptidase 1 (metallopeptidase M20 family)
XLOC_009149	FGGY	0.91	4.73E-03	XM_006274961.1	FGGY carbohydrate kinase domain containing, transcript variant X1	XLOC_008364	HEY2	-0.98	2.63E-03	XM_006266650.1	hes-related family bHLH transcription factor with YRPW motif 2, trans
XLOC_001658	APOA1	0.91	2.63E-03	XM_006259520.1	apolipoprotein A-I	XLOC_001510	LOC102559161	-0.98	2.63E-03	XM_006265238.1	UDP-glucuronosyltransferase 1-9-like
XLOC_007714	LOC102570482	0.90	2.63E-03	XM_006265963.1	cytochrome P450 3A21-like	XLOC_014375	LOC102573199	-0.98	2.63E-03	XM_006273013.1	chromogranin A-like

XLOC_009761	LOC102560621	0.89	2.63E-03	XM_006268113.1	GATA-binding factor 3-like, transcript variant X1		XLOC_016935	LOC102567251	-0.87	2.63E-03	XM_006275615.1	major histocompatibility complex class I-related gene protein-like
XLOC_010298	OTOG	0.89	8.24E-03	XM_006268682.1	otogelin-like		XLOC_007271	SLC18A1	-0.87	2.63E-03	XM_006265496.1	solute carrier family 18 (vesicular monoamine transporter), member
XLOC_009660	HMOX1	0.88	9.85E-03	XM_006268010.1	homeobox containing 1		XLOC_015035	LOC102568567	-0.86	2.63E-03	XM_006273707.1	uncharacterized LOC102568567
XLOC_002739	LOC102566194	0.88	2.63E-03	XM_006260660.1	nuclear receptor subfamily 5 group A member 2-like		XLOC_007516	LOC102560835	-0.83	4.73E-03	XM_006265759.1	monocarboxylate transporter 2-like
XLOC_005977	LOC102562785	0.87	2.63E-03	XM_006264168.1	mucin-4-like		XLOC_017840	MYBL2	-0.82	2.63E-03	XM_006276553.1	v-myb avian myeloblastosis viral oncogene homolog-like 2
XLOC_003318	LOC102577358	0.87	2.63E-03	XM_006261267.1	duplex and mbp-3 related transcription factor 3-like		XLOC_015471	SULF1	-0.82	2.63E-03	XM_006274147.1	sulfatase 1
XLOC_015178	LOC102560270	0.86	2.63E-03	XM_006273834.1	methylcrotonoyl-CoA carboxylase beta chain, mitochondrial-like		XLOC_019982	NMRK2	-0.80	2.63E-03	XM_006278682.1	nicotinamide riboside kinase 2
XLOC_019770	BCL6	0.86	2.63E-03	XM_006278487.1	B-cell CLL/lymphoma 6, transcript variant X1		XLOC_003210	SLC5A8	-0.80	2.63E-03	XM_006261167.1	solute carrier family 5 (sodium/monocarboxylate cotransporter), mem
XLOC_003796	MYO18B	0.86	2.63E-03	XM_006261765.1	myosin XVIIIB		XLOC_014075	SLC5A10	-0.79	2.63E-03	XM_006272714.1	solute carrier family 5 (sodium/sugar cotransporter), member 10, tran
XLOC_018611	LOC102575816	0.84	2.63E-03	XM_006277341.1	mitogen-activated protein kinase 4-like		XLOC_002641	GPX3	-0.79	2.63E-03	XM_006260571.1	glutathione peroxidase 3 (plasma)
XLOC_003273	PREL	0.83	2.63E-03	XM_006261224.1	proline/arginine-rich end leucine-rich repeat protein		XLOC_009005	LOC102569324	-0.78	2.63E-03	XM_006267352.1	vitamin D3 hydroxylase-associated protein-like
XLOC_003061	MFS4	0.82	2.63E-03	XM_006261001.1	major facilitator superfamily domain containing 4		XLOC_0044313	CNN1	-0.77	9.85E-03	XM_006262326.1	calponin 1, basic, smooth muscle
XLOC_006802	LOC102573570	0.82	2.63E-03	XM_006265015.1	solute carrier family 22 member 6-A-like		XLOC_016457	PCBP4	-0.77	4.73E-03	XM_006275137.1	poly(C) binding protein 4
XLOC_004416	LOC102563884	0.80	2.63E-03	XM_006262449.1	polycystin-1-like		XLOC_006860	LOC102569158	-0.76	4.73E-03	XM_006265079.1	protein Wnt-11-like, transcript variant X2
XLOC_018070	LOC102574081	0.80	2.63E-03	XM_006276772.1	chromosome unknown open reading frame, human C1orf63		XLOC_002330	LOC102575357	-0.76	2.63E-03	XM_006260196.1	argininosuccinate lyase-like
XLOC_002123	NTNG2	0.80	2.63E-03	XM_006259990.1	netrin G2		XLOC_002638	SYNPO	-0.74	2.63E-03	XM_006260565.1	synaptopodin
XLOC_002748	SLC5A12	0.79	2.63E-03	XM_006260672.1	solute carrier family 5 (sodium/monocarboxylate cotransporter), member 12		XLOC_000564	LOC102565100	-0.73	2.63E-03	XM_006258355.1	heart- and neural crest derivatives-expressed protein 2-like
XLOC_008224	LOC102562949	0.79	2.63E-03	XM_00626498.1	ammonium transporter Rh type B-B-like		XLOC_001463	LOC102574572	-0.73	8.24E-03	XM_006259299.1	somatostatin-2-like
XLOC_007647	LOC102572713	0.78	4.73E-03	XM_006265890.1	prolactin-releasing peptide receptor-like		XLOC_018671	THBS2	-0.73	2.63E-03	XM_006277394.1	thrombospondin 2, transcript variant X1
XLOC_003026	ID4	0.78	8.24E-03	XM_006260955.1	inhibitor of DNA binding 4, dominant negative helix-loop-helix protein		XLOC_006767	LOC102574741	-0.72	2.63E-03	XM_006264941.1	homeobox protein meis3-B-like
XLOC_014240	LOC102559116	0.77	6.57E-03	XM_006272882.1	chromosome unknown open reading frame, human C10orf90		XLOC_017801	APOC1	-0.69	2.63E-03	XM_006276513.1	apolipoprotein C-I
XLOC_008286	LOC102559326	0.76	2.63E-03	XM_006266561.1	neuroblast differentiation-associated protein AHNAK-like		XLOC_001868	LOC102562999	-0.69	2.63E-03	XM_006259743.1	dehydrogenase/reductase SDR family member 4-like
XLOC_005663	LOC10257135	0.76	2.63E-03	XM_006263807.1	ammonium transporter Rh type C-like		XLOC_015734	SHISA2	-0.69	2.63E-03	XM_006274427.1	shisa family member 2
XLOC_008408	CALB1	0.75	2.63E-03	XM_006266960.1	calbindin 1, 28kDa		XLOC_008801	LOC102572026	-0.69	4.73E-03	XM_006267109.1	GDNF family receptor alpha-4-like
XLOC_005713	AEE01	0.73	2.63E-03	XM_006263861.1	AhpC/TSA antioxidant enzyme domain containing 1		XLOC_012970	DEC R2	-0.69	2.63E-03	XM_006271539.1	2,4-dienoyl CoA reductase 2, peroxisomal
XLOC_013532	MRPL34	0.73	2.63E-03	XM_006272137.1	mitochondrial ribosomal protein L34		XLOC_000771	FRZB	-0.68	2.63E-03	XM_006258581.1	frizzled-related protein
XLOC_015465	LACTB2	0.71	6.57E-03	XM_006274141.1	lactamase, beta 2		XLOC_004236	COL12A1	-0.68	2.63E-03	XM_006262249.1	collagen, type XII, alpha 1
XLOC_016521	P2RX5	0.70	4.73E-03	XM_006275202.1	purinergic receptor P2X, ligand-gated ion channel, 5		XLOC_012939	LOC102557733	-0.68	2.63E-03	XM_006271508.1	fibrillin-2-like
XLOC_019852	IFRD1	0.69	2.63E-03	XM_006278568.1	interferon-related developmental regulator 1, transcript variant X2		XLOC_015551	UHRF1	-0.67	2.63E-03	XM_006274236.1	ubiquitin-like with PHD and ring finger domains 1
XLOC_014354	KCNJ16	0.69	2.63E-03	XM_006273002.1	potassium inwardly-rectifying channel, subfamily J, member 16		XLOC_001405	FBLN5	-0.67	9.85E-03	XM_006259232.1	fblin 5, transcript variant X2
XLOC_015669	CLU	0.69	2.63E-03	XM_006274651.1	clustin		XLOC_001565	MLYK	-0.67	2.63E-03	XM_006259414.1	myosin light chain kinase
XLOC_013007	ACE	0.67	2.63E-03	XM_006271571.1	angiotensin I converting enzyme		XLOC_013636	LOC102560955	-0.66	2.63E-03	XM_006272242.1	protein NEL-like
XLOC_013531	BABAM1	0.66	2.63E-03	XM_006272118.1	BRISC and BRCA1 complex member 1		XLOC_006353	PTRF	-0.64	2.63E-03	XM_006264575.1	polymerase I and transcript release factor
XLOC_014704	SP1	0.66	4.73E-03	XM_006273344.1	Sp1 transcription factor		XLOC_010264	LOC102572032	-0.63	4.73E-03	XM_006268644.1	platelet-derived growth factor D-like
XLOC_018582	NBEAL2	0.66	2.63E-03	XM_006277313.1	neurobeachin-like 2		XLOC_003305	RASL1B	-0.63	6.57E-03	XM_006261252.1	RAS-like, family 11, member B
XLOC_017425	ESPNL	0.65	2.63E-03	XM_006276123.1	espin-like		XLOC_019177	HOXB3	-0.62	2.63E-03	XM_006277919.1	homeobox B3
XLOC_001169	PKD1	0.65	8.24E-03	XM_006268435.1	polycystic kidney disease 1 (autosomal dominant)		XLOC_001112	LOC102563319	-0.61	2.63E-03	XM_006258919.1	dehydrogenase/reductase SDR family member 1-like
XLOC_000925	ROBO3	0.65	2.63E-03	XM_006258733.1	roundabout, axon guidance receptor, homolog 3 (Drosophila)		XLOC_016348	PAX8	-0.61	9.85E-03	XM_006275027.1	paired box 8
XLOC_013843	DCUN1D2	0.64	4.73E-03	XM_006272469.1	DCN1, defective in cullin neddylation 1, domain containing 2, transcript variant X1		XLOC_015530	SPAG5	-0.60	6.57E-03	XM_006274223.1	sperm associated antigen 5
XLOC_003589	LOC102566435	0.64	2.63E-03	XM_006261548.1	small EDRK-rich factor 1-like		XLOC_011181	CTH	-0.58	6.57E-03	XM_006269606.1	cystathionine (cystathione gamma-lyase)
XLOC_004573	USP33	0.63	9.85E-03	XM_006262624.1	ubiquitin specific peptidase 33		XLOC_000678	UCHL1	-0.58	4.73E-03	XM_006258484.1	ubiquitin carboxyl-terminal esterase L1 (ubiquitin thiolesterase)
XLOC_014705	AMHR2	0.63	4.73E-03	XM_006273345.1	anti-Mullerian hormone receptor, type II		XLOC_010513	SLC23A1	-0.58	9.85E-03	XM_006268887.1	solute carrier family 23 (ascorbic acid transporter), member 1
XLOC_010354	PCYOX1	0.62	9.85E-03	XM_006268735.1	prenylcysteine oxidase 1		XLOC_002026	NDUF6	-0.57	6.57E-03	XM_006259892.1	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 6, 14kDa
XLOC_011287	ATP6V0D2	0.62	8.24E-03	XM_006269712.1	ATPase, H <sup>+</sup> -transporting, lysosomal 38kDa, V0 subunit d2		XLOC_004033	SLT3	-0.56	6.57E-03	XM_006262024.1	slit homolog 3 (Drosophila)
XLOC_017330	LOC102566095	0.61	2.63E-03	XR_363683.1	uncharacterized LOC102566095		XLOC_015323	LOC102557886	-0.54	9.85E-03	XM_006273984.1	chromosome unknown open reading frame, human C11orf54
XLOC_015567	LAMA2	0.61	2.63E-03	XM_006274252.1	laminin, alpha 2		XLOC_017563	GLB1L2	-0.52	9.85E-03	XM_006276262.1	galactosidase, beta 1-like 2
XLOC_007382	LOC102561850	0.61	6.57E-03	XM_006265601.1	A.superbus venom factor 1-like							
XLOC_009514	LOC102561484	0.61	4.73E-03	XM_006267878.1	potassium transporting ATPase alpha chain 2-like							
XLOC_011598	CAPSL	0.60	2.63E-03	XM_006270040.1	calcyphosine-like							
XLOC_009799	PHKA1	0.60	6.57E-03	XM_006268154.1	phosphorylase kinase, alpha 1 (muscle)							
XLOC_013747	SDPR	0.60	2.63E-03	XM_006272372.1	serum deprivation response							
XLOC_009597	LOC102561020	0.59	8.24E-03	N/A	CUB and sushi domain-containing protein 1-like							
XLOC_010197	PNRC1	0.58	4.73E-03	XM_006268567.1	proline-rich nuclear receptor coactivator 1							
XLOC_011728	AHDCC1	0.58	8.24E-03	XM_006270214.1	AT hook, DNA binding motif, containing 1							
XLOC_010818	ST6GALNAC2	0.58	2.63E-03	XM_006269266.1	ST6 (alpha-N-acetyl-neuraminy-2,3-beta-galactosyl-1,3)-N-acetylgalactosaminide alpha-2,6-sialyltransferase 2							
XLOC_003053	FTCD	0.57	6.57E-03	XM_006260991.1	formimidoyltransferase cyclodeaminase							
XLOC_012500	LOC102566935	inf	2.63E-03	XM_006271052.1	collagen alpha-1(I) chain-like							
XLOC_007526	LOC102563416	inf	4.73E-03	XR_363102.1	uncharacterized LOC102563416							

Day 3 (MPT) vs Day 6 (MPT)											
Up-regulated							Down-regulated				
Gene_ID	Gene Symbol	LOG2(FC)	FDR	RefSeq Accession	Description	Gene_ID	Gene Symbol	LOG2(FC)	FDR	RefSeq Accession	Description
XLOC_000636	LOC102563794	4.15	2.63E-03	XM_006258433.1	myosin-3-like	XLOC_000709	TAP2	-4.60	4.73E-03	XM_006258513.1	transporter 2, ATP-binding cassette, sub-family B (MDR/TAP)
XLOC_020160	LOC102573463	4.06	2.63E-03	XM_006278908.1	epithelial chloride channel protein-like	XLOC_020054	LOC102559828	-2.84	2.63E-03	XM_006278762.1	acidic mammalian chitinase-like
XLOC_009569	LOC102575456	3.32	2.63E-03	XR_363216.1	uncharacterized LOC102575456, transcript variant X1	XLOC_012454	LOC102565224	-2.53	2.63E-03	XM_006270968.1	neuroblast differentiation-associated protein AHNAK-like
XLOC_011459	COL6A2	3.13	2.63E-03	XM_006269879.1	collagen, type VIII, alpha 2	XLOC_019763	LPP	-2.29	2.63E-03	XM_006278489.1	LIM domain containing preferred translocation partner in lipoma
XLOC_007791	LOC102569784	3.06	2.63E-03	XM_006266039.1	collagen alpha-1(VIII) chain-like	XLOC_018874	RASGEF1C	-2.19	2.63E-03	XM_00627598.1	RasGEF domain family, member 1C
XLOC_009566	ELN	2.97	2.63E-03	XM_006267934.1	elastin	XLOC_010119	PP2D1	-2.05	6.57E-03	XM_006268489.1	protein phosphatase 2C-like domain containing 1
XLOC_017452	CLEC3B	2.84	2.63E-03	XM_006276144.1	C-type lectin domain family 3, member B	XLOC_000041	LOC102566578	-1.99	2.63E-03	XM_006275779.1	neuroblast differentiation-associated protein AHNAK-like
XLOC_003593	AMH	2.80	2.63E-03	XM_006261559.1	anti-Mullerian hormone	XLOC_019398	LOC102575717	-1.91	2.63E-03	XM_006278151.1	avidin-like
XLOC_005250	NOV	2.79	2.63E-03	XM_006263355.1	nephroblastoma overexpressed	XLOC_005150	LOC102559161	-1.83	2.63E-03	XM_0062683238.1	chromodomain-helicase-DNA-binding protein 6-like
XLOC_003144	INHA	2.72	2.63E-03	XM_006261090.1	inhibin, alpha	XLOC_019726	HDXC5	-1.75	2.63E-03	XM_006278452.1	homeobox C5
XLOC_009565	LOC102574916	2.67	2.63E-03	XR_363212.1	uncharacterized LOC102574916	XLOC_012650	MOGAT1	-1.70	8.24E-03	XM_006271177.1	monoacylglycerol O-acyltransferase 1
XLOC_015317	ACTC1	2.60	2.63E-03	XM_006273980.1	actin, alpha, cardiac muscle 1	XLOC_000735	TNRC6B	-1.69	2.63E-03	XM_006268541.1	trinucleotide repeat containing 6B, transcript variant X1
XLOC_004945	LOC102569139	2.45	2.63E-03	XM_006258290.1	cathepsin W-like	XLOC_006538	LOC102565592	-1.66	2.63E-03	XM_006264753.1	BPTI/Kunitz domain-containing protein-like
XLOC_003718	MPO	2.43	2.63E-03	XM_006261680.1	myeloperoxidase	XLOC_007744	LOC102572288	-1.65	8.24E-03	XM_006265988.1	polymeric immunoglobulin receptor-like
XLOC_013006	LOC102575860	2.42	2.63E-03	XM_006271581.1	potassium voltage-gated channel subfamily H member 7-like	XLOC_020621	RC3H1	-1.63	4.73E-03	XM_006272938.1	ring finger and CCCH-type domains 1
XLOC_006201	PLAC9	2.38	2.63E-03	XM_00626408.1	placenta-specific 9, transcript variant X2	XLOC_000049	ERC1	-1.61	2.63E-03	XM_006258283.1	ELKS/RAB6-interacting/CAST family member 1, transcript variant X1
XLOC_010356	LOC102575076	2.26	2.63E-03	XM_006268737.1	butyrophilin subfamily 1 member A1-like	XLOC_003276	ZBED6	-1.57	2.63E-03	XM_006261228.1	zinc finger BED-type containing 6
XLOC_016003	LOC102573440	2.22	2.63E-03	XM_006274686.1	microfibrill-associated glycoprotein 4-like, transcript variant X1	XLOC_012895	TGM3	-1.57	2.63E-03	XM_006271463.1	transglutaminase 3
XLOC_005889	LOC102576921	2.21	6.57E-03	XM_006264068.1	probable RNA-binding protein 46-like, transcript variant X2	XLOC_006565	GYS2	-1.55	2.63E-03	XM_006263801.1	glycogen synthase 2 (liver)
XLOC_002280	TNNC2	2.21	2.63E-03	XM_006260137.1	troponin C type 2 (fast)	XLOC_011273	LOC102574050	-1.55	2.63E-03	XM_006269699.1	SH3 and multiple ankyrin repeat domains protein 3-like
XLOC_006860	LOC102569158	2.20	2.63E-03	XM_006265079.1	protein Wnt-11-like, transcript variant X2	XLOC_017010	AQP2	-1.54	4.73E-03	XM_006275689.1	aquaporin 2 (collecting duct)
XLOC_001548	SMOC2	2.16	2.63E-03	XM_006259389.1	SPARC-related modular calcium binding 2	XLOC_000130	DAAM2	-1.53	2.63E-03	XM_006257879.1	dishevelled associated activator of morphogenesis 2
XLOC_000263	CPA3	2.15	2.63E-03	XM_006258045.1	carboxypeptidase 9, transcript variant X2	XLOC_000909	CCK	-1.52	2.63E-03	XM_006258715.1	cholecytokinin
XLOC_008388	LOC102566921	2.13	2.63E-03	XM_006266674.1	SPARC-like protein 1-like	XLOC_003978	RXRA	-1.50	2.63E-03	XM_006261957.1	retinoid X receptor, alpha, transcript variant X3
XLOC_012124	MFAP5	2.11	2.63E-03	XM_006270600.1	microfibrill-associated protein 5	XLOC_011888	SCN1A	-1.49	2.63E-03	XM_006270357.1	sodium channel, voltage-gated, type I, alpha subunit
XLOC_002516	HSD17B1	2.08	2.63E-03	XM_006260402.1	hydroxysteroid (17-beta) dehydrogenase 1, transcript variant X2	XLOC_003182	SLC22A4	-1.49	2.63E-03	XM_006261136.1	solute carrier family 22 (organic cation/zwitterion transporter), member 4, transcript variant X1
XLOC_010819	CYGB	2.04	2.63E-03	XM_006269221.1	cytoglobin, transcript variant X1	XLOC_003506	KCNJ10	-1.49	8.24E-03	XM_006261467.1	potassium inwardly-rectifying channel, subfamily J, member 10
XLOC_000567	LUM	2.04	2.63E-03	XM_006258358.1	lumican	XLOC_006281	AGTR1	-1.48	2.63E-03	XM_006258044.1	angiotensin II receptor, type 1
XLOC_020119	TNNI2	1.98	2.63E-03	XM_006278383.1	T-tropomyosin 1 type 2 (skeletal, fast)	XLOC_007989	LOC102563022	-1.48	2.63E-03	XM_006266253.1	chromosome unknown open reading frame, human C6orf58
XLOC_013898	CDF	1.97	2.63E-03	XM_006272513.1	complement factor D (adipsin)	XLOC_003565	IGF1R	-1.46	2.63E-03	XM_006263474.1	insulin-like growth factor 1 receptor
XLOC_004294	EPOR	1.96	2.63E-03	XM_006263511.1	erythropoietin receptor	XLOC_006248	LOC102573016	-1.45	2.63E-03	N/A	transcription factor CP2-like protein 1-like
XLOC_008986	LOC102563116	1.96	2.63E-03	XR_363176.1	uncharacterized LOC102563116	XLOC_001371	LOC102567038	-1.44	2.63E-03	XM_006259197.1	WAP four-disulfide core domain protein 5-like
XLOC_016716	TMOD4	1.93	2.63E-03	XM_006275401.1	tropomodulin 4 (muscle)	XLOC_016500	NFIC	-1.44	2.63E-03	XM_006275182.1	nuclear factor I/C (CCAAT-binding transcription factor), transcript variant X1
XLOC_019685	LOC102570913	1.92	2.63E-03	XM_006278416.1	alpha-tectorin-like	XLOC_009466	SLC26A9	-1.41	2.63E-03	XM_006267811.1	solute carrier family 26 (anion exchanger), member 9
XLOC_017046	ACTA2	1.90	2.63E-03	XM_006269140.1	actin, alpha 2, smooth muscle, aorta	XLOC_003128	ACE2	-1.40	2.63E-03	XM_006261087.1	angiotensin I converting enzyme 2
XLOC_012892	EPB42	1.88	2.63E-03	XM_006271454.1	erythrocyte membrane protein band 4.2	XLOC_017576	LOC102571375	-1.39	2.63E-03	XM_006276274.1	stimulator of interferon genes protein-like
XLOC_005991	WSD2	1.86	2.63E-03	XM_006264170.1	WSC domain containing 2	XLOC_002961	AAK1	-1.38	2.63E-03	XM_006260876.1	AP2 associated kinase 1
XLOC_001658	APOA1	1.85	2.63E-03	XM_006259520.1	apolipoprotein A-I	XLOC_015179	LOC102560500	-1.38	4.73E-03	XM_006273835.1	nicotinamide N-methyltransferase-like
XLOC_014873	ANK1	1.77	2.63E-03	XM_006273519.1	ankyrin 1, erythrocytic	XLOC_002025	DCDC2	-1.38	2.63E-03	XM_006260544.1	doublecortin domain containing 2
XLOC_002025	ACTG2	1.72	2.63E-03	XM_006278736.1	actin, gamma 2, smooth muscle, enteric, transcript variant X2	XLOC_017559	EXOC3L4	-1.38	2.63E-03	XM_006276257.1	exocyst complex component 3-like 4
XLOC_004390	ADAMTS15	1.71	2.63E-03	XM_006262430.1	cathelicidin-CH antimicrobial peptide-like	XLOC_011601	RANBP3L	-1.36	2.63E-03	XM_006270043.1	RAN binding protein 3-like
XLOC_015371	TAL1	1.71	2.63E-03	XM_006274037.1	T-cell acute lymphocytic leukemia 1	XLOC_002045	RASGRF1	-1.36	4.73E-03	XM_006259008.1	Ras protein-specific guanine nucleotide-releasing factor 1, transcript variant X1
XLOC_009331	PML	1.71	2.63E-03	XM_006267894.1	premelanosome protein	XLOC_019188	IGFBP1	-1.35	4.73E-03	XM_006277904.1	insulin-like growth factor 2 mRNA binding protein 1, transcript variant X3
XLOC_019258	FAP	1.70	2.63E-03	XM_006277995.1	fibroblast activation protein, alpha	XLOC_014359	GA13	-1.35	2.63E-03	XM_006272999.1	guanine nucleotide binding protein (G protein), alpha 13
XLOC_003869	HBA2	1.68	2.63E-03	XM_006261842.1	hemoglobin, alpha 2	XLOC_011915	FAT2	-1.35	2.63E-03	XM_006270390.1	FAT1 atypical cadherin 2
XLOC_010405	OSTN	1.68	2.63E-03	XM_006268789.1	osteocrin	XLOC_019823	LOC102564018	-1.35	2.63E-03	XM_006278540.1	cytoseine-rich venom protein helothermine-like
XLOC_018071	LOC102557982	1.66	8.24E-03	XM_006276787.1	blood group Rh(D) polypeptide-like	XLOC_015306	HSD17B2	-1.34	2.63E-03	XM_006273972.1	hydroxy steroid (17-beta) dehydrogenase 2
XLOC_014642	FABP7	1.62	2.63E-03	XM_006273281.1	fatty acid binding protein 7, brain	XLOC_011657	LOC102575787	-1.33	2.63E-03	XM_006270115.1	adrenodoxin, mitochondrial-like
XLOC_004389	LOC102558544	1.62	2.63E-03	XM_006262429.1	cathelicidin-2-like	XLOC_001024	ZFH3	-1.33	2.63E-03	XM_006258819.1	zinc finger homeobox 3
XLOC_018075	SLC30A2	1.61	2.63E-03	XM_006276781.1	solute carrier family 30 (zinc transporter), member 2	XLOC_003071	LOC102575599	-1.32	2.63E-03	XM_006261670.1	cytochrome P450 2K4-like
XLOC_003617	MYH11	1.59	2.63E-03	XM_006261582.1	myosin, heavy chain 11, smooth muscle	XLOC_001734	LOC102565647	-1.31	2.63E-03	XM_006259599.1	PR domain zinc finger protein 16-like
XLOC_017096	MATN4	1.59	2.63E-03	XM_006275789.1	matrin 4	XLOC_013605	SLC4A4	-1.29	2.63E-03	XM_006272210.1	solute carrier family 4 (sodium bicarbonate cotransporter), member 4
XLOC_000149	BLVRB	1.57	2.63E-03	XM_006267898.1	biliverdin reductase B (flavin reductase (NADPH))	XLOC_001408	LOC102559600	-1.28	8.24E-03	XM_006259235.1	sodium/hydrogen exchanger 3-like
XLOC_004098	ADAMTS15	1.56	2.63E-03	XM_006262089.1	ADAM metallopeptidase with thrombospondin type 1 motif, 15	XLOC_016538	JPH2	-1.26	2.63E-03	XM_006275231.1	junctophilin 2, transcript variant X1
XLOC_019565	COL15A1	1.55	2.63E-03	XM_006278300.1	collagen, type XV, alpha 1	XLOC_019803	LOC102559056	-1.26	2.63E-03	XM_006278518.1	protein MRP-12-like
XLOC_000025	CA13	1.53	2.63E-03	XM_006257765.1	carbonic anhydrase XIII	XLOC_008541	CNDP1	-1.26	2.63E-03	XM_006266824.1	carnosine dipeptidase 1 (metallopeptidase M20 family)
XLOC_017908	LOC102575941	1.53	2.63E-03	XM_006276617.1	cytochrome P450 26A1-like	XLOC_016644	KCNK3	-1.25	2.63E-03	XM_006257353.1	potassium channel, subfamily K, member 3
XLOC_013202	KEL	1.52	2.63E-03	XM_006271796.1	Keil blood group, metallo-endopeptidase	XLOC_019961	ZBTB7A	-1.24	2.63E-03	XM_006278677.1	zinc finger and BTB domain containing 7A
XLOC_002405	HSPB1	1.52	2.63E-03	XM_006262027.1	heat shock 27kDa protein 1	XLOC_006630	LOC102568382	-1.22	2.63E-03	XM_006264838.1	ficolin-1-like
XLOC_017804	LOC102572053	1.51	4.73E-03	XM_006276523.1	anionic trypsin-1-like	XLOC_009391	LOC102566850	-1.21	2.63E-03	XM_006267730.1	FRAS1-related extracellular matrix protein 2-like
XLOC_002554	ITGA11	1.50	2.63E-03	XM_006260446.1	integrin, alpha 11	XLOC_018611	LOC102575816	-1.20	2.63E-03	XM_006277341.1	mitogen-activated protein kinase 4-like
XLOC_019688	LOC102568737	1.50	9.85E-03	XR_363851.1	uncharacterized LOC102568737	XLOC_016867	LOC102570362	-1.19	2.63E-03	XM_006275551.1	3 beta-hydroxysteroid dehydrogenase/Delta 5-->4-isomerase-like
XLOC_011463	CSR2P	1.49	2.63E-03	XM_006269011.1	cysteine and glycine-rich protein 2	XLOC_016831	FRAS1	-1.19	2.63E-03	XM_006275515.1	Fraser syndrome 1
XLOC_000292	TEX11	1.47	2.63E-03	XM_006258071.1	testis expressed 11						

XL0C_006634	ENTPD2	1.47	2.63E-03	XM_006264847.1	ectonucleoside triphosphate diphosphohydrolase 2		XLOC_011163	LOC102565377	-1.18	2.63E-03	XM_006269585.1	serotriphin-like
XL0C_019721	HOXC10	1.47	4.73E-03	XM_006278447.1	homeobox C10		XLOC_015651	LOC102563772.1	-1.18	6.57E-03	XM_00274340.1	fatty acyl-CoA hydrolase precursor, medium chain-like, liver carboxylesterase-like
XL0C_013143	LOC102567788	1.46	2.63E-03	XM_006271712.1	calretinin-like		XLOC_000414	PDE1C	-1.18	2.63E-03	XM_006258197.1	phosphodiesterase 1C, calmodulin-dependent 70kDa
XL0C_017835	HEMGN	1.46	2.63E-03	XM_006276548.1	hemogen, transcript variant X1		XLOC_001503	LRP2	-1.18	2.63E-03	XM_006268878.1	low density lipoprotein receptor-related protein 2
XL0C_014376	LOC102573435	1.46	2.63E-03	XR_363493.1	uncharacterized LOC102573435		XLOC_001517	LOC102568516	-1.18	2.63E-03	XM_006259359.1	glycine amidinotransferase, mitochondrial-like
XL0C_006771	NFSN541	1.45	2.63E-03	XM_006264947.1	zinc finger protein 541		XLOC_007300	ARAP2	-1.16	2.63E-03	XM_006265523.1	ArfGAP with RhoGAP domain, ankyrin repeat and PH domain 2
XL0C_019338	TAGLN	1.44	2.63E-03	XM_006278069.	transgelin		XLOC_014252	SLC6A18	-1.16	2.63E-03	XM_006272902.1	solute carrier family 6 (neutral amino acid transporter), member 18
XL0C_001359	LOC102565488	1.44	2.63E-03	XM_006259176.1	tubulin alpha-3 chain-like		XLOC_003709	LOC102576203	-1.15	8.24E-03	XM_006261672.1	aryl hydrocarbon receptor-like
XL0C_017357	PDLIM3	1.43	2.63E-03	XM_006276044.1	PDZ and LIM domain 3, transcript variant X1		XLOC_003796	MYO18B	-1.14	2.63E-03	XM_006281765.1	myosin XVIIIB
XL0C_013173	LOC102558340	1.43	2.63E-03	XM_006271749.1	tubulin beta-6 chain-like		XLOC_007821	PPP1R12B	-1.14	8.24E-03	XM_006266086.1	protein phosphatase 1, regulatory subunit 12B
XL0C_012997	SLC4A1	1.42	2.63E-03	XM_006271577.1	solute carrier family 4 (anion exchanger), member 1		XLOC_015981	ADAM28	-1.14	2.63E-03	XM_006274644.1	ADAM metallopeptidase domain 28
XL0C_019900	TIMP1	1.40	2.63E-03	XM_006278610.1	TIMP metalloproteinase inhibitor 1		XLOC_002083	SETBP1	-1.14	2.63E-03	XM_006259959.1	SET binding protein 1, transcript variant X1
XL0C_009875	ITGA2B	1.39	2.63E-03	XM_006268239.1	integrin, alpha 2b (plated glycoprotein IIb/IIIa complex, antigen CD41)		XLOC_017000	LOC102563625	-1.12	2.63E-03	XM_006275682.1	cGMP-dependent 3',5'-cyclic phosphodiesterase-like
XL0C_004860	LOC102574734	1.39	2.63E-03	XM_006262895.1	procollagen C-endopeptidase enhancer 1-like		XLOC_006276	MTPP	-1.11	4.73E-03	XM_00624499.1	microsomal triglyceride transfer protein
XL0C_002987	PIWI1	1.38	2.63E-03	XM_006269010.1	piwi-like RNA-mediated gene silencing 1		XLOC_007725	LOC102573022	-1.11	2.63E-03	XM_006265973.1	protein sidekick-1-like
XL0C_017690	WIF1	1.36	2.63E-03	XM_006273696.1	WNT inhibitory factor 1		XLOC_018116	SOAT1	-1.11	2.63E-03	XM_006276828.1	sterol O-acyltransferase 1
XL0C_016054	GATA1	1.36	2.63E-03	XM_006269039.1	GATA binding protein 1 (globin transcription factor 1)		XLOC_018864	LOC102559287	-1.11	2.63E-03	XM_006277586.1	transmembrane protein FAM155B-like, transcript variant X1
XL0C_003111	FMO1	1.34	2.63E-03	XM_006259132.1	flavin containing monooxygenase 1, transcript variant X2		XLOC_014729	LOC102654645	-1.09	9.85E-03	XM_006273378.1	L-amino-acid oxidase-like
XL0C_002641	GPK3	1.34	2.63E-03	XM_006260571.1	glutathione peroxidase 3 (plasma)		XLOC_006616	UTRN	-1.08	2.63E-03	XM_00624831.1	utrophin
XL0C_000984	LMD01	1.33	2.63E-03	XM_006258800.1	leiomodin 1 (smooth muscle)		XLOC_011397	HSD11B2	-1.08	2.63E-03	XM_006269835.1	hydroxysteroid (11-beta) dehydrogenase 2
XL0C_007861	PIWIL4	1.31	2.63E-03	XM_006266116.1	piwi-like RNA-mediated gene silencing 4		XLOC_014934	LOC102576022	-1.08	2.63E-03	XM_006273577.1	parathyroid hormone/parathyroid hormone-related peptide receptor-like
XL0C_014705	AMHR2	1.31	2.63E-03	XM_006273345.1	anti-Mullerian hormone receptor, type II		XLOC_016487	TFAP2B	-1.06	2.63E-03	XM_006275167.1	transcription factor AP-2 beta (activating enhancer binding protein 2 beta), transcript variant X3
XL0C_000903	PLP1	1.30	2.63E-03	XM_006258708.1	protolipid protein 1, transcript variant X1		XLOC_016258	PLA2R1	-1.06	2.63E-03	XM_006273824.1	phospholipase A2 receptor 1, 180kDa
XL0C_011496	INHBB	1.30	2.63E-03	XM_006269944.1	inhibin, beta B		XLOC_011510	KIF24	-1.05	2.63E-03	XM_006269964.1	kinesin family member 24
XL0C_004413	CNN13	1.30	2.63E-03	XM_006262326.1	calponin 1, basic, smooth muscle		XLOC_013008	TAN2C	-1.05	2.63E-03	XM_006271573.1	tetratricopeptide repeat, ankyrin repeat and coiled-coil containing 2
XL0C_012067	CTGF	1.28	2.63E-03	XM_006270533.1	connective tissue growth factor		XLOC_003210	SLC5A8	-1.04	2.63E-03	XM_006261167.1	solute carrier family 5 (sodium/monocarboxylate cotransporter), member 8
XL0C_015259	LOC102562273	1.28	2.63E-03	XR_36345.1	uncharacterized LOC 102562273		XLOC_007671	ARHGEF17	-1.04	2.63E-03	XM_006265912.1	Rho guanine nucleotide exchange factor (GEF) 17
XL0C_013166	APCD11	1.27	2.63E-03	XM_006271755.1	adenomatous polyposis coli down-regulated 1-like		XLOC_003648	SLC22A16	-1.03	2.63E-03	XM_006261622.1	solute carrier family 22 (organic cation/carnitine transporter), member 16
XL0C_009637	MYCL	1.26	2.63E-03	XM_006267996.1	v-myc avian myelocytomatis viral oncogene lung carcinoma derived homolog		XLOC_001504	LOC102665177	-1.03	2.63E-03	XM_006259345.1	inosine-uridine preferring nucleoside hydrolase-like
XL0C_018671	THBS2	1.26	2.63E-03	XM_006273934.1	thrombospondin 2, transcript variant X1		XLOC_017582	DUOX2	-1.03	2.63E-03	XM_006276282.1	dual oxidase 2
XL0C_015699	CLU	1.26	2.63E-03	XM_006274651.1	clusterin		XLOC_007017	SCRN1	-1.03	2.63E-03	XM_006265245.1	secremin 1
XL0C_013268	LOC102564068	1.25	2.63E-03	XM_006271857.1	aurora kinase B-like		XLOC_002027	TET3	-1.02	2.63E-03	XM_006278741.1	tet methylcytosine dioxygenase 3
XL0C_002001	LOC102567971	1.24	2.63E-03	XM_006278709.1	steroid 17-alpha-hydroxylase/17,20 lyase-like		XLOC_014075	SLC5A10	-1.02	2.63E-03	XM_006272714.1	solute carrier family 5 (sodium/sugar cotransporter), member 10, transcript variant X1
XL0C_019739	NFE2	1.24	2.63E-03	XM_006278456.1	nuclear factor, erythroid 2		XLOC_006223	ALDH8A1	-1.01	2.63E-03	XM_00624434.1	aldehyde dehydrogenase 8 family, member A1, transcript variant X2
XL0C_002852	CHRD	1.20	2.63E-03	XM_006267089.1	chordin		XLOC_019410	LOC102558530	-1.00	2.63E-03	XM_006278126.1	myelin and lymphocyte protein-like, transcript variant X2
XL0C_011416	ACTA1	1.19	2.63E-03	XM_006269852.1	actin, alpha 1, skeletal muscle		XLOC_008919	RASAL2	-0.99	2.63E-03	XM_00627273.1	RAS protein activator like 2
XL0C_012510	NCAN	1.19	2.63E-03	XM_006271033.1	neurocan		XLOC_005298	AFF4	-0.98	2.63E-03	XM_006263400.1	AF4/FMR2 family, member 4
XL0C_015124	PSAT1	1.18	2.63E-03	XM_006273773.1	phosphoserine aminotransferase 1, transcript variant X1		XLOC_015035	LOC102568567	-0.98	2.63E-03	XM_006273707.1	uncharacterized LOC102568567
XL0C_000614	PTRS35	1.17	2.63E-03	XM_006258407.1	protease, serine, 35		XLOC_001438	SOGA1	-0.98	2.63E-03	XM_006259266.1	suppressor of glucose, autophagy associated 1
XL0C_016496	FBLN2	1.17	2.63E-03	XM_006261174.1	fibulin 2		XLOC_009514	LOC102561484	-0.98	2.63E-03	XM_006267878.1	potassium-transporting ATPase alpha chain 2-like
XL0C_011442	LOC102562725	1.17	4.73E-03	XM_006259898.1	angiopoietin-2-like		XLOC_001247	TTLL9	-0.98	2.63E-03	XM_006259082.1	tubulin tyrosine ligase-like family, member 9
XL0C_008285	SLC6A9	1.17	6.57E-03	XM_006266560.1	solute carrier family 6 (neurotransmitter transporter, glycine), member 9		XLOC_012533	INSR	-0.97	2.63E-03	XM_006271026.1	insulin receptor
XL0C_004652	LOC102565041	1.17	2.63E-03	XM_006262948.1	apelin receptor A-like		XLOC_017151	DICER1	-0.97	2.63E-03	XM_00627529.1	dicer 1, ribonuclease type III
XL0C_004200	LOC102567125	1.16	2.63E-03	XM_006262206.1	ribonuclease-like		XLOC_017539	CBX6	-0.97	2.63E-03	XM_006267339.1	chromobox homolog 6
XL0C_015578	SRXN1	1.16	8.24E-03	XM_006268948.1	cadherin 19, type 2		XLOC_009916	ELOVL7	-0.97	2.63E-03	XM_006258721.1	ELOVL fatty acid elongase 7, transcript variant X2
XL0C_011428	PTPR21	1.16	2.63E-03	XM_006269867.1	protein tyrosine phosphatase, receptor-type, Z polypeptide 1		XLOC_009931	LRSAM1	-0.97	2.63E-03	XM_006268287.1	leucine rich repeat and sterile alpha motif containing 1
XL0C_013481	LOC102559263	1.16	2.63E-03	XM_006272068.1	hemoglobin subunit beta-like		XLOC_015249	LOC102559649	-0.97	2.63E-03	XM_006273913.1	voltage-dependent T-type calcium channel subunit alpha-1-like
XL0C_015934	S100A10	1.15	2.63E-03	XM_006274615.1	S100 calcium binding protein A10		XLOC_000476	SALL3	-0.97	2.63E-03	XM_006252626.1	spalt-like transcription factor 3
XL0C_003940	TNNI3	1.14	2.63E-03	XM_006261916.1	tropponin I type 3 (cardiac)		XLOC_007787	TRERF1	-0.97	2.63E-03	XM_006266030.1	transcriptional regulating factor 1, transcript variant X4
XL0C_010569	CDH19	1.14	8.24E-03	XM_006268948.1	cadherin 19, type 2		XLOC_003640	PNLNP	-0.97	2.63E-03	XM_006261603.1	leucyl/cysteinyl aminopeptidase
XL0C_013781	LOC102562818	1.14	2.63E-03	XM_006272414.1	sulfhydryl oxidase 1-like		XLOC_005469	TPPP	-0.97	2.63E-03	XM_006263589.1	tubulin polymerization promoting protein
XL0C_006139	S100A13	1.14	2.63E-03	XM_006264341.1	S100 calcium binding protein A13		XLOC_009542	SLC6A15	-0.96	4.73E-03	XM_006267903.1	solute carrier family 6 (neutral amino acid transporter), member 15
XL0C_006327	LOC102570551	1.13	2.63E-03	XM_006264538.1	keratin, type I cytoskeletal 14-like		XLOC_010738	LOC102575314	-0.96	2.63E-03	XM_0062869131.1	steroid 21-hydroxylase-like
XL0C_015446	LOC102570989	1.12	5.67E-03	XM_006274122.1	endothelin-2-like		XLOC_017090	LOC102566880	-0.96	2.63E-03	XM_006275780.1	1-phosphatidylinositol 4,5-bisphosphate phosphodiesterase beta-1-like
XL0C_002077	CRIP1	1.12	2.63E-03	XM_006259954.1	cysteine-rich protein 1 (intestinal)		XLOC_013836	LOC102575090	-0.96	2.63E-03	XM_006272460.1	insulin-like growth factor-binding protein 4-like
XL0C_015418	LOC102563375	1.12	2.63E-03	XM_006274090.1	protein odd-skipped-related 1-like		XLOC_015629	LOC102565159	-0.95	2.63E-03	XM_006274346.1	cadherin-16-like
XL0C_004684	COL1A1	1.10	2.63E-03	XM_006262736.1	collagen, type XI, alpha 1, transcript variant X3		XLOC_011673	LOC102559489	-0.95	2.63E-03	XM_006270130.1	neuropeptide-like protein C4orf48 homolog
XL0C_019573	LOC102561818	1.09	2.63E-03	XM_006278306.1	class I histocompatibility antigen, Gogo-C'0203 alpha chain-like		XLOC_015729	SPATA13	-0.95	2.63E-03	XM_006274424.1	spermatogenesis associated 13
XL0C_011709	LOC102568633	1.09	2.63E-03	XM_006270170.1	probable vesicular acetylcholine transporter-A-like		XLOC_016502	HIPK2	-0.95	2.63E-03	XM_006275178.1	homeodomain interacting protein kinase 2, transcript variant X2
XL0C_011791	LOC102566081	1.09	2.63E-03	XM_006272035.1	beta-galactoside-binding lectin-like		XLOC_017513	SERPINB5	-0.95	2.63E-03	XM_00627612.1	serpin peptidase inhibitor, clade B (ovalbumin), member 5
XL0C_001405	FBLN5	1.08	2.63E-03	XM_006259232.1	fibulin 5, transcript variant X2		XLOC_019530	LOC102569279	-0.95	2.63E-03	XM_006278253.1	kelch-like protein 4-like
XL0C_013332	MDGA1	1.08	2.63E-03	XM_006271918.1	MAM domain containing glycosylphosphatidylinositol anchor 1		XLOC_005540	AGR2	-0.94	2.63E-03	XM_006263670.1	anterior gradient 2
XL0C_004826	RHBDL1	1.08	8.24E-03	XM_006262887.1	rhomboid, veinlet-like 1 (Drosophila)		XLOC_016988	LOC102560798	-0.94	9.85E-03	XM_006275670.1	chromosome unknown open reading frame, human C1orf116
XL0C_013480	LOC102559498	1.08	2.63E-03	XM_006272069.1	hemoglobin subunit beta-like		XLOC_002162	CELSR2	-0.94	2.63E-03	XM_006260057.1</	

XLOC_007754	TNMD	1.05	2.63E-03	XM_006265998.1	tenomodulin	XLOC_007754	TNMD	1.05	2.63E-03	XM_006265998.1	tenomodulin	XLOC_007754	TNMD	1.05	2.63E-03	XM_006265998.1	tenomodulin
XLOC_004793	LOC102559075	1.05	4.73E-03	XM_006262837.1	endonuclease domain-containing 1 protein-like	XLOC_004793	LOC102559075	1.05	4.73E-03	XM_006262837.1	endonuclease domain-containing 1 protein-like	XLOC_004793	LOC102559075	1.05	4.73E-03	XM_006262837.1	endonuclease domain-containing 1 protein-like
XLOC_000489	A2M	1.05	2.63E-03	XM_006258274.1	alpha-2-macroglobulin	XLOC_000489	A2M	1.05	2.63E-03	XM_006258274.1	alpha-2-macroglobulin	XLOC_000489	A2M	1.05	2.63E-03	XM_006258274.1	alpha-2-macroglobulin
XLOC_017186	CRABP2	1.05	2.63E-03	XM_006275867.1	cellular retinoic acid binding protein 2	XLOC_017186	CRABP2	1.05	2.63E-03	XM_006275867.1	cellular retinoic acid binding protein 2	XLOC_017186	CRABP2	1.05	2.63E-03	XM_006275867.1	cellular retinoic acid binding protein 2
XLOC_017270	LOC102573067	1.05	2.63E-03	XM_006275961.1	retinol-binding protein-like transcript variant X2	XLOC_017270	LOC102573067	1.05	2.63E-03	XM_006275961.1	retinol-binding protein-like transcript variant X2	XLOC_017270	LOC102573067	1.05	2.63E-03	XM_006275961.1	retinol-binding protein-like transcript variant X2
XLOC_010023	TGFBI	1.04	2.63E-03	XM_006283369.1	transforming growth factor, beta 3	XLOC_010023	TGFBI	1.04	2.63E-03	XM_006283369.1	transforming growth factor, beta 3	XLOC_010023	TGFBI	1.04	2.63E-03	XM_006283369.1	transforming growth factor, beta 3
XLOC_018956	EBF3	1.04	2.63E-03	XM_006277689.1	early B-cell factor 3, transcript variant X1	XLOC_018956	EBF3	1.04	2.63E-03	XM_006277689.1	early B-cell factor 3, transcript variant X1	XLOC_018956	EBF3	1.04	2.63E-03	XM_006277689.1	early B-cell factor 3, transcript variant X1
XLOC_004764	LOC102577367	1.03	2.63E-03	XM_006262832.1	vitamin K epoxide reductase complex subunit 1-like protein 1-like	XLOC_004764	LOC102577367	1.03	2.63E-03	XM_006262832.1	vitamin K epoxide reductase complex subunit 1-like protein 1-like	XLOC_004764	LOC102577367	1.03	2.63E-03	XM_006262832.1	vitamin K epoxide reductase complex subunit 1-like protein 1-like
XLOC_010530	GLDC	1.02	8.24E-03	XM_006268906.1	lysine/arginine N-acetyltransferase 2	XLOC_010530	GLDC	1.02	8.24E-03	XM_006268906.1	lysine/arginine N-acetyltransferase 2	XLOC_010530	GLDC	1.02	8.24E-03	XM_006268906.1	lysine/arginine N-acetyltransferase 2
XLOC_012479	TMFS2	1.02	2.63E-03	XM_006271031.1	transmembrane 6 superfamily member 2	XLOC_012479	TMFS2	1.02	2.63E-03	XM_006271031.1	transmembrane 6 superfamily member 2	XLOC_012479	TMFS2	1.02	2.63E-03	XM_006271031.1	transmembrane 6 superfamily member 2
XLOC_006593	LOC102560544	1.01	2.63E-03	XM_006264808.1	elongation factor 1-alpha-like	XLOC_006593	LOC102560544	1.01	2.63E-03	XM_006264808.1	elongation factor 1-alpha-like	XLOC_006593	LOC102560544	1.01	2.63E-03	XM_006264808.1	elongation factor 1-alpha-like
XLOC_000656	COL1A2	1.00	4.73E-03	XM_006258452.1	collagen, type I, alpha 2	XLOC_000656	COL1A2	1.00	4.73E-03	XM_006258452.1	collagen, type I, alpha 2	XLOC_000656	COL1A2	1.00	4.73E-03	XM_006258452.1	collagen, type I, alpha 2
XLOC_020042	CNN3	0.99	2.63E-03	XM_006278766.1	cyclin D3, transcript variant X3	XLOC_020042	CNN3	0.99	2.63E-03	XM_006278766.1	cyclin D3, transcript variant X3	XLOC_020042	CNN3	0.99	2.63E-03	XM_006278766.1	cyclin D3, transcript variant X3
XLOC_006355	PTRF	0.99	2.63E-03	XM_006264575.1	polymerase I and transcript release factor	XLOC_006355	PTRF	0.99	2.63E-03	XM_006264575.1	polymerase I and transcript release factor	XLOC_006355	PTRF	0.99	2.63E-03	XM_006264575.1	polymerase I and transcript release factor
XLOC_003288	PGM5	0.98	2.63E-03	XM_006281237.1	phosphoglumicotase 5	XLOC_003288	PGM5	0.98	2.63E-03	XM_006281237.1	phosphoglumicotase 5	XLOC_003288	PGM5	0.98	2.63E-03	XM_006281237.1	phosphoglumicotase 5
XLOC_010742	LOC102576539	0.98	2.63E-03	XM_006269136.1	zona pellucida sperm-binding protein 3-like	XLOC_010742	LOC102576539	0.98	2.63E-03	XM_006269136.1	zona pellucida sperm-binding protein 3-like	XLOC_010742	LOC102576539	0.98	2.63E-03	XM_006269136.1	zona pellucida sperm-binding protein 3-like
XLOC_003490	F8	0.98	2.63E-03	XM_006261445.1	coagulation factor VIII, procoagulant component	XLOC_003490	F8	0.98	2.63E-03	XM_006261445.1	coagulation factor VIII, procoagulant component	XLOC_003490	F8	0.98	2.63E-03	XM_006261445.1	coagulation factor VIII, procoagulant component
XLOC_015712	CLEC11A	0.97	2.63E-03	XM_006274395.1	C-type lectin domain family 11, member A	XLOC_015712	CLEC11A	0.97	2.63E-03	XM_006274395.1	C-type lectin domain family 11, member A	XLOC_015712	CLEC11A	0.97	2.63E-03	XM_006274395.1	C-type lectin domain family 11, member A
XLOC_002638	SYNO	0.97	2.63E-03	XM_006260565.1	synaptosomal-associated protein 25kDa	XLOC_002638	SYNO	0.97	2.63E-03	XM_006260565.1	synaptosomal-associated protein 25kDa	XLOC_002638	SYNO	0.97	2.63E-03	XM_006260565.1	synaptosomal-associated protein 25kDa
XLOC_015939	TDRKH	0.96	2.63E-03	XM_006274616.1	tudor and KH domain containing	XLOC_015939	TDRKH	0.96	2.63E-03	XM_006274616.1	tudor and KH domain containing	XLOC_015939	TDRKH	0.96	2.63E-03	XM_006274616.1	tudor and KH domain containing
XLOC_007678	LOC102561011	0.96	2.63E-03	XM_006265924.1	chromosome unknown open reading frame, human C2orf40	XLOC_007678	LOC102561011	0.96	2.63E-03	XM_006265924.1	chromosome unknown open reading frame, human C2orf40	XLOC_007678	LOC102561011	0.96	2.63E-03	XM_006265924.1	chromosome unknown open reading frame, human C2orf40
XLOC_003332	ALAS2	0.96	2.63E-03	XM_006281290.1	aminolevulinic acid delta- synthase 2	XLOC_003332	ALAS2	0.96	2.63E-03	XM_006281290.1	aminolevulinic acid delta- synthase 2	XLOC_003332	ALAS2	0.96	2.63E-03	XM_006281290.1	aminolevulinic acid delta- synthase 2
XLOC_004236	COL12A1	0.95	2.63E-03	XM_006262249.1	collagen, type XII, alpha 1	XLOC_004236	COL12A1	0.95	2.63E-03	XM_006262249.1	collagen, type XII, alpha 1	XLOC_004236	COL12A1	0.95	2.63E-03	XM_006262249.1	collagen, type XII, alpha 1
XLOC_014113	LOC102566241	0.95	2.63E-03	XM_006272754.1	beta-microseminoprotein-like	XLOC_014113	LOC102566241	0.95	2.63E-03	XM_006272754.1	beta-microseminoprotein-like	XLOC_014113	LOC102566241	0.95	2.63E-03	XM_006272754.1	beta-microseminoprotein-like
XLOC_003868	LOC102559155	0.95	6.57E-03	XM_006261841.1	hemoglobin subunit pi-like	XLOC_003868	LOC102559155	0.95	6.57E-03	XM_006261841.1	hemoglobin subunit pi-like	XLOC_003868	LOC102559155	0.95	6.57E-03	XM_006261841.1	hemoglobin subunit pi-like
XLOC_007647	LOC102572713	0.93	2.63E-03	XM_006265890.1	prolactin-releasing peptide receptor-like	XLOC_007647	LOC102572713	0.93	2.63E-03	XM_006265890.1	prolactin-releasing peptide receptor-like	XLOC_007647	LOC102572713	0.93	2.63E-03	XM_006265890.1	prolactin-releasing peptide receptor-like
XLOC_011871	HTRA3	0.91	2.63E-03	XM_006270329.1	HTA serine peptidase 3	XLOC_011871	HTRA3	0.91	2.63E-03	XM_006270329.1	HTA serine peptidase 3	XLOC_011871	HTRA3	0.91	2.63E-03	XM_006270329.1	HTA serine peptidase 3
XLOC_008932	ANGPTL1	0.91	2.63E-03	XM_006267260.1	angiopoietin-like 1, transcript variant X2	XLOC_008932	ANGPTL1	0.91	2.63E-03	XM_006267260.1	angiopoietin-like 1, transcript variant X2	XLOC_008932	ANGPTL1	0.91	2.63E-03	XM_006267260.1	angiopoietin-like 1, transcript variant X2
XLOC_017840	MYBL2	0.91	2.63E-03	XM_006276553.1	v-myb avian myeloblastosis viral oncogene homolog-like 2	XLOC_017840	MYBL2	0.91	2.63E-03	XM_006276553.1	v-myb avian myeloblastosis viral oncogene homolog-like 2	XLOC_017840	MYBL2	0.91	2.63E-03	XM_006276553.1	v-myb avian myeloblastosis viral oncogene homolog-like 2
XLOC_004486	PDGFRL	0.90	2.63E-03	XM_006262532.1	platelet-derived growth factor receptor-like	XLOC_004486	PDGFRL	0.90	2.63E-03	XM_006262532.1	platelet-derived growth factor receptor-like	XLOC_004486	PDGFRL	0.90	2.63E-03	XM_006262532.1	platelet-derived growth factor receptor-like
XLOC_003318	LOC102577358	0.90	2.63E-03	XM_006261267.1	duplex and mab-3 related transcription factor 3-like	XLOC_003318	LOC102577358	0.90	2.63E-03	XM_006261267.1	duplex and mab-3 related transcription factor 3-like	XLOC_003318	LOC102577358	0.90	2.63E-03	XM_006261267.1	duplex and mab-3 related transcription factor 3-like
XLOC_001140	SOX10	0.89	2.63E-03	XM_006258551.1	sex determining region Y-box 10	XLOC_001140	SOX10	0.89	2.63E-03	XM_006258551.1	sex determining region Y-box 10	XLOC_001140	SOX10	0.89	2.63E-03	XM_006258551.1	sex determining region Y-box 10
XLOC_012425	TBX1	0.89	2.63E-03	XM_006270926.1	T-box 1	XLOC_012425	TBX1	0.89	2.63E-03	XM_006270926.1	T-box 1	XLOC_012425	TBX1	0.89	2.63E-03	XM_006270926.1	T-box 1
XLOC_016570	LMF2	0.89	2.63E-03	XM_006275259.1	lipase maturation factor 2	XLOC_016570	LMF2	0.89	2.63E-03	XM_006275259.1	lipase maturation factor 2	XLOC_016570	LMF2	0.89	2.63E-03	XM_006275259.1	lipase maturation factor 2
XLOC_003006	LOC102574581	0.89	2.63E-03	XM_006260931.1	myosin-binding protein C, cardiac-type-like	XLOC_003006	LOC102574581	0.89	2.63E-03	XM_006260931.1	myosin-binding protein C, cardiac-type-like	XLOC_003006	LOC102574581	0.89	2.63E-03	XM_006260931.1	myosin-binding protein C, cardiac-type-like
XLOC_001013	LTPB2	0.87	2.63E-03	XM_006268352.1	latent transforming growth factor beta binding protein 2	XLOC_001013	LTPB2	0.87	2.63E-03	XM_006268352.1	latent transforming growth factor beta binding protein 2	XLOC_001013	LTPB2	0.87	2.63E-03	XM_006268352.1	latent transforming growth factor beta binding protein 2
XLOC_002817	OLFML3	0.87	2.63E-03	XM_006260738.1	olfactomedin-like 3	XLOC_002817	OLFML3	0.87	2.63E-03	XM_006260738.1	olfactomedin-like 3	XLOC_002817	OLFML3	0.87	2.63E-03	XM_006260738.1	olfactomedin-like 3
XLOC_013828	LOC102573123	0.86	2.63E-03	XM_006274551.1	transcription factor SOX9-like	XLOC_013828	LOC102573123	0.86	2.63E-03	XM_006274551.1	transcription factor SOX9-like	XLOC_013828	LOC102573123	0.86	2.63E-03	XM_006274551.1	transcription factor SOX9-like
XLOC_015688	CPLX2	0.86	2.63E-03	XM_006274560.1	complexin 2	XLOC_015688	CPLX2	0.86	2.63E-03	XM_006274560.1	complexin 2	XLOC_015688	CPLX2	0.86	2.63E-03	XM_006274560.1	complexin 2
XLOC_003305	IGSF8	0.86	2.63E-03	XM_006261486.1	immunoglobulin superfamily, member 8	XLOC_003305	IGSF8	0.86	2.63E-03	XM_006261486.1	immunoglobulin superfamily, member 8	XLOC_003305	IGSF8	0.86	2.63E-03	XM_006261486.1	immunoglobulin superfamily, member 8
XLOC_001027	GATA6	0.84	2.63E-03	XM_006268397.1	GATA binding protein 6	XLOC_001027	GATA6	0.84	2.63E-03	XM_006268397.1	GATA binding protein 6	XLOC_001027	GATA6	0.84	2.63E-03	XM_006268397.1	GATA binding protein 6
XLOC_001463	LOC102574572	0.84	2.63E-03	XM_006259299.1	somatostatin-2-like	XLOC_001463	LOC102574572	0.84	2.63E-03	XM_006259299.1	somatostatin-2-like	XLOC_001463	LOC102574572	0.84	2.63E-03	XM_006259299.1	somatostatin-2-like
XLOC_007534	CAV1	0.84	2.63E-03	XM_006265774.1	caveolin 1, caveolae protein, 22kDa	XLOC_007534	CAV1	0.84	2.63E-03	XM_006265774.1	caveolin 1, caveolae protein, 22kDa	XLOC_007534	CAV1	0.84	2.63E-03	XM_006265774.1	caveolin 1, caveolae protein, 22kDa
XLOC_006793	LOC102570785	0.84	2.63E-03	XM_006265005.1	sorbin-B-like	XLOC_006793	LOC102570785	0.84	2.63E-03	XM_006265005.1	sorbin-B-like	XLOC_006793	LOC102570785	0.84	2.63E-03	XM_006265005.1	sorbin-B-like
XLOC_000370	C1QTNF5	0.84	2.63E-03	XM_006258146.1	C1q and tumor necrosis factor related protein 5	XLOC_000370	C1QTNF5	0.84	2.63E-03	XM_006258146.1	C1q and tumor necrosis factor related protein 5	XLOC_000370	C1QTNF5	0.84	2.63E-03	XM_006258146.1	C1q and tumor necrosis factor related protein 5
XLOC_005010	MKX	0.83	2.63E-03	XM_006263077.1	mohawk homeobox	XLOC_005010	MKX	0.83	2.63E-03	XM_006263077							

XLOC_018684	LOC102574402	0.77	8.24E-03	XM_006277413.1	GTP-binding protein Di-Ras2-like	XLOC_017842	SGK2	-0.79	2.63E-03	XM_006276556.1	serum/glucocorticoid regulated kinase 2, transcript variant X2
XLOC_000591	DMTN	0.76	2.63E-03	XM_006258386.1	desmatin actin binding protein, transcript variant X1	XLOC_017932	UNC80	-0.79	6.57E-03	XM_006276656.1	unc-80 homolog (C. elegans)
XLOC_016571	NCAPH2	0.75	8.24E-03	XM_006275258.1	non-SMC condensin II complex, subunit H2	XLOC_011419	GPRIN3	-0.79	8.24E-03	XM_006269857.1	GPRIN family member 3
XLOC_018048	LOC102568806	0.75	2.63E-03	XM_006276754.1	gamma-secretase subunit PEN-2-like	XLOC_000685	RBM47	-0.79	2.63E-03	XM_006258481.1	RNA binding motif protein 47
XLOC_006673	LOC102561772	0.75	2.63E-03	XM_006264892.1	probable beta-D-xylidase 5-like	XLOC_005087	LDB3	-0.79	4.73E-03	XM_006263158.1	LIM domain binding 3, transcript variant X2
XLOC_000544	FILIP1L	0.74	2.63E-03	XM_006258334.1	filamin A interacting protein 1-like, transcript variant X3	XLOC_007693	FZD5	-0.78	2.63E-03	XM_006265441.1	frizzled family receptor 5
XLOC_009126	LOC102560553	0.74	2.63E-03	XM_006267475.1	protein S100-A11-like	XLOC_005325	CDHRS	-0.78	2.63E-03	XM_006263422.1	cadherin-related family member 5
XLOC_009321	TIMELESS	0.74	2.63E-03	XM_006267655.1	cytochrome b-245 light chain-like	XLOC_018724	LOC102564013	-0.78	2.63E-03	XM_006277452.1	regucalcin-like
XLOC_009174	THBD	0.73	2.63E-03	XM_006267522.1	thrombomodulin	XLOC_004552	LOC102560535	-0.78	2.63E-03	XM_006262600.1	neuronal membrane glycoprotein M6-a-like
XLOC_000369	MCM4	0.72	2.63E-03	XM_006258155.1	melanoma cell adhesion molecule	XLOC_006944	HAAO	-0.77	2.63E-03	XM_006261601.1	3-hydroxyanthranilate 3,4-dioxygenase
XLOC_005962	XXYL1	0.72	2.63E-03	XM_006264142.1	xyloside xylosyltransferase 1	XLOC_003551	LOC102576907	-0.77	2.63E-03	XM_006261508.1	sulfotransferase 1C1-like
XLOC_003072	TP53	0.72	2.63E-03	XM_006261004.1	tumor protein p53, transcript variant X2	XLOC_019431	XDHD	-0.77	2.63E-03	XM_006278147.1	xanthine dehydrogenase
XLOC_014037	DES	0.72	2.63E-03	XM_006272681.1	desmin	XLOC_016549	HNF4A	-0.77	2.63E-03	XM_006275220.1	hepatocyte nuclear factor 4, alpha
XLOC_017339	LTPB3	0.72	2.63E-03	XM_006276029.1	latent transforming growth factor beta binding protein 3	XLOC_013845	GRTP1	-0.77	2.63E-03	XM_006272474.1	growth hormone regulated TBC protein 1
XLOC_008343	MYL9	0.72	2.63E-03	XM_006266633.1	myosin, light chain 9, regulatory	XLOC_016909	ARNT2	-0.77	2.63E-03	XM_006275591.1	aryl-hydrocarbon receptor nuclear translocator 2
XLOC_010818	STGALNAC2	0.71	2.63E-03	XM_006269266.1	ST6 (alpha-N-acetyl-neuraminyl-2,3-beta-galactosyl-1,3)-N-acetylgalactosaminide	XLOC_003018	PROSER2	-0.76	2.63E-03	XM_006269045.1	proline and serine-rich protein 2
XLOC_014444	CPE	0.71	2.63E-03	XM_006273085.1	carboxypeptidase E	XLOC_011994	EHHADH	-0.76	2.63E-03	XM_006270453.1	enoyl-CoA hydratase 3/hydroxyacyl CoA dehydrogenase
XLOC_014546	LOC102576325	0.71	8.24E-03	XM_006273179.1	serine/threonine-protein kinase PAK 1-like	XLOC_011067	GNE	-0.76	2.63E-03	XM_006269485.1	glucosamine (UDP-N-acetyl)-2-epimerase/N-acetylmannosamine kinase
XLOC_004103	AQP1	0.71	2.63E-03	XM_006262096.1	aquaporin 1	XLOC_005527	LOC102561001	-0.76	2.63E-03	XM_006263661.1	acyl-coenzyme A synthetase ACSM4, mitochondrial-like
XLOC_015397	CREBL3L1	0.71	2.63E-03	XM_006274069.1	cAMP responsive element binding protein 3-like 1	XLOC_015057	LOC102568110	-0.75	2.63E-03	XM_006273705.1	acyl-coenzyme A synthetase ACSM4, mitochondrial-like
XLOC_003305	RASL1B	0.71	2.63E-03	XM_006261252.1	RAS-like, family 11, member B	XLOC_011839	MAOB	-0.75	2.63E-03	XM_006270299.1	monoamine oxidase B
XLOC_003047	LOC102566120	0.70	9.85E-03	XM_006260983.1	protein FAM49A-like	XLOC_000498	WNK1	-0.75	2.63E-03	XM_006252924.1	WNK lysing deficient protein kinase 1
XLOC_014047	TUBA4A	0.70	2.63E-03	XM_006272667.1	tubulin, alpha 4a	XLOC_015444	TRPM6	-0.75	2.63E-03	XM_006274120.1	transient receptor potential cation channel, subfamily M, member 6
XLOC_000427	LOC102570217	0.69	2.63E-03	XM_006258214.1	von Willebrand factor A domain-containing protein 7-like	XLOC_001577	LOC102564479	-0.75	2.63E-03	XM_006259426.1	uncharacterized LOC102564479
XLOC_003243	PRMT5	0.69	2.63E-03	XM_006261178.1	protein arginine methyltransferase 5, transcript variant X2	XLOC_007338	BCAR3	-0.75	2.63E-03	XM_006265558.1	breast cancer anti-estrogen resistance 3
XLOC_019982	NMRK2	0.69	9.85E-03	XM_006278662.1	nicotinamide riboside kinase 2	XLOC_017214	LOC102579798	-0.75	6.57E-03	XM_006275987.1	myeloid protein 1-like
XLOC_015643	CEBPA	0.69	4.73E-03	XM_006274301.1	CCAAT/enhancer binding protein (C/EBP), alpha	XLOC_008876	LOC102574122	-0.75	2.63E-03	XM_006267205.1	cholesterol 24-hydroxylase-like
XLOC_014701	COL2A1	0.68	2.63E-03	XM_006273339.1	collagen, type II, alpha 1, transcript variant X1	XLOC_001026	NFAT5	-0.74	6.57E-03	XM_006258222.1	nuclear factor of activated T-cells 5, tonicity-responsive, transcript variant X1
XLOC_014143	AUP1	0.67	2.63E-03	XM_006272782.1	ancient ubiquitous protein 1	XLOC_005149	LOC10258703J	-0.74	2.63E-03	XM_006274341.1	XM_00626
XLOC_005253	COL14A1	0.67	2.63E-03	XM_006263354.1	collagen, type XIV, alpha 1	XLOC_006854	SPOCK2	-0.73	2.63E-03	XM_006265063.1	sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 2
XLOC_013953	TAGLN2	0.67	2.63E-03	XM_006272585.1	transgelin 2	XLOC_012354	CPEB4	-0.73	2.63E-03	XM_006270850.1	cytoplasmic polyadenylation element binding protein 4
XLOC_003738	MCM3	0.67	2.63E-03	XM_006261703.1	minichromosome maintenance complex component 3	XLOC_012263	RASA4	-0.73	2.63E-03	XM_006270746.1	RAS p21 protein activator 4
XLOC_007162	FOXM1	0.67	2.63E-03	XM_006265401.1	forkhead box M1	XLOC_014354	KCNJ16	-0.73	2.63E-03	XM_006273002.1	potassium inwardly-rectifying channel, subfamily J, member 16
XLOC_006758	POL2A	0.66	2.63E-03	XM_006264969.1	polymerase (DNA directed), alpha 2, accessory subunit	XLOC_015775	APOA2	-0.73	2.63E-03	XM_006274463.1	apolipoprotein A-II
XLOC_000664	LM2O	0.66	2.63E-03	XM_006258461.1	LIM domain only 2 (rhombotin-like 1)	XLOC_009481	LOC102571343	-0.73	2.63E-03	XM_006265822.1	guanidinoacetate N-methyltransferase A-like
XLOC_010986	TUBB3	0.66	6.57E-03	XM_006269387.1	tubulin, beta 3 class III	XLOC_011181	CTH	-0.72	2.63E-03	XM_006269606.1	cystathione lyase (cystathione gamma-lyase)
XLOC_014403	PBK	0.66	4.73E-03	XM_006273043.1	PDZ binding kinase	XLOC_012944	LOC102558789	-0.72	2.63E-03	XM_006271512.1	bifunctional epoxide hydrolase 2-like
XLOC_012175	TM2P	0.66	2.63E-03	XM_006270645.1	TIMP metallopeptidase inhibitor 2	XLOC_017872	PCK1	-0.72	6.57E-03	XM_006276591.1	phosphoenolpyruvate carboxykinase 1 (soluble)
XLOC_001582	BOC	0.66	2.63E-03	XM_006259427.1	BOC cell adhesion associated, oncogene regulated	XLOC_010094	LOC102567929	-0.71	2.63E-03	XM_006268475.1	sulfotransferase 1 family member D1-like
XLOC_003052	COL6A2	0.65	2.63E-03	XM_006260988.1	collagen, type VI, alpha 2, transcript variant X1	XLOC_014010	KIF21A	-0.71	2.63E-03	XM_006272649.1	kinesin family member 21A
XLOC_001524	LOC102571069	0.65	2.63E-03	XM_006259370.1	nicotinamide riboside kinase 2-like	XLOC_006973	LOC10257796	-0.71	4.73E-03	XM_006265187.1	receptor-type tyrosine-protein phosphatase U-like
XLOC_004033	SLT3	0.64	6.57E-03	XM_006262024.1	slit homolog 3 (Drosophila)	XLOC_018531	LOC102573613	-0.71	4.73E-03	XM_006277247.1	nicotinamide N-methyltransferase-like
XLOC_014690	NCKIPSD	0.64	2.63E-03	XM_006273332.1	NCK interacting protein with SH3 domain, transcript variant X1	XLOC_010506	LOC102564848	-0.70	2.63E-03	XM_006273691.1	acyl-coenzyme A synthetase ACSM3, mitochondrial-like
XLOC_014654	ADAMTS4	0.63	6.57E-03	XM_006273298.1	ADAMTS-like 4	XLOC_012377	CERKL	-0.70	9.85E-03	XM_006270876.1	ceramide kinase-like
XLOC_015530	SPAG5	0.63	6.57E-03	XM_006274223.1	sperm associated antigen 5	XLOC_016024	INADL	-0.70	2.63E-03	XM_006274712.1	InAD-like (Drosophila)
XLOC_019475	LOC102576659	0.63	8.24E-03	XM_006278203.1	HAUS augmin-like complex subunit 7-like	XLOC_015218	GRIP2	-0.70	6.57E-03	XM_006273884.1	glutamate receptor interacting protein 2
XLOC_018126	H1C1	0.63	8.24E-03	XM_006276838.1	hypermethylated in cancer 1	XLOC_015630	LOC102565395	-0.70	4.73E-03	XM_006274437.1	cadherin-16-like
XLOC_018367	SRPX	0.63	2.63E-03	XM_006270689.1	sushi-repeat containing protein, X-linked	XLOC_018107	ABL2	-0.70	8.24E-03	XM_006276829.1	c-abl oncogene 2, non-receptor tyrosine kinase
XLOC_018917	EMP3	0.63	8.24E-03	XM_006277629.1	epithelial membrane protein 3	XLOC_019031	LOC102563225	-0.69	2.63E-03	XM_006277765.1	beta-1,3-galactosyl-O-glycosyl-glycoprotein beta-1,6-N-acetylgalactosaminyltransferase-like
XLOC_016460	LOC102570282	0.62	2.63E-03	XM_006275148.1	semaphorin-3D-like	XLOC_009612	LOC102570493	-0.69	2.63E-03	XM_006267988.1	microtubule-actin cross-linking factor 1-like
XLOC_006023	CXPX1	0.61	4.73E-03	XM_006264207.1	carboxypeptidase X (M14 family), member 1	XLOC_018760	ABCD5	-0.69	8.24E-03	XM_006277487.1	ATP-binding cassette, sub-family D (ALD), member 3
XLOC_011864	IP04	0.60	8.24E-03	XM_006259737.1	importin 4	XLOC_008577	KMT2A	-0.69	2.63E-03	XM_006266862.1	lysine (K)-specific methyltransferase 2A
XLOC_018798	CYR61	0.60	2.63E-03	XM_006277505.1	cysteine-rich, angiogenic inducer, 61	XLOC_000217	ARHGAP32	-0.69	2.63E-03	XM_006257965.1	Rho GTPase activating protein 32
XLOC_011804	ERF	0.60	4.73E-03	XM_006270269.1	ets2 repressor factor	XLOC_017566	TSHZ1	-0.69	2.63E-03	XM_00627266.1	teashirt zinc finger homeobox 1
XLOC_007378	LOC102561163	0.60	2.63E-03	XM_006265598.1	tubulin beta-4B chain-like	XLOC_007512	LOC102559932	-0.69	2.63E-03	XM_006265755.1	collagen alpha-1(XXVI) chain-like
XLOC_005989	TFRC	0.60	2.63E-03	XM_006264159.1	transferrin receptor	XLOC_007888	STAR	-0.69	4.73E-03	XM_006266133.1	steroidogenic acute regulatory protein
XLOC_015551	UHRF1	0.60	6.57E-03	XM_006274236.1	ubiquitin-like with PHD and ring finger domains 1	XLOC_011621	LOC102565143	-0.68	2.63E-03	XM_006270070.1	RE1-silencing transcription factor A-like
XLOC_018290	LOC102571606	0.59	9.85E-03	XM_006277002.1	derlin-2-like	XLOC_011287	ATP6V0D2	-0.68	2.63E-03	XM_006269712.1	ATPase, H <sup>+</sup> transporting, lysosomal 38kDa, V0 subunit d2
XLOC_002515	NAGLU	0.59	2.63E-03	XM_006260415.1	N-acetylglucosaminidase, alpha	XLOC_018203	CLCNKB	-0.67	2.63E-03	XM_006276925.1	chloride channel, voltage-sensitive K <sup>b</sup>
XLOC_014786	ILK	0.59	2.63E-03	XM_006273435.1	integrin-linked kinase	XLOC_013703	RTTN	-0.67	2.63E-03	XM_006272311.1	rotatin
XLOC_005068	SF3B4	0.58	6.57E-03	XM_006263136.1	splicing factor 3b, subunit 4, 49kDa	XLOC_003907	SLC12A1	-0.67	2.63E-03	XM_006261880.1	solute carrier family 12 (sodium/potassium/chloride transporter), member 1, transcript variant X1
XLOC_018274	LOC102570282	0.58	2.63E-03	XM_006263136.1	splicing factor 3b, subunit 4, 49kDa	XLOC_018884	KHL3	-0.67	8.24E-03	XM_006277619.1	kelch-like family member 3
XLOC_004741	GALEN5	0.58	2.63E-03	XM_006277505.1	gamma-secretase subunit PEN-2-like	XLOC_004741	GALEN5	-0.67	8.24E-03	XM_006262802.1	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylglucosaminyltransferase 5 (GalNAc-
XLOC_002717	TMEM52B	0.58	2.63E-03	XM_006276528.1	transmembrane protein 52B	XLOC_002717	TMEM52B	-0.66	6.57E-03	XM_006260421.1	transmembrane protein 52B
XLOC_010294	ACSS3	0.58	2.63E-03	XM_006268678.1	acyl-CoA synthetase short-chain family member 3	XLOC_019303	LOC102571763	-0.66	2.63E-03	XM_006278035.1	transforming protein p54/c-ets-1-like
XLOC_005061	NDNF	0.58	2.63E-03	XM_006263128.1	neuron-derived neurotrophic factor, transcript variant X2	XLOC_005061	NDNF	-0.66	2.63E-03	XM_006263128.1	neuron-derived neurotrophic factor, transcript variant X2

XLOC_012336	SPTB	0.57	2.63E-03	XM_006270827.1	spectrin, beta, erythrocytic, transcript variant X1	XLOC_003833	MYO7B	-0.66	2.63E-03	XM_006261792.1	myosin VIIb
XLOC_010044	PLK1	0.57	8.24E-03	XM_006268449.1	polo-like kinase 1	XLOC_017810	NDRG1	-0.66	2.63E-03	XM_006276526.1	N-myc downstream regulated 1
XLOC_010436	MCM4	0.57	8.24E-03	XM_006268816.1	minichromosome maintenance complex component 4	XLOC_018228	LOC102559361	-0.66	4.73E-03	XM_006276953.1	endothelin B receptor-like
XLOC_001671	RPRM1	0.55	9.85E-03	XM_006259539.1	ribonucleotide reductase M1	XLOC_002569	CBS	-0.66	4.73E-03	XM_006260475.1	cystathione-beta-synthase, transcript variant X3
XLOC_013672	FBL	0.55	9.85E-03	XM_006272275.1	fibrillarin	XLOC_010069	KD1	-0.65	4.73E-03	XM_006268435.1	polycystic kidney disease 1 (autosomal dominant)
XLOC_003241	LOC102558609	0.55	9.85E-03	XM_006261193.1	matrix metalloproteinase-14-like	XLOC_008408	CALB1	-0.65	2.63E-03	XM_006266690.1	calbindin 1, 28kDa
XLOC_004287	NF1X	0.54	9.85E-03	XM_006262319.1	nuclear factor I/X (CCAAT-binding transcription factor), transcript variant X3	XLOC_009610	LOC102564364	-0.65	2.63E-03	XM_006267961.1	neurofilament, light polypeptide
XLOC_017183	HDGF	0.54	8.24E-03	XM_006275864.1	hepatoma-derived growth factor	XLOC_018099	NEFL	-0.65	6.57E-03	XM_006276810.1	tetraspanin 9, transcript variant X1
						XLOC_007156	TSPAN9	-0.65	4.73E-03	XM_006265390.1	prostaglandin reductase 1-like
						XLOC_007138	LOC102573310	-0.65	2.63E-03	XM_006259209.1	cytochrome P450 3A21-like
						XLOC_007714	LOC102570482	-0.64	6.57E-03	XM_006265963.1	cubilin (intrinsic factor-cobalamin receptor)
						XLOC_007617	CUBN	-0.64	8.24E-03	XM_006265866.1	DIP2 disco-interacting protein 2 homolog B (Drosophila)
						XLOC_006400	DIP2B	-0.64	2.63E-03	XM_006264640.1	ferredoxin reductase
						XLOC_004405	FDXR	-0.63	2.63E-03	XM_006262447.1	solute carrier family 37, member 3
						XLOC_008853	SLC37A3	-0.63	6.57E-03	XM_006268207.1	cysteine conjugate-beta lyase 2
						XLOC_017667	CCLB2	-0.63	2.63E-03	XM_006276369.2	Niemann-Pick disease, type C1
						XLOC_018826	NPC1	-0.63	4.73E-03	XM_006277553.1	aldehyde dehydrogenase 1 family, member A3, transcript variant X2
						XLOC_005431	ALDH1A3	-0.62	2.63E-03	XM_006263543.1	nicotinamide nucleotide transhydrogenase
						XLOC_010553	NNT	-0.62	2.63E-03	XM_006268917.1	leucine rich repeat containing 8 family, member D
						XLOC_007455	LRRC8D	-0.62	2.63E-03	XM_006265697.1	myotubularin related protein 12
						XLOC_009422	MTMR12	-0.62	8.24E-03	XM_006267762.1	empty spiracles homeobox 1
						XLOC_003353	EMX1	-0.62	2.63E-03	XM_006261299.1	cadherin, EGF LAG seven-pass G-type receptor 1
						XLOC_006464	CELSR1	-0.62	6.57E-03	XM_006264688.1	inter-alpha-trypsin inhibitor heavy chain family, member 5
						XLOC_006522	ITIH5	-0.61	2.63E-03	XM_006264736.1	Rho guanine nucleotide exchange factor (GEF) 28
						XLOC_009958	ARHGEF28	-0.61	4.73E-03	XM_006264684.1	glutathione S-transferase zeta 1, transcript variant X2
						XLOC_005632	GSTZ1	-0.61	4.73E-03	XM_006263770.1	selenide binding protein 1
						XLOC_016720	SELENBP1	-0.61	4.73E-03	XM_006275408.1	eukaryotic translation initiation factor 3 subunit A-like
						XLOC_008886	LOC102577065	-0.61	4.73E-03	XM_006267219.1	alanine-glyoxylate aminotransferase 2
						XLOC_011596	AGXT2	-0.61	8.24E-03	XM_006270044.1	glycosyphosphatidylinositol specific phospholipase D1
						XLOC_002618	GPLD1	-0.61	8.24E-03	XM_006260536.1	succinyl-CoA-3-ketobid coenzyme A transferase 1, mitochondrial-like
						XLOC_016042	LOC102564628	-0.61	5.75E-03	XM_006274734.1	carbonic anhydrase 2-like
						XLOC_000021	LOC102559447	-0.60	2.63E-03	XM_006257749.1	alpha-methylacyl-CoA racemase
						XLOC_009417	AMACR	-0.60	2.63E-03	XM_006267758.1	Rho guanine nucleotide exchange factor (GEF) 12
						XLOC_001823	ARHGEF12	-0.60	4.73E-03	XM_006259693.1	KIAA1239 ortholog
						XLOC_003428	KIAA1239	-0.60	8.24E-03	XM_006261374.1	interferon gamma receptor 1-like
						XLOC_011011	LOC102566228	-0.60	2.63E-03	XM_006269424.1	thiosulfate sulfurtransferase (rhodanese)
						XLOC_011785	TST	-0.60	2.63E-03	XM_006270248.1	pseudopodium-enriched atypical kinase 1, transcript variant X1
						XLOC_013776	PEAK1	-0.60	9.85E-03	XM_006272401.1	espin-like
						XLOC_017425	ESPNL	-0.60	4.73E-03	XM_006276123.1	fucokinase
						XLOC_014131	FUK	-0.60	8.24E-03	XM_006272777.1	urocanate hydratase 1
						XLOC_014459	UROC1	-0.60	4.73E-03	XM_006273094.1	N-acylsphingosine amidohydrolase (acid ceramidase) 1
						XLOC_004496	ASA1H	-0.60	2.63E-03	XM_006262540.1	glycerate kinase
						XLOC_016454	GLYCTK	-0.60	6.57E-03	XM_006275130.1	inositol polyphosphate multikinase
						XLOC_007186	IPMK	-0.59	9.85E-03	XM_006265421.1	ras responsive element binding protein 1, transcript variant X3
						XLOC_008084	RREB1	-0.59	2.63E-03	XM_006266346.1	uncharacterized LOC102564038
						XLOC_004242	LOC102564038	-0.58	4.73E-03	XM_006262282.1	UDP-glucuronosyltransferase 1-E-like
						XLOC_005148	LOC102558477	-0.58	4.73E-03	XM_006263235.1	pyruvate dehydrogenase kinase, isozyme 4
						XLOC_013100	PDK4	-0.58	6.57E-03	XM_006271681.1	PTPRF interacting protein, binding protein 2 (liprin beta 2), transcript variant X3
						XLOC_008091	PPFBP2	-0.57	9.85E-03	XM_006266353.1	REST corepressor 1
						XLOC_015907	RCOR1	-0.57	4.73E-03	XM_006274592.1	low-density lipoprotein receptor-related protein 2-like
						XLOC_016043	LOC102565081	-0.57	8.24E-03	N/A	pterin-4 alpha-carbinolamine dehydratase/dimerization cofactor of hepatocyte nuclear factor 1 alp
						XLOC_017046	PCBD1	-0.57	8.24E-03	XM_006275727.1	major histocompatibility complex class I-related gene protein-like
						XLOC_009448	LOC102562567	-0.57	8.24E-03	XM_006267800.1	succinate-CoA ligase, GDP-forming, beta subunit
						XLOC_010297	PTPRQ	-0.57	9.85E-03	XM_006268681.1	probable proline dehydrogenase 2-like
						XLOC_007514	SUCLG2	-0.57	9.85E-03	XM_006265758.1	signal-induced proliferation-associated 1 like 1
						XLOC_002665	LOC102567357	-0.57	8.24E-03	XM_006260586.1	arginine-glutamic acid dipeptide repeats protein-like
						XLOC_003044	SIPA1L1	-0.56	6.57E-03	XM_006260980.1	adenosylhomocysteinase-like 1, transcript variant X1
						XLOC_016841	LOC102563541	-0.56	6.57E-03	XM_006275525.1	sorbitol dehydrogenase
						XLOC_001486	AHCYL1	-0.56	8.24E-03	XM_006259321.1	Na(+)/H(+) exchange regulatory cofactor NHE-RF3-like
						XLOC_017584	SORD	-0.56	4.73E-03	XM_006276283.1	intracellular transport 80 homolog (Chlamydomonas), transcript variant X1
						XLOC_004275	LOC102563808	-0.55	4.73E-03	XM_006262281.1	80
						XLOC_014217	IFT80	-0.54	4.73E-03	XM_006272855.1	

Day 6 (MPT) vs Day 12 (MPT)											
Up-regulated						Down-regulated					
Gene_ID	Gene Symbol	LOG2(FC)	FDR	RefSeq Accession	Description	Gene_ID	Gene Symbol	LOG2(FC)	FDR	RefSeq Accession	Description
XLOC_000709	TAP2	5.00	9.85E-03	XM_006258513.1	transporter 2, ATP-binding cassette, sub-family B (MDR/TAP)	XLOC_016935	LOC102567251	-4.97	8.24E-03	XM_006275615.1	major histocompatibility complex class I-related gene protein-like
XLOC_017214	LOC102557978	3.85	2.63E-03	XM_006275897.1	myeloid protein 1-like	XLOC_001261	LOC102563321	-2.73	2.63E-03	XM_006259088.1	hemoglobin subunit epsilon-like
XLOC_002864	AHSG	3.23	8.24E-03	XM_006260768.1	alpha-2-HS-glycoprotein	XLOC_000636	LOC102563794	-2.6	2.63E-03	XM_006258433.1	myosin-3-like
XLOC_017096	MATN4	2.82	2.63E-03	XM_006275789.1	matrin 4	XLOC_010405	OSTN	-2.12	2.63E-03	XM_006268789.1	osteocrin
XLOC_000041	LOC102566578	2.55	2.63E-03	XM_006257779.1	avidin-like	XLOC_007791	LOC102569784	-2.09	2.63E-03	XM_006260393.1	collagen alpha-1(VIII) chain-like
XLOC_006538	LOC102565592	2.04	2.63E-03	XM_006264753.1	BPTI/Kunitz domain-containing protein-like	XLOC_019721	HOCX10	-1.71	2.63E-03	XM_006278447.1	homeobox C10
XLOC_002340	PNMT	1.97	2.63E-03	XM_006260210.1	phenylethanolamine N-methyltransferase	XLOC_003796	MYO18B	-1.47	2.63E-03	XM_006261765.1	myosin XIIIB
XLOC_014252	SLC6A18	1.93	2.63E-03	XM_006272902.1	solute carrier family 6 (neutral amino acid transporter), member 18	XLOC_013480	LOC102559498	-1.44	2.63E-03	XM_006272069.1	hemoglobin subunit beta-like
XLOC_009365	GGT1	1.93	2.63E-03	XM_006267703.1	gamma-glutamyltransferase 1	XLOC_003968	LOC102559155	-1.42	2.63E-03	XM_006261841.1	hemoglobin subunit pi-like
XLOC_020054	LOC102559828	1.91	2.63E-03	XM_006278762.1	acidic mammalian chitinase-like	XLOC_006659	EPHA10	-1.41	4.73E-03	XM_006264881.1	EPH receptor A10
XLOC_000903	PLP1	1.83	2.63E-03	XM_006258708.1	protolipid protein 1, transcript variant X1	XLOC_014376	LOC102573435	-1.36	2.63E-03	XR_363493.1	uncharacterized LOC102573435
XLOC_018339	LOC102567962	1.82	6.57E-03	XM_006277068.1	protein Niban-like	XLOC_011989	LOC102574848	-1.23	2.63E-03	XM_006270435.1	mast cell protease 1A-like
XLOC_005081	COL9A1	1.81	2.63E-03	XM_006263154.1	collagen, type IX, alpha 1	XLOC_017446	LOC102558523	-0.96	2.63E-03	XM_006276142.1	musculin-like
XLOC_012871	LOC102560787	1.80	2.63E-03	XM_006271440.1	xylosyltransferase 1-like	XLOC_004274	GJA5	-0.88	2.63E-03	XM_006262278.1	gap junction protein, alpha 5, 40kDa
XLOC_000495	LOC102569139	1.77	2.63E-03	XM_006258290.1	cathepsin W-like	XLOC_017835	HEMN	-0.88	2.63E-03	XM_006276548.1	hemogen, transcript variant X1
XLOC_018954	LOC102563224	1.75	6.57E-03	XM_006277686.1	lysozyme g-like	XLOC_020025	ACTG2	-0.85	2.63E-03	XM_006278736.1	actin, gamma 2, smooth muscle, enteric, transcript variant X2
XLOC_001371	LOC102570382	1.74	2.63E-03	XM_006259197.1	WAP four-disulfide core domain protein 5-like	XLOC_012168	NPTX1	-0.85	2.63E-03	XM_006270639.1	neuronal pentrax I
XLOC_009583	NRN1	1.74	2.63E-03	XM_006267940.1	neuritin 1	XLOC_016716	TMOD4	-0.80	4.73E-03	XM_006275401.1	tropomodulin 4 (muscle)
XLOC_014638	LOC102561113	1.71	2.63E-03	XM_006273280.1	solute carrier family 22 member 2-like	XLOC_017186	CRABP2	-0.79	2.63E-03	XM_006275867.1	cellular retinoic acid binding protein 2
XLOC_005150	LOC102559161	1.67	2.63E-03	XM_006263238.1	UDP-glucuronosyltransferase 1-9-like	XLOC_002638	SYNPO	-0.78	4.73E-03	XM_006260565.1	synaptopodin
XLOC_009466	SLC26A9	1.65	2.63E-03	XM_006267934.1	solute carrier family 26 (anion exchanger), member 9	XLOC_001548	SMOC2	-0.77	6.57E-03	XM_006259389.1	SPARC related modular calcium binding 2
XLOC_018953	LOC102562523	1.64	2.63E-03	XM_006277684.1	lysozyme g-like	XLOC_007825	GPR37L1	-0.77	2.63E-03	XM_006260677.1	G protein-coupled receptor 37 like 1
XLOC_015777	MPZ	1.64	2.63E-03	XM_006274464.1	myelin protein zero	XLOC_004294	EPOR	-0.75	2.63E-03	XM_006262351.1	erythropoietin receptor
XLOC_003593	AMH	1.58	2.63E-03	XM_006261559.1	anti-Mullerian hormone	XLOC_003940	TNNI3	-0.73	2.63E-03	XM_006261916.1	troponin I type 3 (cardiac)
XLOC_009706	LOC102566308	1.55	2.63E-03	XM_006268053.1	matrix Gla protein-like	XLOC_006767	LOC102574741	-0.70	8.24E-03	XM_006264941.1	homeobox protein meis3-B-like
XLOC_017122	LOC102574633	1.54	2.63E-03	XM_006275810.1	cytochrome P450 2A5-like	XLOC_012997	SLC4A1	-0.70	2.63E-03	XM_006271577.1	solute carrier family 4 (anion exchanger), member 1
XLOC_009056	LOC102561092	1.47	8.24E-03	XM_006267396.1	cysteine-rich venom protein hethermine-like	XLOC_004684	COL1A1	-0.65	6.57E-03	XM_00626736.1	collagen, type XI, alpha 1, transcript variant X3
XLOC_020001	LOC102567971	1.39	2.63E-03	XM_006278707.1	steroid 17-alpha-hydroxylase/17,20 lyase-like	XLOC_013481	LOC102559263	-0.65	9.85E-03	XM_006272068.1	hemoglobin subunit beta-like
XLOC_012895	TGM3	1.36	2.63E-03	XM_006271463.1	transglutaminase 3	XLOC_009748	LOC102573884	-0.63	4.73E-03	XM_006268087.1	cystatin-like
XLOC_009567	LOC102575071	1.36	2.63E-03	XR_363213.1	uncharacterized LOC102575071, transcript variant X1	XLOC_014038	SPEG	-0.58	4.73E-03	XM_006272682.1	SPEG complex locus
XLOC_012311	LOC102567318	1.36	4.73E-03	XR_363379.1	uncharacterized LOC102567318	XLOC_005823	ALDH1A2	-0.56	6.57E-03	XM_006263988.1	aldehyde dehydrogenase 1 family, member A2, transcript variant X1
XLOC_014542	ISLR2	1.34	2.63E-03	XM_006273158.1	immunoglobulin superfamily containing leucine-rich repeat 2, transcript variant X1	XLOC_001928	ARX	-0.56	6.57E-03	XM_006259798.1	aristless related homeobox
XLOC_009566	ELN	1.33	2.63E-03	XM_006267934.1	elastin	XLOC_018147	LOC102557983	-0.55	8.24E-03	XM_006276865.1	ovocalyxin-32-like
XLOC_017114	LOC102574160	1.32	2.63E-03	XM_006275808.1	plasminogen-like						
XLOC_004611	BCAS1	1.32	2.63E-03	XM_006262658.1	breast carcinoma amplified sequence 1						
XLOC_013799	TH	1.29	2.63E-03	XM_006272424.1	tyrosine hydroxylase						
XLOC_003210	SLC5A8	1.20	2.63E-03	XM_006261167.1	solute carrier family 5 (sodium/monocarboxylate cotransporter), member 8						
XLOC_016644	KCNK3	1.19	4.73E-03	XM_006275335.1	potassium channel, subfamily K, member 3						
XLOC_013641	IFIT5	1.19	2.63E-03	XM_006272248.1	interferon-induced protein with tetrapeptide repeats 5						
XLOC_009569	LOC102575456	1.18	2.63E-03	XR_363216.1	uncharacterized LOC102575456, transcript variant X1						
XLOC_003435	LOC102566361	1.18	2.63E-03	XM_006261381.1	ovotransferrin-like						
XLOC_018282	LOC102573693	1.17	2.63E-03	XM_006277011.1	solute carrier family 2, facilitated glucose transporter member 11-like						
XLOC_017415	KIF1A	1.12	2.63E-03	XM_006276111.1	kinesin family member 1A, transcript variant X1						
XLOC_014427	STMN3	1.12	2.63E-03	XM_006273066.1	stathmin-like 3						
XLOC_020160	LOC102573463	1.10	2.63E-03	XM_006278908.1	epithelial chloride channel protein-like						
XLOC_011163	LOC102565377	1.07	2.63E-03	XM_006269585.1	serotriptin-like						
XLOC_008557	MPZL2	1.06	2.63E-03	XM_006266847.1	myelin protein zero-like 2						
XLOC_006327	LOC102570551	1.06	2.63E-03	XM_006264538.1	keratin, type I cytoskeletal 14-like						
XLOC_007233	LOC102567139	1.04	2.63E-03	XM_006265470.1	multidrug and toxin extrusion protein 1-like						
XLOC_013393	LOC102557664	1.04	2.63E-03	XM_006271986.1	acyl-CoA-binding protein-like						
XLOC_000283	CPA3	1.04	4.73E-03	XM_006265045.1	carboxypeptidase A3 (mast cell)						
XLOC_008541	CNDP1	1.03	2.63E-03	XM_006266824.1	camosine dipeptidase 1 (metallopeptidase M20 family)						
XLOC_003701	LOC102575599	1.02	2.63E-03	XM_006261670.1	cytochrome P450 2K4-like						
XLOC_002641	GPX3	1.02	2.63E-03	XM_006260571.1	glutathione peroxidase 3 (plasma)						
XLOC_003357	AB13BP	1.01	4.73E-03	XM_006261304.1	ABI family, member 3 (NES) binding protein						
XLOC_007516	LOC102560835	0.98	2.63E-03	XM_006265759.1	monocarboxylate transporter 2-like						
XLOC_006415	LOC102561161	0.97	2.63E-03	XM_006264659.1	peripherin-like						
XLOC_017690	WIF1	0.97	2.63E-03	XM_006276396.1	WNT inhibitory factor 1						
XLOC_004096	ADAMTS8	0.94	2.63E-03	XM_006262090.1	ADAM metallopeptidase with thrombospondin type 1 motif, 8						
XLOC_016705	MLLT11	0.93	8.24E-03	XM_006275396.1	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 11						

XLOC_011397	HSD11B2	0.93	2.63E-03	XM_006269835.1	hydroxysteroid (11-beta) dehydrogenase 2
XLOC_010513	SLC23A1	0.91	2.63E-03	XM_006268887.1	solute carrier family 23 (ascorbic acid transporter), member 1
XLOC_001686	RET	0.91	4.73E-03	XM_006259549.1	ret proto-oncogene
XLOC_001517	LOC102568516	0.90	2.63E-03	XM_006259359.1	glycine amidinotransferase, mitochondrial-like
XLOC_002973	DBH	0.89	2.63E-03	XM_006260879.1	dopamine beta-hydroxylase (dopamine beta-monoxygenase)
XLOC_005942	GAP43	0.89	2.63E-03	XM_006264120.1	growth associated protein 43
XLOC_008690	SLC5A1	0.88	2.63E-03	XM_006266970.1	solute carrier family 5 (sodium/glucose cotransporter), member 1, transcript variant X1
XLOC_006416	LOC102561391	0.88	4.73E-03	XM_006264660.1	peripherin-like
XLOC_005818	PTPRR	0.87	2.63E-03	XM_006263984.1	protein tyrosine phosphatase, receptor type, R
XLOC_001463	LOC102574572	0.87	2.63E-03	XM_006259299.1	somatostatin-2-like
XLOC_008095	G6PC	0.86	2.63E-03	XM_006266359.1	glucose-6-phosphatase, catalytic subunit
XLOC_019823	LOC102564018	0.85	2.63E-03	XM_006278540.1	cysteine-rich venom protein helothermine-like
XLOC_006802	LOC102573570	0.85	2.63E-03	XM_006265015.1	solute carrier family 22 member 6-A-like
XLOC_014833	SRGN	0.84	2.63E-03	XM_006273478.1	serglycin
XLOC_017872	PCK1	0.84	2.63E-03	XM_006276591.1	phosphoenolpyruvate carboxykinase 1 (soluble)
XLOC_011267	LOC102572104	0.82	2.63E-03	XM_006269693.1	reticulin-1-A-like, transcript variant X3
XLOC_014075	SLC5A10	0.82	2.63E-03	XM_006272714.1	solute carrier family 5 (sodium/sugar cotransporter), member 10, transcript variant X1
XLOC_007107	UPK3A	0.81	2.63E-03	XM_006265339.1	uroplakin 3A
XLOC_018099	NEFL	0.81	2.63E-03	XM_006276810.1	neurofilament, light polypeptide
XLOC_011483	MBNL3	0.81	4.73E-03	XM_006269919.1	muscleblind-like splicing regulator 3, transcript variant X1
XLOC_015057	LOC102568110	0.80	2.63E-03	XM_006273705.1	acyl-coenzyme A synthetase ACSM4, mitochondrial-like
XLOC_008706	CADPS	0.80	2.63E-03	XM_006267004.1	Ca++-dependent secretion activator
XLOC_013828	LOC102573123	0.80	2.63E-03	XM_006272455.1	transcription factor SOX-9-like
XLOC_019137	C7	0.79	2.63E-03	XM_006277786.1	complement component 7
XLOC_001658	APOA1	0.79	2.63E-03	XM_006259520.1	apolipoprotein A-I
XLOC_011453	LOC102576383	0.79	6.57E-03	XR_363324.1	uncharacterized LOC102576383
XLOC_004662	SLC18A2	0.78	9.85E-03	XM_006262699.1	solute carrier family 18 (vesicular monoamine transporter), member 2
XLOC_003127	TMEM27	0.77	2.63E-03	XM_006261086.1	transmembrane protein 27
XLOC_017473	UHMK1	0.76	2.63E-03	XM_006276174.1	U2AF homology motif (UHM) kinase 1
XLOC_003591	DOT1L	0.76	2.63E-03	XM_006261154.1	DOT1-like histone H3K79 methyltransferase, transcript variant X1
XLOC_005579	SERINC5	0.75	2.63E-03	XM_006263715.1	serine incorporator 5
XLOC_002556	CALML4	0.74	2.63E-03	XM_006260456.1	calmodulin-like 4
XLOC_002692	LOC102575737	0.74	2.63E-03	XM_006260622.1	cytochrome P450 11B, mitochondrial-like
XLOC_010738	LOC102575314	0.73	2.63E-03	XM_006269131.1	steroid 21-hydroxylase-like
XLOC_001313	LOC102575660	0.73	2.63E-03	XM_006259135.1	dimethylallylline monooxygenase [N-oxide-forming] 1-like, transcript variant X3
XLOC_010742	LOC102576539	0.73	2.63E-03	XM_006269136.1	zona pellucida sperm-binding protein 3-like
XLOC_007888	STAR	0.72	2.63E-03	XM_006266133.1	steroidogenic acute regulatory protein
XLOC_007714	LOC102570482	0.71	2.63E-03	XM_006265963.1	cytochrome P450 3A21-like
XLOC_018173	FKBP5	0.69	2.63E-03	XM_006276891.1	FK506 binding protein 5
XLOC_002016	SLC25A15	0.69	6.57E-03	XM_006259877.1	solute carrier family 25 (mitochondrial carrier; ornithine transporter) member 15
XLOC_008171	ARG2	0.68	8.24E-03	XM_006266445.1	arginase 2
XLOC_018203	CLCNKB	0.68	2.63E-03	XM_006276925.1	chloride channel, voltage-sensitive Kb
XLOC_015376	LOC102571448	0.66	2.63E-03	XM_006274041.1	cytochrome P450 4B1-like
XLOC_005967	LOC102577145	0.65	4.73E-03	XM_006264145.1	D-beta-hydroxybutyrate dehydrogenase, mitochondrial-like
XLOC_013605	SLC4A4	0.65	2.63E-03	XM_006272210.1	solute carrier family 4 (sodium bicarbonate cotransporter), member 4
XLOC_011994	EHHADH	0.63	4.73E-03	XM_006270453.1	enoyl-CoA, hydratase/3-hydroxyacyl CoA dehydrogenase
XLOC_008801	LOC102572026	0.63	9.85E-03	XM_006267109.1	GDNF family receptor alpha-4-like
XLOC_008160	LOC102567071	0.62	8.24E-03	XM_006266432.1	pleckstrin-2-like
XLOC_010986	TUBB3	0.61	2.63E-03	XM_006269387.1	tubulin, beta 3 class III
XLOC_007156	TSPAN9	0.61	6.57E-03	XM_006265390.1	tetraspanin 9, transcript variant X1
XLOC_016831	FRAS1	0.59	4.73E-03	XM_006275515.1	Fraser syndrome 1
XLOC_014444	CPE	0.59	4.73E-03	XM_006273085.1	carboxypeptidase E
XLOC_015438	LOC102569264	0.58	9.85E-03	XM_006274116.1	cytochrome P450 2D14-like
XLOC_017810	NDRG1	0.58	6.57E-03	XM_006276526.1	N-myc downstream regulated 1
XLOC_001357	TM4SF4	0.57	6.57E-03	XM_006259172.1	transmembrane 4 L six family member 4
XLOC_016580	LOC102558436	inf	2.63E-03	XM_006275267.1	zinc finger protein 184-like

## Day 0 (FPT) vs Day 3 (FPT)

Up-regulated							Down-regulated						
Gene ID	Gene Symbol	LOG2(FC)	FDR	RefSeq Accession	Description	Gene ID	Gene Symbol	LOG2(FC)	FDR	RefSeq Accession	Description		
XLOC_012142	PI15	2.16	8.24E-03	XM_00627616.1	peptidase inhibitor 15	XLOC_007791	LOC102569784	-3.56	2.63E-03	XM_006266309.1	collagen alpha-1(VIII) chain-like		
XLOC_012722	TTR	1.98	2.63E-03	XM_006271257.1	transthyretin	XLOC_019721	HOXC10	-2.67	2.63E-03	XM_006278447.1	homeobox C10		
XLOC_011871	HTRA3	1.96	2.63E-03	XM_006270329.1	Htr4 serine peptidase 3	XLOC_010405	OSTN	-2.24	2.63E-03	XM_006268789.1	osteocrin		
XLOC_004389	LOC102558544	1.79	2.63E-03	XM_006262429.1	cathelicidin-2-like	XLOC_002973	DBH	-2.05	2.63E-03	XM_006260879.1	dopamine beta-hydroxylase (dopamine beta-monooxygenase)		
XLOC_000735	TNRCEB	1.77	2.63E-03	XM_006258541.1	trinucleotide repeat containing 6B, transcript variant X1	XLOC_007271	SLC18A1	-2.05	2.63E-03	XM_006265496.1	solute carrier family 18 (vesicular monoamine transporter), member 1		
XLOC_03593	AMH	1.69	4.73E-03	XM_006261559.1	anti-Mullerian hormone	XLOC_005250	NOV	-1.85	2.63E-03	XM_006263355.1	nephroblastoma overexpressed		
XLOC_004390	LOC102558761	1.69	2.63E-03	XM_006262430.1	cathelicidin-OH antimicrobial peptide-like	XLOC_002977	LOC102566431	-1.76	6.57E-03	XM_006260896.1	chromosome unknown open reading frame, human C9orf96		
XLOC_010686	LOC102561252	1.67	2.63E-03	XM_006269073.1	phospholipase A2 inhibitor subunit gamma B-like	XLOC_014375	LOC102573199	-1.74	2.63E-03	XM_006273013.1	chromogranin A-like		
XLOC_007754	TNMD	1.66	2.63E-03	XM_006265998.1	tenomodulin	XLOC_000909	CCK	-1.74	2.63E-03	XM_006258715.1	cholecytokinin		
XLOC_006977	MAMD2	1.59	2.63E-03	XM_006265197.1	MAM domain containing 2	XLOC_007130	HOXA10	-1.66	2.63E-03	XM_006265365.1	homeobox A10		
XLOC_012454	LOC102656224	1.58	2.63E-03	XM_006270968.1	neuroblast differentiation-associated protein AHNAK-like	XLOC_017562	B3GAT1	-1.63	2.63E-03	XM_006276261.1	beta-1,3-glucuronidyltransferase 1 (glucuronosyltransferase P)		
XLOC_012085	LOC102565682	1.58	2.63E-03	XM_006270554.1	serpin B11-like	XLOC_004479	ROS1	-1.60	2.63E-03	XM_006262520.1	c-ros oncogene 1, receptor tyrosine kinase		
XLOC_001634	ERBB4	1.52	4.73E-03	XM_006259492.1	v-erb-b2 avian erythroblastic leukemia viral oncogene homolog 4	XLOC_005966	ACADVL	-1.53	2.63E-03	XM_006264144.1	acyl-CoA dehydrogenase, very long chain		
XLOC_011989	LOC102574848	1.45	2.63E-03	XM_006270435.1	mast cell protease 1A-like	XLOC_000062	ADAM19	-1.49	2.63E-03	XM_006257806.1	ADAM metallopeptidase domain 19		
XLOC_003878	FABP4	1.42	2.63E-03	XM_006261857.1	fatty acid binding protein 4, adipocyte	XLOC_013799	TH	-1.47	2.63E-03	XM_006272424.1	tyrosine hydroxylase		
XLOC_020119	TNNI2	1.39	2.63E-03	XM_006278838.1	troponin type 2 (skeletal, fast)	XLOC_012101	TAGLN3	-1.46	2.63E-03	XM_006270572.1	transgelin 3		
XLOC_010819	CYGB	1.38	2.63E-03	XM_006269221.1	cytoglobin, transcript variant X1	XLOC_001686	RET	-1.46	2.63E-03	XM_006259549.1	ret proto-oncogene		
XLOC_019823	LOC102564018	1.38	2.63E-03	XM_006278540.1	cysteine-rich venous protein helothermine-like	XLOC_015651	LOC102563772.1	-1.38	2.63E-03	36274340.1, XM_00627-fatty acyl-CoA hydrolase precursor, medium chain-like, liver carboxylesterase-like			
XLOC_014376	LOC102573435	1.33	2.63E-03	XM_363493.1	uncharacterized LOC102573435	XLOC_014102	SEZ6	-1.33	2.63E-03	XM_006272745.1	seizure related 6 homolog (mouse)		
XLOC_007678	LOC1026561011	1.32	2.63E-03	XM_006266924.1	chromosome unknown open reading frame, human C2orf40	XLOC_006687	CHCB	-1.33	2.63E-03	XM_006264900.1	chromogranin B (secretogranin 1)		
XLOC_010524	LOC102577390	1.31	2.63E-03	XM_006268897.1	uncharacterized LOC102577390, transcript variant X1	XLOC_004513	LOC102570622	-1.32	2.63E-03	XM_006262559.1	insulin gene enhancer protein ISL-1-like		
XLOC_005063	LOC102573091	1.31	2.63E-03	XM_006263132.1	7-alpha-hydroxycholest-4-en-3-one 12-alpha-hydroxylase-like	XLOC_005656	GY2	-1.31	2.63E-03	XM_006263801.1	glycogen synthase 2 (liver)		
XLOC_011653	LOC102570571	1.25	6.57E-03	XM_006270012.1	growth arrest-specific protein 1-like	XLOC_006292	SLC15A2	-1.31	2.63E-03	XM_006264513.1	solute carrier family 15 (oligopeptide transporter), member 2		
XLOC_000567	LUM	1.25	2.63E-03	XM_006258358.1	lumican	XLOC_002988	RIMPBP2	-1.29	2.63E-03	XM_006260911.1	RIMS binding protein 2		
XLOC_010503	LRP2	1.22	2.63E-03	XM_006268878.1	low density lipoprotein receptor-related protein 2	XLOC_011459	COL8A2	-1.27	2.63E-03	XM_006269879.1	collagen, type VIII, alpha 2		
XLOC_003026	ID4	1.22	2.63E-03	XM_006260955.1	inhibitor of DNA binding 4, dominant negative helix-loop-helix protein	XLOC_000564	LOC102565100	-1.24	2.63E-03	XM_006258355.1	heart- and neural crest derivatives-expressed protein 2-like		
XLOC_013332	MDGA1	1.21	2.63E-03	XM_006271918.1	MDM domain containing glycosylphosphatidylinositol anchor 1	XLOC_007888	STAR	-1.22	2.63E-03	XM_006261633.1	steroidogenic acute regulatory protein		
XLOC_014000	SLC15A1	1.16	2.63E-03	XM_006272640.1	solute carrier family 15 (oligopeptide transporter), member 1	XLOC_019573	LOC102561818	-1.20	2.63E-03	XM_006278306.1	class I histocompatibility antigen, Gogo-C'0203 alpha chain-like		
XLOC_003959	JSRP1	1.15	2.63E-03	XM_006261560.1	junctional sarcoplasmic reticulum protein 1	XLOC_001548	SMOC2	-1.19	2.63E-03	XM_006259389.1	SPARC related modular calcium binding 2		
XLOC_012892	EPB42	1.15	2.63E-03	XM_006271454.1	erythrocyte membrane protein band 4.2	XLOC_000984	LMOD1	-1.18	4.73E-03	XM_006258800.1	leiomodin 1 (smooth muscle)		
XLOC_005010	MKX	1.15	2.63E-03	XM_006263075.1	mohawk homeobox	XLOC_016540	EY42	-1.18	8.24E-03	XM_006275234.1	eyes absent homolog 2 ( <i>Drosophila</i> )		
XLOC_001311	FMO1	1.15	4.73E-03	XM_006259132.1	flavin containing monooxygenase 1, transcript variant X2	XLOC_005999	MYO1H	-1.17	8.24E-03	XM_006264194.1	myosin IIH		
XLOC_019268	LAMA3	1.13	2.63E-03	XM_006278007.1	laminin, alpha 3	XLOC_016538	JPH2	-1.17	2.63E-03	XM_006275231.1	junctophilin 2, transcript variant X1		
XLOC_014454	LOC102573200	1.13	2.63E-03	XM_006273095.1	netrin-4-like, transcript variant X1	XLOC_012549	F5TL	-1.17	4.73E-03	XM_006271075.1	folistatin-like 5		
XLOC_002987	PWIL1	1.12	4.73E-03	XM_006269010.1	pwil-like RNA-mediated gene silencing 1	XLOC_004031	LOC102562544	-1.16	6.57E-03	XM_006262022.1	ovochymase-2-like		
XLOC_009221	LOC102565053	1.12	2.63E-03	XM_006267562.1	lipocalin-kinin	XLOC_003893	SCARB1	-1.16	2.63E-03	XM_006261864.1	scavenger receptor class B, member 1		
XLOC_007647	LOC102572713	1.11	2.63E-03	XM_006285890.1	proactin-releasing peptide receptor-like	XLOC_001483	LOC102574572	-1.14	2.63E-03	XM_006259299.1	somatostatin-2-like		
XLOC_010743	LOC102576768	1.11	2.63E-03	XM_006269137.1	lysosomal acid lipase/cholesterol ester hydrolase-like	XLOC_020025	ACTG2	-1.13	2.63E-03	XM_006276736.1	actin, gamma 2, smooth muscle, enteric, transcript variant X2		
XLOC_012453	LOC102564995	1.11	2.63E-03	XM_006270967.1	neuroblast differentiation-associated protein AHNAK-like	XLOC_001510	LOC102559161	-1.11	2.63E-03	XM_006263238.1	UDP-glucuronyltransferase 1-9-like		
XLOC_012787	LOC102558510	1.10	8.24E-03	XM_006271342.1	uncharacterized LOC102558510	XLOC_008541	CNDP1	-1.11	2.63E-03	XM_006266824.1	carnosine dipeptidase 1 (metalloproteinase M20 family)		
XLOC_014317	LOC102559691	1.09	2.63E-03	XM_006272968.1	vasopressin V1a receptor-like	XLOC_002633	SYNPQ	-1.11	2.63E-03	XM_006260565.1	synaptotagmin		
XLOC_009466	SLC26A9	1.09	2.63E-03	XM_006267811.1	solute carrier family 26 (anion exchanger), member 9	XLOC_018099	NFL	-1.10	2.63E-03	XM_006267680.1	neurofiliament, light polypeptide		
XLOC_003435	LOC102566361	1.09	2.63E-03	XM_006261381.1	ovoferrin-like	XLOC_017932	UNC80	-1.10	2.63E-03	XM_006267666.1	unc-80 homolog (C. elegans)		
XLOC_015366	STARD5	1.08	2.63E-03	XM_006274032.1	STAR-related lipid transfer (START) domain containing 5	XLOC_017067	GPR116	-1.10	6.57E-03	XM_006275758.1	G protein-coupled receptor 116		
XLOC_003318	LOC102577358	1.08	2.63E-03	XM_006261267.1	duplex and mab-3 related transcription factor 3-like	XLOC_010858	MGAT5B	-1.07	4.73E-03	XM_00626915.1	mannosyl (alpha-1,6)-glycoprotein beta-1,6-N-acetyl-glucosaminyltransferase, isoform 1		
XLOC_002265	LOC102559838	1.05	2.63E-03	XM_006260135.1	WAP four-disulfide core domain protein 2-like	XLOC_010400	LOC102566853	-1.00	8.24E-03	XM_006268766.1	receptor-type tyrosine-protein phosphatase N2-like		
XLOC_009294	PPR13C	1.04	2.63E-03	XM_006267634.1	protein phosphatase 1, regulatory subunit 3C	XLOC_009005	LOC102569324	-0.97	2.63E-03	XM_006267352.1	Vitamin D3 hydroxylase-associated protein-like		
XLOC_013143	LOC102567788	1.02	2.63E-03	XM_006271712.1	calretinin-like	XLOC_007303	LOC102563735	-0.97	2.63E-03	XM_006265526.1	BMP/retninoic acid-inducible neural-specific protein 1-like		
XLOC_045489	ST6GALNAC5	1.02	4.73E-03	XM_006262626.1	TBC1 domain family, member 3 (beta-neuraminyl-2,3-beta-galactosyl-1,3-N-acetylgalactosaminyltransferase)	XLOC_016196	FBLN2	-0.97	2.63E-03	XM_006275174.1	fibrillin 2		
XLOC_006290	CRISPLD2	1.02	2.63E-03	XM_006263395.1	cysteine-rich secretory protein LCLC domain containing 2	XLOC_001760	STEAP1	-0.97	2.63E-03	XM_00626626.1	six transmembrane epithelial antigen of the prostate 1, transcript variant X2		
XLOC_009539	PXDN	0.99	4.73E-03	XM_00628304.1	peroxidasin (Drosophila)-like	XLOC_004313	CNN1	-0.96	2.63E-03	XM_00626228.1	calponin 1, basic, smooth muscle		
XLOC_019803	LOC102559056	0.99	2.63E-03	XM_00627815.1	protein MRP-12-like	XLOC_016935	LOC102567251	-0.95	2.63E-03	XM_006275615.1	major histocompatibility complex class I-related gene protein-like		
XLOC_013522	MRPL34	0.99	2.63E-03	XM_006272137.1	mitochondrial ribosomal protein L34	XLOC_017756	SCG2	-0.95	2.63E-03	XM_006276487.1	secretogranin II		
XLOC_004240	LOC102567125	0.97	2.63E-03	XM_006262206.1	ribonuclease-like	XLOC_014643	PKIB	-0.93	8.24E-03	XM_006273282.1	protein kinase (cAMP-dependent, catalytic) inhibitor beta		
XLOC_012957	UPK1B	0.94	2.63E-03	XM_006271528.1	uroplakin 1B	XLOC_008364	HEY2	-0.93	4.73E-03	XM_006266650.1	res-related family bHLH transcription factor with YRPW motif 2, transcript variant X		
XLOC_019258	FAP	0.93	8.24E-03	XM_006277995.1	fibroblast activation protein, alpha	XLOC_015050	LOC102564848	-0.92	2.63E-03	XM_006273691.1	acyl-coenzyme A synthetase ACSM3, mitochondrial-like		
XLOC_004871	LOC102562472	0.92	8.24E-03	XM_006262925.1	cytochrome P450 2J6-like	XLOC_012888	SLC35C2	-0.92	2.63E-03	XM_006271460.1	solute carrier family 35 (GDP-fucose transporter), member C2		
XLOC_014270	LOC102567098	0.92	9.85E-03	XM_006272922.1	cadherin-10-like	XLOC_016348	PAX6	-0.92	2.63E-03	XM_006275027.1	paired box 8		
XLOC_016716	TMOD4	0.91	8.24E-03	XM_006275401.1	tropomodulin 4 (muscle)	XLOC_018293	LOC102574944	-0.90	4.73E-03	XM_006277016.1	interleukin-15-like, transcript variant X1		
XLOC_014705	AMHR2	0.88	2.63E-03	XM_006273345.1	anti-Mullerian hormone receptor, type II	XLOC_007693	FZD5	-0.90	2.63E-03	XM_006265941.1	fizzled family receptor 5		
XLOC_009660	HMBOX1	0.88	6.57E-03	XM_006268010.1	homeobox containing 1	XLOC_016687	LOC102570362	-0.90	2.63E-03	XM_006275551.1	3 beta-hydroxy steroid dehydrogenase/Delta 5->4-isomerase-like		
XLOC_013303	OSGIN1	0.86	4.73E-03	XM_006271885.1	oxidative stress induced growth inhibitor 1	XLOC_017258	TBX18	-0.89	2.63E-03	XM_006275946.1	T-box 18		
XLOC_016502	HIPK2	0.84	2.63E-03	XM_006275178.1	homeodomain interacting protein kinase 2, transcript variant X2	XLOC_002641	GPX3	-0.89	2.63E-03	XM_006260571.1	glutathione peroxidase 3 (plasma)		
XLOC_008602	TBC1D9	0.84	2.63E-03	XM_006266891.1	TBC1 domain family, member 9 (with GRAM domain)	XLOC_011657	LOC102575787	-0.89	2.63E-03	XM_006270115.1	adrenodoxin, mitochondrial-like		
XLOC_017632	CORIN	0.84	2.63E-03	XM_006276336.1	corin, serine peptidase	XLOC_015332	LOC102560570	-0.88	2.63E-03	XM_006273996.1	disintegrin and metalloproteinase domain-containing protein 19-like		
XLOC_0													

XLOC_008408 CALB1	0.77	2.63E-03	XM_006266690.1	calbindin 1, 28kDa	XLOC_017468 RGS4	-0.81	6.57E-03	XM_006276158.1	regulator of G-protein signaling 4
XLOC_009391 LOC102566850	0.76	2.63E-03	XM_006267730.1	FRAS1-related extracellular matrix protein 2-like	XLOC_002692 LOC102575737	-0.80	2.63E-03	XM_006260622.1	cytochrome P450 11B, mitochondrial-like
XLOC_007825 GPR37L1	0.76	4.73E-03	XM_006266077.1	G protein-coupled receptor 37 like 1	XLOC_002220 LOC102569061	-0.79	2.63E-03	XM_006260099.1	glycine N-acetyltransferase-like protein 3-like
XLOC_012236 COL21A1	0.76	2.63E-03	XM_006270716.1	collagen, type XXI, alpha 1	XLOC_015664 GATA5	-0.78	4.73E-03	XM_006274328.1	GATA binding protein 5
XLOC_011791 LOC102566081	0.76	2.63E-03	XM_006270235.1	beta-galactoside-binding lectin-like	XLOC_003145 LOC102572230	-0.78	6.57E-03	XM_006261091.1	transmembrane protein 198-B-like
XLOC_007512 LOC102559932	0.75	2.63E-03	XM_006265755.1	collagen alpha-1(XXVI) chain-like	XLOC_007178 MYO1A	-0.77	4.73E-03	XM_006265411.1	myosin IA
XLOC_014618 LOC102575170	0.74	2.63E-03	XM_006273256.1	cystatin-B-like	XLOC_017000 LOC102563625	-0.76	2.63E-03	XM_006275682.1	cGMP-dependent 3',5'-cyclic phosphodiesterase-like
XLOC_000177 LOC102561900	0.74	2.63E-03	XM_006257927.1	semaphorin-3D-like	XLOC_002786 SLC25A29	-0.76	2.63E-03	XM_006260708.1	solute carrier family 25 (mitochondrial carnitine/acylcarnitine carrier), member 29
XLOC_002516 HSD17B1	0.72	2.63E-03	XM_006260402.1	hydroxysteroid (17-beta) dehydrogenase 1, transcript variant X2	XLOC_010746 ACTA2	-0.76	2.63E-03	XM_006269140.1	actin, alpha 2, smooth muscle, aorta
XLOC_010256 LOC102570029	0.71	2.63E-03	XM_006268638.1	vascular cell adhesion protein 1-like, transcript variant X2	XLOC_008801 LOC102572026	-0.75	8.24E-03	XM_006267109.1	GDNF family receptor alpha-4-like
XLOC_003273 PRELP	0.71	2.63E-03	XM_006261224.1	proline/arginine-rich end leucine-rich repeat protein	XLOC_004684 COL11A1	-0.74	4.73E-03	XM_006262736.1	collagen, type XI, alpha 1, transcript variant X3
XLOC_009174 THBD	0.70	2.63E-03	XM_006267522.1	thrombomodulin	XLOC_016034 OSR2	-0.74	2.63E-03	XM_006274725.1	odd-skipped related transcription factor 2, transcript variant X2
XLOC_016824 GAS2	0.68	4.73E-03	XM_006275507.1	growth arrest-specific 2	XLOC_005967 LOC102577145	-0.73	2.63E-03	XM_006264145.1	D-beta-hydroxybutyrate dehydrogenase, mitochondrial-like
XLOC_015934 S100A10	0.68	2.63E-03	XM_006274615.1	S100 calcium binding protein A10	XLOC_008706 CADPS	-0.73	8.24E-03	XM_006267004.1	Ca++-dependent secretion activator
XLOC_012235 LOC102575186	0.66	2.63E-03	XM_006277977.1	transmembrane protein 47-like	XLOC_011701 OGDHL	-0.72	2.63E-03	XM_006270166.1	oxoglutarate dehydrogenase-like, transcript variant X2
XLOC_013512 GJA1	0.65	2.63E-03	XM_006272096.1	gap junction protein, alpha 1, 43kDa	XLOC_008999 LOC102565364	-0.72	2.63E-03	XM_006267336.1	alanine aminotransferase 2-like
XLOC_001181 ME3	0.65	2.63E-03	XM_006258999.1	malic enzyme 3, NADP(+)-dependent, mitochondrial	XLOC_015306 HSD17B2	-0.72	2.63E-03	XM_006273972.1	hydroxysteroid (17'-beta) dehydrogenase 2
XLOC_018761 F3	0.64	2.63E-03	XM_006277486.1	coagulation factor III (thromboplastin, tissue factor)	XLOC_012067 CTGF	-0.71	2.63E-03	XM_006270533.1	connective tissue growth factor
XLOC_005663 LOC102575135	0.63	6.57E-03	XM_006263807.1	ammonium transporter Rh type C-like	XLOC_003407 CHRNA3	-0.69	2.63E-03	XM_006261354.1	cholinergic receptor, nicotinic, alpha 3 (neuronal)
XLOC_017835 HEMGN	0.62	4.73E-03	XM_006276548.1	hemogen, transcript variant X1	XLOC_009930 SLC31A1	-0.68	9.85E-03	XM_006268285.1	solute carrier family 31 (copper transporter), member 1
XLOC_013747 SDPR	0.62	2.63E-03	XM_006272372.1	serum deprivation response	XLOC_006525 LOC102562243	-0.68	6.57E-03	XM_006264740.1	ectonucleotide pyrophosphatase/phosphodiesterase family member 3-like
XLOC_006296 SFRP2	0.60	4.73E-03	XM_006264518.1	secreted frizzled-related protein 2	XLOC_015832 LOC102572203	-0.68	4.73E-03	XM_006274533.1	contarin-1-like
XLOC_018247 LOC102563631	0.55	6.57E-03	XR_363745.1	uncharacterized LOC102563631	XLOC_018173 FKBP5	-0.67	2.63E-03	XM_006276891.1	FK506 binding protein 5
XLOC_001291 LOC102570689	inf	2.63E-03	XM_006259113.1	norrin-like	XLOC_008171 ARG2	-0.66	8.24E-03	XM_006266445.1	arginase 2
XLOC_012500 LOC102566935	inf	2.63E-03	XM_006271052.1	collagen alpha-1(II) chain-like	XLOC_018116 SOAT1	-0.66	2.63E-03	XM_006276828.1	sterol O-acyltransferase 1
XLOC_001053 LOC102568912	inf	6.57E-03	XR_362717.1	uncharacterized LOC102568912	XLOC_006767 LOC102574741	-0.65	2.63E-03	XM_006264941.1	homeobox protein meis3-B-like
XLOC_009696 LOC102563028	inf	9.85E-03	XM_006268040.1	histone H2B 1/2/3/4/6-like	XLOC_011181 CTH	-0.63	2.63E-03	XM_006269606.1	cystathionase (cystathione gamma-lyase)
					XLOC_001112 LOC102563319	-0.63	2.63E-03	XM_006258919.1	dehydrogenase/reductase SDR family member 1-like
					XLOC_019177 HOXB3	-0.61	2.63E-03	XM_006277919.1	homeobox B3
					XLOC_002963 SARDH	-0.58	4.73E-03	XM_006260892.1	sarcosine dehydrogenase
					XLOC_015775 APOA2	-0.57	9.85E-03	XM_006274463.1	apolipoprotein A-II
					XLOC_005771 LOC102563338	-inf	2.63E-03	XM_006263922.1	thioredoxin domain-containing protein 17-like
					XLOC_001066 LOC102573078	-inf	4.73E-03	XM_006258789.1	chromosome unknown open reading frame, human C2orf50

Day 3 (FPT) vs Day 6 (FPT)											
Up-regulated						Down-regulated					
Gene_ID	Gene_Symbol	LOG2(FC)	FDR	RefSeq_Accession	Description	Gene_ID	Gene_Symbol	LOG2(FC)	FDR	RefSeq_Accession	Description
XLOC_007791	LOC102569784	4.15	2.63E-03	XM_006266039.1	collagen alpha-1(VIII) chain-like	XLOC_012454	LOC102565224	-2.09	2.63E-03	XM_006270968.1	neuroblast differentiation-associated protein AHNAK-like
XLOC_020160	LOC102573463	3.60	2.63E-03	XM_006278908.1	epithelial chloride channel protein-like	XLOC_019763	LPP	-1.96	4.73E-03	XM_006278489.1	LIM domain containing preferred translocation partner in lipoma
XLOC_018519	LOC102570910	3.35	1.90E-02	XM_006277236.1	uncharacterized LOC102570910	XLOC_012085	LOC102565682	-1.71	2.63E-03	XM_006270554.1	serpin B11-like
XLOC_017452	CLEC3B	3.23	2.63E-03	XM_006276144.1	C-type lectin domain family 3, member B	XLOC_000735	TNRC6B	-1.70	2.63E-03	XM_006258541.1	trinucleotide repeat containing 6B, transcript variant X1
XLOC_009569	LOC102575456	2.99	2.63E-03	XR_363216.1	uncharacterized LOC102575456, transcript variant X1	XLOC_020054	LOC102559828	-1.70	2.63E-03	XM_006278762.1	acidic mammalian chitinase-like
XLOC_005250	NOV	2.95	2.63E-03	XM_006263355.1	nephroblastoma overexpressed	XLOC_012453	LOC102564995	-1.62	2.63E-03	XM_006270967.1	neuroblast differentiation-associated protein AHNAK-like
XLOC_009568	LOC102575306	2.87	4.00E-02	XR_363215.1	uncharacterized LOC102575306	XLOC_012239	LOC102566083	-1.56	6.57E-03	XR_363368.1	uncharacterized LOC102566083
XLOC_009566	ELN	2.83	2.63E-03	XM_006267934.1	elastin	XLOC_001633	ERBB4	-1.54	2.63E-03	XM_006259492.1	v-erb-b2 avian erythroblastic leukemia viral oncogene homolog 4
XLOC_009565	LOC102574916	2.62	2.63E-03	XR_363212.1	uncharacterized LOC102574916	XLOC_003435	LOC102566361	-1.51	2.63E-03	XM_006261381.1	ovotransferrin-like
XLOC_019721	HOCX10	2.56	2.63E-03	XM_006278447.1	homeobox C10	XLOC_017010	AQP2	-1.51	2.63E-03	XM_006275689.1	aquaporin 2 (collecting duct)
XLOC_011459	COLBA2	2.47	2.63E-03	XM_006269879.1	collagen, type VIII, alpha 2	XLOC_010680	LOC102561252	-1.44	2.63E-03	XM_006269073.1	phospholipase A2 inhibitor subunit gamma B-like
XLOC_003079	SEZBL	2.29	1.54E-02	XM_006261766.1	seizure related 6 homolog (mouse)-like	XLOC_019803	LOC102559056	-1.44	2.63E-03	XM_006278518.1	protein MRP-126-like
XLOC_017827	PTHHL	2.22	4.64E-02	XM_006276542.1	parathyroid hormone-like hormone	XLOC_003171	LOC102570382	-1.44	2.63E-03	XM_006259197.1	WAP four-disulfide core domain protein 5-like
XLOC_006201	PLAC9	2.19	2.63E-03	XM_006264408.1	placenta-specific 9, transcript variant X2	XLOC_017214	LOC102567978	-1.44	2.63E-03	XM_006275897.1	myeloid protein 1-like
XLOC_015777	MPZ	1.99	4.00E-02	XM_006274464.1	myelin protein zero	XLOC_000780	LOC102561446	-1.43	4.56E-02	XM_006258588.1	urotensin-2 receptor-like
XLOC_001548	SMOC2	1.96	2.63E-03	XM_006259389.1	SPARC related modular calcium binding 2	XLOC_015972	RFX3	-1.40	3.67E-02	XM_006274655.1	regulatory factor X, 3 (influences HLA class II expression)
XLOC_010405	OSTN	1.95	2.63E-03	XM_006268897.1	osteocrin	XLOC_008040	LOC102574911	-1.39	2.85E-02	XM_006266302.1	FRAS1-related extracellular matrix protein 1-like
XLOC_020025	ACTG2	1.74	2.63E-03	XM_006278736.1	actin, gamma 2, smooth muscle, enteric, transcript variant X2	XLOC_019726	HOCX5	-1.39	3.58E-02	XM_006278452.1	homeobox C5
XLOC_002667	CNL3	1.72	2.63E-03	XM_006260587.1	ceroid-lipofuscinosis, neuronal 3	XLOC_010500	LRP2	-1.34	2.63E-03	XM_006268878.1	low density lipoprotein receptor-related protein 2
XLOC_020053	LOC102563158	1.65	1.54E-02	XM_006278776.1	acidic mammalian chitinase-like	XLOC_009221	LOC102565053	-1.28	2.63E-03	XM_006267562.1	lipocalin-like
XLOC_002638	SYNPO	1.65	2.63E-03	XM_006260555.1	synaptopodin	XLOC_012895	TGM3	-1.26	2.63E-03	XM_006271463.1	transglutaminase 3
XLOC_006415	LOC102561161	1.61	2.63E-03	XM_006264659.1	peripherin-like	XLOC_000012	LOC102558385	-1.26	4.79E-02	XM_006257745.1	serpin B4-like
XLOC_004313	CNN1	1.59	2.63E-03	XM_006262326.1	calponin 1, basic, smooth muscle	XLOC_019398	LOC102575717	-1.23	3.83E-02	XM_006278115.1	chromodomain-helicase-DNA-binding protein 6-like
XLOC_016003	LOC102573440	1.59	2.63E-03	XM_006274666.1	microfibril-associated glycoprotein 4-like, transcript variant X1	XLOC_006977	MAMDC2	-1.21	2.63E-03	XM_006265197.1	MAM domain containing 2
XLOC_012124	MFPAT5	1.56	2.63E-03	XM_006270600.1	microfibrillar associated protein 5	XLOC_006532	LOC102565592	-1.19	2.63E-03	XM_006264753.1	BPT1/Kunitz domain-containing protein-like
XLOC_019573	LOC102561818	1.56	2.63E-03	XM_006278306.1	class I histocompatibility antigen, Gogo-C*0203 alpha chain-like	XLOC_009391	LOC102566850	-1.17	2.63E-03	XM_006267730.1	FRAS1-related extracellular matrix protein 2-like
XLOC_012148	CDDC3	1.56	1.27E-02	XM_006270625.1	coiled-coil domain containing 3	XLOC_0030663	LOC102565963	-1.17	4.73E-03	XM_006261629.1	tripartite motif-containing protein 16-like
XLOC_017122	LOC102574633	1.54	4.25E-02	XM_006275810.1	cytochrome P450 2A5-like	XLOC_001445	HMG2A	-1.16	4.73E-03	XM_006259276.1	high mobility group AT-hook 2
XLOC_010746	ACTA2	1.54	2.63E-03	XM_006269140.1	actin, alpha 2, smooth muscle, aorta	XLOC_002312	LOC102575826	-1.15	2.75E-02	XM_006260198.1	autism susceptibility gene 2 protein-like
XLOC_017091	LOC102567104	1.53	1.13E-02	XM_006275781.1	paired mesoderm homeobox protein 1-like	XLOC_003689	LOC102572382	-1.13	2.35E-02	XM_006261657.1	transcription factor TFIIB component B' homolog
XLOC_003144	INHA	1.53	1.54E-02	XM_006261090.1	inhibin, alpha	XLOC_012095	ANKEF1	-1.10	4.33E-02	XM_006270570.1	ankyrin repeat and EF-hand domain containing 1
XLOC_000984	LMD01	1.53	2.63E-03	XM_006258800.1	leiomodin 1 (smooth muscle)	XLOC_005290	CRISPLD2	-1.09	2.63E-03	XM_006263385.1	cysteine-rich secretory protein LCLL domain containing 2
XLOC_020158	LOC102572993	1.47	4.48E-02	XM_006278906.1	neuronal acetylcholine receptor subunit alpha-4-like	XLOC_011214	LOC102558416.L	-1.05	4.94E-02	XM_006269636.1, XM_006261269.1	centrosome-associated protein 350-like
XLOC_005991	WSCD2	1.47	2.63E-03	XM_006264170.1	WSC domain containing 2	XLOC_010298	OTGL	-1.00	8.24E-03	XM_006268682.1	otogelin-like
XLOC_016496	FBLN2	1.47	2.63E-03	XM_006275174.1	fibulin 2	XLOC_018953	LOC102562523	-1.00	6.57E-03	XM_006277684.1	lysosome g-like
XLOC_008971	STK32B	1.44	3.92E-02	XM_006267315.1	serine/threonine kinase 32B	XLOC_000408	PP1R17	-0.98	2.63E-03	XM_006258196.1	protein phosphatase 1, regulatory subunit 17
XLOC_010986	TUBB3	1.43	2.63E-03	XM_006269387.1	tubulin, beta 3 class III	XLOC_009056	LOC102561092	-0.98	2.85E-02	XM_006267396.1	cysteine-rich venom protein helothermine-like
XLOC_006235	PRDM6	1.43	8.24E-03	XM_006264455.1	PR domain containing 6	XLOC_000041	LOC102566578	-0.97	2.63E-03	XM_006257779.1	avidin-like
XLOC_014102	SEZ6	1.42	2.63E-03	XM_006272745.1	seizure related 6 homolog (mouse)	XLOC_017556	EXOC3L4	-0.94	2.85E-02	XM_006276257.1	exocyst complex component 3-like 4
XLOC_015941	LOC102576792	1.42	3.41E-02	XM_006274617.1	CUGBP1 Elav-like family member 3-like	XLOC_017513	SERPNB5	-0.92	6.57E-03	XM_006276121.1	serpin peptidase inhibitor, clade B (ovalbumin), member 5
XLOC_007589	NEFH	1.41	3.75E-02	XM_006265847.1	neurofilament, heavy polypeptide	XLOC_001281	CMC2	-0.91	8.24E-03	XM_006259101.1	C(x)-y-C motif containing 2
XLOC_007271	SLC18A1	1.38	2.63E-03	XM_006265496.1	solute carrier family 18 (vesicular monoamine transporter), member 1	XLOC_001335	IGSF10	-0.90	2.63E-03	XM_006259179.1	immunoglobulin superfamily, member 10
XLOC_013166	APCD11L	1.37	2.63E-03	XM_006271755.1	adenomatous polyposis coli down-regulated 1-like	XLOC_003858	CERC5	-0.89	2.65E-02	XM_006261832.1	cat eye syndrome chromosome region, candidate 5
XLOC_013674	LOC102570506	1.37	3.04E-02	XM_006272278.1	kallikrein 15-like	XLOC_013422	PREM1	-0.87	1.13E-02	XM_006272014.1	FRAS1 related extracellular matrix 1
XLOC_012067	CTGF	1.36	2.63E-03	XM_006270533.1	connective tissue growth factor	XLOC_002617	DCCD2	-0.86	2.56E-02	XM_006260544.1	doublecortin domain containing 2
XLOC_006416	LOC102561391	1.36	2.63E-03	XM_006264660.1	peripherin-like	XLOC_015736	TNFSF19	-0.85	3.67E-02	XM_006274425.1	tumor necrosis factor receptor superfamily, member 19
XLOC_001095	PP2R2C	1.32	4.00E-02	XM_006258906.1	protein phosphatase 2, regulatory subunit B, gamma	XLOC_000499	ERC1	-0.85	4.25E-02	XM_006258283.1	ELKS/RAB6-interacting/CAST family member 1, transcript variant
XLOC_015709	LOC102576789	1.30	9.85E-03	XM_006274392.1	protein kinase C and casein kinase substrate in neurons protein 2-like	XLOC_003858	CERC2	-0.84	1.90E-02	XM_006261831.1	cat eye syndrome chromosome region, candidate 2
XLOC_004793	LOC102559075	1.30	2.63E-03	XM_006262837.1	endonuclease domain-containing 1 protein-like	XLOC_009660	HMBQX1	-0.84	1.66E-02	XM_006268031.1	homeobox containing 1
XLOC_014533	CPLX3	1.29	3.75E-02	XM_006273142.1	complexin 3	XLOC_013231	CCDC181	-0.83	2.35E-02	XM_006271813.1	coiled-coil domain containing 181, transcript variant X2
XLOC_001463	LOC102574572	1.26	2.63E-03	XM_006259299.1	somatostatin-2-like	XLOC_019823	LOC102564018	-0.83	2.63E-03	XM_006278540.1	cysteine-rich venom protein helothermine-like
XLOC_004684	COL1A1	1.25	2.63E-03	XM_006262766.1	collagen, type XI, alpha 1, transcript variant X3	XLOC_014022	BMP5	-0.81	4.73E-03	XM_006272661.1	bone morphogenic protein 5
XLOC_003593	AMH	1.24	2.63E-03	XM_006261559.1	anti-Mullerian hormone	XLOC_003183	SLC22A5	-0.81	3.23E-02	XM_006261139.1	solute carrier family 22 (organic cation/carnitine transporter), mem
XLOC_002641	GPK3	1.23	2.63E-03	XM_006260571.1	glutathione peroxidase 3 (plasma)	XLOC_016502	HIPK2	-0.80	2.63E-03	XM_006275178.1	homeodomain interacting protein kinase 2, transcript variant X2
XLOC_006139	S100A13	1.22	2.63E-03	XM_006264341.1	S100 calcium binding protein A13	XLOC_011513	DNAI1	-0.78	8.24E-03	XM_006269950.1	dynein, axonemal, intermediate chain 1
XLOC_010796	LOC102570032	1.20	2.63E-03	XM_006269192.1	NAC-alpha domain-containing protein 1-like	XLOC_016041	LOC102564391	-0.78	1.54E-02	XM_006274733.1	relaxin receptor 1-like
XLOC_013888	CFD	1.20	2.63E-03	XM_006272513.1	complement factor D (adipsin)	XLOC_001261	LOC102563321	-0.74	2.63E-03	XM_006259088.1	hemoglobin subunit epsilon-like
XLOC_011709	LOC102568633	1.20	2.63E-03	XM_006270170.1	probable vesicular acetylcholine transporter-A-like	XLOC_014833	SRGN	-0.73	4.25E-02	XM_006273478.1	serglycan
XLOC_004513	LOC102570622	1.18	8.24E-03	XM_006262559.1	insulin gene enhancer protein ISL-1-like	XLOC_014934	LOC102576022	-0.73	4.08E-02	XM_006273577.1	parathyroid hormone/parathyroid hormone-related peptide receptor
XLOC_010356	LOC102575076	1.18	2.63E-03	XM_006268737.1	butyrophilin subfamily 1 member A1-like	XLOC_005365	IGF1R	-0.72	2.01E-02	XM_006263474.1	insulin-like growth factor 1 receptor
XLOC_014375	LOC102573199	1.16	2.63E-03	XM_006273013.1	chromogranin A-like	XLOC_000170	ATP8V1C2	-0.71	2.63E-03	XM_006257922.1	ATPase, H+-transporting, lysosomal 42kDa, V1 subunit C2
XLOC_017562	B3GAT1	1.16	3.14E-02	XM_006276261.1	beta-1,3-glycuronidyltransferase 1 (glucuronosyltransferase P)	XLOC_015268	LOC102564300	-0.70	3.92E-02	XM_006273932.1	zinc finger protein 42-like
XLOC_019688	LOC102568737	1.15	1.54E-02	XR_363851.1	uncharacterized LOC102568737	XLOC_001438	SOGA1	-0.70	4.73E-03	XM_006259266.1	suppressor of glucose, autophagy associated 1
XLOC_015967	SCARA3	1.15	1.13E-02	XM_006274653.1	scavenger receptor class A, member 3	XLOC_004476	DCBLD1	-0.70	2.24E-02	XM_006262521.1	uncharacterized LOC102564479
XLOC_000204	UPC2	1.14	2.63E-03	XM_006257947.1	uncoupling protein 2 (mitochondrial, proton carrier)	XLOC_007449	SLC6A12	-0.70			

XLOC_002973	DBH	1.12	2.63E-03	XM_006260879.1	dopamine beta-hydroxylase (dopamine beta-monoxygenase)	XLOC_003595	JSRP1	-0.69	1.90E-02	XM_006261560.1	junctional sarcoplasmic reticulum protein 1
XLOC_008706	CADPS	1.09	2.63E-03	XM_006267004.1	Ca++-dependent secretion activator	XLOC_018110	CERP350	-0.69	3.50E-02	XM_006267681.1	centrosomal protein 350kDa
XLOC_017756	SCG2	1.09	2.63E-03	XM_006276487.1	secretogranin II	XLOC_006616	UTRN	-0.68	2.13E-02	XM_006264831.1	utrophin
XLOC_001656	APOA1	1.08	2.63E-03	XM_006259520.1	apolipoprotein A-I	XLOC_007092	ADAMTS9	-0.68	6.57E-03	XM_006265332.1	ADAM metallopeptidase with thrombospondin type 1 motif, 9
XLOC_015975	STMN4	1.08	6.57E-03	XM_006274659.1	stathmin-like 4	XLOC_015958	STC1	-0.67	2.63E-03	XM_006274642.1	stanniocalcin 1
XLOC_006687	CHGB	1.08	2.63E-03	XM_006264900.1	chromogranin B (secretogranin 1)	XLOC_019946	LOC102574878	-0.66	1.27E-02	XM_006278659.1	fatty acyl-CoA reductase 1-like
XLOC_017067	GPR116	1.08	2.65E-02	XM_006275758.1	G protein-coupled receptor 116	XLOC_007512	LOC102559932	-0.66	2.63E-03	XM_006265755.1	collagen alpha-1(XXVI) chain-like
XLOC_015418	LOC102563375	1.07	2.63E-03	XM_006274090.1	protein odd-skipped-related 1-like	XLOC_014517	EDC3	-0.66	1.27E-02	XM_006273147.1	enhancer of mRNA deadapping 3
XLOC_009120	LOC102559409	1.07	1.27E-02	XM_006267472.1	calcitonin receptor-like	XLOC_020027	TET3	-0.65	1.27E-02	XM_006278741.1	tet methylcytosine dioxygenase 3
XLOC_012101	TAGLN3	1.07	2.63E-03	XM_006270572.1	transgelin 3	XLOC_009418	SLC45A2	-0.65	4.72E-02	XM_006267764.1	solute carrier family 45, member 2
XLOC_005026	MARVELD1	1.07	1.66E-02	XM_006263087.1	MARVEL domain containing 1	XLOC_013405	ENPP5	-0.65	3.14E-02	XM_006271995.1	ectonucleotid pyrophosphatase/phosphodiesterase 5 (putative), t
XLOC_018292	LOC102570383	1.06	4.25E-02	XM_006259696.1	high affinity choline transporter 1-like	XLOC_012416	ARVCF	-0.64	9.85E-03	XM_006270920.1	armadillo repeat gene deleted in velocardiofacial syndrome
XLOC_004860	LOC102574734	1.04	2.63E-03	XM_006262895.1	procollagen C-endopeptidase enhancer 1-like	XLOC_000457	LOC102576424	-0.61	2.01E-02	XM_006258238.1	heat shock factor protein 3-like
XLOC_003490	F8	1.04	2.63E-03	XM_006261445.1	coagulation factor VIII, procoagulant component	XLOC_013636	LOC102560955	-0.61	2.63E-03	XM_006272242.1	protein NEL-like
XLOC_010569	CDH19	1.02	1.13E-02	XM_006268948.1	cadherin 19, type 2	XLOC_000177	LOC102561900	-0.60	1.78E-02	XM_006257927.1	semaphorin-3D-like
XLOC_018747	PDZD7	1.01	8.24E-03	XM_006277481.1	PDZ domain containing 7	XLOC_008172	PLEKH11	-0.60	2.46E-02	XM_006266446.1	pleckstrin homology domain containing, family H (with MyTH4 dom
XLOC_014542	ISLR2	1.00	2.63E-03	XM_006273158.1	immunoglobulin superfamily containing leucine-rich repeat 2, transcript	XLOC_001486	AHCYL1	-0.60	2.63E-03	XM_006259321.1	adenosylhomocysteinase-like 1, transcript variant X1
XLOC_000062	ADAM19	1.00	4.00E-02	XM_006257005.1	ADAM metallopeptidase domain 19	XLOC_004183	HYDIN	-0.59	3.32E-02	XM_006262199.1	HYDIN, axonemal central pair apparatus protein
XLOC_012889	SLC35C2	1.00	2.63E-03	XM_006271460.1	solute carrier family 35 (GDP-fucose transporter), member C2	XLOC_014046	MRP1P	-0.59	2.35E-02	XM_006272696.1	myosin phosphatase Rho interacting protein
XLOC_002692	LOC102575737	0.99	2.63E-03	XM_006260622.1	cytochrome P450 11B, mitochondrial-like	XLOC_006622	MANB1	-0.59	3.58E-02	XM_006264834.1	mannosidase, alpha, class 1B, member 1
XLOC_008364	HEY2	0.97	2.63E-03	XM_006266650.1	hes-related family bHLH transcription factor with YRPW motif 2, transcr	XLOC_008408	CALB1	-0.59	1.78E-02	XM_006266690.1	calbindin 1, 28kDa
XLOC_002697	LOC1025747810	0.97	1.27E-02	XM_006260618.1	riboflavin transporter 2-like	XLOC_015444	TRPM6	-0.59	1.54E-02	XM_006274120.1	transient receptor potential cation channel, subfamily M, member 6
XLOC_006431	NCKAP5L	0.97	2.63E-03	XM_006264647.1	NCK-associated protein 5-like	XLOC_004420	PAMR1	-0.58	1.13E-02	XM_006262454.1	peptidase domain containing associated with muscle regeneration
XLOC_000564	LOC102565100	0.97	2.63E-03	XM_006256355.1	heart- and neural crest derivatives-expressed protein 2-like	XLOC_011288	ATP4A	-0.58	2.63E-03	XM_006269708.1	ATPase, H+K+ -exchanging, alpha polypeptide
XLOC_004236	COL12A1	0.97	2.63E-03	XM_006262249.1	collagen, type XI, alpha 1	XLOC_019410	LOC102558530	-0.58	3.83E-02	XM_006278126.1	myelin and lymphocyte protein-like, transcript variant X2
XLOC_000656	COL1A2	0.96	4.73E-03	XM_009259452.1	collagen, type I, alpha 2	XLOC_011042	STGALNAC4	-0.58	1.90E-02	XM_006269463.1	ST6 (alpha-N-acetylgalactosaminyl-2,3-beta-galactosyl-1,3)-N-acetylgl
XLOC_011603	LOC102560255	0.96	3.41E-02	XM_006270048.1	cytochrome P450 1B1-like	XLOC_004919	LOC102575133	-0.58	1.27E-02	XM_006262981.1	zinc finger protein 55A-like
XLOC_014873	ANK1	0.95	2.63E-03	XM_006273519.1	ankyrin 1, erythrocyte	XLOC_011067	GNE	-0.58	1.13E-02	XM_006269485.1	glucosamine (UDP-N-acetyl)-2-epimerase/N-acetylmannosamine k
XLOC_002686	TONS1	0.95	2.63E-03	XM_006260614.1	tonosku-like, DNA repair protein	XLOC_011207	UGT8	-0.57	4.56E-02	XM_006269623.1	UDP glycosyltransferase 8, transcript variant X1
XLOC_017270	LOC102573067	0.94	4.73E-03	XM_006275961.1	reticulin-4 receptor-like, transcript variant X2	XLOC_001024	ZFXH3	-0.57	1.54E-02	XM_006258919.1	zinc finger homeobox 3
XLOC_018332	LOC102565404	0.94	1.90E-02	XM_006277058.1	collagen alpha-(1) chain-like	XLOC_015778	LOC102574469	-0.57	4.56E-02	XM_006274466.1	uncharacterized LOC102574469
XLOC_015332	LOC102560570	0.94	2.63E-03	XM_006273996.1	desintegrin and metalloproteinase domain-containing protein 19-like	XLOC_003740	PKHD1	-0.57	2.46E-02	XM_006261706.1	polycystic kidney and hepatic disease 1 (autosomal recessive)
XLOC_004652	LOC102565041	0.92	1.27E-02	XM_006262695.1	apelin receptor A-like	XLOC_003155	CLDN8	-0.56	2.13E-02	XM_006261102.1	claudin 8
XLOC_013173	LOC102558340	0.92	1.41E-02	XM_006271749.1	tubulin beta-6 chain-like	XLOC_017842	SGK2	-0.56	3.41E-02	XM_006276558.1	serum/glucocorticoid regulated kinase 2, transcript variant X2
XLOC_003701	LOC102575599	0.92	2.63E-03	XM_006261670.1	cytochrome P450 2K4-like	XLOC_018884	KHL3	-0.55	2.85E-02	XM_006277619.1	kelch-like family member 3
XLOC_008099	CYHR1	0.91	1.41E-02	XM_006267338.1	cysteine/histidine-rich 1	XLOC_008805	EFHC2	-0.55	4.25E-02	XM_006271114.2	EF-hand domain (C-terminal) containing 2
XLOC_012665	LOC102563914	0.91	3.50E-02	XM_006271199.1	17-beta-hydroxysteroid dehydrogenase type 6-like	XLOC_009298	PPP1R3C	-0.55	3.41E-02	XM_006267634.1	protein phosphatase 1, regulatory subunit 3C
XLOC_002601	FNDC1	0.90	2.63E-03	XM_006260531.1	fibronectin type III domain containing 1	XLOC_014252	SLC6A18	-0.55	4.00E-02	XM_006269708.1	solute carrier family 6 (neutral amino acid transporter), member 18
XLOC_018279	MMP11	0.90	4.73E-03	XM_006277009.1	matrix metalloproteinase 11 (stromelysin 3)	XLOC_009419	ADAMTS12	-0.54	3.23E-02	XM_006267776.1	ADAM metallopeptidase with thrombospondin type 1 motif, 12
XLOC_004294	EPOR	0.90	2.63E-03	XM_006262351.1	erythropoietin receptor	XLOC_014327	LOC102562589	-0.53	2.13E-02	XM_006272978.1	probable glutamate receptor-like
XLOC_010654	GATA1	0.90	1.13E-02	XM_006269039.1	GATA binding protein 1 (globin transcription factor 1)	XLOC_005663	LOC102575135	-0.53	2.13E-02	XM_006263807.1	ammonium transporter Rh type C-like
XLOC_019338	TAGLN	0.89	2.63E-03	XM_006270869.1	transgelin	XLOC_002541	LOC102572301	-0.53	3.50E-02	XM_006260435.1	suppressor of hairless protein homolog, transcript variant X2
XLOC_011267	LOC102572104	0.88	2.63E-03	XM_006269693.1	reticulin-1A-like, transcript variant X3	XLOC_009563	LOC102574213	-0.53	3.14E-02	XM_006267928.1	claudin-4-like
XLOC_011810	ATP1A3	0.88	2.63E-03	XM_006270272.1	ATPase, Na+/K+ transporting, alpha 3 polypeptide	XLOC_017095	SDC4	-0.53	4.08E-02	XM_006275788.1	syndecan 4
XLOC_011442	LOC102562725	0.88	3.67E-02	XM_006269898.1	angiopoietin-2-like	XLOC_003884	FABP5	-0.53	3.32E-02	XM_006261858.1	fatty acid binding protein 5 (psoriasis-associated)
XLOC_015371	TAL1	0.88	2.63E-03	XM_006274037.1	T-cell acute lymphocytic leukemia 1	XLOC_004416	LOC102563884	-0.52	2.85E-02	XM_006262449.1	polycomb-1-like
XLOC_008080	LOC102572026	0.88	2.63E-03	XM_006267109.1	GDNT family receptor alpha-4-like	XLOC_004125	BNC1	-0.52	3.23E-02	XM_006262115.1	basonuclin 1
XLOC_001140	SOX10	0.86	6.57E-03	XM_006259855.1	SRY (sex determining region Y)-box 10	XLOC_007725	LOC102573022	-0.51	2.85E-02	XM_006265973.1	protein sidekick-1-like
XLOC_004098	ADAMTS15	0.85	2.63E-03	XM_006262089.1	ADAM metallopeptidase with thrombospondin type 1 motif, 15	XLOC_017707	TGFBI	-0.50	2.94E-02	XM_006276411.1	transforming growth factor, beta-induced, 68kDa
XLOC_019944	RARG	0.84	2.63E-03	XM_006278647.1	retinoic acid receptor, gamma	XLOC_003745	LOC102566123	-0.50	2.94E-02	XM_006261707.1	spondin-1-like
XLOC_020135	SLC5A2	0.84	2.63E-03	XM_006278885.1	solute carrier family 5 (sodium/glucose cotransporter), member 2	XLOC_013512	GJA1	-0.50	2.65E-02	XM_006272096.1	gap junction protein, alpha 1, 43kDa
XLOC_018671	THBS2	0.83	2.63E-03	XM_006277394.1	thrombospondin 2, transcript variant X1	XLOC_015907	RCOR1	-0.50	3.67E-02	XM_006274592.1	REST corepressor 1
XLOC_012997	SLC4A1	0.82	2.63E-03	XM_006271577.1	solute carrier family 4 (anion exchanger), member 1	XLOC_016831	FRAS1	-0.50	3.58E-02	XM_006275515.1	Fraser syndrome 1
XLOC_010400	LOC102566853	0.82	4.40E-02	XM_006268788.1	neurofilament, light polypeptide	XLOC_008569	DDX6	-0.50	4.33E-02	XM_006266836.1	DEAD (Asp-Glu-Ala-Asp) box helicase 6
XLOC_009338	ITGA7	0.81	2.63E-03	XM_006267700.1	integrin, alpha 7	XLOC_010884	NUDT4	-0.49	3.23E-02	XM_006262985.1	nudix (nucleoside diphosphate linked moiety X)-type motif 4
XLOC_010738	LOC102575314	0.81	2.63E-03	XM_006269131.1	steroid 17beta-hydroxylase-like	XLOC_004912	LOC102575365	-0.47	4.87E-02	XM_006262982.1	transmembrane protein 72-like
XLOC_014076	PIPOX	0.80	1.13E-02	XM_006272746.1	pepcidic acid oxidase	XLOC_007028	LOC102573251	-0.46	3.83E-02	XM_006265256.1	aquaporin-3-like
XLOC_002221	LOC102569293	0.80	3.32E-02	XM_006260100.1	glycine N-acyltransferase-like protein 3-like	XLOC_009696	LOC102563028	-inf	2.63E-03	XM_006268040.1	histone H2B 1/2/3/4/6-like
XLOC_001649	KLF2	0.79	2.63E-03	XM_006259500.1	Kruppel-like factor 2	XLOC_010349	LOC102573503	-inf	2.63E-03	XR_363249.1	uncharacterized LOC102573503
XLOC_018099	NEFL	0.79	2.63E-03	XM_006276810.1	neurofilament, light polypeptide	XLOC_017996	LOC102559443	-inf	1.27E-02	XR_363733.1	uncharacterized LOC102559443
XLOC_011416	ACTA1	0.78	2.63E-03	XM_006269852.1	actin, alpha 1, skeletal muscle	XLOC_006509	LOC102558484	-inf	2.46E-02	XR_363004.1	uncharacterized LOC102558484

XLOC_014144	DQX1	0.71	3.58E-02	XM_006272784.1	DEAQ box RNA-dependent ATPase 1
XLOC_004875	ECEL1	0.70	2.85E-02	XM_006262936.1	endothelin converting enzyme-like 1
XLOC_006178	LOC102572775	0.70	4.73E-03	XM_006264382.1	mothers against decapentaplegic homolog 4-like
XLOC_008795	SLC34A1	0.69	2.63E-03	XM_006267103.1	solute carrier family 34 (type II sodium/phosphate cotransporter), member 1
XLOC_014042	SLC23A3	0.69	2.63E-03	XM_006272671.1	solute carrier family 23, member 3
XLOC_007534	CAV1	0.69	2.63E-03	XM_006265774.1	caveolin 1, caveolae protein, 22kDa
XLOC_012234	LOC102565383	0.69	2.63E-03	XM_006270714.1	neuronal acetylcholine receptor subunit alpha-7-like
XLOC_019869	LOC102571991	0.69	6.57E-03	XM_006278573.1	polymerase I and transcript release factor-like, transcript variant X2
XLOC_010742	LOC102576539	0.69	3.58E-02	XM_006269136.1	zona pellucida sperm-binding protein 3-like
XLOC_007888	STAR	0.69	1.66E-02	XM_006266133.1	steroidogenic acute regulatory protein
XLOC_003288	PGM5	0.68	4.73E-03	XM_006261237.1	phosphoglucomutase 5
XLOC_002559	LOC102577353	0.68	3.67E-02	XM_006260458.1	fibroblast growth factor 13-like, transcript variant X2
XLOC_006353	PTRF	0.68	2.63E-03	XM_006264575.1	polymerase I and transcript release factor
XLOC_003145	LOC102572230	0.67	3.50E-02	XM_006261091.1	transmembrane protein 198-B-like
XLOC_013799	TH	0.67	4.40E-02	XM_006272424.1	tyrosine hydroxylase
XLOC_000771	FRZB	0.67	2.63E-03	XM_006258581.1	frizzled-related protein
XLOC_006311	HTRA1	0.67	2.63E-03	XM_006264531.1	HtrA serine peptidase 1
XLOC_017186	CRABP2	0.67	4.73E-03	XM_006275867.1	cellular retinoic acid binding protein 2
XLOC_019005	NFKB1	0.66	4.73E-03	XM_006277754.1	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, beta
XLOC_006702	AOC1	0.66	6.57E-03	XM_006264919.1	amine oxidase, copper containing 1
XLOC_019900	TIMP1	0.66	2.63E-03	XM_006278610.1	TIMP metalloproteinase inhibitor 1
XLOC_008638	LOC102568241	0.66	2.63E-03	XM_006266925.1	von Willebrand factor-like
XLOC_015832	LOC102572203	0.66	2.63E-03	XM_006274533.1	contactin-1-like
XLOC_019890	CFP	0.66	2.63E-03	XM_006278617.1	complement factor properdin
XLOC_002077	CRIP1	0.66	1.13E-02	XM_006259954.1	cysteine-rich protein 1 (intestinal)
XLOC_015386	AP5B1	0.65	4.40E-02	XM_006274050.1	adaptor-related protein complex 5, beta 1 subunit
XLOC_005818	PTPRR	0.64	3.14E-02	XM_006263984.1	protein tyrosine phosphatase, receptor type, R
XLOC_018350	LOC102569355	0.63	2.63E-03	XM_006277074.1	collagen alpha-1(XI) chain-like
XLOC_003569	CDO1	0.63	2.63E-03	XM_006261528.1	cysteine dioxygenase type 1
XLOC_000149	BLVRB	0.63	2.63E-03	XM_006257898.1	biliverdin reductase B (flavin reductase (NADPH))
XLOC_014654	ADAMTSL4	0.62	8.24E-03	XM_006273298.1	ADAMTS-like 4
XLOC_006827	HSD17B11	0.62	2.65E-02	XM_006265040.1	hydroxysteroid (17-beta) dehydrogenase 11, transcript variant X2
XLOC_012770	OLFM2A	0.62	2.63E-03	XM_006271324.1	olfactomedin-like 2A
XLOC_011913	PRNP	0.62	1.27E-02	XM_006270385.1	prion protein
XLOC_016538	JPH2	0.61	2.85E-02	XM_006275231.1	junctophilin 2, transcript variant X1
XLOC_014143	AUP1	0.61	1.54E-02	XM_006272782.1	ancient ubiquitous protein 1
XLOC_009005	LOC102569324	0.61	6.57E-03	XM_006267352.1	vitamin D3 hydroxylase-associated protein-like
XLOC_017215	EMILIN1	0.61	2.63E-03	XM_006275898.1	elastin microfibril interfacer 1
XLOC_002134	ASS1	0.60	6.57E-03	XM_006260002.1	argininosuccinate synthase 1
XLOC_004612	LOC102574966	0.60	1.41E-02	XM_006262659.1	1,25-dihydroxyvitamin D(3) 24-hydroxylase, mitochondrial-like
XLOC_002748	SLC5A12	0.60	4.73E-03	XM_006260672.1	solute carrier family 5 (sodium/monocarboxylate cotransporter), member 12
XLOC_015712	CLEC11A	0.59	2.94E-02	XM_006274395.1	C-type lectin domain family 11, member A
XLOC_003617	MYH11	0.59	8.24E-03	XM_006261582.1	myosin, heavy chain 11, smooth muscle
XLOC_000591	DMTN	0.58	3.75E-02	XM_006258386.1	desmatin actin binding protein, transcript variant X1
XLOC_014047	TUBA4A	0.58	1.27E-02	XM_006272667.1	tubulin, alpha 4a
XLOC_014444	CPE	0.58	1.27E-02	XM_006273085.1	carboxypeptidase E
XLOC_002902	SALL2	0.56	9.85E-03	XM_006260826.1	spalt-like transcription factor 2
XLOC_015382	LOC102572890	0.56	4.73E-03	XM_006274047.1	solute carrier family 22 member 6-A-like
XLOC_010951	LOC102568868	0.56	1.41E-02	XM_006269351.1	rho-related GTP-binding protein Rho-like
XLOC_008568	TREH	0.56	4.72E-02	XM_006266854.1	trehalase (brush-border membrane glycoprotein)
XLOC_003724	ALPL	0.55	2.46E-02	XM_006261695.1	alkaline phosphatase, liver/bone/kidney
XLOC_007477	NUPR1	0.55	3.58E-02	XM_006265711.1	nuclear protein, transcriptional regulator, 1
XLOC_018173	FKBP5	0.54	2.85E-02	XM_006276891.1	FK506 binding protein 5
XLOC_004287	NFX1	0.54	1.27E-02	XM_006262319.1	nuclear factor I(X) (CCAAT-binding transcription factor), transcript variant X3
XLOC_005418	ADAMTS2	0.54	3.58E-02	XM_006263538.1	ADAM metallopeptidase with thrombospondin type 1 motif, 2
XLOC_012939	LOC102557733	0.54	2.01E-02	XM_006271508.1	fibrillin-2-like
XLOC_014691	CELSR3	0.54	4.16E-02	XM_006273334.1	cadherin, EGF LAG seven-pass G-type receptor 3
XLOC_006860	LOC102569158	0.53	3.14E-02	XM_006265079.1	protein Wnt-11-like, transcript variant X2
XLOC_006801	LOC102573333	0.53	2.56E-02	XM_006265014.1	solute carrier family 22 member 6-A-like
XLOC_008746	EEF1A2	0.53	2.01E-02	XM_006267053.1	eukaryotic translation elongation factor 1 alpha 2
XLOC_003005	LOC102574190	0.53	4.33E-02	XR_362827.1	uncharacterized LOC102574190
XLOC_011804	ERF	0.53	3.75E-02	XM_006270269.1	Ets2 repressor factor
XLOC_007478	SULT1A1	0.51	2.94E-02	XM_006265713.1	sulfotransferase family, cytosolic, 1A, phenol-prefering, member 1
XLOC_013775	LINGO1	0.51	3.14E-02	XM_006272399.1	leucine rich repeat and Ig domain containing 1, transcript variant X3
XLOC_003774	LOC102571925	0.50	1.90E-02	XM_006261728.1	tyrosine-protein kinase receptor Tie-1-like
XLOC_002042	AP3S2	0.50	3.67E-02	XM_006259906.1	adaptor-related protein complex 3, sigma 2 subunit
XLOC_019742	ITG45	0.49	3.75E-02	XM_006278464.1	integrin, alpha 5 (fibronectin receptor, alpha polypeptide)
XLOC_006411	CACNB3	0.49	4.16E-02	XM_006264650.1	calcium channel, voltage-dependent, beta 3 subunit
XLOC_000158	LTBP4	0.48	4.08E-02	XM_006257901.1	latent transforming growth factor beta binding protein 4
XLOC_000369	MCAM	0.48	2.56E-02	XM_006258155.1	melanoma cell adhesion molecule
XLOC_018524	JAG1	0.47	4.87E-02	XM_006277242.1	jagged 1
XLOC_006023	CPXM1	0.47	4.64E-02	XM_006264207.1	carboxypeptidase X (M14 family), member 1

XLOC_002679	SERPINF1	0.47	4.79E-02	XM_006260604.1	serpin peptidase inhibitor, clade F (alpha-2 antiplasmin, pigment epithelium derived factor), member 1
XLOC_000048	LOC102564090	0.47	4.40E-02	XM_006257769.1	tropomyosin alpha-4 chain-like, transcript variant X4
XLOC_015969	CLU	0.47	4.79E-02	XM_006274651.1	clusterin
XLOC_000387	TAC1	inf	2.63E-03	XM_006258170.1	tachykinin, precursor 1, transcript variant X2
XLOC_019004	LOC102558904	inf	2.63E-03	XM_006277748.1	synaptosomal-associated protein 25-like
XLOC_003232	LOC102575047	inf	3.41E-02	XR_362840.1	uncharacterized LOC102575047
XLOC_020082	LOC102569673	inf	3.50E-02	XR_363878.1	uncharacterized LOC102569673

Day 6 (FPT) vs Day 12 (FPT)											
Up-regulated						Down-regulated					
Gene ID	Gene Symbol	LOG2(FC)	FDR	RefSeq Accession	Description	Gene ID	Gene Symbol	LOG2(FC)	FDR	RefSeq Accession	Description
XLOC_014016	LOC102561033	2.43	2.63E-03	XM_006272653.1	mesotocin receptor-like	XLOC_001261	LOC102563321	-3.82	2.63E-03	XM_006259088.1	hemoglobin subunit epsilon-like
XLOC_009036	TBXA2R	2.22	2.63E-03	XM_006267376.1	thromboxane A2 receptor	XLOC_010405	OSTN	-1.90	2.63E-03	XM_006268798.1	osteocrin
XLOC_017690	WIF1	2.15	2.63E-03	XM_006276396.1	WNT inhibitory factor 1	XLOC_011459	COL8A2	-1.80	2.63E-03	XM_006269879.1	collagen, type VIII, alpha 2
XLOC_001005	LOC102577040	2.15	2.63E-03	XM_006258812.1	forkhead box protein L2-like	XLOC_009120	LOC102559409	-1.49	2.63E-03	XM_006267472.1	calcitonin receptor-like
XLOC_013006	LOC102575860	2.01	2.63E-03	XM_006271581.1	potassium voltage-gated channel subfamily H member 7-like	XLOC_002692	LOC102575737	-1.49	2.63E-03	XM_006260622.1	cytochrome P450 11B, mitochondrial-like
XLOC_010742	LOC102576539	1.89	2.63E-03	XM_006269136.1	zona pellucida sperm-binding protein 3-like	XLOC_002221	LOC102569293	-1.29	2.63E-03	XM_006260100.1	glycine N-acyltransferase-like protein 3-like
XLOC_002517	LOC102565261	1.82	6.57E-03	XR_362801.1	uncharacterized LOC102565261	XLOC_006235	PRDM6	-1.28	8.24E-03	XM_006264455.1	PR domain containing 6
XLOC_002516	HSD17B1	1.78	2.63E-03	XM_006260402.1	hydroxysteroid (17-beta) dehydrogenase 1, transcript variant X2	XLOC_007791	LOC102569784	-1.25	2.63E-03	XM_006266039.1	collagen alpha-1(VIII) chain-like
XLOC_015777	Mpz	1.75	2.63E-03	XM_006274464.1	myelin protein zero	XLOC_019573	LOC102561818	-1.22	2.63E-03	XM_006278306.1	class I histocompatibility antigen, Gogo-C-2023 alpha chain-like
XLOC_017214	LOC102557978	1.70	2.63E-03	XM_006275897.1	myeloid protein 1-like	XLOC_001548	SMOC2	-1.18	2.63E-03	XM_006259389.1	SPARC related modular calcium binding 2
XLOC_010819	CYGB	1.65	2.63E-03	XM_006269221.1	cytoglobin, transcript variant X1	XLOC_003886	LOC102559155	-1.17	2.63E-03	XM_006261841.1	hemoglobin subunit pi-like
XLOC_013393	LOC102557664	1.61	2.63E-03	XM_006271986.1	acyl-CoA-binding protein-like	XLOC_012722	TTR	-1.16	2.63E-03	XM_006271257.1	transferrin
XLOC_004830	LOC102570004	1.57	2.63E-03	XM_006262875.1	galanin receptor type 2-like	XLOC_002667	CLN3	-1.11	2.63E-03	XM_006260587.1	ceroid-lipofuscinosis, neuronal 3
XLOC_013143	LOC102567788	1.53	2.63E-03	XM_006271712.1	calretinin-like	XLOC_004684	COL11A1	-1.04	2.63E-03	XM_006262736.1	collagen, type XI, alpha 1, transcript variant X3
XLOC_003617	MYH1	1.42	2.63E-03	XM_006261582.1	myosin, heavy chain 11, smooth muscle	XLOC_005582	THBS4	-1.04	2.63E-03	XM_006263716.1	thrombospondin 4
XLOC_000795	PCSK9	1.40	2.63E-03	XM_006258599.1	proprotein convertase subtilisin/kexin type 9	XLOC_005250	NOV	-1.00	2.63E-03	XM_006263356.1	nephroblastoma overexpressed
XLOC_000532	COL4A4	1.39	2.63E-03	XM_006258324.1	collagen, type IV, alpha 4	XLOC_003701	LOC102575599	-0.99	2.63E-03	XM_006261670.1	cytochrome P450 2K-like
XLOC_014642	FABP7	1.39	2.63E-03	XM_006273281.1	fatty acid binding protein 7, brain	XLOC_013480	LOC102559498	-0.94	2.63E-03	XM_006272069.1	hemoglobin subunit beta-like
XLOC_011490	LOC102570959	1.35	2.63E-03	XM_006269934.1	proactivator polypeptide-like	XLOC_004274	GJA5	-0.91	2.63E-03	XM_006262278.1	gap junction protein, alpha 5, 40kDa
XLOC_009583	NNR1	1.27	6.57E-03	XM_006267940.1	neuritin 1	XLOC_016496	FBLN2	-0.90	2.63E-03	XM_006275174.1	fibulin 2
XLOC_003119	GLDN	1.25	2.63E-03	XM_006261068.1	gliomedin	XLOC_017186	CRABP2	-0.88	2.63E-03	XM_006275867.1	cellular retinol acid binding protein 2
XLOC_017738	NOS2	1.21	4.73E-03	XM_006278456.1	nitric oxide synthase 2, inducible	XLOC_012067	CTGF	-0.87	2.63E-03	XM_006270533.1	connective tissue growth factor
XLOC_020001	LOC102567971	1.18	2.63E-03	XM_006278707.1	steroid 17-alpha-hydroxylase/17,20 lyase-like	XLOC_013013	OIT3	-0.86	2.63E-03	XM_006271585.1	oncoprotein induced transcript 3
XLOC_012957	UPK1B	1.18	2.63E-03	XM_006275128.1	uroplakin 1B	XLOC_001517	LOC102568516	-0.84	2.63E-03	XM_006263359.1	glycine amidinotransferase, mitochondrial-like
XLOC_015124	PSAT1	1.16	2.63E-03	XM_006273773.1	phosphoserine aminotransferase 1, transcript variant X1	XLOC_005061	NDNF	-0.82	2.63E-03	XM_006263128.1	neuron-derived neurotrophic factor, transcript variant X2
XLOC_020119	TNNI2	1.15	2.63E-03	XM_006278838.1	troponin I type 2 (skeletal, fast)	XLOC_001360	LOC102567816	-0.81	8.24E-03	XM_006259186.1	LIM/homeobox protein LMX-1.2-like
XLOC_000524	COL4A3	1.12	2.63E-03	XM_006258325.1	collagen, type IV, alpha 3 (Glycopaste antigen)	XLOC_015332	LOC102560570	-0.81	2.63E-03	XM_006273996.1	disintegrin and metalloproteinase domain-containing protein 19-like
XLOC_014542	ISLR2	1.08	2.63E-03	XM_006273158.1	immunoglobulin superfamily containing leucine-rich repeat 2, transcript variant X1	XLOC_013007	ACE	-0.80	2.63E-03	XM_006271571.1	angiotensin I converting enzyme
XLOC_015182	LM30	1.05	2.63E-03	XM_006273840.1	LM domain only 3 (rhombotin-like 2), transcript variant X5	XLOC_000440	LOC102573225	-0.79	8.24E-03	XM_006258225.1	GDFN family receptor alpha-4-like
XLOC_009637	MYCL	1.04	2.63E-03	XM_006267966.1	v-myc avian myelocytomatis viral oncogene lung carcinoma derived homolog	XLOC_002638	SYNPO	-0.78	2.63E-03	XM_006260565.1	synaptosomal
XLOC_002739	LOC102566194	1.04	2.63E-03	XM_006260660.1	nuclear receptor subfamily 5 group A member 2-like	XLOC_016867	LOC102570362	-0.77	2.63E-03	XM_006275551.1	3 beta-hydroxysteroid dehydrogenase/Delta-5->4-isomerase-like
XLOC_002887	PWIL1	1.00	2.63E-03	XM_006260910.1	piwi-like RNA-mediated gene silencing 1	XLOC_017899	LOC102574476	-0.77	8.05E-03	XM_00627614.1	uncharacterized LOC102574476
XLOC_013332	MDCA1	0.97	2.63E-03	XM_006271918.1	MDA domain containing glycosylphosphateisitol anchor 1	XLOC_017984	FOXC2	-0.75	2.63E-03	XM_006276695.1	forkhead box C2 (MFH-1, mesenchyme forkhead 1)
XLOC_016705	MLLT11	0.96	2.63E-03	XM_006275396.1	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 11	XLOC_018212	LOC102575256	-0.74	4.73E-03	XM_006276937.1	zinc finger protein 655-like
XLOC_004826	RHBDL1	0.95	2.63E-03	XM_006262887.1	rhomboid, veinlet-like 1 (Drosophila)	XLOC_018037	NPHS1	-0.73	2.63E-03	XM_006276765.1	nephrosis 1, congenital, Finnish type (nephrin)
XLOC_003317	DMRT1	0.95	2.63E-03	XM_006261265.1	doublesex and mab-3 related transcription factor 1, transcript variant X1	XLOC_012898	SLC25C2	-0.72	2.63E-03	XM_006271460.1	solute carrier family 35 (GDP-fucose transporter), member C2
XLOC_003299	SNC4	0.95	9.85E-03	XM_006261248.1	synuclein, alpha (non A4 component of amyloid precursor)	XLOC_010738	LOC102575314	-0.71	2.63E-03	XM_006269131.1	steroid 21-hydroxylase-like
XLOC_000903	PLP1	0.94	2.63E-03	XM_006258708.1	proteolipid protein 1, transcript variant X1	XLOC_018106	NPHS2	-0.70	2.63E-03	XM_006276826.1	nephrosis 2, idiopathic, steroid-resistant (podocin)
XLOC_019253	LOC102559669	0.93	2.63E-03	XM_006277993.1	frizzled-10like	XLOC_015734	SHISA2	-0.69	2.63E-03	XM_006276427.1	shisa family member 2
XLOC_008416	LOC102561391	0.91	2.63E-03	XM_006264660.1	peripherin-like	XLOC_007703	LOC102567612	-0.68	9.85E-03	XM_006265914.1	cytochrome P450 2B6-like
XLOC_003006	LOC102574581	0.90	2.63E-03	XM_006260931.1	myosin-binding protein C, cardiac-type-like	XLOC_016538	JPH2	-0.68	6.57E-03	XM_006275231.1	junctophilin 2, transcript variant X1
XLOC_015259	LOC102562273	0.89	4.73E-03	XR_363545.1	uncharacterized LOC102562273	XLOC_020135	SLC5A2	-0.65	2.63E-03	XM_006278885.1	solute carrier family 5 (sodium/glucose cotransporter), member 2
XLOC_013022	SEMA5A	0.88	2.63E-03	XM_006273154.1	sema domain, seven thrombospondin repeats (type 1 and type 1-like), transmembrane domain (TM)	XLOC_002731	PODXL	-0.63	9.85E-03	XM_006260653.1	podocalyxin-like
XLOC_005010	MKX	0.88	2.63E-03	XM_006263075.1	mohawk homeobox	XLOC_012997	SLC4A1	-0.61	6.57E-03	XM_006271577.1	solute carrier family 4 (anion exchanger), member 1
XLOC_007754	TNMD	0.86	2.63E-03	XM_006265998.1	tenomodulin	XLOC_019197	PALMD	-0.61	6.57E-03	XM_006277941.1	palmelphin
XLOC_014555	LOC102558114	0.85	2.63E-03	XM_006273185.1	lysine--tRNA ligase-like	XLOC_002665	LOC102567357	-0.60	4.73E-03	XM_006260586.1	probable proline dehydrogenase 2-like
XLOC_006860	LOC102569158	0.85	2.63E-03	XM_006265079.1	protein Wnt-11-like, transcript variant X2	XLOC_004098	ADAMTS15	-0.60	8.24E-03	XM_006262089.1	ADAM metallopeptidase with thrombospondin type 1 motif, 15
XLOC_005818	PTPRK	0.85	2.63E-03	XM_006263984.1	protein tyrosine phosphatase, receptor type, R	XLOC_019177	HOXB3	-0.60	4.73E-03	XM_006277919.1	homeobox B3
XLOC_012479	TMSF52	0.83	2.63E-03	XM_006271031.1	transmembrane 6 superfamily member 2	XLOC_002043	ANPEP	-0.59	8.24E-03	XM_006259907.1	alanyl (membrane) aminopeptidase
XLOC_014520	SEMA7A	0.80	2.63E-03	XM_006273154.1	semaphorin 7A, GPI membrane anchor (John Milton Hagen blood group)	XLOC_001821	ID2	-0.58	6.57E-03	XM_006259688.1	inhibitor of DNA binding 2, dominant negative helix-loop-helix protein
XLOC_003318	LOC102573558	0.78	2.63E-03	XM_006271267.1	duplex and mab-3 related transcription factor 3-like	XLOC_010297	PTPRQ	-0.57	4.73E-03	XM_006268681.1	protein tyrosine phosphatase, receptor type, Q
XLOC_014521	LOC102569028	0.76	2.63E-03	XM_006273155.1	cholesterol side-chain cleavage enzyme, mitochondrial-like complexin 2	XLOC_005823	ALDH1A2	-0.55	8.24E-03	XM_006263981.1	aldehyde dehydrogenase 1 family, member A2, transcript variant X1
XLOC_006627	EYA1	0.75	2.63E-03	XM_006264490.1	eyes absent homolog 1 (Drosophila), transcript variant X1						
XLOC_000325	KIAA1024	0.74	6.57E-03	XM_006273179.1	serine/threonine-protein kinase PAK 1-like						
XLOC_014546	LOC102576325	0.74	2.63E-03	XM_006273179.1	N-acetylglycosaminidase, alpha						
XLOC_002515	NAGLU	0.74	2.63E-03	XM_006260415.1	cyclin J-like						
XLOC_019047	CCNJL	0.74	2.63E-03	XM_006277780.1	matrix metallopeptidase 23B						
XLOC_004468	MMP23B	0.73	2.63E-03	XM_006259289.1	glutathione S-transferase 3-like						
XLOC_004381	LOC102573555	0.72	2.63E-03	XM_006262407.1	lymphocyte antigen 86-like						
XLOC_017860	LOC102565559	0.72	8.24E-03	XM_006276579.1	tubulin, beta 3 class III						
XLOC_010986	TUBB3	0.72	2.63E-03	XM_006269387.1	tubulin, beta 3 class III						
XLOC_017020	LOC102564773	0.71	2.63E-03	XM_006275687.1	keratin, type II cytoskeletal coatechile-like						
XLOC_015969	CLU	0.70	2.63E-03	XM_006274651.1	clusten						
XLOC_014705	AMHR2	0.70	2.63E-03	XM_006273345.1	anti-Mullerian hormone receptor, type II						
XLOC_011267	LOC102572104	0.70	2.63E-03	XM_006269693.1	reticulin-1-like, transcript variant X3						
XLOC_011098	NDC80	0.69	2.63E-03	XM_006269514.1	NDC80 kinetochore complex component						
XLOC_018290	LOC102571606	0.69	2.63E-03	XM_006277002.1	derlin-2-like						
XLOC_012510	NCAN	0.68	2.63E-03	XM_006271033.1	neuropin						
XLOC_017840	MYBL2	0.68	2.63E-03	XM_006275653.1	v-myc avian myeloblastosis viral oncogene homolog-like 2						
XLOC_001168	MGM	0.68	9.85E-03	XM_006258986.1	maltase-glucosidase (alpha-glucosidase)						
XLOC_006069	LOC102562318	0.68	8.24E-03	XM_006264248.1	kinetochore protein Spc2-like		</				

XLOC_015352	LOC102567023	0.65	2.63E-03	XM_006274023.1	smoothelin-like protein 2-like
XLOC_003129	PIR	0.64	2.63E-03	XM_006261077.1	pirin (iron-binding nuclear protein)
XLOC_001463	LOC102574572	0.64	2.63E-03	XM_006259299.1	somatostatin-2-like
XLOC_001658	APOA1	0.62	6.57E-03	XM_006259520.1	apolipoprotein A-I
XLOC_004506	SALL1	0.62	2.63E-03	XM_006262552.1	spalt-like transcription factor 1, transcript variant X4
XLOC_002641	GPX3	0.58	9.85E-03	XM_006260571.1	glutathione peroxidase 3 (plasma)
XLOC_011119	MSH6	0.57	2.63E-03	XM_006269539.1	mutS homolog 6

**Table 2-2.** Annotation of sexually dimorphic genes in gonad during Day 0-12

Day 3 FPT vs MPT											
Female-biased						Male-biased					
Gene ID	Gene Symbol	LOG2(FC)	FDR	RefSeq Accession	Description	Gene ID	Gene Symbol	LOG2(FC)	FDR	RefSeq Accession	Description
XLOC_019258 FAP	-2.34	2.63E-03	XM_006277095.1	fibroblast activation protein, alpha	XLOC_006325 LOC102570319	2.37	2.63E-03	XM_006264537.1	keratin, type I cytoskeletal 10-like		
XLOC_012142 P115	-2.15	9.85E-03	XM_006270616.1	peptidase inhibitor 15	XLOC_003796 MYO1B	1.55	2.63E-03	XM_006261765.1	myosin XVIB		
XLOC_001325 ISGF10	-2.09	2.63E-03	XM_006259179.1	immunoglobulin superfamily, member 10	XLOC_013841 IFIT5	1.43	2.63E-03	XM_006272248.1	interferon-induced protein with tetratricopeptide repeats 5		
XLOC_015448 DKK2	-1.99	2.63E-03	XM_006274125.1	dickkopf WNT signaling pathway inhibitor 2	XLOC_002004 UCP2	1.36	2.63E-03	XM_006257947.1	uncoupling protein 2 (mitochondrial, proton carrier)		
XLOC_009221 LOC102660503	-1.89	2.63E-03	XM_006267562.1	lipocalin-like	XLOC_010995 LOC102568168	1.35	9.85E-03	XM_006268476.1	sulfotransferase family cytosolic 18 member 1-like		
XLOC_017214 LOC102597978	-1.87	2.63E-03	XM_006275987.1	myeloid protein 1-like	XLOC_007271 SLC18A1	1.18	2.63E-03	XM_006254908.1	solute carrier family 18 (vesicular monoamine transporter), member 1		
XLOC_000567 LUM	-1.83	2.63E-03	XM_006253858.1		XLOC_007482 LOC102570403	1.16	9.85E-03	XM_006265717.1	sulfotransferase 1C2-like		
XLOC_013275 KDM6B	-1.75	2.63E-03	XM_006271864.1	lysine (K)-specific demethylase 6B	XLOC_007988 STAR	1.13	2.63E-03	XM_006266133.1	steroidogenic acute regulatory protein		
XLOC_004098 ADAMTS15	-1.67	2.63E-03	XM_006262089.1	ADAM metallopeptidase with thrombospondin type 1 motif, 15	XLOC_016940 LOC102563300	1.11	8.24E-03	XM_006275524.1	up-regulator of cell proliferation-like		
XLOC_011871 HTRA3	-1.66	2.63E-03	XM_006270329.1	HtrA serine peptidase 3	XLOC_006045 LOC102561161	1.11	6.57E-03	XM_006264659.1	peripherin-like		
XLOC_007678 LOC102561011	-1.65	2.63E-03	XM_006265924.1	chromosome unknown open reading frame, human C2orf40	XLOC_003593 AMH	1.07	2.63E-03	XM_006261559.1	anti-Mullerian hormone		
XLOC_019048 C1QTNF2	-1.65	8.24E-03	XM_006277782.1	C1q and tumor necrosis factor related protein 2, transcript variant X2	XLOC_016538 JPH2	1.06	2.63E-03	XM_006275231.1	junctophilin 2, transcript variant X1		
XLOC_012144 LOC102561337	-1.65	2.63E-03	XM_006270617.1	protein Junmori-like	XLOC_012055 LOC102558568	1.06	6.57E-03	XM_006270527.1	panthenate kinase-like		
XLOC_012145 LOC102562106	-1.58	2.63E-03	XM_006270621.1	protein Junmori-like	XLOC_002973 DBH	1.05	2.63E-03	XM_006260879.1	dopamine beta-hydroxylase (dopamine beta-monooxygenase)		
XLOC_006977 MAMDC2	-1.55	2.63E-03	XM_006265197.1	MAM domain containing 2	XLOC_001523 TMPRSS9	1.04	2.63E-03	XM_006265937.1	transmembrane protease, serine 9		
XLOC_015366 STARD5	-1.44	2.63E-03	XM_006274032.1	STAR-related lipid transfer (START) domain containing 5	XLOC_004741 GALNT5	1.01	2.63E-03	XM_006262802.1	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 5 (GalNAc-T5)		
XLOC_008388 LOC102566921	-1.42	2.63E-03	XM_006266674.1	SPARC-like protein 1-like	XLOC_015057 LOC102568110	1.01	2.63E-03	XM_006273705.1	acyl-coenzyme A synthetase ACSM4, mitochondrial-like		
XLOC_008932 ANGPTL1	-1.40	2.63E-03	XM_006267260.1	angiopoietin-like 1, transcript variant X2	XLOC_018747 PDZD7	1.01	8.24E-03	XM_006277481.1	PDZ domain containing 7		
XLOC_005290 CRISPLD2	-1.30	2.63E-03	XM_006263385.1	cysteine-rich secretory protein LCC1 domain containing 2	XLOC_012101 TGLNL3	0.99	5.67E-03	XM_006270572.1	translin 3		
XLOC_0102527032	-1.26	2.63E-03	XM_006268644.1	platelet-derived growth factor D-like	XLOC_015178 LOC102567020	0.96	2.63E-03	XM_006273834.1	methylcrotonyl-CoA carboxylase beta chain, mitochondrial-like		
XLOC_000614 PRSS35	-1.25	2.63E-03	XM_006258407.1	protease, serine, 35	XLOC_017498 PPP1R36	0.94	4.73E-03	XM_006276195.1	protein phosphatase 1, regulatory subunit 36		
XLOC_018832 MRKX5	-1.25	2.63E-03	XM_006277550.1	matrix-remodeling associated 5	XLOC_000587 TRPC4AP	0.94	2.63E-03	XM_006258376.1	transient receptor potential cation channel, subfamily C, member 4 associated protein		
XLOC_013834 LOC102574466	-1.25	2.63E-03	XM_006272459.1	R-spondin-like	XLOC_004035 EIF4A2	0.93	2.63E-03	XM_006262029.1	eukaryotic translation initiation factor 4A2		
XLOC_014376 LOC102573435	-1.23	2.63E-03	XR_363493.1	uncharacterized LOC102573435	XLOC_007978 BFM15	0.92	8.24E-03	XM_006268153.1	bone morphogenetic protein 15		
XLOC_012085 LOC102566862	-1.18	4.73E-03	XM_006270554.1	serpin B11-like	XLOC_000559 KMO	0.92	4.73E-03	XM_006258349.1	kyurenine 3-monooxygenase (kyurenine 3-hydroxylase)		
XLOC_010868 LOC102561252	-1.17	6.57E-03	XM_006269073.1	phospholipase A2 inhibitor subunit gamma 2-like	XLOC_011364 GUCY2C	0.89	6.57E-03	XM_006269980.1	guanylate cyclase 2C (heat stable enterotoxin receptor)		
XLOC_011459 COL8A2	-1.16	2.63E-03	XM_006269879.1	collagen, type VIII, alpha 2	XLOC_017000 LOC102563625	0.86	2.63E-03	XM_006275682.1	cGMP-dependent 3'-5'-cyclic phosphodiesterase-like		
XLOC_013143 LOC102567788	-1.12	2.63E-03	XM_006271712.1	catelin-like	XLOC_007989 LOC102563022	0.86	9.85E-03	XM_0062626253.1	chromosome unknown open reading frame, human C6orf158		
XLOC_016910 ARSD	1.09	4.73E-03	XM_006274505.1	arylsulfatase D	XLOC_010738 LOC102575314	0.86	2.63E-03	XM_006269131.1	steroid 21-hydroxylase-like		
XLOC_002001 LOC102567971	-1.07	2.63E-03	XM_006278707.1	sterol 17-alpha-hydroxylase/17,20 lyase-like	XLOC_006790 SAC3D1SNX15	0.85	8.24E-03	XM_006265001.1	SAC3D1 domain containing 1, sorting nexin 15		
XLOC_003664 GLTB02	-1.06	4.73E-03	XM_006261630.1	glycosidase, family 8 domain containing 2	XLOC_007993 FZD5	0.83	2.63E-03	XM_006265941.1	frizzled family receptor 5		
XLOC_006860 LOC102569158	-1.06	2.63E-03	XM_006265079.1	protein Wnt-11-like, transcript variant X2	XLOC_013070 ALDOB	0.82	2.63E-03	XM_006268753.1	aldo-keto reductase family 1, member 1B		
XLOC_001633 LOC102569382	-1.06	2.63E-03	XM_006259197.1	WAP four-disulfide core domain protein 5-like	XLOC_016867 LOC102570362	0.82	8.24E-03	XM_006275512.1	3 beta-hydroxysteroid dehydrogenase/Delta 5->4-isomerase-like		
XLOC_009569 LOC102575456	-1.02	2.63E-03	XR_363216.1	uncharacterized LOC102575456, transcript variant X1	XLOC_019197 PALMD1	0.81	2.63E-03	XM_006277941.1	palmdelphin		
XLOC_013035 RASL1B	-1.01	6.57E-03	XM_006277024.1	epidermal retinol dehydrogenase 2-like	XLOC_003053 FTCD	0.79	2.63E-03	XM_006260991.1	formimidoyltransferase cyclodeaminase		
XLOC_009174 THBD	-1.00	2.63E-03	XM_006267522.1	thrombomodulin	XLOC_004612 LOC102574966	0.76	2.63E-03	XM_006262659.1	2,3-dihydroxyvitamin D(3) 24-hydroxylase, mitochondrial-like		
XLOC_018671 THBS2	-1.00	2.63E-03	XM_006277394.1	thrombospondin 2, transcript variant X1	XLOC_007305 LOC102563735	0.76	2.63E-03	XM_006265526.1	BMP/retnic acid-inducible neural-specific protein 1-like		
XLOC_013636 LOC102560955	-0.99	2.63E-03	XM_006272242.1	protein NEL-like	XLOC_014375 LOC102573119	0.76	2.63E-03	XM_006273013.1	chromogranin-A-like		
XLOC_018956 EEF2	-0.97	6.57E-03	XM_006277689.1	early B-cell factor 3, transcript variant X1	XLOC_010126 LOC102576076	0.76	2.63E-03	XM_006268502.1	long-chain fatty acid transport protein 6-like		
XLOC_007033 HPGDS	-0.97	4.73E-03	XM_006265263.1	hematopoietic prostaglandin D synthase	XLOC_018497 RIMS1	0.75	2.63E-03	XM_006272714.1	regulating synaptic membrane exocytosis 1		
XLOC_012093 LOC102566081	-0.95	2.63E-03	XM_006270235.1	beta-galactosidase-binding lectin-like	XLOC_002636 LOC102575734	0.74	2.63E-03	XM_006260622.1	cytochrome P450 11B, mitochondrial-like		
XLOC_018421 LOC102566886	-0.95	9.85E-03	XM_006277143.1	anosmin-1-like	XLOC_018070 LOC102574081	0.74	2.63E-03	XM_006276772.1	chromosome unknown open reading frame, human C1orf63		
XLOC_009566 ELN	-0.94	6.57E-03	XM_006267934.1	elastin	XLOC_007107 UPRO3A	0.73	2.63E-03	XM_006265339.1	uproplakin 3A		
XLOC_015685 COLA3	-0.94	2.63E-03	XM_006274385.1	collagen, type VI, alpha 3	XLOC_015643 CEBPA	0.73	9.85E-03	XM_006274301.1	CCAAT/enriched binding protein (C/EBP), alpha		
XLOC_011463 CSRP2	-0.92	2.63E-03	XM_006269901.1	cysteine and glycine-rich protein 2	XLOC_016611 LOC10255996	0.72	2.63E-03	XM_006275273.1	diamine acetyltransferase 2-like, transcript variant X1		
XLOC_019338 TAGLN	-0.90	2.63E-03	XM_006278069.1	translin	XLOC_014555 LOC102558114	0.72	2.63E-03	XM_006273185.1	lysine-tRNA ligase-like		
XLOC_006686 MCM8	-0.85	4.73E-03	XM_006264898.1	minichromosome maintenance complex component 8	XLOC_006252 SCL15A2	0.71	6.57E-03	XM_0062624513.1	solute carrier family 15 (oligopeptide transporter), member 2		
XLOC_003878 FABP4	-0.84	2.63E-03	XM_006261857.1	fatty acid binding protein 4, adipocyte	XLOC_011510 KIF24	0.71	8.24E-03	XM_006269964.1	kinesin family member 24		
XLOC_011513 DNAI1	-0.84	6.57E-03	XM_006269950.1	dynein, intermediate chain 1	XLOC_002636 LOC102561378	0.71	2.63E-03	XM_006260563.1	serpin H1-like		
XLOC_002405 HSPB1	-0.84	4.73E-03	XM_006262078.1	heat shock 27kDa protein 1	XLOC_002418 WDRL6	0.69	8.24E-03	XM_006260316.1	WD repeat domain 6		
XLOC_004200 LOC102567125	-0.81	2.63E-03	XM_006262206.1	ribonuclease-like	XLOC_003790 ALDH4A1,LOC10257334	0.68	4.73E-03	XM_006261753.1	aldehyde dehydrogenase 4 family, member 1A, taste receptor type 1 member 2-like		
XLOC_014113 LOC102566241	-0.79	2.63E-03	XM_006272754.1	beta-microseminoprotein-like	XLOC_013109 PHF1	0.68	4.73E-03	XM_006271689.1	PHD finger protein 1		
XLOC_012052 PCDH18	-0.78	2.63E-03	XM_006270525.1	protocadherin 18, transcript variant X2	XLOC_002205 LOC102567904	0.67	2.63E-03	XM_006260094.1	aspartate/butyrate-2-like		
XLOC_002265 LOC102559836	-0.77	2.63E-03	XM_006261555.1	WAP four-disulfide core domain protein 2-like	XLOC_018116 SCAT1	0.67	2.63E-03	XM_006276828.1	sterol O-acyltransferase 1		
XLOC_019803 LOC102559056	-0.77	2.63E-03	XM_006278518.1	protein MRP-126-like	XLOC_017043 SLC45A1	0.67	2.63E-03	XM_006275726.1	solute carrier family 45, member 1		
XLOC_017186 CRABP2	-0.77	2.63E-03	XM_006275867.1	cellular retinoic acid binding protein 2	XLOC_015611 BLNK	0.66	4.73E-03	XM_006274294.1	B-cell linker		
XLOC_005476 ACAT2	-0.77	6.57E-03	XM_006263994.1	acetyl-CoA acetyltransferase 2	XLOC_019852 IFRD1	0.66	2.63E-03	XM_006278568.1	interferon-related developmental regulator 1, transcript variant X2		
XLOC_017840 MYBL2	-0.77	2.63E-03	XM_006276553.1	v-myc avian myeloblastosis viral oncogene homolog-like 2	XLOC_006694 SLC1A4	0.66	2.63E-03	XM_006264916.1	solute carrier family 1 (glutamate/neuronal amino acid transporter), member 4		
XLOC_013781 LOC102562818	-0.76	4.73E-03	XM_006272414.1	sulphydryl oxidase 1-like	XLOC_004405 FDXR	0.65	2.63E-03	XM_006262447.1	ferredoxin reductase		
XLOC_012895 TGGM3	-0.75	2.63E-03	XM_006271463.1	transglutaminase 3	XLOC_010354 PCYOX1	0.65	8.24E-03	XM_006268735.1	penrylcysteine oxidase 1		
XLOC_019137 C7	-0.74	2.63E-03	XM_006277876.1	complement component 7	XLOC_005325 CDHR5	0.64	2.63E-03	XM_006263422.1	cadherin-related family member 5		
XLOC_006599 LOC102561468	-0.74	2.63E-03	XM_006264812.1	peptidyl-prolyl cis-trans isomerase CWC27 homolog	XLOC_015146 LOC102577042	0.63	4.73E-03	XM_006263934.1	sulfotransferase 6S1-like		
XLOC_002516 HSD17B1	-0.73	2.63E-03	XM_006260402.1	hydroxysteroid (17-beta) dehydrogenase 1, transcript variant X2	XLOC_005967 LOC102577145	0.61	9.85E-03	XM_006264145.1	D-beta-hydroxybutyrate dehydrogenase, mitochondrial-like		
XLOC_017707 TGFB1	-0.73	2.63E-03	XM_006276411.1	transforming growth factor, beta-induced, 68kDa	XLOC_002618 GPLD1	0.58	9.85E-03	XM_006260536.1	glycosylphosphatidylinositol specific phospholipase D1		

XLOC_001261	LOC102563321	-0.73	2.63E-03	XM_006250088.1	hemoglobin subunit epsilon-like	XLOC_017425	ESPNL	0.58	9.85E-03	XM_006276123.1	espin-like
XLOC_004763	EDNRA	-0.72	2.63E-03	XM_006267252.1	endothelin receptor type A, transcript variant X1	XLOC_018826	NPC1	0.57	6.57E-03	XM_006277553.1	Niemann-Pick disease, type C1
XLOC_003288	PGMS	-0.70	4.73E-03	XM_006261237.1	phosphoglucomutase 5	XLOC_007526	LOC102563416	inf	4.73E-03	XR_363102.1	uncharacterized LOC102563416
XLOC_017597	SCG5	-0.69	9.85E-03	XM_006272629.1	secretogranin V (782 protein), transcript variant X1						
XLOC_006833	TGFBI2	-0.69	4.73E-03	XM_006265048.1	transforming growth factor, beta 2						
XLOC_003617	MYH11	-0.69	6.57E-03	XM_006261582.1	myosin, heavy chain 11, smooth muscle						
XLOC_010256	LOC102570029	-0.69	2.63E-03	XM_006268638.1	vascular cell adhesion protein 1-like, transcript variant X2						
XLOC_017835	HEMGN	-0.68	2.63E-03	XM_006276548.1	hemogen, transcript variant X1						
XLOC_006538	LOC102565592	-0.68	2.63E-03	XM_006264753.1	BPTI/Kunitz domain-containing protein-like						
XLOC_017724	FN1	-0.67	9.85E-03	XM_00627433.1	fibronectin 1, transcript variant X4						
XLOC_001036	LRIG3	-0.67	2.63E-03	XM_006258847.1	leucine-rich repeats and immunoglobulin-like domains 3						
XLOC_006984	RINT1	-0.67	4.73E-03	XM_006265209.1	RAD50 interactor 1, transcript variant X1						
XLOC_004684	COL1A1	-0.67	8.24E-03	XM_006262736.1	collagen, type XI, alpha 1, transcript variant X3						
XLOC_001309	LOC102576189	-0.66	2.63E-03	XM_006259136.1	dimethylaminolemonoxygenase [N-oxide-forming] 3-like						
XLOC_013855	LOC102560862	-0.66	6.57E-03	XM_006272484.1	ribonucleoside-diphosphate reductase subunit M2-like						
XLOC_009126	LOC102560553	-0.65	2.63E-03	XM_006267475.1	protein S100-A11-like						
XLOC_004860	LOC102574734	-0.64	2.63E-03	XM_006262895.1	procollagen C-endopeptidase enhancer 1-like						
XLOC_003054	LSS	-0.62	4.73E-03	XM_006260992.1	lanosterol synthase (2,3-oxidosqualane-lanosterol cyclase)						
XLOC_013090	NUAK1	-0.60	6.57E-03	XM_006271673.1	NUAK family, SNF1-like kinase, 1						
XLOC_015352	LOC102567023	-0.60	6.57E-03	XM_006274023.1	smoothelin-like protein 2-like						
XLOC_010661	BGN	-0.59	2.63E-03	XM_006269028.1	biginican						
XLOC_003940	TNNI3	-0.58	6.57E-03	XM_006261916.1	troponin I type 3 (cardiac)						
XLOC_011391	CMTM3	-0.57	9.85E-03	XM_006269851.1	CKLF-like MARVEL transmembrane domain containing 3						
XLOC_000678	UCHL1	-0.56	6.57E-03	XM_006258484.1	ubiquitin carboxy-terminal esterase L1 (ubiquitin thioesterase)						
XLOC_010162	SMAD1	-0.55	9.85E-03	XM_006268534.1	SMAD family member 1						
XLOC_012065	MOXD1	-0.53	9.85E-03	XM_006270532.1	monooxygenase, DBH-like 1						
XLOC_018826	LOC102563028	-inf	2.63E-03	XM_006268040.1	histone H2B 1/2/3/4/6-like						

Day 6 FPT vs MPT											
Female-biased						Male-biased					
Gene_ID	Gene Symbol	LOG2(FC)	FDR	RefSeq Accession	Description	Gene_ID	Gene Symbol	LOG2(FC)	FDR	RefSeq Accession	Description
XLOC_000709	TAP2	-4.88	4.73E-03	XM_006258513.1	transporter 2, ATP-binding cassette, sub-family B (MDR/TAP)	XLOC_000636	LOC102563794	2.96	2.63E-03	XM_006258433.1	myosin-3-like
XLOC_005656	GY52	-1.79	2.63E-03	XM_006263801.1	glycogen synthase 2 (liver)	XLOC_006327	LOC102570551	2.92	2.63E-03	XM_006264534.1	keratin, type I cytoskeletal 14-like
XLOC_013275	KDM6B	-1.66	2.63E-03	XM_006271864.1	lysine (K)-specific demethylase 6B	XLOC_003593	AMH	2.63	2.63E-03	XM_006215591.1	anti-Mullerian hormone
XLOC_000041	LOC102566578	-1.65	2.63E-03	XM_006257779.1	avidin-like	XLOC_006325	LOC102570319	2.29	2.63E-03	XM_006264537.1	keratin, type I cytoskeletal 10-like
XLOC_002667	CLN3	-1.64	2.63E-03	XM_006260587.1	ceroid-lipofuscinosis, neuronal 3	XLOC_017096	MATN4	1.90	2.63E-03	XM_006275789.1	matrin 4
XLOC_012144	LOC102561337	-1.49	2.63E-03	XM_006270617.1	protein Jumonji-like	XLOC_015317	ACTC1	1.84	2.63E-03	XM_006273980.1	actin, alpha, cardiac muscle 1
XLOC_005150	LOC102559161	-1.45	2.63E-03	XM_006263238.1	UDP-glucuronosyltransferase 1-9-like	XLOC_020119	TNNI2	1.68	2.63E-03	XM_006278838.1	troponin I type 2 (skeletal, fast)
XLOC_015035	LOC102568567	-1.42	2.63E-03	XM_006273707.1	uncharacterized LOC102568567	XLOC_002239	LOC102573233	1.64	2.63E-03	XM_006261010.1	somatomedin-B and thrombospondin type-1 domain-containing protein-like
XLOC_012145	LOC102562106	-1.41	8.24E-03	XM_006270621.1	protein Jumonji-like	XLOC_008936	TBX2R	1.64	6.57E-03	XM_006267376.1	thromboxane A2 receptor
XLOC_003701	LOC102575599	-1.39	2.63E-03	XM_006261670.1	cytochrome P450 2K-like	XLOC_006442	DHH	1.59	9.85E-03	XM_006264655.1	desert hedgehog
XLOC_0035128	ACE2	-1.37	2.63E-03	XM_006261087.1	angiotensin I converting enzyme 2	XLOC_003144	INHA	1.54	2.63E-03	XM_006261090.1	inhibin, alpha
XLOC_009120	LOC102559409	-1.32	2.63E-03	XM_006267472.1	calcitonin receptor-like	XLOC_003718	MPO	1.41	2.63E-03	XM_006261680.1	myeloperoxidase
XLOC_011884	SCN1A	-1.29	2.63E-03	XM_006270357.1	sodium channel, voltage-gated, type I, alpha subunit	XLOC_014968	TCP23	1.41	2.63E-03	XM_006273614.1	transcription factor 23
XLOC_001309	LOC102576189	-1.22	2.63E-03	XM_006259136.1	dimethylaminolethione monooxygenase [N-oxide-forming] 3-like	XLOC_002035	CpxM2	1.39	2.63E-03	XM_006259901.1	carboxypeptidase X (M14 family), member 2
XLOC_009542	SLC6A15	-1.18	2.63E-03	XM_006267903.1	solute carrier family 6 (neutral amino acid transporter), member 15	XLOC_010819	CYGB	1.37	2.63E-03	XM_006269221.1	cytoglobin, transcript variant X1
XLOC_017214	LOC102557978	-1.18	2.63E-03	XM_006257897.1	myeloid protein 1-like	XLOC_000025	CA13	1.35	2.63E-03	XM_006257756.1	carbonic anhydrase XIII
XLOC_001517	LOC102568516	-1.17	2.63E-03	XM_006259359.1	glycine amidinotransferase, mitochondrial-like	XLOC_018940	LOC102559753	1.25	2.63E-03	XM_006277671.1	inactive serine/threonine-protein kinase TEX14-like
XLOC_007033	HPGDS	-1.17	2.63E-03	XM_006265263.1	hematopoietic prostaglandin D synthase	XLOC_006593	LOC102560544	1.22	2.63E-03	XM_006264808.1	elongation factor 1-alpha-like
XLOC_009466	SLC26A9	-1.16	8.24E-03	XM_006267811.1	solute carrier family 26 (anion exchanger), member 9	XLOC_013202	KEL	1.21	2.63E-03	XM_006271796.1	Kell blood group, metallo-endopeptidase
XLOC_006538	LOC102556592	-1.15	2.63E-03	XM_006264753.1	BPT1/Kunitz domain-containing protein-like	XLOC_000495	LOC102569139	1.21	4.73E-03	XM_006258290.1	cathepsin W-like
XLOC_002692	LOC102575737	-1.11	2.63E-03	XM_006260622.1	cytochrome P450 11B, mitochondrial-like	XLOC_015969	CLU	1.19	2.63E-03	XM_006274651.1	clusterin
XLOC_001371	LOC102570382	-1.06	2.63E-03	XM_006259197.1	WAP four-disulfide core domain protein 5-like	XLOC_000292	TEX11	1.12	8.24E-03	XM_006258071.1	testis expressed 11
XLOC_012895	TGM3	-1.06	2.63E-03	XM_006271463.1	transglutaminase 3	XLOC_015939	TDRKH	1.10	2.63E-03	XM_006274616.1	tudor and KH domain containing
XLOC_019132	LOC102568973	-1.05	2.63E-03	XM_006277688.1	complement C4-like	XLOC_008388	LOC102566921	1.09	2.63E-03	XM_006266674.1	SPARC-like protein 1-like
XLOC_002697	LOC102574810	-1.04	6.57E-03	XM_006260618.1	riboflavin transporter 2-like	XLOC_018070	LOC102574081	1.06	2.63E-03	XM_006276772.1	chromosome unknown open reading frame, human C1orf63
XLOC_008611	LOC102561244	-1.04	4.73E-03	XM_006266989.1	metabotropic glutamate receptor 7-like	XLOC_007647	LOC102572713	1.05	2.63E-03	XM_006265890.1	prolactin-releasing peptide receptor-like
XLOC_003210	SLC5A8	-1.03	2.63E-03	XM_006261167.1	solute carrier family 5 (sodium/monocarboxylate cotransporter), member 8	XLOC_016041	LOC102564391	1.04	2.63E-03	XM_006274733.1	relaxin receptor 1-like
XLOC_000020	LOC102562135	-0.98	6.57E-03	XM_006257759.1	solute carrier family 7 member 13-like	XLOC_002516	HSD17B1	1.01	2.63E-03	XM_006260402.1	hydroxy steroid (17-beta) dehydrogenase 1, transcript variant X2
XLOC_001504	LOC102565171	-0.97	2.63E-03	XM_006259345.1	inosine-uridine preferring nucleoside hydrolase-like	XLOC_003317	DMRT1	1.00	2.63E-03	XM_006261265.1	doublesex and mab-3 related transcription factor 1, transcript variant X1
XLOC_004098	ADAMTS15	-0.96	2.63E-03	XM_006262089.1	ADAM metallopeptidase with thrombospondin type 1 motif, 15	XLOC_007575	GAS2L2	0.99	2.63E-03	XM_006265831.1	growth arrest-specific 2 like
XLOC_016867	LOC102570362	-0.92	2.63E-03	XM_006275551.1	3 beta-hydroxysteroid dehydrogenase/Delta 5->4-isomerase-like	XLOC_000200	UCP2	0.99	2.63E-03	XM_006257947.1	uncoupling protein 2 (mitochondrial, proton carrier)
XLOC_010738	LOC102575314	-0.91	2.63E-03	XM_006269131.1	steroid 21-hydroxylase-like	XLOC_005519	HSPH1	0.98	2.63E-03	XM_006263641.1	heat shock 105kDa/110kDa protein 1, transcript variant X1
XLOC_011657	LOC102575787	-0.90	2.63E-03	XM_006270151.1	adrenodoxin, mitochondrial-like	XLOC_000226	HPD	0.96	4.73E-03	XM_006257986.1	4-hydroxyphenylpyruvate dioxygenase
XLOC_012970	DECR2	-0.89	2.63E-03	XM_006271539.1	2,4-dienoyl CoA reductase 2, peroxisomal	XLOC_001319	CABP1	0.95	2.63E-03	XM_006259142.1	calcium binding protein 1
XLOC_018302	LOC102577108	-0.88	8.24E-03	XM_006277024.1	epidermal retinol dehydrogenase 2-like	XLOC_003058	LOC102568919	0.95	9.85E-03	XM_006260995.1	uncharacterized LOC102568919
XLOC_019823	LOC102564018	-0.88	2.63E-03	XM_006278540.1	cysteine-rich venom protein heliotremine-like	XLOC_002739	LOC102566194	0.93	2.63E-03	XM_006260660.1	nuclear receptor subfamily 5 group A member 2-like
XLOC_017932	UNC80	-0.87	2.63E-03	XM_006276656.1	unc-80 homolog (C. elegans)	XLOC_015259	LOC102562273	0.93	2.63E-03	XR_363545.1	uncharacterized LOC102562273
XLOC_010924	LOC102564214	-0.87	2.63E-03	XM_006269330.1	zinc finger RNA-binding protein-like	XLOC_0026236	LOC102561378	0.92	2.63E-03	XM_006260563.1	serpin H1-like
XLOC_019258	FAP	-0.86	9.85E-03	XM_006277995.1	fibroblast activation protein, alpha	XLOC_002987	PWIL1	0.92	2.63E-03	XM_006260910.1	piwi-like RNA-mediated gene silencing 1
XLOC_008413	LOC102571256	-0.85	2.63E-03	XM_006266691.1	Y-L amino acid transporter 2-like	XLOC_004390	LOC102558761	0.92	2.63E-03	XM_006262430.1	cathecidin-OH antimicrobial peptide-like
XLOC_011387	BEAN1	-0.82	2.63E-03	XM_006269828.1	brain expressed, associated with NEDD4, 1	XLOC_012957	UPK1B	0.92	2.63E-03	XM_006271528.1	uroplakin 1B
XLOC_004684	COL11A1	-0.82	2.63E-03	XM_006262736.1	collagen, type XI, alpha 1, transcript variant X3	XLOC_012892	EPB42	0.90	2.63E-03	XM_006271454.1	erythrocyte membrane protein band 4.2
XLOC_016538	JPH2	-0.81	2.63E-03	XM_006275231.1	junctophilin 2, transcript variant X1	XLOC_015976	LOC102567479	0.89	2.63E-03	XM_006274681.1	zinc finger protein 208-like
XLOC_005657	SLC35F2	-0.81	8.24E-03	XM_006263806.1	myosin-10-like	XLOC_011490	LOC102570959	0.88	6.57E-03	XM_006269934.1	proactivator polypeptide-like
XLOC_015775	APOA2	-0.81	2.63E-03	XM_006274463.1	apolipoprotein A-II	XLOC_015124	PSAT1	0.87	2.63E-03	XM_006273773.1	phosphoserine aminotransferase 1, transcript variant X1
XLOC_009566	ELEN	-0.80	4.73E-03	XM_006267934.1	elastin	XLOC_015643	CEBPA	0.87	2.63E-03	XM_006274301.1	CCAAT/enhancer binding protein (C/EBP), alpha
XLOC_018099	NEFL	-0.80	2.63E-03	XM_006276810.1	neurofilament, light polypeptide	XLOC_004294	EPOR	0.87	2.63E-03	XM_006262351.1	erythropoietin receptor
XLOC_002784	SLC25A47	-0.79	2.63E-03	XM_006260709.1	solute carrier family 25, member 47	XLOC_001658	APOA1	0.86	2.63E-03	XM_006259520.1	apolipoprotein A-I
XLOC_008706	CADPS	-0.77	2.63E-03	XM_006267004.1	Ca++-dependent secretion activator	XLOC_003395	DNAJA4	0.85	2.63E-03	XM_006261339.1	DnaJ (Hsp40) homolog, subfamily A, member 4
XLOC_001197	SLC5F2	-0.76	2.63E-03	XM_006259020.1	solute carrier family 35, member F2	XLOC_004035	EIF4A2	0.85	2.63E-03	XM_006262029.1	eukaryotic translation initiation factor 4A2
XLOC_013845	GRTP1	-0.76	2.63E-03	XM_006272474.1	growth hormone regulated TBC protein 1	XLOC_000489	A2M	0.84	2.63E-03	XM_006258274.1	alpha-2-macroglobulin
XLOC_002665	LOC102567357	-0.76	2.63E-03	XM_006260586.1	probable proline dehydrogenase 2-like	XLOC_013143	LOC102567788	0.83	2.63E-03	XM_006271712.1	calretinin-like
XLOC_008932	ANGPTL1	-0.75	2.63E-03	XM_006267260.1	angiopoietin-like 1, transcript variant X2	XLOC_013828	LOC102573123	0.83	9.85E-03	XM_006272455.1	transcription factor SOX-9-like
XLOC_001247	TTL9	-0.74	2.63E-03	XM_006259082.1	tubulin tyrosine ligase-like family, member 9	XLOC_003318	LOC102577358	0.83	2.63E-03	XM_006261267.1	duplex and mab-3 related transcription factor 3-like
XLOC_006419	LOC102562082	-0.73	2.63E-03	XM_006264663.1	spermatogenesis-associated serine-rich protein 2-like	XLOC_013332	MDGA1	0.82	2.63E-03	XM_006271918.1	MAM domain containing glycosylphosphatidylinositol anchor 1
XLOC_011181	CTH	-0.72	2.63E-03	XM_006269606.1	cystathione lyase (cystathione gamma-lyase)	XLOC_014873	ANK1	0.81	2.63E-03	XM_006273519.1	ankyrin 1, erythrocytic
XLOC_015332	LOC102560570	-0.72	2.63E-03	XM_006273996.1	disintegrin and metalloproteinase domain-containing protein 19-like	XLOC_019852	IFRD1	0.81	2.63E-03	XM_006278568.1	interferon-related developmental regulator 1, transcript variant X2
XLOC_006977	MAMDC2	-0.72	2.63E-03	XM_006265197.1	MAM domain containing 2	XLOC_015846	LOC102575246	0.79	6.57E-03	XM_006274545.1	antigen peptide transporter 1-like
XLOC_011704	GLUD1	-0.71	2.63E-03	XM_006270156.1	glutamate dehydrogenase 1	XLOC_014555	LOC102558114	0.79	2.63E-03	XM_006273185.1	lysine-N-acetyltransferase 1
XLOC_014252	SLC6A18	-0.71	2.63E-03	XM_006272902.1	solute carrier family 6 (neutral amino acid transporter), member 18	XLOC_016521	PRX2	0.79	2.63E-03	XM_006276202.1	purinergic receptor P2X, ligand-gated ion channel, 5
XLOC_001112	LOC102563319	-0.71	2.63E-03	XM_006258919.1	dehydronoease/reductase SDR family member 1-like	XLOC_019505	LOC102564244	0.77	2.63E-03	XM_006278233.1	probable E3 ubiquitin-protein ligase MID2-like

XLOC_004380	GSTA4	-0.71	9.85E-03	XM_006262426.1	glutathione S-transferase alpha 4		XLOC_004389	LOC102558544	0.77	2.63E-03	XM_006262429.1	cathelicidin-2-like
XLOC_003367	STEAP4	-0.70	2.63E-03	XM_006261315.1	STEAP family member 4		XLOC_010356	LOC102575076	0.76	2.63E-03	XM_006268737.1	butyrophilin subfamily 1 member A1-like
XLOC_011163	LOC102565377	-0.70	2.63E-03	XM_006269585.1	serotriphin-like		XLOC_013658	PCED1A	0.76	9.85E-03	XM_006272260.1	PC-esterase domain containing 1A
XLOC_008928	ZBTB6	-0.69	2.63E-03	XM_006267251.1	zinc finger and BTB domain containing 6		XLOC_011927	HSP90AA1	0.76	2.63E-03	XM_006270404.1	heat shock protein 90kDa alpha (cytosolic), class A member 1
XLOC_018724	LOC102564013	-0.69	4.73E-03	XM_006277452.1	regucalcin-like		XLOC_014546	LOC102576325	0.74	6.57E-03	XM_006273179.1	serine/threonine-protein kinase PAK 1-like
XLOC_010094	LOC102567929	-0.69	2.63E-03	XM_006268475.1	sulfotransf erase 1 family member D1-like		XLOC_001468	MMP23B	0.74	2.63E-03	XM_006259289.1	matrix metallopeptidase 23B
XLOC_014605	DNAH5	-0.69	8.24E-03	XM_006273245.1	dynein, axonemal, heavy chain 5		XLOC_017446	LOC102558523	0.73	9.85E-03	XM_006276142.1	musculin-like
XLOC_009005	LOC102569324	-0.69	2.63E-03	XM_006267352.1	vitamin D3 hydroxylase-associated protein-like		XLOC_014705	AMHR2	0.73	2.63E-03	XM_006273345.1	anti-Mullerian hormone receptor, type II
XLOC_018094	NEFM	-0.68	2.63E-03	XM_006276809.1	neurofilament, medium polypeptide		XLOC_005111	LOC102568149	0.72	2.63E-03	XM_006263192.1	nuclear receptor subfamily 0 group B member 1-like
XLOC_007684	LOC102562558	-0.67	2.63E-03	XM_006265929.1	3-ketoady-CoA thiolase B, peroxisomal-like		XLOC_000149	BLVRB	0.71	2.63E-03	XM_006257989.1	biliverdin reductase B (flavin reductase (NADPH))
XLOC_018601	RRM2B	-0.67	2.63E-03	XM_006277330.1	ribonucleotide reductase M2 B (TP53 inducible)		XLOC_017860	LOC102565559	0.70	9.85E-03	XM_006276579.1	lymphocyte antigen 86-like
XLOC_000655	LOC102570455	-0.66	2.63E-03	XM_006258459.1	probable acyl-CoA dehydrogenase 6-like		XLOC_009637	MYCL	0.70	2.63E-03	XM_006267966.1	v-myc avian myelocytomatosis viral oncogene lung carcinoma derived homolog
XLOC_008616	GPD2	-0.66	2.63E-03	XM_006266903.1	glycerol-3-phosphate dehydrogenase 2 (mitochondrial)		XLOC_019253	LOC102559669	0.70	4.73E-03	XM_006277993.1	frizzled-10-like
XLOC_007017	SCRN1	-0.66	2.63E-03	XM_006265245.1	secernin 1		XLOC_012763	NR5A1	0.69	2.63E-03	XM_006271311.1	nuclear receptor subfamily 5, group A, member 1
XLOC_015056	LOC102564848	-0.65	2.63E-03	XM_006273691.1	acyl-coenzyme A synthetase ACSM3, mitochondrial-like		XLOC_006205	TPR1	0.68	2.63E-03	XM_006264421.1	transmembrane protein, adipocyte associated
XLOC_013605	SLC4A4	-0.64	8.24E-03	XM_006272210.1	solute carrier family 4 (sodium bicarbonate cotransporter), member 4		XLOC_012997	SLC4A1	0.67	2.63E-03	XM_006271577.1	solute carrier family 4 (anion exchanger), member 1
XLOC_014253	SLC6A19	-0.64	4.73E-03	XM_006272903.1	solute carrier family 6 (neutral amino acid transporter), member 19		XLOC_016032	LOC102561962	0.67	4.73E-03	XM_006274722.1	parvalbumin, muscle-like
XLOC_006854	SPOCK2	-0.63	2.63E-03	XM_006265063.1	spark/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 2		XLOC_011428	PTPRZ1	0.66	6.57E-03	XM_006269867.1	protein tyrosine phosphatase, receptor-type, Z polypeptide 1
XLOC_003353	EMX1	-0.63	2.63E-03	XM_006261299.1	empty spiracles homeobox 1		XLOC_005256	ENPP2	0.66	2.63E-03	XM_006263351.1	ectonucleotide pyrophosphatase/phosphodiesterase 2, transcript variant X2
XLOC_009514	LOC102561484	-0.62	4.73E-03	XM_006267878.1	potassium-transporting ATPase alpha chain 2-like		XLOC_009636	TRIT1	0.65	2.63E-03	XM_006267965.1	tRNA isopentenylyltransferase 1
XLOC_002055	LOC102568673	-0.62	8.24E-03	XM_006259931.1	uncharacterized LOC102568673		XLOC_002515	NAGLU	0.64	2.63E-03	XM_006260411.1	N-acetylglucosaminidase, alpha
XLOC_009610	LOC102564364	-0.62	6.57E-03	XM_006267961.1	ornithine decarboxylase 2-like		XLOC_001582	BOC	0.63	2.63E-03	XM_006259427.1	BOC cell adhesion associated, oncogene regulated
XLOC_006431	NCKAP5L	-0.62	2.63E-03	XM_006264647.1	NCK-associated protein 5-like		XLOC_003589	LOC102566435	0.63	4.73E-03	XM_006261548.1	small EDRK-rich factor 1-like
XLOC_019177	HOXB3	-0.59	2.63E-03	XM_006277191.1	homeobox B3		XLOC_006860	LOC102569158	0.61	6.57E-03	XM_006265079.1	protein Wnt-11-like, transcript variant X2
XLOC_017921	WDR26	-0.58	2.63E-03	XM_006276637.1	WD repeat domain 26		XLOC_007754	TNMD	0.60	2.63E-03	XM_006265998.1	tenomodulin
XLOC_005828	MPI	-0.59	8.24E-03	XM_006264007.1	mannose phosphate isomerase		XLOC_005633	AHS1	0.59	2.63E-03	XM_006263776.1	AHA1, activator of heat shock 90kDa protein ATPase homolog 1 (yeast)
XLOC_010264	LOC102572032	-0.58	2.63E-03	XM_006268644.1	platelet-derived growth factor D-like		XLOC_010818	ST6GALNAC2	0.59	4.73E-03	XM_006269266.1	ST6 (alpha-N-acetyl-neuraminy-2,3-beta-galactosyl-1,3)-N-acetylgalactosam
XLOC_018671	THBS2	-0.57	4.73E-03	XM_006277394.1	thrombospondin 2, transcript variant X1		XLOC_009748	LOC102573884	0.59	4.73E-03	XM_006268087.1	cystatin-like
XLOC_018228	LOC102559361	-0.57	4.73E-03	XM_006276953.1	endothelin B receptor-like		XLOC_005629	MST1	0.59	4.73E-03	XM_006263766.1	macrophage stimulating 1 (hepatocyte growth factor-like)
XLOC_001384	LOC102573310	-0.54	9.85E-03	XM_006259209.1	prostaglandin reductase 1-like		XLOC_014282	BRINP2	0.59	6.57E-03	XM_006272949.1	bone morphogenic protein/retinoic acid inducible neural-specific 2
XLOC_018473	LOC102559751	-0.52	8.24E-03	XM_006277194.1	vitamin K-dependent protein S-like		XLOC_007028	LOC102573251	0.59	4.73E-03	XM_006265256.1	aquaporin 3-like
XLOC_009837	LOC102558436	-inf	2.63E-03	XM_006275267.1	zinc finger protein 184-like		XLOC_019928	LOC102573222	0.57	2.63E-03	XM_006278652.1, XM_006277tensin-like C1 domain-containing phosphatase-like	
							XLOC_012336	SPTB	0.57	6.57E-03	XM_006270827.1	spectrin, beta, erythrocytic, transcript variant X1
							XLOC_018338	COLGALT1	0.57	2.63E-03	XM_006277067.1	collagen beta(1-O)galactosyltransferase 1
							XLOC_018060	LOC102575942	0.57	8.24E-03	XM_006276780.1	exostosin-1c-like
							XLOC_009845	LOC102564670	0.55	2.63E-03	XM_006268214.1	3-oxo-5-beta-steroid 4-dehydrogenase-like

Day 12 FPT vs MPT											
Female-biased					Male-biased						
Gene_ID	Gene Symbol	LOG2(FC)	FDR	RefSeq Accession	Description						
XLOC_016935	LOC102567251	-4.05	8.24E-03	XM_006275615.1	major histocompatibility complex class I-related gene protein-like	XLOC_003593	AMH	4.70	2.63E-03	XM_006261559.1	anti-Mullerian hormone
XLOC_017683	LOC102559514	-2.30	2.63E-03	XM_006276390.1	complement receptor type 1-like	XLOC_017096	MATN4	3.94	2.63E-03	XM_006275789.1	matrin 4
XLOC_017010	AQP2	-2.06	4.73E-03	XM_006275689.1	aquaporin 2 (collecting duct)	XLOC_002864	AHSG	3.55	6.57E-03	XM_006260768.1	alpha-2-HS-glycoprotein
XLOC_012145	LOC102562106	-2.01	2.63E-03	XM_006270621.1	protein Jumonji-like	XLOC_006327	LOC102570551	3.02	2.63E-03	XM_006264538.1	keratin, type I cytoskeletal 14-like
XLOC_013275	KDM6B	-1.78	2.63E-03	XM_006271864.1	lysine (K)-specific demethylase 6B	XLOC_006325	LOC102570319	2.80	2.63E-03	XM_006264537.1	keratin, type I cytoskeletal 10-like
XLOC_019721	HOXC10	-1.67	2.63E-03	XM_006278474.1	homeobox C10	XLOC_005081	COL9A1	2.55	2.63E-03	XM_006263154.1	collagen, type IX, alpha 1
XLOC_012144	LOC102561337	-1.66	2.63E-03	XM_006270617.1	protein Jumonji-like	XLOC_007742	LOC102573967	2.46	2.63E-03	XM_006265651.1	serum albumin-like
XLOC_001006	LOC102570740	-1.50	2.63E-03	XM_006258812.1	forkhead box protein L2-like	XLOC_013641	IFIT5	2.42	2.63E-03	XM_006272248.1	interferon-induced protein with tetratricopeptide repeats 5
XLOC_007791	LOC102569784	-1.48	2.63E-03	XM_006266039.1	collagen alpha-1(VII) chain-like	XLOC_016834	LOC102561886	2.09	8.24E-03	XM_006275518.1	fibrinogen alpha chain-like
XLOC_002517	LOC102565261	-1.47	2.63E-03	XR_362801.1	uncharacterized LOC102565261	XLOC_012311	LOC102567318	2.02	4.73E-03	XR_363379.1	uncharacterized LOC102567318
XLOC_005656	GYS2	-1.47	2.63E-03	XM_006263801.1	glycogen synthase 2 (liver)	XLOC_007414	LOC102574207	1.91	2.63E-03	XM_006265652.1	serum albumin-like
XLOC_016389	LOC102568572	-1.34	8.24E-03	XM_006275056.1	synaptotagmin-12-like	XLOC_000495	LOC102569139	1.91	2.63E-03	XM_006258290.1	cathepsin W-like
XLOC_008087	ASPG	-1.32	4.73E-03	XM_006266348.1	asparagine synthetase homolog (S. cerevisiae)	XLOC_000283	CAP3	1.86	2.63E-03	XM_006258045.1	carboxypeptidase A3 (mast cell)
XLOC_013006	LOC102575860	-1.30	2.63E-03	XM_006271581.1	potassium voltage-gated channel subfamily H member 7-like	XLOC_018282	LOC102573693	1.72	2.63E-03	XM_006277011.1	solute carrier family 2, facilitated glucose transporter member 11-like
XLOC_013344	LOC102561495	-1.27	6.57E-03	XR_363430.1	uncharacterized LOC102561495	XLOC_003144	INHA	1.63	2.63E-03	XM_006261090.1	inhibin, alpha
XLOC_000795	PCSK9	-1.25	2.63E-03	XM_006258599.1	proprotein convertase subtilisin/kexin type 9	XLOC_005927	FGB	1.62	6.57E-03	XM_006264103.1	fibrinogen beta chain
XLOC_019132	LOC102568973	-1.23	2.63E-03	XM_006277868.1	complement C4-like	XLOC_017367	LOC10257980	1.60	9.85E-03	XM_006276059.1	sodium/nucleoside cotransporter 2-like
XLOC_015035	LOC102568567	-1.09	2.63E-03	XM_006273707.1	uncharacterized LOC102568567	XLOC_012871	LOC102560787	1.58	2.63E-03	XM_006271440.1	xylosyltransferase 1-like
XLOC_017904	LOC102575941	-1.09	2.63E-03	XM_006276617.1	cytochrome P450 26A1-like	XLOC_009180	M0V10	1.56	8.24E-03	XM_006267531.1	M0V10, Moloney leukemia virus 10, homolog (mouse)
XLOC_012164	NPTX1	-1.09	2.63E-03	XM_006270639.1	neuronal pentraxin I	XLOC_011776	LGALS2	1.51	2.63E-03	XM_006270258.1	lectin, galactoside-binding, soluble, 2
XLOC_012052	COL4A3	-1.05	2.63E-03	XM_006258325.1	collagen, type IV, alpha 3 (Goodpasture antigen)	XLOC_013828	LOC102573123	1.50	2.63E-03	XM_006274551.1	transcription factor SOX-9-like
XLOC_017934	CPS1	-1.02	4.73E-03	XM_006276652.1	carbamoyl-phosphate synthase 1, mitochondrial	XLOC_017122	LOC102574633	1.49	9.85E-03	XM_006275810.1	cytochrome P450 2A5-like
XLOC_015868	CPLX2	-0.99	2.63E-03	XM_006274560.1	complexin 2	XLOC_017114	LOC102574160	1.43	2.63E-03	XM_006275808.1	plasminogen-like
XLOC_017936	CPN4	-0.99	2.63E-03	XM_006276640.1	copine IV	XLOC_017091	LOC102568476	1.36	2.63E-03	XM_006269186.1	interferon-induced very large GTPase 1-like
XLOC_006272	EYAI	-0.97	2.63E-03	XM_006264490.1	eyes absent homolog 1 (Drosophila), transcript variant X1	XLOC_002340	PNMT	1.35	2.63E-03	XM_006260210.1	phenylethanolamine N-methyltransferase
XLOC_001064	GREB1	-0.97	2.63E-03	XM_006258874.1	growth regulation by estrogen in breast cancer 1	XLOC_001732	LOC102563781	1.31	2.63E-03	XM_006276493.1	tapsasin-related protein-like
XLOC_004986	CNTN4	-0.92	2.63E-03	XM_006263050.1	contactin 4	XLOC_018169	GSTP1	1.27	2.63E-03	XM_006276880.1	glutathione S-transferase pi 1
XLOC_009448	LOC102562567	-0.90	2.63E-03	XM_006276800.1	major histocompatibility complex class I-related gene protein-like	XLOC_000323	LOC102561902	1.25	2.63E-03	XM_006258095.1	tripartite motif-containing protein 7-like
XLOC_003617	MYH11	-0.89	2.63E-03	XM_006261582.1	myosin, heavy chain 11, smooth muscle	XLOC_003435	LOC102566361	1.25	2.63E-03	XM_006261381.1	ovotransferrin-like
XLOC_002516	HSD17B1	-0.88	2.63E-03	XM_006260402.1	hydroxysteroid (17-beta) dehydrogenase 1, transcript variant X2	XLOC_014516	LOC102566943	1.22	2.63E-03	XM_006273145.1	cytochrome P450 1A5-like, transcript variant X1
XLOC_001929	ARX	-0.84	2.63E-03	XM_006259798.1	aristless related homeobox	XLOC_006802	LOC102573570	1.21	2.63E-03	XM_006265015.1	solute carrier family 22 member 6-A-like
XLOC_011708	LOC102568633	-0.82	2.63E-03	XM_006270170.1	probable vesicular acetylcholine transporter A-like	XLOC_009365	GGT1	1.18	2.63E-03	XM_006276703.1	gamma-glutamyltransferase 1
XLOC_010162	SMAD1	-0.79	2.63E-03	XM_006268534.1	SMAD family member 1	XLOC_015902	LOC102567478	1.18	2.63E-03	XM_006274585.1	interferon-induced GTP-binding protein Mx-like
XLOC_010742	LOC102576539	-0.78	2.63E-03	XM_006269136.1	zona pellucida sperm-binding protein 3-like	XLOC_002692	LOC102575737	1.12	2.63E-03	XM_006260622.1	cytochrome P450 11B, mitochondrial-like
XLOC_017020	LOC102564773	-0.75	2.63E-03	XM_006275687.1	keratin, type II cytoskeletal coiled-coil-like	XLOC_007233	LOC102567139	1.11	2.63E-03	XM_006265470.1	multidrug and toxin extrusion protein 1-like
XLOC_008617	VSTM2	-0.74	6.57E-03	XM_006269938.1	V-set and transmembrane domain containing 2B	XLOC_001261	LOC102563321	1.11	2.63E-03	XM_006259988.1	hemoglobin subunit epsilon-like
XLOC_015775	APOA2	-0.73	2.63E-03	XM_006274463.1	apolipoprotein A-II	XLOC_015057	LOC102568110	1.10	2.63E-03	XM_006273705.1	acyl-coenzyme A synthetase ACSM4, mitochondrial-like
XLOC_012510	NCAN	-0.71	2.63E-03	XM_006271033.1	neurocan	XLOC_002221	LOC102569293	1.09	6.57E-03	XM_006260100.1	glycine-N-acetyltransferase-like protein 3-like
XLOC_001200	ELMOD1	-0.68	9.85E-03	XM_006259016.1	ELMO/CED-12 domain containing 1, transcript variant X1	XLOC_014638	LOC102561113	1.08	2.63E-03	XM_006273280.1	solute carrier family 22 member 2-like
XLOC_008602	TBC1D9	-0.68	2.63E-03	XM_006266891.1	TBC1 domain family, member 9 (with GRAM domain)	XLOC_009466	SLC2A9	1.08	2.63E-03	XM_006267811.1	solute carrier family 26 (anion exchanger), member 9
XLOC_015841	COL20A1	-0.67	2.63E-03	XM_006274540.1	collagen, type XX, alpha 1	XLOC_004035	EIF4A2	1.07	2.63E-03	XM_006262029.1	eukaryotic translation initiation factor 4A2
XLOC_003878	FABP4	-0.67	6.57E-03	XM_006261857.1	fatty acid binding protein 4, adipocyte	XLOC_014670	LOC102567399	1.07	2.63E-03	XM_006273306.1	sulfotransferease family cytosolic 2B member 1-like
XLOC_014007	TENN2	-0.67	2.63E-03	XM_006272641.1	teneurin transmembrane protein 2	XLOC_015166	ITGB6	1.05	2.63E-03	XM_006273817.1	integrin, beta 6, transcript variant X2
XLOC_017694	WIF1	-0.66	2.63E-03	XM_006276396.1	WNT inhibitory factor 1	XLOC_004741	GALNT5	1.04	2.63E-03	XM_006262802.1	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 5 (GalNAc-T5)
XLOC_013243	UBE2E2	-0.64	4.73E-03	XM_006271829.1	ubiquitin-conjugating enzyme E2 E	XLOC_001978	CREB3L3	1.04	8.24E-03	XM_006278692.1	cAMP responsive element binding protein 3-like 3
XLOC_020025	ACTG2	-0.64	2.63E-03	XM_006278736.1	actin, gamma 2, smooth muscle, enteric, transcript variant X2	XLOC_005087	TRPC4AP	1.03	2.63E-03	XM_006258376.1	transient receptor potential cation channel, subfamily C, member 4 associated protein
XLOC_012410	TXND5	-0.63	4.73E-03	XM_006270909.1	thioredoxin domain containing 5 (endoplasmic reticulum), transcript variant X1	XLOC_019505	LOC102564244	1.03	2.63E-03	XM_00627233.1	probable E3 ubiquitin-protein ligase MID2-like
XLOC_005828	MPI	-0.63	2.63E-03	XM_006264007.1	mannose phosphate isomerase	XLOC_001658	APOA1	1.03	2.63E-03	XM_006259620.1	apolipoprotein A-I
XLOC_018087	SLC30A9	-0.62	6.57E-03	XM_006276803.1	solute carrier family 30 (zinc transporter), member 9	XLOC_000204	UCP2	1.03	2.63E-03	XM_006275947.1	uncoupling protein 2 (mitochondrial, proton carrier)
XLOC_000678	UCHL1	-0.62	4.73E-03	XM_006258484.1	ubiquitin carboxyl-terminal esterase L1 (ubiquitin thiolesterase)	XLOC_019259	IFIH1	1.02	2.63E-03	XM_006277996.1	interferon induced with helicase C domain 1
XLOC_000344	DPYSL4	-0.60	6.57E-03	XM_006258120.1	dihydropyrimidinase-like 4	XLOC_017452	CLEC3B	1.02	2.63E-03	XM_006276144.1	C-type lectin domain family 3, member B
XLOC_013616	RDH10	-0.58	2.63E-03	XM_006272222.1	retinol dehydrogenase 10 (all-trans)	XLOC_010034	SLC5A11	1.00	4.73E-03	XM_006268442.1	solute carrier family 5 (sodium/inositol cotransporter), member 11
XLOC_013344	TSHZ3	-0.58	6.57E-03	XM_006271924.1	teashirt zinc finger homeobox 3	XLOC_016865	LOC102569893	1.00	2.63E-03	XM_006275549.1	dermatopontin-like
					XLOC_002035	CPXM2	1.00	2.63E-03	XM_006259901.1	carboxypeptidase X (M14 family), member 2	
					XLOC_010871	LOC102570957	0.98	8.24E-03	XM_006269278.1	unconventional myosin-XV-like	
					XLOC_017214	LOC102575978	0.97	2.63E-03	XM_006275897.1	myeloid protein 1-like	
					XLOC_009583	NRN1	0.97	2.63E-03	XM_006267940.1	neuritin 1	
					XLOC_013428	LOC102566162	0.97	2.63E-03	XM_006272019.1	uncharacterized LOC102566162	
					XLOC_011589	TEX15	0.96	2.63E-03	XM_006270036.1	testis expressed 15	
					XLOC_015178	LOC102560270	0.96	2.63E-03	XM_006273834.1	methylocrotonyl-CoA carboxylase beta chain, mitochondrial-like	
					XLOC_015969	CLU	0.93	2.63E-03	XM_006274651.1	clusterin	
					XLOC_018953	LOC102562523	0.93	2.63E-03	XM_006277684.1	lysosome g-like	
					XLOC_000903	PLP1	0.92	2.63E-03	XM_006258708.1	proteolipid protein 1, transcript variant X1	
					XLOC_017425	ESPNL	0.92	2.63E-03	XM_006276123.1	espin-like	
					XLOC_005028	HOGA1	0.91	2.63E-03	XM_006263089.1	4-hydroxy-2-oxoglutarate aldolase 1	
					XLOC_002636	LOC102561378	0.91	2.63E-03	XM_006260653.1	serpin H1-like	

XLOC_0002043	ANPEP	0.88	2.63E-03	XM_006259907.1	alanyl (membrane) aminopeptidase
XLOC_014240	LOC102559116	0.88	6.57E-03	XM_006272882.1	chromosome unknown open reading frame, human C1orf90
XLOC_007107	UPK3A	0.88	2.63E-03	XM_006265339.1	uroplakin 3A
XLOC_019890	CFP	0.86	2.63E-03	XM_006278617.1	complement factor properdin
XLOC_013067	CPT1B	0.86	2.63E-03	XM_006271642.1	carnitine palmitoyltransferase 1B (muscle)
XLOC_008388	LOC102566921	0.85	2.63E-03	XM_006266674.1	SPARC-like protein 1-like
XLOC_001938	ACSF3	0.83	2.63E-03	XM_006259815.1	acyl-CoA synthetase family member 3
XLOC_007730	AGMAT	0.83	2.63E-03	XM_006265981.1	arginine ureidohydrolase (agmatinase)
XLOC_005663	LOC102575135	0.82	2.63E-03	XM_006263807.1	ammonium transporter Rh type C-like
XLOC_001313	LOC102575660	0.82	2.63E-03	XM_006259135.1	dimehylinoline monooxygenase [N-oxide-forming] 1-like, transcript variant X3
XLOC_004855	TFR2	0.82	4.73E-03	XM_006262912.1	transferrin receptor 2
XLOC_000026	CA13	0.81	2.63E-03	XM_006257756.1	carbonic anhydrase XIII
XLOC_009566	ELN	0.81	2.63E-03	XM_006267934.1	elastin
XLOC_007228	DDX58	0.81	2.63E-03	XM_006265462.1	DEAD (Asp-Glu-Ala-Asp) box polypeptide 58
XLOC_010370	ALDOB	0.80	2.63E-03	XM_006268753.1	aldolase B, fructose-bisphosphate, transcript variant X2
XLOC_003095	JSRP1	0.80	6.57E-03	XM_006261560.1	junctional sarcoplasmic reticulum protein 1
XLOC_003790	ALDH4A1.LOC10	0.80	2.63E-03	XM_006261753.1	aldehyde dehydrogenase 4 family, member A1, taste receptor type 1 member 2-like
XLOC_017558	AMN	0.79	2.63E-03	XM_006274258.1	ammon associated transmembrane protein
XLOC_018070	LOC102574081	0.79	2.63E-03	XM_006276772.1	chromosome unknown open reading frame, human C1orf63
XLOC_003589	LOC102566435	0.78	2.63E-03	XM_006261548.1	small EDKR-rich factor 1-like
XLOC_015976	LOC102567479	0.78	2.63E-03	XM_006274661.1	zinc finger protein 208-like
XLOC_004612	LOC102574966	0.77	2.63E-03	XM_006262659.1	1,25-dihydroxyvitamin D(3)-24-hydroxylase, mitochondrial-like
XLOC_010354	PCYOX1	0.77	2.63E-03	XM_006268735.1	prenylcysteine oxidase 1
XLOC_001624	LOC102576428	0.76	9.85E-03	XM_006259479.1	cytochrome P450 4F22-like
XLOC_016914	CLEC18A	0.76	2.63E-03	XM_006275598.1	C-type lectin domain family 18, member A
XLOC_004420	PAMR1	0.76	2.63E-03	XM_006262454.1	peptidase domain containing associated with muscle regeneration 1, transcript variant X1
XLOC_003061	MFSD4	0.76	2.63E-03	XM_006261001.1	major facilitator superfamily domain containing 4
XLOC_000041	LOC102566578	0.75	6.57E-03	XM_006257779.1	avidin-like
XLOC_016610	LOC102566253	0.74	6.57E-03	XM_006275298.1	diamine acetyltransferase 2-like
XLOC_003184	P4HA2	0.74	2.63E-03	XM_006261132.1	prolyl 4-hydroxylase, alpha polypeptide II, transcript variant X1
XLOC_014252	SLC6A18	0.73	2.63E-03	XM_006272902.1	solute carrier family 6 (neutral amino acid transporter), member 18
XLOC_008408	CALB1	0.72	2.63E-03	XM_006266690.1	calbindin 1, 28kDa
XLOC_004857	GIGYF1	0.72	2.63E-03	XM_006262914.1	GRB10 interacting GYF protein 1
XLOC_003053	FTCD	0.72	2.63E-03	XM_006260991.1	formimidoyltransferase cycloaminase
XLOC_012802	PDZD3	0.71	2.63E-03	XM_006271363.1	PDZ domain containing 3
XLOC_006538	LOC102565592	0.70	2.63E-03	XM_006264753.1	BPTI/Kunitz domain-containing protein-like
XLOC_014342	AMDHD1	0.70	2.63E-03	XM_006272991.1	amidohydrolase domain containing 1
XLOC_013750	STAT1	0.70	4.73E-03	XM_006272369.1	signal transducer and activator of transcription 1, 91kDa
XLOC_014873	ANK1	0.70	9.85E-03	XM_006273519.1	ankyrin 1, erythrocytic
XLOC_000299	GJB1	0.68	8.24E-03	XM_006259059.1	gap junction protein, beta 1, 32kDa
XLOC_016032	LOC102561962	0.68	2.63E-03	XM_006274722.1	parvalbumin, muscle-like
XLOC_002205	LOC102567904	0.68	4.73E-03	XM_006260094.1	aspartoacylase-2-like
XLOC_007714	LOC102570482	0.68	2.63E-03	XM_006265963.1	cytochrome P450 3A21-like
XLOC_004389	LOC102558544	0.67	2.63E-03	XM_006262429.1	cathelicidin-2-like
XLOC_009584	F13A1	0.67	2.63E-03	XM_006267941.1	coagulation factor XIII, A1 polypeptide
XLOC_001181	ME3	0.66	2.63E-03	XM_006259999.1	malic enzyme 3, NADP(+)-dependent, mitochondrial
XLOC_007888	STAR	0.65	4.73E-03	XM_006266133.1	steroidogenic acute regulatory protein
XLOC_019852	IFRD1	0.65	2.63E-03	XM_006278568.1	interferon-related developmental regulator 1, transcript variant X2
XLOC_001310	FMO2	0.65	8.24E-03	XM_006259130.1	flavin containing monooxygenase 2 (non-functional)
XLOC_002641	GPX3	0.64	2.63E-03	XM_006260571.1	glutathione peroxidase 3 (plasma)
XLOC_006702	AOC1	0.64	6.57E-03	XM_006264919.1	amine oxidase, copper containing 1
XLOC_002679	SERPINF1	0.63	2.63E-03	XM_006260604.1	serpin peptidase inhibitor, clade F (alpha-2 antiprotease, pigment epithelium derived factor), member 1
XLOC_007638	LOC10257107	0.63	2.63E-03	XM_006265883.1	poly [ADP-ribose] polymerase 14-like
XLOC_007175	LOC102573334	0.62	5.97E-03	XM_006265415.2	low-density lipoprotein receptor-related protein 1-like
XLOC_007156	TPSPAN9	0.61	5.97E-03	XM_006265390.1	tetraspanin 9, transcript variant X1
XLOC_004838	LOC102558546	0.61	N/A		zinc finger protein 850-like
XLOC_003127	TMEM27	0.61	2.63E-03	XM_006261086.1	transmembrane protein 27
XLOC_016572	MIOX	0.60	2.63E-03	XM_006275260.1	myo-inositol oxygenase
XLOC_020119	TNNI2	0.60	9.85E-03	XM_006278938.1	troponin I type 2 (skeletal, fast)
XLOC_009465	PM20D1	0.60	2.63E-03	XM_006267821.1	peptidase M20 domain containing 1
XLOC_019094	HIF3A	0.59	4.73E-03	XM_006277828.1	hypoxia inducible factor 3, alpha subunit
XLOC_016611	LOC102559968	0.58	8.24E-03	XM_006275273.1	transmembrane protein 27
XLOC_010513	SLC23A1	0.57	6.57E-03	XM_006268887.1	solute carrier family 23 (ascorbic acid transporter), member 1
XLOC_001517	LOC102568516	0.57	4.73E-03	XM_006259359.1	glycine amidinotransferase, mitochondrial-like
XLOC_001546	LOC102577042	0.57	8.24E-03	XM_006259394.1	sulfotransferase 6B1-like
XLOC_009799	PHKA1	0.57	8.24E-03	XM_006268154.1	phosphorylase kinase, alpha 1 (muscle)
XLOC_020135	SLC5A2	0.56	9.85E-03	XM_006278885.1	solute carrier family 5 (sodium/glucose cotransporter), member 2
XLOC_019480	RENBP	0.56	9.85E-03	XM_006278205.1	renin binding protein
XLOC_009845	LOC102564670	0.56	8.24E-03	XM_006268214.1	3-oxo-5-beta-steroid 4-dehydrogenase-like

**Table 2-3.** Candidate temperature-responsive genes.

Day 0 – Day 3 MPT: MPT dimorphic (up-regulated)				
Description	RefSeq Accession No.	Log <sub>2</sub> (FC)	FDR	Primary Ontology
uncoupling protein 2 (mitochondrial, proton carrier)	XM_006257947.1	1.47	2.63E-03	P: liver regeneration
UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 5	XM_006262802.1	1.46	2.63E-03	C: Golgi membrane
eukaryotic translation initiation factor 4A2	XM_006262029.1	1.18	2.63E-03	F: translation initiation factor activity
uroplakin 3A	XM_006265339.1	1.09	2.63E-03	C: integral to membrane
low-density lipoprotein receptor-related protein 1-like	XM_006265415.1	1.09	2.63E-03	P: lipoprotein transport
acyl-coenzyme A synthetase ACSM4, mitochondrial-like	XM_006273705.1	1.01	2.63E-03	F: catalytic activity
solute carrier family 1 (glutamate/neutral amino acid transporter), member 4	XM_006264916.1	0.97	2.63E-03	P: proline transmembrane transport
transient receptor potential cation channel, subfamily C, member 4 associated protein	XM_006258376.1	0.91	2.63E-03	C: Cul4A-RING ubiquitin ligase complex
CCAAT/enhancer binding protein (C/EBP), alpha	XM_006274301.1	0.90	2.63E-03	P: regulation of cell proliferation
methylcrotonoyl-CoA carboxylase beta chain, mitochondrial-like	XM_006273834.1	0.86	2.63E-03	F: ligase activity
myosin XVIIIB	XM_006261765.1	0.86	2.63E-03	C: nucleolus
chromosome unknown open reading frame, human C1orf63	XM_006276772.1	0.80	2.63E-03	N/A
interferon-related developmental regulator 1, transcript variant X2	XM_006278568.1	0.69	2.63E-03	P: myoblast fate determination
espin-like	XM_006276123.1	0.65	2.63E-03	N/A
prenylcysteine oxidase 1	XM_006268735.1	0.62	9.85E-03	C: lysosome
formimidoyltransferase cyclodeaminase	XM_006260991.1	0.57	6.57E-03	C: cytosol
uncharacterized LOC102563416	XR_363102.1	infinite	4.73E-03	C: cytosol
Day 0 – Day 3 MPT: FPT dimorphic (down-regulated)				
Description	RefSeq Accession No.	Log <sub>2</sub> (FC)	FDR	Primary Ontology
lysine (K)-specific demethylase 6B	XM_006271864.1	-1.42	2.63E-03	P: positive regulation of transcription from RNA polymerase II promoter
protein Jumonji-like	XM_006270621.1	-1.32	2.63E-03	P: negative regulation of transcription from RNA polymerase II promoter
protein Jumonji-like	XM_006270617.1	-1.32	2.63E-03	P: negative regulation of transcription from RNA polymerase II promoter
cysteine and glycine-rich protein 2	XM_006269901.1	-1.31	2.63E-03	P: multicellular organismal development
myeloid protein 1-like	XM_006275897.1	-1.30	2.63E-03	P: granulocyte differentiation
protease, serine, 35	XM_006258407.1	-1.24	2.63E-03	C: extracellular region
ADAM metallopeptidase with thrombospondin type 1 motif, 15	XM_006262089.1	-1.24	2.63E-03	F: metalloendopeptidase activity
cellular retinoic acid binding protein 2	XM_006275867.1	-1.18	2.63E-03	F: retinoic acid binding
angiopoietin-like 1, transcript variant X2	XM_006267260.1	-1.18	2.63E-03	C: extracellular space
transgelin	XM_006278069.1	-1.14	2.63E-03	F: protein binding, bridging
dimethylaniline monooxygenase [N-oxide-forming] 3-like	XM_006259136.1	-1.06	2.63E-03	C: endoplasmic reticulum membrane
elastin	XM_006267934.1	-1.05	2.63E-03	N/A
uncharacterized LOC102575456, transcript variant X1	XR_363216.1	-1.03	2.63E-03	N/A
hematopoietic prostaglandin D synthase	XM_006265263.1	-1.01	4.73E-03	C: cytoplasm
hemoglobin subunit epsilon-like	XM_006259088.1	-0.95	2.63E-03	P: oxygen transport
matrix-remodelling associated 5	XM_006277556.1	-0.94	2.63E-03	C: extracellular region
epidermal retinol dehydrogenase 2-like	XM_006277024.1	-0.90	8.24E-03	P: retinal metabolic process
v-myb avian myeloblastosis viral oncogene homolog-like 2	XM_006276553.1	-0.82	2.63E-03	P: spindle assembly involved in mitosis
protein Wnt-11-like, transcript variant X2	XM_006265079.1	-0.76	4.73E-03	P: positive regulation of apoptotic process
thrombospondin 2, transcript variant X1	XM_006277394.1	-0.73	2.63E-03	C: basement membrane
protein NEL-like	XM_006272242.1	-0.66	2.63E-03	F: kinase activity
platelet-derived growth factor D-like	XM_006268644.1	-0.63	4.73E-03	P: regulation of peptidyl-tyrosine phosphorylation
RAS-like, family 11, member B	XM_006261252.1	-0.63	6.57E-03	P: small GTPase mediated signal transduction
ubiquitin carboxyl-terminal esterase L1 (ubiquitin thioesterase)	XM_006258484.1	-0.58	4.73E-03	F:cysteine-type endopeptidase activity

**Table 2-4.** Annotation of critical genes involved in sex determination.

Day 0 vs Day 3							
FPT			MPT				
Gene symbol	Regulation	0-3 log2[FC]	Gene symbol	Regulation	0-3 log2[FC]		
DBH	DOWN	-2.05	dopamine beta-hydroxylase (dopamine beta-monooxygenase)	FAP	DOWN	-1.41	fibroblast activation protein, alpha
SLC18A1	DOWN	-2.05	solute carrier family 18 (vesicular monoamine transporter), member 1	LOC102557978	DOWN	-1.30	myeloid protein 1-like
LOC102563199	DOWN	-1.74	chloride channel A-like	LOC102557979	DOWN	-1.42	lysophosphatidic acid acyltransferase 6B
TAGLN3	DOWN	-1.46	transferrin receptor 3	ADMATTS15	DOWN	-1.41	ADAM metallopeptidase with thrombospondin type 1 motif, 15
SLC15A2	DOWN	-1.31	solute carrier family 15 (oligopeptide transporter), member 2	LOC102561337	DOWN	-1.27	protein Junonii-like
STAR	DOWN	-1.22	steroidogenic acute regulatory protein	LOC102562106	DOWN	-1.32	protein Junonii-like
JPH2	DOWN	-1.17	junctophilin 2, transcript variant X1	ANGPTL1	DOWN	-1.18	angiopoietin-like 1, transcript variant X2
LOC102563735	DOWN	-0.97	BMP/relinic acid-inducible neural-specific protein 1-like	LOC102572032	DOWN	-0.63	platelet-derived growth factor D-like
FZD5	DOWN	-0.96	frizzled family receptor 5	PRSS35	DOWN	-1.24	protease, serine, 35
LOC1025670362	DOWN	-0.95	3-beta-hydroxyestrogen dehydrogenase/Delta 5->4-isomerase-like	MXRA5	DOWN	-0.94	retinol binding protein-associated 5
PLAU	DOWN	-0.93	plasminogen activator	C4orf145	DOWN	-2.43	collagen-type VI alpha 1
LOC102576075	DOWN	-0.82	long-chain fatty acid transport protein 6-like	LOC102569158	DOWN	-0.76	protein Wnt-11-like, transcript variant X2
LOC102575314	DOWN	-0.82	steroid 21-hydroxylase-like	LOC102575456	DOWN	-1.03	uncharacterized LOC102575456, transcript variant X1
LOC102575373	DOWN	-0.80	cytochrome P450 11B, mitochondrial-like	LOC102577108	DOWN	-0.90	epidermal retinoic dehydrogenase 2-like
LOC102563623	DOWN	-0.76	cGMP-dependent 3',5'-cyclic phosphodiesterase-like	THBS5	DOWN	-0.73	thrombospondin 2, transcript variant X1
LOC102577145	DOWN	-0.73	D-beta-hydroxybutrate dehydrogenase, mitochondrial-like	LOC102560955	DOWN	-0.66	protein NELU-like
SOAT1	DOWN	-0.66	sterol O-acyltransferase 1	HIPGD	DOWN	-1.01	hematopoietic prostaglandin D synthase
PHTK1	UP	2.16	phosphotransferase	ELL	DOWN	-1.02	elliptin
HTR4S	UP	2.15	5-htr2a serine phosphoprotein 3	CBRP2	DOWN	-1.31	cysteine and glycine-rich protein 2
LOC102561252	UP	1.67	phospholipase A2 inhibitor subunit gamma B-like	TAGLN	DOWN	-1.14	tanglein
MAMD2C	UP	1.59	MAM domain containing 2	RASL1B	DOWN	-0.63	RAS-fac, family 11, member B
LOC102565682	UP	1.58	serpin B1-like	CRABP2	DOWN	-1.18	cellular retinoic acid binding protein 2
FABP4	UP	1.42	fatty acid binding protein 4, adipocyte	MYBL2	DOWN	-0.82	v-myc avian myeloblastosis viral oncogene homolog-like 2
LOC102573435	UP	1.33	uncharacterized LOC102573435	LOC102563321	DOWN	-0.95	hemoglobin subunit epsilon-like
LOC102561011	UP	1.32	chromosome unknown open reading frame, human C2orf40	COL11A1	DOWN	-1.41	collagen, type XI, alpha 1, transcript variant X3
LUU	UP	1.25	lipocalin	LOC102567169	DOWN	-1.04	dehydrogenase/lyase (N-oxide-forming) 3-like
LOC102565053	UP	1.12	lipocalin-like	LOC102561101	DOWN	-0.59	ubiquitin carboxy-terminal esterase L1 (ubiquitin thiolesterase)
STAR05	UP	1.08	SMN-related lipid transfer (START) domain containing 5	AMH	UP	2.78	anti-Mullerian hormone
LOC102598538	UP	1.05	WAV-four-dissulfide core domain protein 2-like	UCP2	UP	1.47	uncoupling protein 2 (mitochondrial proton carrier)
LOC102567788	UP	1.02	catenin-like	GALNT5	UP	1.46	N-acetyl-D-galactosamine:peptide N-acetylgalactosaminyltransferase 5 (GalNAc-T5)
CRISPLD2	UP	1.02	cysteine-rich secretory protein LCC1 domain containing 2	EIF4A2	UP	1.18	eukaryotic translation initiation factor 4A2
LOC102569054	UP	0.99	protein MRP-126-like	UFPK3A	UP	1.09	uprakrin 3A
LOC102567125	UP	0.97	ribonuclease 3	LOC102573334	UP	1.09	low-density lipoprotein receptor-related protein 1-like
NCAP	UP	0.95	androgen receptor protein, alpha	LOC102568810	UP	1.09	alpha-1-proteinase inhibitor, acidic
MYH11	UP	0.83	myosin, heavy chain 11, smooth muscle	SLC14A	UP	0.97	solute carrier family 1 (glutathione reductase), member 4
MCM8	UP	0.82	microtubule maintenance complex component 8	TRPC4AP	UP	0.91	transient receptor potential cation channel, subfamily C, member 4 associated protein
RINT1	UP	0.78	RAD50 interacting 1, transcript variant X1	CEBPA	UP	0.90	CEBP-alpha enhancer binding protein (C/EBP), alpha
LOC102566081	UP	0.76	beta-galactoside-binding lectin-like	LOC102560270	UP	0.86	methylcytochrome-CoxI carboxylase beta chain, mitochondrial-like
HSD17B1	UP	0.72	hydroxysteroid (17-beta) dehydrogenase 1, transcript variant X2	MYO18B	UP	0.86	myosin XVIII
LOC102570022	UP	0.71	vascular adhesion protein 1-like, transcript variant X2	LOC102574081	UP	0.80	chromosome unknown open reading frame, human C1orf63
THRH	UP	0.70	thyroid hormone receptor, alpha	IFRD1	UP	0.69	interferon-related developmental regulator 1, transcript variant X2
HEMN	UP	0.62	hemogen, hemizygous variant X1	BDNL	UP	0.69	synapsin
LOC102569028	UP	0.61	histone H2B 1/2346-like	PCYOX1	UP	0.62	pyruvate oxidase 1
			FTCD	UP	0.57	formylmethionyltransferase cycloheximide	
			LOC102563416	UP	inf	uncharacterized LOC102563416	
Day 3 vs Day 6							
FPT			MPT				
Gene symbol	Regulation	3-6 log2[FC]	Gene symbol	Regulation	3-6 log2[FC]		
LOC102564391	DOWN	-0.78	relaxin receptor 1-like	TAP2	DOWN	-4.60	transporter, 2 ATP-binding cassette, sub-family B (MDR/TAP)
LOC102573251	DOWN	-0.46	aquaporin-9-like	LOC102566578	DOWN	-1.99	afadin-like
ELN	UP	2.83	elastin	LOC102591161	DOWN	-1.83	CCAAT/enrichment factor binding protein 1-like
DEUS	UP	1.75	deoxyuridine triphosphate nucleotidase, neuronal 3	LOC102565952	DOWN	-1.79	SPFH-domain-containing protein-like
COL11A1	UP	1.25	collagen, type XI, alpha 1, transcript variant X3	TGM3	DOWN	-1.57	transglutaminase 3
CADPS	UP	1.09	Ca++-dependent secretion activator	GYS2	DOWN	-1.55	glycogen synthase 2 (liver)
LOC102594040	UP	1.07	caltonium receptor-like	SCN1A	DOWN	-1.49	sodium channel, voltage-gated, type I, alpha subunit
LOC102575737	UP	0.99	cytochrome P450 11B, mitochondrial-like	LOC102570382	DOWN	-1.44	WAP four-dissulfide core domain protein 5-like
LOC102574810	UP	0.97	riboflavin transporter 2-like	SLC26A9	DOWN	-1.41	solute carrier family 26 (anion exchanger), member 9
NCKAP1	UP	0.97	NCK-associated kinase-like	ACE2	DOWN	-1.40	alpha-1 converting enzyme 2
LOC102569570	UP	0.94	oleoylegacyl and methylacylome-thane domain-containing protein 19-like	LOC102564018	DOWN	-1.35	oleoylegacyl and methylacylome-thane domain-containing protein 19-like
LOC102565959	UP	0.92	cytochrome P450 2K4-like	LOC102575787	DOWN	-1.33	adrenodoxin, mitochondrial-like
ADAMTS15	UP	0.85	ADAM metallopeptidase with thrombospondin type 1 motif, 15	SLC10A9	DOWN	-1.32	cytochrome P450 2K4-like
THBS2	UP	0.83	thrombospondin 2, transcript variant X1	SLC44A	DOWN	-1.29	solute carrier family 4 (sodium bicarbonate cotransporter), member 4
LOC102575314	UP	0.81	steroid 21-hydroxylase-like	JPH2	DOWN	-1.26	junctophilin 2, transcript variant X1
NEFL	UP	0.79	neurofilament, light polypeptide	LOC102570382	DOWN	-1.19	Delta-hydroxy steroid dehydrogenase 5-like
JPH2	UP	0.61	junctophilin 2, transcript variant X1	LOC102565377	DOWN	-1.18	serotinin-like
LOC102568924	UP	0.61	vitamin D3 hydroxylase-associated protein-like	SLC10A9	DOWN	-1.18	gamma-glutamyl transferase, mitochondrial-like
			SLC5A8	DOWN	-1.04	solute carrier family 6 (neutral amino acid transporter), member 8	
			SCRN1	DOWN	-1.03	secernin 1	
			LOC102568587	DOWN	-0.98	uncharacterized LOC102568587	
			LOC102561484	DOWN	-0.98	potassium-translocating ATPase alpha chain 2-like	
			TTLL9	DOWN	-0.98	tryptophanyl tRNA ligase, family 1, member 9	
			BDNF	DOWN	-0.96	solute carrier family 6 (neutral amino acid transporter), member 15	
			LOC102575314	DOWN	-0.95	transferrin 2-like	
			LOC102571256	DOWN	-0.86	Y+L amino acid transporter 2-like	
			LOC102575737	DOWN	-0.86	cytochrome P450 11B, mitochondrial-like	
			DNAH4	DOWN	-0.84	dynein, axonemal, heavy chain 5	
			NEFM	DOWN	-0.81	neurofilament, medium polypeptide	
			SLC6A19	DOWN	-0.81	solute carrier family 6 (neutral amino acid transporter), member 19	
			UNC90	DOWN	-0.79	unc-90 homolog (C. elegans)	
			LOC102568403	DOWN	-0.78	retinol dehydrogenase	
			GRTP1	DOWN	-0.77	growth hormone regulated TBC protein 1	
			LOC102575978	DOWN	-0.75	myeloid protein 1-like	
			SPOCK2	DOWN	-0.73	sparcostatin, ovo and kazal-like domains proteoglycan (testican) 2	
			APOA2	DOWN	-0.73	apolipoprotein A-II	
			CTH	DOWN	-0.72	cystathionase (cystathione gamma-lyase)	
			LOC102567929	DOWN	-0.71	sulfotransferase 1 family member D1-like	
			LOC10256448	DOWN	-0.70	anthropin A 4 synthase ACSM3, mitochondrial-like	
			LOC102593061	DOWN	-0.69	endothelin B receptor	
			LOC102593494	DOWN	-0.65	smthine desmosine 2-like	
			NEFL	DOWN	-0.65	neurofilament, light polypeptide	
			LOC102573310	DOWN	-0.65	prostaglandin endoperoxide 1-like	
			EMX1	DOWN	-0.62	empty spiracles homeobox 1	
			LOC102567357	DOWN	-0.57	probable proline dehydrogenase 2-like	
			LOC102563794	UP	4.15	myosin-3-like	
			ANXA1	UP	2.80	anti-Mullerian hormone	
			INVA	UP	2.72	zeta 1 sialin	
			ACTC1	UP	2.60	actin, alpha, cardiac muscle 1	
			LOC102569139	UP	2.45	cathepsin W-like	
			MPO	UP	2.43	myeloperoxidase	
			LOC102575076	UP	2.26	butyrophilin subfamily 1 member A1-like	
			LOC102569158	UP	2.20	protein Wnt-11-like, transcript variant X2	
			LOC102566921	UP	2.13	SLC4C-like protein 1-like	
			LOC102565781	UP	1.71	cysteinidin-2-OH antimicrobial peptide-like	
			LOC102558544	UP	1.62	cathepsin D-like	
			MATN4	UP	1.59	matrin 4	
			BIVRB	UP	1.57	biliverdin reductase B (favin reductase (NADPH))	
			CA13	UP	1.53	carbonic anhydrase XIII	
			KEL	UP	1.52	Kell blood group, metallo-endopeptidase	
			TEX11	UP	1.47	testis expressed 11	
			LOC102567788	UP	1.46	calreticulin-like	
			SLC4A1	UP	1.42	solute carrier family 4 (anion exchanger), member 1	
			PWHL1	UP	1.39	anti-Mullerian hormone receptor, type II	
			AMHR2	UP	1.31	anti-Mullerian hormone receptor, type II	
			LOC102582273	UP	1.28	uncharacterized LOC102582273	
			MYCL	UP	1.26	v-myc avian myelocytomatosis viral oncogene lung carcinoma derived homolog	
			CLU	UP	1.25	clusterrin	
			PSAT1	UP	1.18	phosphoserine aminotransferase 1, transcript variant X1	
			PTPRZ1	UP	1.16	protein tyrosine phosphatase, receptor-type, Z polypeptide 1	
			LOC102570551	UP	1.13	keratin, type I cytoskeletal 14-like	

Day 6 vs Day 12					
FPT			MPT		
Gene symbol	Regulation	6-12 log2(FC)	Gene symbol	Regulation	6-12 log2(FC)
NDGA1	UP	1.08	MAM domain containing glycosylphosphatidylinositol anchor 1		
LOC102570959	UP	1.07	proteolipid polypeptide-like		
TNMD	UP	1.05	tenomodulin		
A2M	UP	1.05	alpha-2-macroglobulin		
LOC102560544	UP	1.01	elongation factor 1-alpha-like		
TDRKH	UP	0.96	tudor and KH domain containing		
LOC102572713	UP	0.93	prolactin-releasing peptide receptor-like		
LOC102577358	UP	0.90	duplex and mbt-3 related transcription factor 3-like		
LOC102573123	UP	0.86	transcription factor SOX-9-like		
LOC102575942	UP	0.80	exostosin-1c-like		
UPK1B	UP	0.79	uroplakin 1B		
MMP23B	UP	0.78	matrix metallopeptidase 23B		
UCP2	UP	0.77	uncoupling protein 2 (mitochondrial, proton carrier)		
ST6GALNAC2	UP	0.71	ST6 (alpha-N-acetyl-neuraminy-2,3-beta-galactosyl)3-N-acetylgalactosaminide alpha-2,6-sialyltransferase 2		
LOC102576325	UP	0.71	serine/threonine-protein kinase PAK 1-like		
CEBP $\alpha$	UP	0.69	CCAAT/enhancer binding protein (CEBP), alpha		
BOC	UP	0.66	BOC cell adhesion associated, oncogene regulated		
LOC102573884	UP	0.62	cystatin-like		
NAGLU	UP	0.59	N-acetylglycosaminidase, alpha		
SPTB	UP	0.57	spectrin, beta, erythrocytic, transcript variant X1		
Day 6 vs Day 12					
Gene symbol	Regulation	6-12 log2(FC)	Gene symbol	Regulation	6-12 log2(FC)
LOC102563321	DOWN	-3.82	hemoglobin subunit epsilon-like	LOC102567251	DOWN
LOC102575737	DOWN	-1.49	cytochrome P450 11B, mitochondrial-like	LOC102569784	DOWN
LOC102569293	DOWN	-1.29	glycine N-acyltransferase-like protein 3-like	HDXC10	DOWN
LOC102568516	DOWN	-0.84	glycine amidinotransferase, mitochondrial-like	ACTG2	DOWN
SLC5A2	DOWN	-0.65	solute carrier family 5 (sodium/glucose cotransporter), member 2	NPTX1	DOWN
AVPR1A	DOWN	-0.58	altrophycocyanin/nitroporphyrin	AVPR1A	DOWN
WIF1	UP	2.15	WNT inhibitor factor 1	LOC102557978	UP
			forkhead box protein L3-like	AHSN	UP
LOC102575960	UP	2.15	potassium voltage-gated channel subfamily H member 7-like	MATN4	UP
LOC102576539	UP	1.89	zona pellucida sperm-binding protein 3-like	LOC102566578	UP
LOC102565261	UP	1.82	uncharacterized LOC102565261	LOC102566592	UP
HSD17B1	UP	1.78	hydroxysteroid (17-beta) dehydrogenase 1, transcript variant X2	PNMT	UP
MYH11	UP	1.42	myosin, heavy chain 11, smooth muscle	SLC6A18	UP
PCSK9	UP	1.40	proprotein convertase subtilisin/kenin type 9	GGT1	UP
COL4A3	UP	1.12	collagen, type IV, alpha 3 (Goodpasture antigen)	PLP1	UP
CPLX2	UP	0.76	complexin 2	COL9A1	UP
EYA1	UP	0.75	eyes absent homolog 1 (Drosophila), transcript variant X1	LOC102560787	UP
LOC102564773	UP	0.71	keratin, type II cytoskeletal coiled-coil-like	LOC102569139	UP
NCAN	UP	0.68	neurocan	NRN1	UP
			LOC102561113	UP	1.71
			SLC26A9	UP	1.65
			LOC102562523	UP	1.64
			AMH	UP	1.58
			LOC102574633	UP	1.54
			LOC102567318	UP	1.36
			ELN	UP	1.33
			LOC102574160	UP	1.32
			IFT15	UP	1.19
			LOC102566361	UP	1.18
			LOC102573893	UP	1.17
			LOC102570551	UP	1.16
			LOC102567139	UP	1.04
			CPAS	UP	1.04
			GPX3	UP	1.02
			SLC23A1	UP	0.91
			LOC102568516	UP	0.90
			LOC102573570	UP	0.85
			UPK3A	UP	0.81
			LOC102568110	UP	0.80
			LOC102573123	UP	0.80
			AP0A1	UP	0.79
			TMEM27	UP	0.77
			LOC102575737	UP	0.74
			LOC102575760	UP	0.73
			STAR	UP	0.72
			LOC102570482	UP	0.71
			CLCNKB	UP	0.68
			TSPAN9	UP	0.61

**Table 2-5.** Candidate critical genes with putative regulatory functions.

Candidate transcriptional regulator					
Gene ID	Gene symbol	Description	Molecule type	Expression	Timespan
<b>MPT Day 0 vs MPT Day 3</b>					
XLOC_015643	<i>CEBPA</i>	CCAAT/enhancer binding protein (C/EBP), alpha	Transcription factor	Up	Short
XLOC_013275	<i>KDM6B</i>	Lysine (K)-specific demethylase 6B	Transcription regulator	Down	Long
XLOC_012144	<i>LOC102562106</i>	Protein Jumonji-like	Transcription regulator	Down	Long
XLOC_012145	<i>LOC102561337</i>	Protein Jumonji-like	Transcription regulator	Down	Long
XLOC_017186	<i>CRABP2</i>	Cellular retinoic acid binding protein 2	Transporter	Down	Short
XLOC_017840	<i>MYBL2</i>	v-myb avian myeloblastosis viral oncogene homolog-like 2	Transcription factor	Down	Short
XLOC_006860	<i>LOC102569158</i>	Protein Wnt-11-like, transcript variant X2	Other	Down	Short
<b>MPT Day 3 vs MPT Day 6</b>					
XLOC_006860	<i>LOC102569158</i>	Protein Wnt-11-like, transcript variant X2	Other	Up	Short
XLOC_020119	<i>TNNI2</i>	Troponin I type 2 (skeletal, fast)	Enzyme	Up	Short
XLOC_009637	<i>MYCL</i>	v-myc avian myelocytomatisis viral oncogene lung carcinoma derived homolog	Transcription factor	Up	Short
XLOC_006593	<i>LOC102560544</i>	Elongation factor 1-alpha-like	Other	Up	Short
XLOC_003318	<i>LOC102577358</i>	Duplex and mab-3 related transcription factor 3-like	Transcription factor	Up	Long
XLOC_013828	<i>LOC102573123</i>	Transcription factor SOX-9-like	Transcription factor	Up	Long
XLOC_014546	<i>LOC102576325</i>	Serine/threonine-protein kinase PAK 1-like	Protein kinase	Up	Long
XLOC_015643	<i>CEBPA</i>	CCAAT/enhancer binding protein (C/EBP), alpha	Transcription factor	Up	Short
XLOC_012336	<i>SPTB</i>	Spectrin, beta, erythrocytic, transcript variant X1	Other	Up	Short
XLOC_018228	<i>LOC102559361</i>	Endothelin B receptor-like	Receptor	Down	Ambiguous
XLOC_003353	<i>EMX1</i>	Empty spiracles homeobox 1	Transcription factor	Down	Short
<b>MPT Day 6 vs MPT Day 12</b>					
XLOC_013828	<i>LOC102573123</i>	Transcription factor SOX-9-like	Transcription factor	Up	Long
XLOC_019721	<i>HOXC10</i>	Homeobox C10	Transcription factor	Down	Ambiguous
XLOC_001928	<i>ARX</i>	Aristless related homeobox	Transcription factor	Down	Long
<b>FPT Day 0 vs FPT Day 3</b>					
XLOC_003878	<i>FABP4</i>	Fatty acid binding protein 4, adipocyte	Transporter	Up	Ambiguous
XLOC_000567	<i>LUM</i>	Lumican	Other	Up	Short
XLOC_012101	<i>TAGLN3</i>	Transgelin 3	Other	Down	Short
XLOC_007693	<i>FZD5</i>	Frizzled family receptor 5	Receptor	Down	Short
XLOC_017000	<i>LOC102563625</i>	cGMP-dependent 3',5'-cyclic phosphodiesterase-like	Enzyme	Down	Short
<b>FPT Day 6 vs FPT Day 12</b>					
XLOC_001005	<i>LOC102577040</i>	Forkhead box protein L2-like	Transcription factor	Up	Long
XLOC_006272	<i>EYAI</i>	Eyes absent homolog 1 (Drosophila), transcript variant X1	Phosphatase	Up	Long

## **General discussion**

In this thesis, integrated use of classical methodology (pharmacological administration experiments) and modern methodology (next generation RNA sequencing analysis) were employed to potentially elucidate and comprehensively characterize molecular mechanism underlying TSD in *Alligator mississippiensis*. In chapter 1, I was able to suggest for potential model of temperature sensation mechanism during TSD in the developing embryo. Expression analysis of the gonad during sex determination period indicated expression of the thermosensitive cation channel TRPV4 (Figure 1-1). Electrophysiological analysis indicated that channel was activated at warm temperatures, near temperature range associated with alligator sex determination, and the channel activation led to intracellular  $\text{Ca}^{2+}$  influx (Figure 1-5). By selective activation and inhibition of TRPV4 channel activity using administration of TRPV4-specific pharmacological agents during sex determination period, I was able to demonstrate that TRPV4 channel activity can influence the expression of genes related to testis-determination in the long term. Expression levels of *AMH* and *SOX9*, genes critical for testis formation, were significantly altered several weeks after the chemical administration, and partial feminization was observed at histological level in male producing temperature (Figure 1-6,9). In conclusion, TRPV4 was able to influence genetic cascade related with testicular formation. Hence, for the first time a biomolecule, TRPV4, was able to directly associate temperature and sex determination in TSD species.

In chapter 2, I was able to comprehensively characterize the global transcriptome in the embryonic gonad at female- and male-producing temperature during sex determination using RNA-sequencing (RNA-seq) analysis (Figure 2-1).

RNA-seq data was collected, and I was able to track differentially expressed genes between adjacent time points at same temperature conditions, and also between the two temperature conditions at corresponding time points (Figure 2-3), and by cross-comparison, 230 genes with both development-wise and sex-wise differential expression were screened out (Figure 2-7). Forty-one genes expressions were observed to be temperature-responsive, including jumonji proteins *KDM6B*, *JARID2*, transcription factor *C/EBPA*, and Wnt signaling factor *WNT11* (Table 2-3). Furthermore, twenty-five transcriptional regulators were highly regulated in a sexually dimorphic manner. These include *SOX9*, *FOXL2*, *MYBL2*, *MYCL* and *HOXC10* (Table 2-5). In conclusion, utilization of the high-throughput RNA-seq analysis provided novel insights into the genetic framework underlining alligator TSD, and establishes the much needed gene expression data for future studies.

Two experiments presented in thesis cover the aspect of temperature sensation from both upstream and downstream. TRPV4 channel addresses how temperature, a physical energy, can be translated to chemical signaling via channel activation and  $\text{Ca}^{2+}$  influx. Global transcriptome data presents potential targets, and direct results of the  $\text{Ca}^{2+}$  influx, and also provides short- and long-term gene expression changes during sex determination. Both results from chapter 1 and 2 were not able to explain female sex determination as much as male sex determination, and much of the ovarian sex determination cascade remains unclear. Much of this is only speculation at this stage, however, and more robust evidence is required in the future. Classical methodology such as pharmacological administration experiments can be difficult to provide robust results, unlike modern genome editing and such. However, with advent of modern methodologies such as reporter assays and chromatin immunoprecipitation (ChIP) as

mentioned in chapter 2, as well as organ culture experiments, it would be possible to conduct experiments and validate the role of TRPV4. Additionally, with plethora of observations made in chapter 2 during sex determination, TSD can now be researched from variety of ways, including epigenetic, metabolomics, stress-response.

Sex of species that display GSD is determined at fertilization, and the sexually dimorphic heterochromosomes (XX/XY, ZW/ZZ) have been noted since the beginning of 20th century. However, the molecular mechanisms itself were not identified until the functional characterization of *Sry* gene on the eutherian Y chromosome, almost three decades ago, followed by discovery of many other vertebrate sex determining genes. Generally speaking, in contrast to the binary determination mechanism seen in GSD (presence/absence of heteromorphic sex chromosomes), TSD tends to work in a gradient manner (low to high temperature), meaning screening of sexually dimorphic gene expression alone cannot easily provide clues to elusive sex determining factor.

In the past, several comparative analyses were performed between TSD and GSD organisms, such as mouse, chicken, turtles and alligators. However, the genes in focus were genes found to be crucial in GSD sex determination. This resulted in dependency on GSD model organism for answer to TSD mechanism. When *sry* was first described as master sex determination switch in mammals, reptiles with TSD were immediately theorized to possess thermosensitive *sry* homolog, which later were found to be untrue (Lance, 2009). While comparative analyses are powerful tool, it alone is not enough to study TSD. Furthermore, temperature, in practice, is the measure of particle kinetic energy, and heat radiation. This implies that temperature shift affects the system from the atomic level, rather than specific receptor. In comparison with other

ESD systems, temperature have the ability to influence both specific thermosensors, and non-targets unlike other biotic and physical cues used in ESD such as stress (cortisol level), and photoperiod (photoreceptor) and hence there is greater difficulty in pinpointing the molecular level in which the temperature works during TSD. This is part of reason why so much mechanisms have been theorized, as temperature effects have been observed through DNA bending, RNA stem-loop, protein dimerization, and enzyme efficiency (Sengupta, 2013). Because of temperature's global influence, an alternative method was required.

There is an innate assumption that TSD among reptiles share similar mode of TSD mechanism. In practice, it is necessary to make such assumption, due to relatively limited selection of previous literatures. However, it is becoming increasingly apparent that deep evolutionary division exists among these reptiles; via pattern of gene expression such as timing of *AMH* and *SOX9*, germ cell movement patterns, and pattern of TSD. Current understanding of sex determination indicates that the high diversity is present during the initial activation mechanism, according to researches on GSD organisms. Hence, it should be expected that other reptiles might possess their own unique method of thermosensation, and opens potential for further exotic molecular mechanism of sex determination. Likewise, TRPV4 could not account for all of sex determination in alligator, and another novel element may be present. Therefore, these conclusions only press the further need for more research on TSD. Integration of the classical data with global transcriptomic data, new ideas can be attained. By sharing the RNAseq reads and proposing a novel mechanism of sex determination in alligators, I hope to contribute to the ever-increasing understanding of TSD, and by extension, other ESD systems as well.

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## **Acknowledgments**

I am especially grateful to my supervisor Professor Iguchi Taisen of SOKENDAI (Graduate University for Advanced Studies) and Okazaki Institute for Integrative Bioscience for all the mentoring and academic advices. I am grateful to my supervisors Assistant professors Dr. Shinichi Miyagawa and Dr. Yukiko Ogino for direct supervisions and all their help. I am grateful to Professor Makoto Tominaga and Assistant professor Shigeru Saito for the help with patch clamp studies, and kind support. I would like to thank the members of Iguchi laboratory, Professor Yoshinao Katsu, Professor Ohta for all their advice and help. I would like to thank late Professor Louis J. Guillette Jr. for this collaboration, and his kind support, as this research would not have been possible without him. I would like to thank Dr. Satomi Kohno, Dr. Benjamin B. Parrott, Mr. Russell H. Lowers, and members of Dr. Guillette laboratory for all advices and help with alligator embryo experiments. I would like to thank my family members for all their support. Finally, I would like to thank Dr. David Crews and members of Crews laboratory for inviting me to field of TSD research and recommending me to Dr. Iguchi.