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## 論文内容の要旨

There has been great controversy between neutralists and selectionists over what proportion of mutants contributed to gene evolution as advantageous mutants. Several reports of sequence comparisons have shown by statistical analysis that there were some particular genes at the nucleotide sequence level on which positive selection operates, but no one had been able to estimate the proportion of genes on which positive selection operates among all the genes available. This is because conducting such research requires a large amount of DNA sequence data and coordinated analysis for large-scale search for candidate genes by full use of computers. The purpose of this dissertation is to reveal the role of positive selection in the course of gene evolution. For the first attempt, the proportion of the genes on which positive selection may operate was estimated by a large-scale search. In PART I, the strategy and the results of a large-scale search for the genes on which positive selection may operate were discussed. In this study, a large-scale search is defined as the search for the genes on which can pass certain criteria by utilizing a large amount of DNA sequence data with the high processibility of computers including super computer. The search was performed by the following strategies: 1) alignment construction of the homologous sequences of non-partial coding sequences available in the DDBJ DNA database release 11; 2) comparison between the numbers of synonymous and nonsynonymous substitutions. From the search, seventeen homologous gene groups were obtained as the candidate genes on which positive selection may operate. They constitutes 0.47% of all the gene groups examined in the study. Interestingly enough, nine out of the seventeen gene groups were for the surface proteins of viruses and parasites. A window analysis for the numbers of synonymous and nonsynonymous substitutions was performed to locate the possible within-gene regions being subject to positive selection. The analysis indicated that a region where the number of nonsynonymous substitutions was larger than that of synonymous substitutions corresponded to the known antigenic epitope region.

In PART II, further search was performed to find the genes which contains a region or a segment within the gene subject to positive selection. This search was performed because the nucleotide sites responsible for positive selection usually does not spread to all over the entire gene even when positive selection operates on a gene. This fact led us to the inability to obtain the MHC genes by search in PART I, because only antigenic sites in the MHC genes are selected. In the new search shown in part II, 192 gene groups were obtained as the candidate genes having the within-gene regions where positive selection may operate. They constituted about five percents of all the genes examined.

## 論文の審査結果の要旨

遠藤俊徳君はDNA塩基配列の大量解析によって分子進化の一般的原理を明らかにすることを試みた。分子進化の中立説対自然淘汰説論争では、有利な自然淘汰による突然変異の置換がどれ程存在するかが焦点である。有利な自然淘汰の存在については個々の場合についての報告がいくつかあるが、全体についての解析は未だなされていない。そこで遠藤君は大量のDNA塩基配列を用いて解析した。

PART I では、大量検索の結果について報告している。まづ相同な配列のアラインをし、ついで同義置換と非同義置換の比較を行う。相同遺伝子群のpairwiseな比較で非同義置換が同義置換を上回るpairが半数以上の場合を正の淘汰の候補として取り出した。この検索から17の相同な遺伝子群が有利な淘汰の候補であることがわかった。これは全体の0.47%にすぎない。17の中で9の遺伝子グループはウイルスや他の病原菌の膜蛋白質であった。

PART II では遺伝子内の特定の領域で正の淘汰が働いているような場合の検索を行った。これはウインドウ解析による。20のコドンのウインドウで非同義置換が同義置換の2倍以上であるような場合を正の淘汰の候補とした。その結果192の遺伝子群で特定領域での有利な淘汰の可能性が見い出された。これは全体のほぼ5%である。DNA塩基配列の大量情報解析による研究として充分学位論文に値するものと判断した。