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MHC DQA基因的分子进化研究:Ⅰ.等位基因多态性保持机制及GC含量对基因结构的影响

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摘要 对7种哺乳动物MHC DQA座位的23个等位基因不同外显子(EN)、抗原识别位点(ARS)和EN2的非ARS(NAEN2)的核苷酸同义替换率(Ps)和异义替换率(P~N|)进行了分析,发现在HLA-DQA1的7个等位基因之间的IαAα8个等位基因之间,即同一物种DQA1基因座位内,ARS的PN均显著高于Ps 2倍以上,表现超显性选择;而不同物种DQA基因(DQA1或DQA2)或同一物种的不同DQA基因(DQA1和DQA2)的ARS之间和各比较组的NAEN2之间, 则Ps与PN大致相等,即近似地符合中性进化的预期;EN4和EN3不仅替换率远比ARS低, Ps/PN比值亦非常大,在IαAα等位基因之间达到近20倍,不同基因座位之间也达到4倍左右,呈明显的纯化选择,GC含量分析显示GC峰值大致于某些功能区相应序列的中央部分;EN4的GC含量最高且稳定;密码子第三位GC含量(GCIII)的变化与Ps存在一定程度的负相关关系。上述结果表明, 同一MHC DQA基因的相应于不同功能区(或ARS)的不同外显子(或密码子群)具有特定的相应于其功能的等位基因多态性保持机制, 并提示GCIII是在选择压力下维持分子结构和功能的一种重要机制。本文还修改了核苷酸替换率的估算方法。

关键词 MHC DQA基因 等位基因多态性 超显性选择 纯化选择 GC含量

分类号

Molecular Evolution of MHC DQA Genes I.The Maintenance of Interallelic Divergence and the influence of GC Content on Gene Structure

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Abstract

The analyses of the proportion of synonymous and missense nucleotide substitution (Ps and Pn)in different exons,antigen recognition sites (ARS) and non-ARS of EN2 (NAEN2) of 23 alleles at MHC DQA loci in 7 mammal species gave rise to the following findings.(1) Pn was about twice as much as Ps in ARS among the alleles at DQA1 of any given species,i.e. 7 alleles at HLA-DQA1 or 8 alleles at IaAa. this accords with overdominant selection;(2)Ps showed more or less the same as Pn in ARS among different loci (DQA1 or DQA2 in different species, or DQA1 and DQA2 in one species) or NAEN2 of all comparative pairs, this conforms the expectation of neutral selection;(3)In exon4 and exon3, not only was the substitution proportion extremely low, but also Ps was much higher than Pn(the ratio Ps over Pn is 19.5 in alleles at IaAa of mouse and 4 among alleles at different loci). this coincides obviously with purification selection.The analysis of GC content of MHCDQA showed that its peaks were in the regions corresponding to the middle bulks of some domains,that the highest and constant level was in exon4 and that GC content in the third codon position (GC Ⅲ content) associates inversely with Ps. These results in dicate that the specified maintenance mechanisms of interallelic diversity relevant to their functions exist in given exons corresponding to some domains of the same MHC DQA locus and GC Ⅲ content is an important factor in keeping the structure and function of gene under selection constraint.The method for estimating nucleotide substitution proportion was modified.

Key words MHC DQA genes Interallelic divergence divergence Overdominant selection Purifying selection GC content

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