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原著

Hb Miyada:βδ融合遺伝子による異常ヘモグロビンの構造とその遺伝子解析

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Hb Miyada : Analyses of the Structure and the Gene of Abnormal Hemoglobin with βδ-Hybrid Globin Gene

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Abstract

Isoelectric focusing of hemolysate from peripheral blood of the patient, which was detected during an assay of the Hb A_{1c} level, showed the presence of a slow-moving abnormal hemoglobin located at the same position to Hb A_2. Its content, including the Hb A_2 content, in the total Hb by DEAE-HPLC amounted to 19.8%. Structural analysis indicated that the abnormal globin consisted of the β-like globin from the N-terminus to amino acid 12 and of theδ-like globin from amino acid 22 through the C-terminus. Thus, this Hb was predicted to be identical to Hb Miyada. Analyses of the globin gene arrangement by the Southern-blot-hybridization method and the nucleotide sequence of the clone prepared from DNA amplified by PCR showed that the crossover must have occurred without loss of bases within the first nucleotide of the 18th and the first nucleotide of the 22nd codon of theseβ- and (δ-genes. Reticulocyte in peripheral blood of the patient was incubated with 3H-Leu. The individual globin chains were separated and the incorporated radioactivity determined. The synthesis of the normalα- and β-chains was well-balanced (β/α = 1 .06) for 2 hour incubation, but during this time there was no radioactivity

incorporated into the Miyada (βδ) −chain. It seems, therefore, that the synthesis of the Miyada (βδ)−chain occurs early during erythroid maturation and is completed before the reticulocyte stage as reported for the δ− and (βδ) −chains of Hb A_2 and Hb Lepore.

要 約

HbA_{1c}。値測定の際に,異常Hbの保因者が検出された.末梢血液から調製された溶血液の等電点分画はHbA_2と同様の挙動を示すslow−movingの異常Hbの存在を示した.DEAE−HPLC分析による異常Hb含量はHbA_2を含め19.8%であった.このHbの構造解析は,グロビンのアミノ酸組成分析からβ鎖とδ鎖遺伝子間のCrossoverによって生じる融合型(βδ)グロビンをもつHb Miyadaと推定された.サザンブロットバイブリダイゼーションによる遺伝子配列解析やDNAクローンの塩基配列の解析から,この異常グロビンはN−末端から17位までがβ鎖で,22位からC−末端がδ鎖から成り立っており,この18位の第1塩基と22位の第1塩基間がcrossover siteと考えられた.患者の末梢血液の網状赤血球での合成グロビン分析は,β/α=1.06で合成均衡を示したが,(βδ)融合グロビンへの放射活性物質の取り込みは観察されなかった.このことは,HbA_2やHb Lepore のδ鎖や(βδ)鎖グロビンに見られると同様に,(βδ)融合グロビンの合成能は赤血球の成熟過程において急速にその機能を低下し,網状赤血球の前段階で終わってしまうためと考えられる.