ヒト血清アルブミンの体内動態に及ぼす表面電荷とα-ヘリックス含量の影響

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Changes of net charge and alpha-helical content affect the pharmacokinetic properties of human serum albumin

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ABSTRACT The pharmacokinetics of 17 genetic variants of human serum albumin with single-residue mutations and their corresponding normal albumin were studied in mice. In all cases, the plasma half-life was affected, but only variants with +2 changes in charge prolonged it, whereas changes in hydrophobicity decreased it. Good positive and negative correlations were found between changes in alpha-helical content taking place in domains I+III and domain II, respectively, and changes in half-lives. Liver and kidney uptake clearances were also modified: alpha-helical changes of domains I+III showed good negative correlations to both types of clearances, whereas changes in domain II only had a good positive correlation to kidney uptake clearance. The present information should be useful when designing recombinant, therapeutical albumins or albumin products with a modified plasma half-life.

抄録　ヒト血清アルブミンの17個の１残基変異体（バリアント）の体内動態を正常アルブミンと比較検討した。その結果、バリアントによる構造変化の中でもその表面電荷及びαヘリックス含量の変化と体内動態変化が相関することが明らかとなった。今回得られた結果はアルブミン製剤の設計において、重要な基礎資料として期待される。

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