

# ヒト血清アルブミンの熱安定性に及ぼす遺伝多型の影響

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## Effect of genetic variation on the thermal stability of human serum albumin

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**ABSTRACT** : Reversible thermal denaturation of 33 genetic variants of human serum albumin (HSA) appeared to be a two-state process when studied by circular dichroism (CD). Fourteen single-residue variants have  $T_m$  values higher than, and nine have  $T_m$  values lower than, their endogenous, wild-type counterpart. Nine single-residue variants have  $\Delta H_v$  values higher than, and 14 have  $\Delta H_v$  values lower than, normal albumin. All types of combinations of positive and negative  $\Delta T_m$  values and  $\Delta H_v$  values were found. Good linear correlations between mutation-induced changes of alpha-helical content and  $\Delta H_v$  values, but not  $\Delta T_m$  values, were found especially for the variants mutated in domains I and III. The effect of altered chain length and glycosylation on  $T_m$  and  $\Delta H_v$  was also studied. For all variants, no clear relationship was found between the changes in the thermodynamic parameters and the type of substitution, changes in protein charge or hydrophobicity. However, the protein changes taking place in domain I have a rather uniform effect. The present results can be of both protein chemical relevance and of clinical interest, because they could be useful when designing stable, recombinant HSAs for clinical applications.

**抄録** 我々は、ヒト血清アルブミン(HSA)の熱安定性に及ぼす遺伝多型の影響を円二色性CDスペクトルにより評価した。HSAを構成するドメインIとIIIに位置するアミノ酸残基の変異において、熱安定性と構造変化に有意な相関が観察された。一方、それ以外のドメインにおける変異において熱安定性との相関は観察されなかった。今回得られた知見は、今後、遺伝子組換え型アルブミンの作製における重要な基礎資料になるものと思われる。

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