THE EVOLUTION OF POLARITY RELATIONS IN GLOBINS

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1. Introduction

The well known correlation between the hydrophobicity of amino acid residues and their position in the interior of protein molecules was predicted long ago (Kauzmann [9]) and was more recently verified by X-ray diffraction studies (Kendrew [10]).

At the Rutgers conference in 1964, the examination of substitution patterns in globins showed that "there are more sites that seem to specialize in carrying residues fit for apolar bonding than any other sites at which the residues found are limited to one given chemical category." Apolar bonding, it was said, "may be the most specifically determined business of molecular sites in globular proteins" and, further: "we may venture the generalization that the outside of the globin molecule, and perhaps of globular proteins in general, is more variable than the inside" (Zuckerkandl and Pauling [19]).

This presumption was based in part on the already available knowledge that the majority of the polar amino acid residues are on the outside of the globins [10] and in part on the observation [19] that charged sites and other polar sites are more variable, on the average, than apolar sites, with the exception notably of glycine and of alanine sites.

In 1967, it was shown, by counting the minimal number of base substitutions on a deduced molecular phylogenetic tree, that maximum variability of sites coincided mostly with exteriority of the sites. This was established for a stretch representing two thirds of the globin chain (Derancourt, Lebor, and Zuckerkandl [5]).

On the basis of their study of the structural and functional implications of amino acid substitutions found in abnormal human hemoglobins, Perutz and Lehmann concluded in 1968 [12] that, whereas the conditions of amino acid substitutions are functionally restrictive in the interior of the hemoglobin molecule, they are liberal at its surface. The surface should be more variable than the interior, as Epstein [7] has also shown.

It was therefore unexpected to find (Zuckerkandl, Derancourt, and Vogel [18]), on the basis of an inventory of the different types of probable amino acid

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