

“Structure and Function of Binding Site Mutations in Transferrin: Crystals Structures of the Asp63Glu and Arg121Ala Mutants of the N-Lobe of Human Transferrin”

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Serum transferrin high affinity to bond Fe^{3+} is essential in human metabolism. It has been determined that the transferrin has a structure of two globular lobes with a cleft between the two lobes, in which the iron binds. The two prime residues involved in the binding are an aspartate residue, Asp63, in the N-lobe which hydrogen bonds between the two domains and an arginine residue, Arg124, in the N-lobe that binds the iron-bound carbonate ion. To examine the binding conditions further D63E and R124A mutants of the N-lobe of human transferrin were produced and crystal structure of each was determined. The structure of the D63E mutant was determined at 1.9 Å resolution ($R=0.245$, $R_{\text{free}} = 0.261$), indicated that the carboxyl group still binds to the iron despite the larger Glu side chain, with slight displacement. The structure of the R124A mutant was determine at 2.4 Å resolution ($R = 0.219$ and $R_{\text{free}} = 0.288$), indicated that the loss of the Arg side chain caused a 0.3 Å displacement of the carbonate ion and correlating movement of the iron atom. Both mutations cause the iron coordination to change slightly and release iron more readily than the wild type.

Bibliography

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