

**P022** Albumin as a zinc carrier - properties of its high-affinity zinc-binding site

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Although details of the molecular mechanisms for the uptake of the essential nutrient zinc into the blood stream and its subsequent delivery to zinc-requiring organs and cells are poorly understood, it is clear that in vertebrates the majority of plasma zinc (ca. 75%, 9-14  $\mu\text{M}$  in humans) is bound to serum albumin, constituting part of the so-called exchangeable pool.

The binding of zinc to serum albumins has been the subject of decades of studies, employing a multitude of techniques, but only recently the identity and putative structure of the major zinc site on albumin has been reported. Intriguingly, this site is located at the interface between two domains, and involves two residues each from domains I and II. Comparisons of X-ray crystal structures of free and fatty-acid bound human serum albumin have suggested that zinc binding to this site and fatty acid binding to one of the five major sites are mutually exclusive.

We have employed isothermal titration calorimetry (ITC),  $^1\text{H}$  NMR spectroscopy, and molecular modelling to study this hypothesis in detail. Our results suggest that simultaneous binding of the short chain fatty acid octanoate and zinc to the domain interface is possible, but that the binding of longer chain fatty acids (e.g. myristate) to this site prevents zinc binding to its major site. Interactive binding of zinc and long chain fatty acids to albumin may have physiological implications.