

Analysis of Human Serum Albumin Metal Complexes

Vanessa A Bijak¹, Michal Gucwa², Michal Szczygiel³, Katarzyna Handing⁴, Wlodek Minor⁵

¹University of Virginia, ²University of Virginia, Jagiellonian University, ³University of Virginia, Jagiellonian University ⁴University of Virginia, Tango Therapeutics, ⁵University of Virginia
vab3n@virginia.edu

The abundance of serum albumin (SA) in plasma and its ability to bind and transport a variety of metal ions underlies its critical role in maintaining metal ion homeostasis, particularly for Zn²⁺, Cu²⁺, Ca²⁺, and Mg²⁺. SA acts as the main transporter of these ions and can mitigate the harmful effects of toxic metals like Ni²⁺, Co²⁺, and Cd²⁺. Due to its involvement in drug delivery and transport, SA is an important research target.

Despite the importance of metal binding to SA, limited structural data exists on the metal-binding sites and properties. Our work addresses this by focusing on human serum albumin (HSA). Building on our prior success in obtaining the crystal structure of equine serum albumin (ESA) in complexes with Cu²⁺, Ni²⁺, Pt²⁺, Hg²⁺, and Au³⁺, we are currently exploring the structure of HSA in complexes with these same metals. Recently, we showed that ketoprofen exhibits different binding-site preferences when interacting with human serum albumin compared with other mammalian albumins. For that reason, we are expanding our investigation to HSA to gain a deeper understanding of metal ion homeostasis in humans.