Structural Study of Hepatitis B Virus Capsid Polymorphism and Stabilization

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The amino acid changes between different strains of HBV affect biological properties [1] and crystallization [2]. We hypothesize that these differences manifest as capsid polymorphism within an icosohedral framework.

We have crystallized strain *adyw* HBV T=4 capsids for comparison to the previously determined *adw*-like HBV capsid [1]. To obtain this structure we engineered disulfide cross-links between the dimer building blocks, resulting in a stabalization of the capsid within the crystallographic lattice. To asses the role of this cross-link, data was also collected on a crystal without cross-linking. A critical advance for our structures was the ability to cryo-cool them, which was only possible when free capsid was included in the artificial mother liquor.

Data were collected at the APS synchrotron, beamline 14BMC. The data sets were isomorphous in *C*2 space group with one capsid per asymmetric unit. The cross-linked capsid data set is 81% complete overall to 3.95Å, while the non-cross-linked capsid is 94.9% complete to 3.95Å.

Current efforts are focused on phasing these structures with molecular replacement methods and refinement of the solution. This will allow us to visualize structural polymorphism between strains of HBV capsid and the effect of cross-linking capsid subunits.

[1] Ceres P., Stray S., Zlotnick A., *J. Virol.,* 2004, **78**, 9538. [2] Wynne S., Crowther R., Leslie A., *Mol. Cell.,* 1999, **3**, 771.

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