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# Structural studies of the human drug-metabolising protein CYP3A4

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A highly flexible protein with an active site that changes its volume to fit a wide variety of ligands. A lid made of loops changes conformation based on ligand-size. Inhibition of this enzyme stops metabolism of drugs. This is an automatic disqualification of a drug candidate. Room temperature SSX shows better definition of some flexible loops, even at worse resolution. SSX data collection at tens of kilo Gray produces a similar active-site to our XFEL structure. I present an internal distance matrix analysis of a subset of PDB CYP3A4 structures to determine that crystal form, resolution and to some extent ligand-size dominates the clustering of global similarity with little difference caused by temperature. The protein crystalises as a monomer in the ASU but SAX, cryo-EM and SEC-MALS shows a homo-tetramer in solution bringing it into the perfect size range for cryo-EM. I present initial data for the volume of the tetramer solved through single particle analysis at SciLifeLab Solna.

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