

## **Crystal Structure of the Protease Domain of *Plasmodium falciparum* SERA-5**

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The multi-gene *SERA* family of *Plasmodium* produces proteins of varying abundance called the serine repeat antigens (SERAs). Full-length SERA molecules (~120 kDa) undergo processing into several smaller fragments, one of which (the protease domain) has significant homology to papain-like cysteine proteases. SERAs exhibit intriguing differences in putative enzyme active site residues; for example SERA-5, the dominantly-expressed member of the *P. falciparum* gene family, has serine substituted for the active site cysteine, whereas SERA-6 retains cysteine at the catalytic position.

The protease domain of SERA-5 was produced as both native and SeMet-substituted recombinant proteins in *E. coli*, refolded in the presence of a glutathione redox pair, and purified by affinity and ion exchange chromatography. Crystals grown from native and SeMet proteins diffracted to 1.8 Å and 2.5 Å resolution, respectively. Native diffraction data were collected at SLS, Villigen and MAD data were collected at APS, Chicago. The crystal structure was solved by MAD analysis. Interestingly, although SeMet crystals were grown in the absence of reducing agent in an effort to preserve several disulfide bonds, the Se atoms remained reduced.

As predicted, the overall fold of SERA-5 enzyme domain is that of a papain-family cysteine protease. Details of the active site geometry will be presented and interpreted in the light of our other experimental results.