

P002 Crystal structure of foot-and-mouth disease virus 3C protease
**James R. Birtley¹, Stephen R. Knox², Agnès M. Jaulent²,
Peter Brick¹, Robin J. Leatherbarrow² and Stephen Curry¹**
*¹Biophysics Section, Department of Biological Sciences and
²Biological and Biophysical Chemistry Section, Department of
Chemistry, Imperial College, South Kensington Campus,
Exhibition Road, London SW7 2AZ, UK*

Picornaviruses are absolutely reliant upon virally encoded proteases for the liberation of mature viral protein products from the polyprotein. The foot-and-mouth disease virus 3C protease (FMDV 3C^{pro}) is a key enzyme as it processes 10 of the 13 FMDV polyprotein cleavage junctions, making this enzyme a highly attractive target for antiviral drugs.

Picornaviral 3C proteases also play a role in the down regulation of host translation initiation by specifically cleaving translation initiation factors, such as eIF4A1, PABP and PTB.

The creation of suitable surface-exposed amino acid substitutions (C95K and C142S) enhanced the solubility and improved the aggregation state of FMDV 3C^{pro}, as determined by dynamic light scattering whilst maintaining cleavage characteristics indistinguishable from wild-type. N- and C- terminal truncated forms of this mutant were entered into extensive crystallisation trials and after the development of a novel method for screening additives, crystals were grown that diffracted to high resolution. Multi-wavelength anomalous dispersion experiments with selenomethionine-labelled crystals was used to tackle the phase problem and the structure was determined to 1.9 Å resolution by X-ray diffraction.