

W0297

**Crystal Structure of the Aspartic Protease Plasmepsin 4 from the Malarial Parasite *P. malariae*.** A. Madabushi<sup>a</sup>, S. Chakraborty<sup>a</sup>, S.Z. Fisher<sup>a</sup>, J.C. Clemente<sup>a</sup>, C. Yowell<sup>b</sup>, M. Agbandje-McKenna<sup>a</sup>, J.B. Dame<sup>b</sup>, B.M. Dunn<sup>a</sup>, R. McKenna<sup>a\*</sup>, <sup>a</sup>Dept of Biochem. & Mol. Biol. & <sup>b</sup>Dept. of Pathol., Univ. of Florida, Gainesville, FL 32610.

Plasmepsin 4 (PmPM4) is a member of the plasmepsins from the malarial parasite *Plasmodium malariae*. Plasmepsins are pepsin-like aspartic acid proteases involved in haemoglobin degradation in the parasite food vacuole. Recombinant PmPM4 has been overexpressed, purified from inclusion bodies and activated. Crystals of PmPM4 in complex with the small molecule inhibitor AG1776 have been grown from a precipitant of 15 % PEG 4000 and 200 mM ammonium sulfate in 100 mM sodium acetate pH 4.5. X-ray diffraction data were collected on a Rigaku rotating anode generator from a single crystal under cryo conditions. The crystals are shown to be orthorhombic and belong to the space group P2<sub>1</sub>2<sub>1</sub>2, with unit cell dimensions a=95.88, b=112.58, and c=90.40 Å. Packing considerations and self-rotation function results indicated two molecules per asymmetric unit. The structure of PmPM4 has been determined at 3.3 Å resolution using molecular replacement methods using the phase information obtained from previously determined plasmepsin structures. Elucidation of the structure of PmPM4 in complex with inhibitors may be paramount to producing new anti - malarial therapeutic agents.