

## **Structural Studies of Mammalian Protein Geranylgeranyltransferase Type I**

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Beamline(s): **X12B**

Protein geranylgeranyltransferase type-I (GGTase-I) attaches a geranylgeranyl lipid to a conserved cysteine residue near the C-terminus of proteins; including Rho, Rac, and most heterotrimeric G protein gamma subunits. Lipid attachment (prenylation) promotes membrane association and is required for the function of these proteins. The majority of prenylated proteins in the cell are geranylgeranylated, and inhibition of GGTase-I function can prevent cells from proceeding from G1 to S phase in the cell cycle. GGTase-I is being pursued as a target in several clinical areas, including cancer and heart disease.

The three-dimensional structure and functional mechanism of mammalian protein geranylgeranyltransferase type-I (GGTase-I) is under study by X-ray crystallography. Determination of the high-resolution three-dimensional structure of the mammalian GGTase-I will provide the first structural information on any GGTase-I. GGTase-I crystallizes in the orthorhombic space group I222 with cell dimensions  $a=184 \text{ \AA}$ ,  $b=204 \text{ \AA}$ ,  $c=270 \text{ \AA}$ . The large unit cell makes collecting diffraction data difficult on a rotating anode X-ray source, and so data were collected at the NSLS beam line X12B. In addition, the beam energy was adjusted during collection of data from a platinum derivative, to maximize the anomalous signal. These data lead to the successful determination of experimental phases using the SIRAS technique. Model refinement is currently in progress.