

Crystallographic study of universal stress protein Rv2623 from *Mycobacterium tuberculosis* H37Rv

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Introduction

Approximately one-third of the population is infected with *Mycobacterium tuberculosis*, but in over 90% of infections remains clinically latent (1). Unfortunately, the mechanism of the host-pathogen interaction is poorly understood, mainly the mechanisms employed by *M. tuberculosis* to survive in a nutritionally deprived and an anoxic environment during latency (2). The adaptation to such an extreme environment involves differential expression of genes that respond to iron limitation, alternative carbon metabolism and hypoxia (3). Consequently, anaerobic and nutritionally starved cultures can be used as models for study of the physiological state of *M. tuberculosis* during latency (4). Using these approaches, it has been discovered that oxygen-starved *M. tuberculosis*, *M. bovis* BCG and *M. smegmatis* express a novel class of proteins whose counterparts in other organisms comprise the universal stress protein (USP), or UspA, family (5, 6, 7).

Universal stress protein Rv2623 has been found to be expressed under hypoxia in 2-D gel analysis of *M. tuberculosis* and *M. bovis* BCG (5, 6). Furthermore, since it has also been observed that Rv2623 is expressed following phagocytosis of *M. tuberculosis* (8), the universal stress proteins, particularly Rv2623, might play a role in the resistance of the bacterial cells against different stress factors encountered during infection of macrophages.

We determined the structure of the first universal stress protein Rv2623 from *M. tuberculosis* containing two tandem Usp domains.

Results and discussion

The structure of the selenomethione substituted MtUSP was determined using single anomalous wavelength diffraction method (SAD) and refined to resolution of 3.2Å.

The MtUSP crystallizes as a monomer in space group P6₄22 with one molecule per asymmetric unit, the water content of the crystal is 70%. The topology of a single domain shows α/β fold, the five parallel β -sheets are connected with four α -helices (Figure 1a). The domainA (residues 1-150) and domainB (residues 151-297) are connected between β -5 and β -6 sheet resulted in an arrangement resembling the composition of the two protomers observed in the asymmetric unit of

JM5077 (Figure1). The MtUSP proteins homodimerize in the crystal on the crystallographic two-fold axis via intermolecular hydrogen bonds between anti parallel β -sheets.

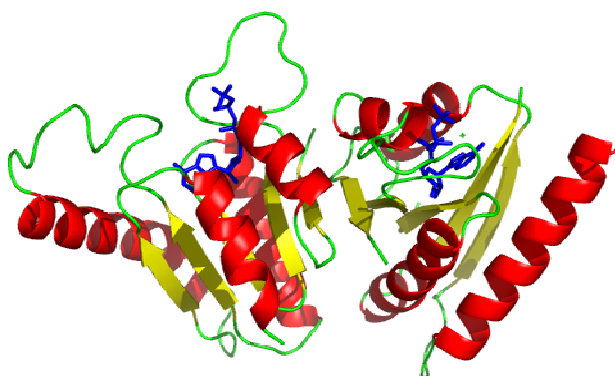


Figure 1. Cartoon representation of MtUSP complexed with ATP.

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