ESRF

ESRF	**Experiment title:** STRUCTURE OF MYCOBACTERIUM TUBERCULOSIS NAD KINASE	**Experiment number**: MX129
Beamline: ID29 ID14-EH1 ID14-EH4	**Date of experiment**: from:21/06/03 to:23/06/03 from :05/08/03 to:06/08/03 from:14/10/03 to:15/10/03	**Date of report**: 21th June 2004
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Report:

Background – NAD kinase catalyses the magnesium dependent phosphorylation of NAD, representing the sole source of freshly synthesized NADP in all organisms. The enzyme is essential for the growth of the deadly multidrug-resistant pathogen *Mycobacterium tuberculosis* and is an attractive target for novel antitubercular agents. The crystal structure of NAD kinase has been solved by multiwavelength anomalous dispersion at a resolution of 2.3 Å in its T state. Two crystal forms have been obtained revealing either a dimer or a tetramer. The enzyme architecture discloses a novel molecular arrangement, with each subunit consisting of an α/β N-terminal domain and a C-terminal 12-stranded β sandwich domain, connected by swapped β strands (Figure1). The C-terminal domain shows a striking internal approximate 222 symmetry and an unprecedented topology, revealing a novel fold within the family of all-β structures. The catalytic site is located in the long crevice defining the domains interface. The conserved GGDG structural fingerprint of the catalytic site is reminiscent of the related region in 6-phopshofructokinase, supporting the hypothesis that NAD kinase belongs to a newly reported superfamily of kinases.

FIGURE 3B

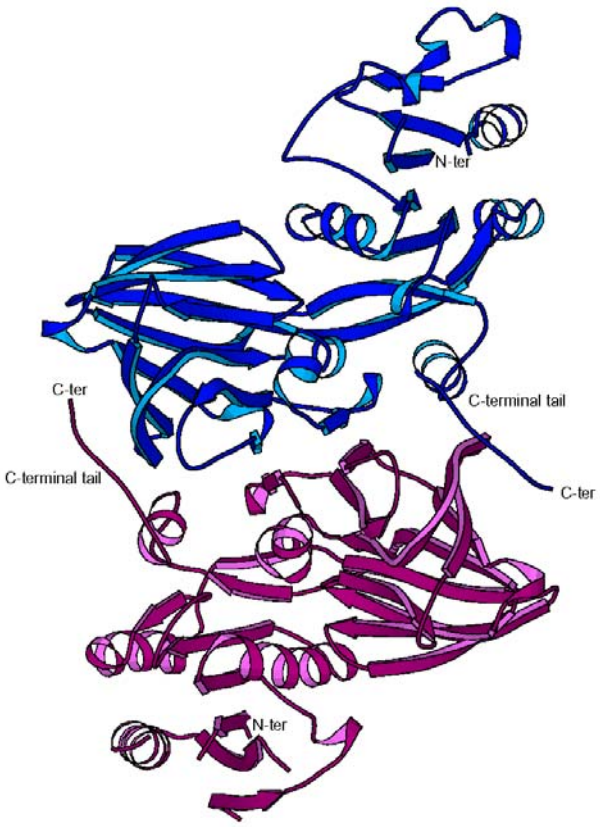

Figure 1: Ribbon representation of the M. tuberculosis NAD kinase dimer

1. Silvia Garavaglia, Nadia Raffaelli, Lucia Finaurini, Giulio Magni, and Menico Rizzi.
A novel fold revealed by *Mycobacterium tuberculosis* NAD kinase, a key allosteric enzyme in NADP biosynthesis. (2004) submitted