Is MgtC, a Potential Drug Target in *M. tuberculosis*, Inhibited by MgtR

F. Jean-Francois, T.A. Cross (NHMFL, FSU Chemistry & Biochemistry)

**Introduction**

MgtR, a highly hydrophobic 30 amino acids peptide, is expressed naturally in *Salmonella typhimurium*. It has been shown that within the macrophage, the over expression of MgtR leads to a decrease of Salmonella replication rate. This process was shown to involve an interaction between MgtR and a membrane protein of salmollena (MgtC) which is required for the bacteria survival at low magnesium concentration (intramacrophage conditions) [1]. Throughout the literature, MgtC has proven to be one of the key factors in *Mycobacterium tuberculosis* latent state [2]. Using the sequence homology between *Salmonella typhimurium* MgtC and *Mycobacterium tuberculosis* MgtC as a good argument, the interaction between MgtR from *Salmonella typhimurium* and *Mycobacterium tuberculosis* MgtC will be studied.

**Experimental**

With the aim to study the interaction between MgtR and MgtC TB, we first focused on the synthesis and characterization of the potential drug. The 30 amino acid residue hydrophobic peptide, MgtR, was chemically synthesized and purified over 95% by using cation exchange chromatography on an FLPC system. Circular Dichroism was used to perform a preliminary structural study in LUV made of DMPC/DMPG (4:1), Fig. 2. The solid state NMR structural characterization has been started by acquiring, on the 400 MHz 89mm at the NHMFL, a PISEMA spectrum of a selectively labeled peptide embedded in DMPC/DMPG membranes, Fig. 1.

**Results and Discussion**

![Figure 1: PISEMA spectrum of MgtR specifically 15N labeled (Ala 10, Leu 15, Ile 16, Ala24) in DMPC/DMPG membranes.](image1)

![Figure 2: Circular dicroism spectrum of MgtR embedded in DMPC/DMPG.](image2)

**Conclusions**

The CD spectrum suggests that this peptide is mainly α helical structured (75%) in DMPC/DMPG membranes. The PISEMA spectrum depicts a PISA wheel pattern that suggests an α helix tilted at 38° with respect to the bilayer normal. These results will be used as the starting point for the study of the interaction between MgtR and its potential target MgtC.

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**References**
