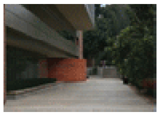

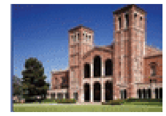

The *M.tuberculosis* virulence factor trehalose dimycolate imparts desiccation resistance to a model mycobaterial membrane

Chris Harland[1], David Rabuka[2], Carolyn Bertozzi[3], Raghuveer Parthasarathy[4]

[1]Materials Science Institute, Department of Physics, University of Oregon
[2]Lawrence Berkeley National Laboratory
[3]Department of Chemistry, University of California
[4]Department of Molecular and Cell Biology, and Howard Hughes Medical Institute, University of California

Abstract: The resurgence of tuberculosis in the developed world and its continued persistence in the developing world are well known public health concerns: roughly one-third of the human population is infected with Mycobacterium tuberculosis and each year two million people die as a result. The physical properties of the bacterium outer envelope are suspected to play a key role in its persistence. All mycobacteria, including Mycobacterium tuberculosis, have a dense outer membrane consisting of large fatty acids of which the glycolipid trehalose 6,6' dimycolate (TDM) is a major component. Most studies of TDM and other envelope molecules, especially in recent years, have focused on the molecular biology of their expression and their interactions with host immune cells, leaving the physical properties of the envelope and the advantages it confers on pathogenic bacteria poorly delineated.

Given the ability of mycobacteria to withstand desiccation and the ability of soluble α,α- trehalose to protect proteins, cellular membranes, and whole organisms during desiccation, we hypothesized that TDM may alone be sufficient to confer upon its constituent membranes resistance to dehydration. To test this, we devised an experimental model that mimics the structure of mycobacterial cell envelopes, in which a TDM-rich, fluid outer leaflet is supported by an immobile hydrocarbon layer. We demonstrate, for the first time, the formation of two-dimensionally fluid TDM membranes, and find that they can be dehydrated and rehydrated without loss of membrane integrity or fluidity. More strikingly, this protection from dehydration extends to TDM-phospholipid mixtures in which TDM is a minority component, down to only 20 mol% TDM.

The Frontiers in Microrheology Workshop
February 6 - February 9, 2008
at the CNSI, UCLA
http://www.cnsi.ucla.edu/conferences/microrheology/