

## E0046

**Structural Basis of Lipid Antigen Presentation by CD1.** I.A. Wilson, D.M. Zajonc, D. Wu, G. Painter, V. Kumar, M. Kronenberg, D.B. Moody, C.-H. Wong, L. Teyton, The Scripps Research Institute, La Jolla, CA.

The human CD1 family of cell surface receptors, CD1a to CD1d, presents a variety of lipid antigens to CD1-restricted T cell receptors (TCRs) in order to elicit a specific immune response against invading pathogens, or to carry out immuno-regulatory functions. Many classes of lipid antigens have been identified including self-antigens, such as glycerolipids and sphingolipids, as well as foreign lipids, such as phosphatidylinositol mannosides (PIMs), mycolates, phosphoisoprenoids, small hydrophobic molecules and lipopeptides. To elucidate how such structurally diverse antigens can be presented by a limited number of CD1 receptors, we have determined multiple CD1-lipid structures. Structural differences among the CD1 binding grooves confer antigen binding specificity. All ligands bind with their lipid tails buried within the hydrophobic CD1 binding groove, whereas their diverse headgroups are exposed for TCR recognition at the CD1 surface. Whereas only a few specific polar interactions are observed between the glycolipid headgroups bound to either CD1a or CD1b, a specific hydrogen bond network is found in CD1d, which orients and stabilizes different classes of CD1d ligands, such as the highly stimulatory  $\alpha$ -GalCer.