

**P073** Deciphering the structure/function relationships of lipoglycans signaling via Toll-like receptor-2  
**Jérôme Nigou<sup>1</sup>, Thierry Vasselon<sup>2</sup>, Aurélie Ray<sup>1</sup>, Patricia Constant<sup>1</sup>, Martine Gilleron<sup>1</sup>, Gérard Tiraby<sup>3</sup> and Germain Puzo<sup>1</sup>**

1. Institut de Pharmacologie et de Biologie Structurale, CNRS UMR 5089, Toulouse, France

2. Institut de Génétique Moléculaire de Montpellier, CNRS UMR 5535, Montpellier, France

3. Cayla-Invivogen, Toulouse, France

Lipoglycans are TLR2 agonists found in some genera of the phylogenetic order *Actinomycetales*, among which *Mycobacterium*. They are built from a mannosyl-phosphatidyl-*myo*-inositol (MPI) anchor linked to a polysaccharidic moiety composed of a ( $\alpha$ 1 $\rightarrow$ 6)-linked D-mannopyranosyl chain whose units can be substituted by D-mannopyranosyl and/or D-arabinofuranosyl units. So far little is known about the molecular bases underlying their ability to induce signaling via this receptor. We have recently shown that MPI anchor must be at least triacylated, however the contribution of the glycosidic moiety is not clearly defined. We show here that lipoglycan activity is directly determined by their mannan chain length. Indeed, activity increases with the number of units constituting the ( $\alpha$ 1 $\rightarrow$ 6)-Mannopyranosyl backbone and is critically dependant on the substitution type of the OH-2 of these units that must be free or glycosylated by mannopyranosyl, but not arabinofuranosyl, units. Moreover, we demonstrate that lipoglycans can bind cell surface expressed TLR2 and that their ability to induce signaling might be, at least in part, dictated by their affinity for the receptor.