

**Toll2006, Recent advances in Pattern Recognition
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Since the recent discovery of toll-like receptors, the field of innate pathogen recognition has been exploding. Not surprisingly, two years ago the first meeting was organized that was totally dedicated to TLRs and related pathogen recognition receptors. This year's congress in Salvador (Brazil) was the second of its kind and provided an excellent opportunity for me to meet the leading scientists in this area of research and to get a full update on the current status of this rapidly progressing field. Because during these 4 days only two parallel sessions were scheduled, I was able to attend almost all presentations.

Most signaling pathways downstream of TLRs are already fairly well characterized. As a result, this was clearly not the main topic of this meeting. Instead, there was more emphasis on the molecular characterization of the interaction between TLRs and their ligands, and the motif requirements of RNA and DNA –strands to be recognized by these receptors. Furthermore, a large part of this meeting was dedicated to a very recently discovered family of intracellular cytosolic pathogen recognition receptors (RIG-I and MDA-5), that are particularly activated by viral ss- and dsRNA's. Homologous cytosolic receptors had already been described in *Drosophila*, in which of course initially Toll was identified. These presentations, further highlight how incredibly similar and conserved these innate immune responses are throughout the whole animal kingdom.

Of particular interest were the two parasite recognition sessions, in which several speakers presented their recent work on *Leishmania*, malaria, and *Trypanosoma*. Most, if not all, research focusing on the role of TLRs in parasite infection, uses the powerful tool of TLR knockout mouse models. Generally speaking it becomes evident from these studies that although TLRs play important roles in resistance to these infections, they also clearly indicate that there are also other factors (receptors?) involved that determine the outcome of these infectious diseases. Another very interesting talk was that of Reis e Sousa. In his presentation he provided evidence for the absolute need for TLR activation on APC to allow polarized T cell responses to occur. Since I am working on effects of helminth antigens on dendritic cells via TLRs, this talk was particularly interesting for my own research.

My contribution to this meeting was a poster, which I presented during the poster session. In my poster I presented data on the differential effects on dendritic cells in terms of T helper cell polarizing capacity induced by TLR2 activating helminths derived lipids and TLR2 activating bacterial antigens (see abstract below). Interestingly, during this session I met people from a Brazilian group who are also working on these helminths derived lipids. This opens up an opportunity to start collaboration in the near future.

Molecular comparison of human dendritic cells activated by Th1 and Th2 promoting Toll-like receptor 2 ligands

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Dendritic cells (DCs) are pivotal in determining the class of adaptive immune response, in which Toll-like receptors (TLRs) play an important role. DCs activated via TLR2 have been shown to induce both Th1 and Th2 responses, depending on the ligand. Yet, the molecular changes following TLR2 activation in DCs responsible for the induction of these opposite T cell responses are still largely unknown.

Here we show that lipid fractions derived from the helminths *Schistosoma mansoni* and *Ascaris lumbricoides* activate TLR2 and are able to instruct monocyte-derived DCs to induce Th2 skewed responses. These DCs were compared with DCs stimulated with the Th1 inducing TLR2 activating bacteria *Escherichia coli* and Heat Killed *Lysteria monocytogenes* (HKLM). For an initial analysis of the molecular effects in DC, real time PCR was used to study messenger RNA expression levels of molecules that are involved in downstream signalling events of TLR2 both positively or negatively, Th1/Th2 associated molecules and pro- and anti-inflammatory factors. Both helminth-derived TLR2 ligands induced a very similar gene expression pattern, yet very different from the bacterial TLR2 ligands. In the lipid stimulated DCs there was a clear downregulation of pro-inflammatory/Th1-associated molecules, but an increase in expression of transcription factor c-Fos. Conversely, mRNA levels of pro-inflammatory/Th1 associated molecules, including notch ligand delta-4, were elevated in HKLM/*E.coli* treated DCs, whereas c-Fos was unchanged. Thus, expression levels of delta4 and c-Fos are associated with Th1 and Th2 responses, respectively, in DCs that were stimulated with different TLR2 ligands.