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The role of Toll-like receptor 13 in pneumococcal recognition by macrophages

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Authors declare no conflict of interests

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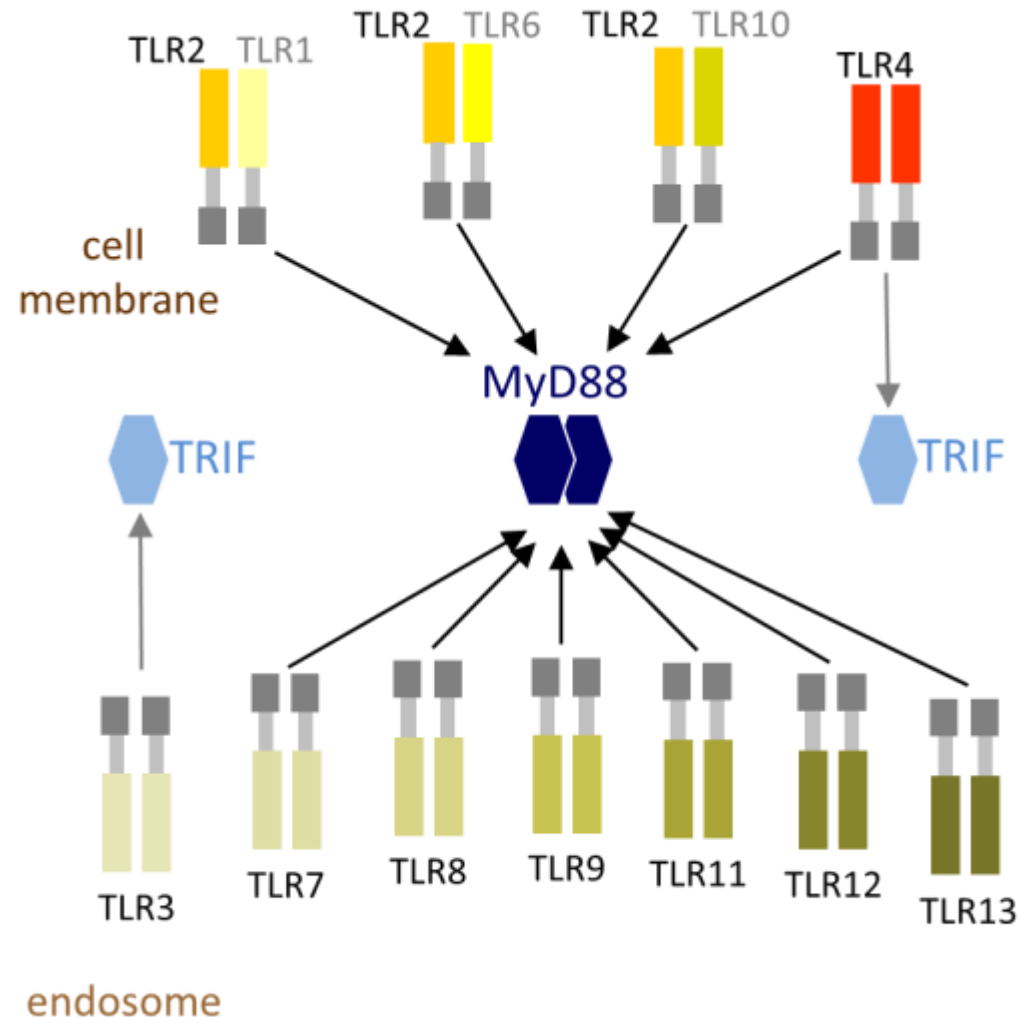


M. Rohde (Braunschweig)
S. Hammerschmidt
(Greifswald)

- ◎ Over 1.2 million of BM per year worldwide
- ◎ Most common etiologic agent of BM in Europe and the United States (~ 60% of all cases)
- ◎ Case fatality rates vary between 10-15% in high-income countries
- ◎ Intracranial complications may be due to the powerful inflammatory response in the brain

Toll-like receptors:

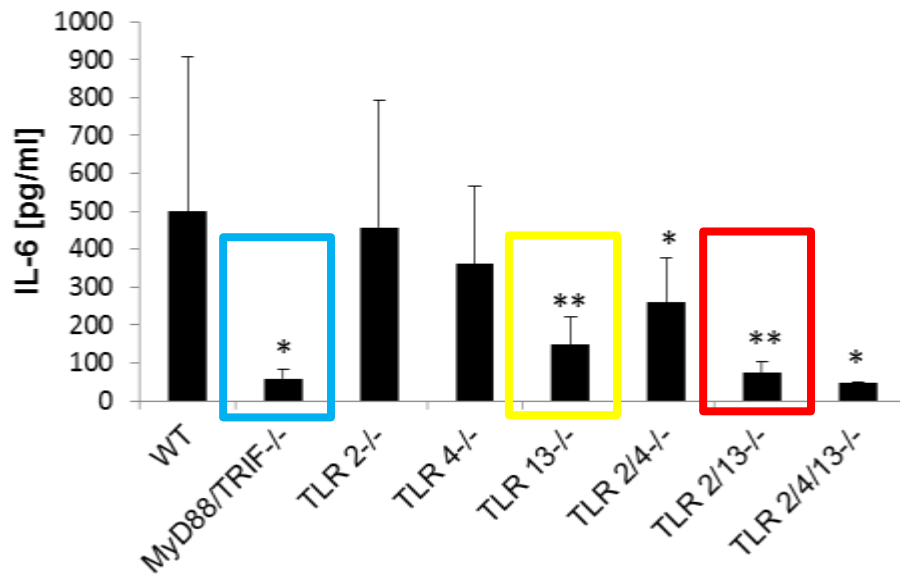
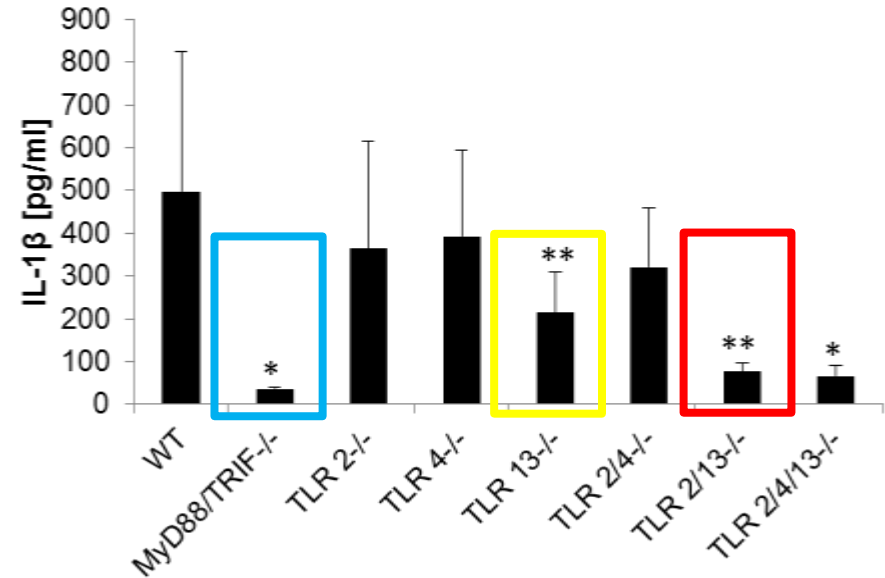
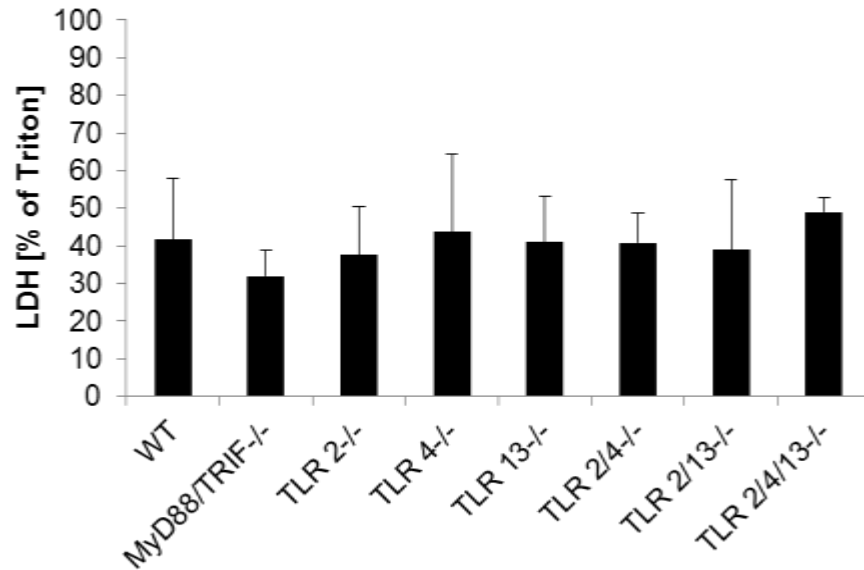
- TLR 1-10 in humans
- TLR 1-13 (without TLR10) in mice
- TLR 2 & 4: involved in pneumococcal recognition in murine meningitis



Which Toll-like receptors are responsible for recognition of *S. pneumoniae* by macrophages?

- Cells:
 - Murine bone-marrow derived macrophages (BMDM) from wild-type or transgenic mutant mice
 - Human THP-1 cells
 - Human monocyte-derived macrophages (hMDM)
 - Human peripheral blood mononuclear cells (PBMC)
- Bacteria:
 - *S.pneumoniae* serotypes: 2, 3, 4, 7F, 14, 19A, 2 Δ Ply
- Assays:
 - LDH release (Cytotoxicity)
 - Interleukin (IL)-1 β and IL-6 production (Cytokines)

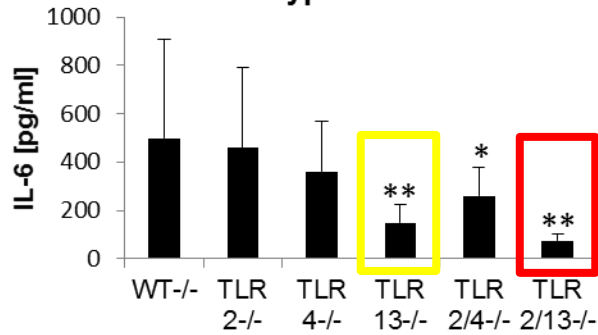
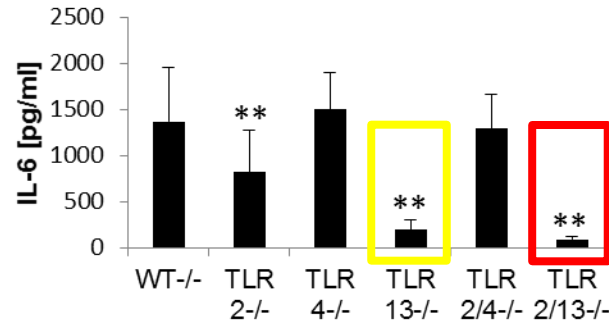
Recognition of *S. pneumoniae* D39 by murine BMDM: transgenic approach



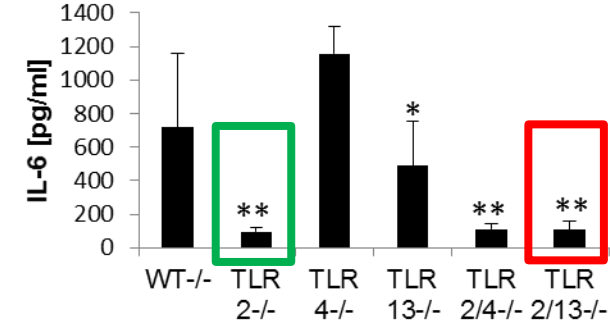
*: $p < 0,05$ compared with WT

** : $p < 0,001$ compared with WT

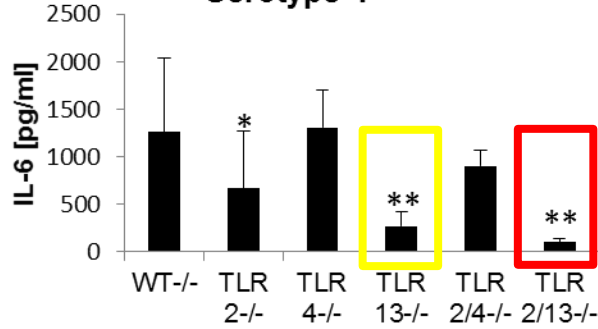
Serotype 2

Serotype 2 Δ PLY

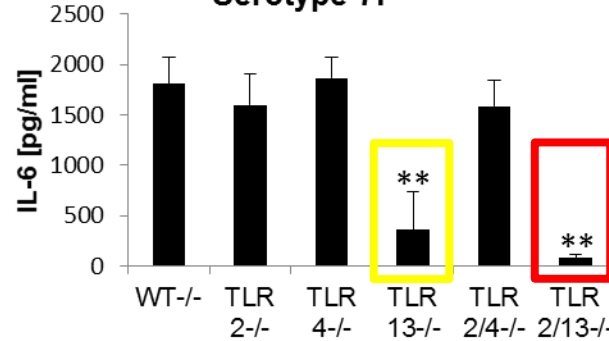
Serotype 3



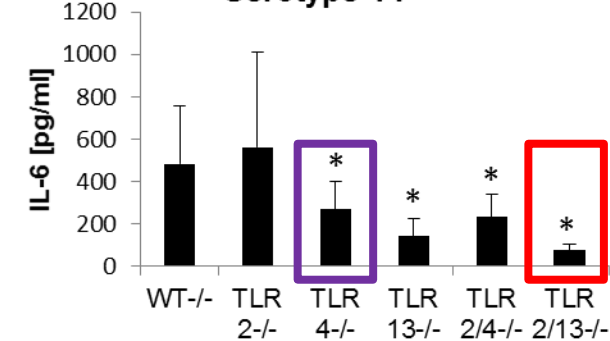
Serotype 4



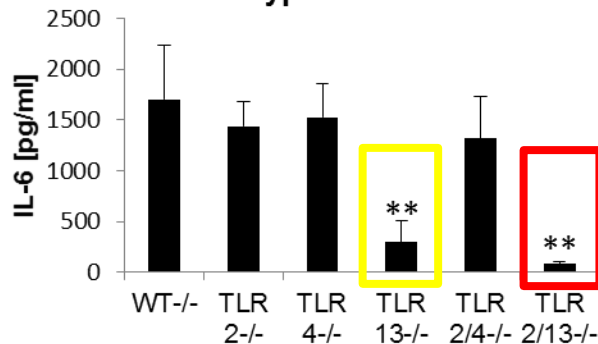
Serotype 7F



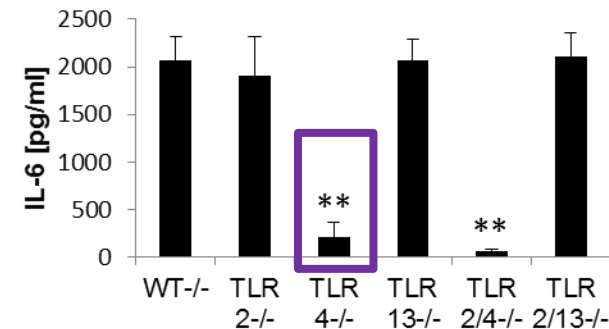
Serotype 14



Serotype 19A



LPS/Nigericin

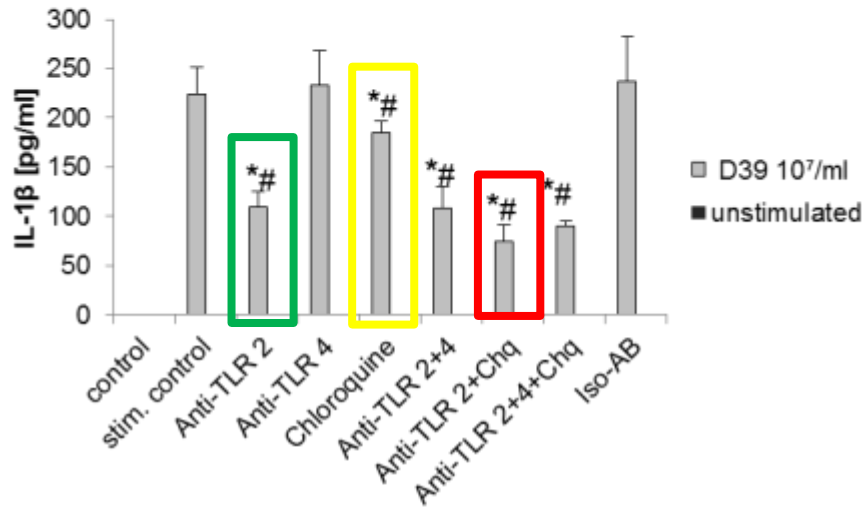


* : p<0,05 compared with WT

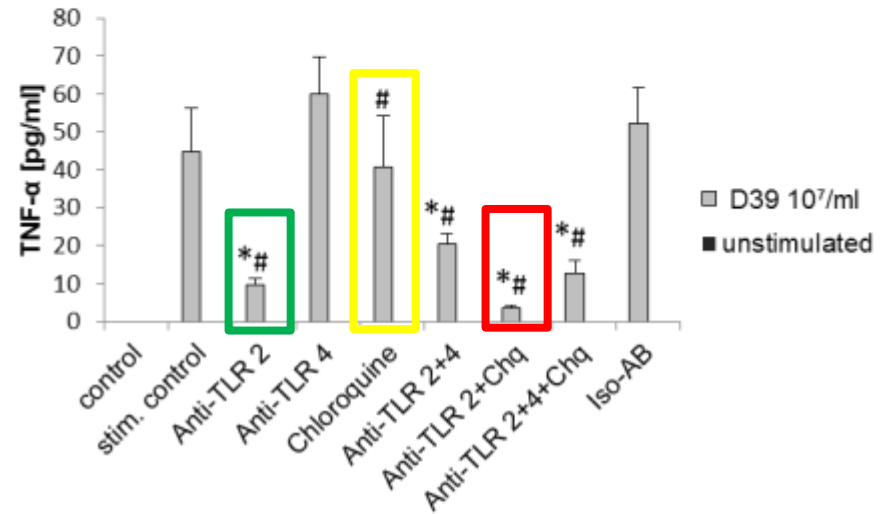
** : p<0,001 compared with WT

Recognition of *S. pneumoniae* D39 by human macrophages and PBMC

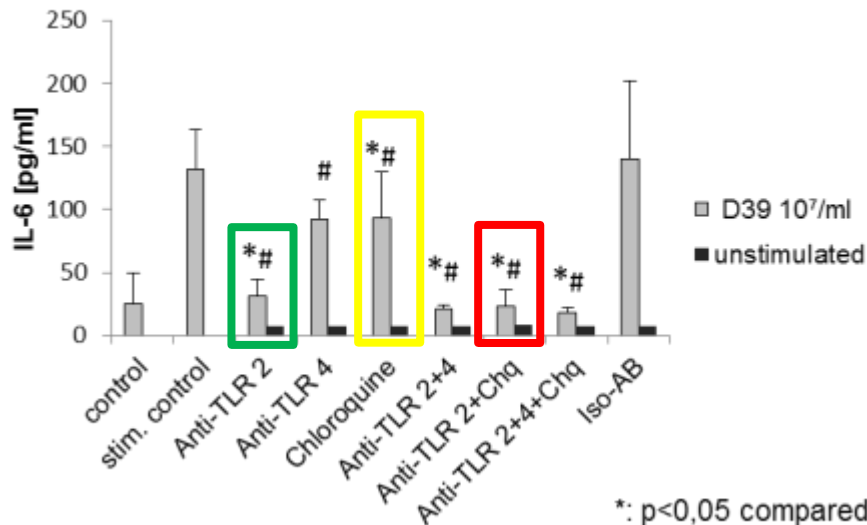
THP-1



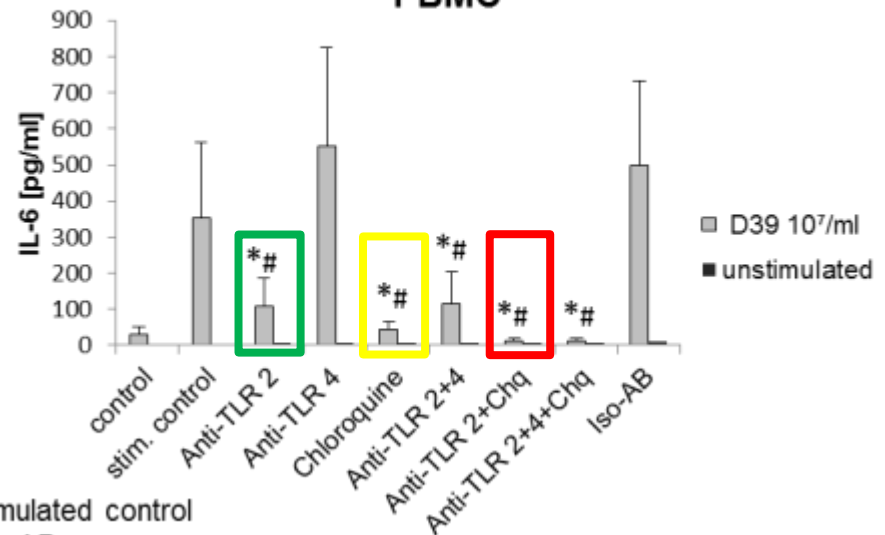
THP-1



hMDM



PBMC



*: p < 0,05 compared with stimulated control
#: p < 0,05 compared with Iso-AB

Recognition of *S. pneumoniae*

- Murine macrophages: TLR 2 + TLR 13
- Human macrophages: TLR 2 + (endosomal TLR)
- Human mononuclear cells: TLR 2 + endosomal TLR

- Differences between various serotypes

- Carsten Kirschning
- Thomas Scholtysik
- Sven Hammerschmidt
- Barbara Angele
- Uwe Koedel
- Philipp Oldemeier
- Hans-Walter Pfister
- Institute for Medical Microbiology, University of Essen, Germany (*transgenic knockout mice*)
- Department of Genetics of Microorganisms, Interfaculty Institute for Genetics and Functional Genomics, University Greifswald, Germany (*S. pneumoniae strains*)
- Department of Neurology, Clinic of the University of Munich, Germany