

FOR 1336

CD14 as a Gate Keeper in Microglial Responses to PAMPs and DAMPs



**Funding Period:
from 2010 to 2017**

Project Leader

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Project Description:

The sentinel and immune functions of microglia require rapid and adequate reactions to CNS infection and damage. Toll-like receptors (TLRs) enable the cells to respond to both threats as they sense a range of microbial agents as well as self-derived factors termed pathogen and damage-associated molecular patterns (PAMPs, DAMPs). We found that especially the TLR4 complex organizes adapted microglial responses to these exogenous and endogenous danger signals—with a remarkable agonist discrimination as well as cell type- and subsetspecific consequences. The coreceptor CD14 thereby demonstrated previously unanticipated roles in gating and shaping the reactive phenotype, including mandatory support for DAMPs, protection against overshooting responses in PAMP challenges and distinct involvement in the organization of microglial functions. These contributions cannot be explained by a simple assistance in agonist binding. They rather suggest own CD14 signaling at a decision-making position. We will address mechanisms and outcomes of CD14 involvement for (i) managing distinct microglial responsiveness to PAMPs and DAMPs in infection and injury, (ii) with a focus on signaling control in TLR4-triggered reactions and (iii) considering the importance of IFN β in the CD14-guided competition of PAMPs and DAMPs for functional dominance.

Reference: <https://gepris.dfg.de/gepris/projekt/165157162?language=en>