

DFG Au338/3-1: Regulation of dendritic cells and their progenitors in infectious diseases

Upon the fight against invading pathogens mechanisms and events such as mobilization to the sites of infection or apoptosis lead to the consumption of immune cells. Dendritic cells (DCs) are key players of the adaptive immune response and important components in immunity against infections. Therefore, the regulation of DCs and their progenitors upon infection/inflammation is an emerging field of interest.

Using the model pathogen *Yersinia enterocolitica* (Ye) in an experimental mouse infection model we found that Yeinfection causes a pronounced reduction of the number of splenic DCs. This effect was dependent on TLR4 and TRIF signaling, and the net result of Ye-induced faster DC turnover and suppression of *de novo*DC generation. However, the mechanism underlying this remains elusive.

We hypothesize that Ye may affect hematopoietic stem and progenitor cells (HSPCs) and DC precursors by microbial and/or inflammatory signals, such as TLR ligands, pathogenicity factors andinterferonsand that this might influence immunity against the pathogen. Therefore, the regulation of HSPCs and their progeny with focus on DC progenitors will be analyzed upon infection with different bacterial pathogens to elucidate possible general regulation mechanisms. Specifically we will focus on analyzing the basic influence of microbial (TLR signaling, direct and indirect effects) and inflammatory (interferons, chemokines and growth factors) signals on survival/proliferation, migration and differentiation of HSPCs and DC precursors (see Figure 2). Knowledge about this will not only give new insights into basic DC biology, but may also identify new therapeutic targets/diagnostic markers in infectious diseases.

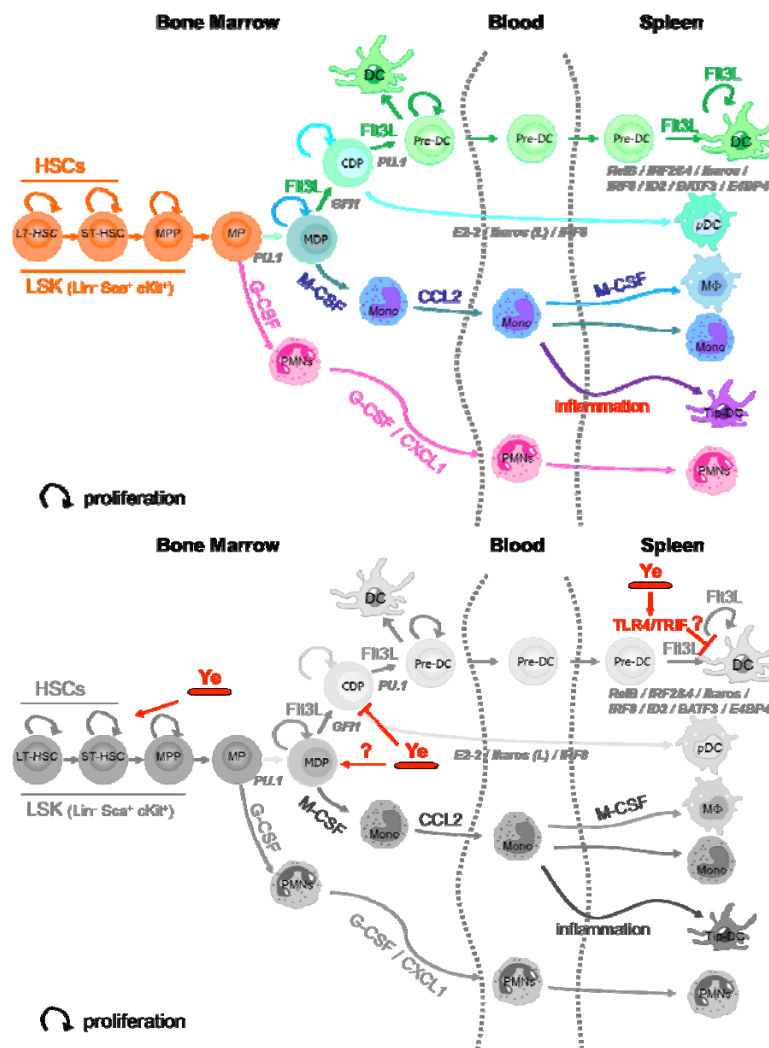


Figure 2: Possible mechanisms how Ye may affect DC homeostasis