Abstract

Granulocytes represent the first line of defense against bacteria and fungi. Daily production of granulocytes is sustained by steady state granulopoiesis but under stress (e.g., bacterial infection) this program switches to emergency granulopoiesis (EG) which ensures the production of granulocytes at enhanced and accelerated rates. Very little is known about the regulation of EG. In this thesis, we showed that disruption of the β-catenin-TCF/LEF mediated transcription impairs EG *in vivo*. Further, we demonstrated that lipopolysaccharide (LPS) administration in mice induces accumulation of active β-catenin in hematopoietic stem and progenitor cells (HSPCs) as early as 4 hours (H) after stimulation, with highest increase at 24H. This effect was at least partially mediated in a niche independent manner, since LPS stimulation *in vitro* induced β-catenin accumulation in c-Kit+ cells after 2H, with a peak activation at 4H. Using single cell RNA sequencing, we determined the cell cluster dynamics of HSPCs following 4H LPS stimulation. Interestingly, we identified a possible upstream activator of β-catenin in one of the clusters – Wnt10b. Indeed, *Wnt10b* showed a similar expression pattern as EG master regulator *Cebpb* and β-catenin activation, following *in vitro* treatment with LPS. Altogether, our data point at a critical role of the Wnt/β-catenin-TCF/LEF signaling pathway in activation of the EG program at the HSPC level at early stages upon infection.

Key words: Granulocytes, Emergency Granulopoiesis, Inflammation, β-catenin, Hematopoietic Stem and Progenitor Cell