

WORKPACKAGE 5:

T and B cell interplay in the allogeneic stem cell transplantation (collaboration Ellen Meijer, Saskia Ebeling)

Chronic graft-versus-host-disease (GVHD) is the major long term complication of allogeneic stem-cell-transplantation (allo-SCT) as up to 70% of all patients receiving allo-SCT and surviving beyond day 100 develop chronic GVHD. With characteristics of auto-immune diseases like scleroderma and idiopathic lungfibrosis, this complication is invalidating and can be lethal. Several lines of investigation indicate that B-cells are involved in the development of chronic GVHD and the clinical importance of B-cells in chronic GVHD is indicated by the observation that treatment of steroid refractory chronic GVHD with the B-cell depleting monoclonal anti-CD20 antibody rituximab has been successful in up to 70% of patients. However, it is to date unclear whether host or graft B-cells are involved in this process, which would be the best timing of B-cell-depletion and whether a pre-emptive B-cell-depletion can reduce the incidence of this quality of life and life threatening complication. So far, our data indicate that host B-cells are important during both, acute and chronic GVHD following reduced intensity conditioning transplantation but in completely different aspects. While host B-cell-depletion is beneficial in terms of substantially reducing extensive chronic GVHD, it is detrimental once acute GVHD occurs as it seems to shape the host T cell repertoire against self but not cancer tissue. Aim of this research project is therefore to further elucidate the B and T cell interplay in stem cell transplantation.