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Mechanisms of immune evasion in aggressive B cell lymphomas

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Chemoimmunotherapy is the standard of care treatment for aggressive B cell lymphomas, like Diffuse large B cell lymphoma (DLBCL) and Burkitt lymphoma (BL). However, 30-40% of patients relapse or have refractory disease. Innovative therapy approaches focus on tumor infiltrating T cells and their potential capacity to mediate killing of malignant B cell clones. To leverage the therapeutic benefit of those approaches, it is essential to have in-depth knowledge about the tumor microenvironment (TME) and understand immune evasion strategies. Interestingly, the malignant cells in aggressive B cell lymphomas originate from lymphocytes, physiologically prone to recognize antigens with their B cell receptor (BCR) and interact with other immune cells like follicular dendritic cells (FDCs) or T follicular helper cells (TfHs). During lymphomagenesis, the cells need to find mechanisms to prevent recognition and killing from other immune cells.

By studying lymphomagenesis in autochthonous mouse models, we characterize the T cell landscape of aggressive B cell lymphomas. Using innovative technologies, including single-cell RNA sequencing (scRNA seq) and spectral flow cytometry, we gain information about the transcriptomic and proteomic landscape of the TME.

Like the human disease, murine BL tumors predominantly consist of tumor cells (>90% of cells in the tumor bulk). Non-tumor cells, including T cells and myeloid cells, are infrequently detectable, and heterogeneity exists between the individual tumors.
In contrast, DLBCL-like tumors often harbor rich infiltration of immune cells in the affected organs. The tumors have an increased CD8/CD4 T cell ratio and show increased expression of activation and exhaustion markers, while T follicular helper cell proportions decrease in the tumors.
These insights will provide the basis for further analyses of immune escape mechanisms during lymphomagenesis.