

ISOLATION AND CHARACTERIZATION OF A MURINE SPONTANEOUS DLBCL LYMPHOMA WITH RESTRICTED IN VIVO SPREADING – A MODEL FOR VISCERAL LYMPHATIC METASTASIS?

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Introduction: Spontaneous or induced malignant lymphomas in mice are valuable tools for studying both physiological lymphoid development and the microenvironmental factors influencing the survival and spreading of tumor cells, including migration between peripheral lymphoid organs and subsequent positioning in distinct tissue compartments. In this presentation the isolation, phenotypic and genetic characterization and in vivo propagation of a novel BALB/c-derived B-cell lymphoma with the cytological characteristics of high-grade diffuse large B-cell lymphoma (Bc-DLBCL.1) showing restricted tissue distribution and metastasis formation will be reported.

Results: The original tumor was identified in an aged BALB/c mouse as an incidental finding presenting as a soft tissue mass engulfing the mesenterium and the mesenteric lymph nodes (mLN). Subsequent intraperitoneal injection into both syngeneic BALB/c and allogeneic RAG-1-deficient hosts led to the successful propagation of tumor, with extensive splenomegaly and enlarged mLN in tumor-bearing recipients. Bc-DLBCL.1 cells express CD19, B220, MHC II, surface IgG2a/kappa chain as well as dual rearrangement of VhQ52 and Vh7183 regions of the IgH gene consistent with the B-cell origin of lymphoma, possibly of post-germinal center (GC) stage. Despite its aggressive high-grade features, Bc-DLBCL.1 lymphoma cells did not expand into extraabdominal locations upon intraperitoneal passage, and only exceptionally produced hepatic metastasis. In addition, attempts to establish in vitro adopted sublines were unsuccessful, indicating dependence for in vivo tissue microenvironment. In mLNs the high endothelial venules (HEVs) contained only few tumor cells (corresponding to low-level expression of L-selectin), while the LYVE-1-positive lymphatic vessels were almost completely filled with lymphoma cells. Preferential association of Bc-DLBCL.1 cells with lymphatics was further indicated by the mesenteric tumor expansion where in the peritoneal sheath the tumor cells in perivascular cuffs were intermingled with LYVE-1-positive cysts containing lymphoma cells.

Conclusion: Based upon these findings, Bc-DLBCL.1 lymphoma cells likely propagate in mLN primarily via the lymphatic circulation, therefore this tumor may serve as a model to investigate the physiological as well as pathological aspects of cell migration via the lymphatic circulation from the peritoneal cavity.

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