Institute of Pathology

Gene Expression Profiling and SNP Analysis of B Cell Lymphoma of the Gastrointestinal Tract

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As a national reference center for lymphoma diagnostics, the Institute of Pathology at Ulm University has been engaged for many years in the characterization of Hodgkin and non-Hodgkin lymphoma. Based on a large collection of fresh-frozen lymphoma tissue, the aim of the project is to analyze oncogenesis and the progression of extranodal marginal zone B cell lymphoma (MZBL) of the gastrointestinal (GI) tract by means of gene expression profiling and SNP analysis of microdissected lymphoma tissue.

MZBL, consisting of small cells, and aggressive diffuse large B cell lymphoma (DLBCL) of the GI tract are extranodal lymphomas with immunological, cytogenetic and clinical features that differ from nodal B cell lymphomas. It is well known that indolent MZBL and aggressive DLBCL can coexist in the GI tract. Within an inflammatory context caused by Helicobacter pylori infection, clonal evolution from the small to the large cell variant has been proven by means of molecular cytogenetics.
Composite lymphoma of an extranodal marginal B cell lymphoma of the stomach.
A: Hematoxylin-Eosin staining of the small cell component of a composite B cell lymphoma of the stomach. Cells have a lymphocytic appearance.
B: Hematoxylin-Eosin staining of the large cell component of the same lymphoma.
C: Immunostaining with the proliferation marker Ki-67. The large cell compartment shows a higher proliferation index than the small cell areas.
D: Immunostaining with an antibody specific for Bcl6. The small cell compartment is negative, while the large cell compartment shows strong expression of the Bcl6 protein.

Therefore, these tumors are referred to as “composite lymphoma” and represent a model of lymphoma progression. In a former study, we showed by transcriptional profiling that there is a close relationship between GI MALT lymphoma and their large cell variants. From these results, we concluded that DLBCL of the GI tract is a blastic, aggressive variant of MZBL.

We have identified that c-REL and BCL6, as candidate genes for lymphoma progression, can be activated by gene amplification or translocations. We have shown that an amplification of c-REL is frequently accompanied by a nuclear accumulation of REL protein in the nucleus of lymphoma cells. Our goal is to further characterize this finding of GI B cell lymphomas by using Affymetrix platforms for gene expression profiling and SNP analysis. Our aim is to identify specific markers associated with lymphoma progression from MZBL to DLBCL.

FISH with a probe for c-REL on a large B cell lymphoma of the stomach. The cloudy red signals reflect massive amplification on 2p16 that includes the c-REL gene.

Selected Publications: