**Tumor progression in gastric marginal zone B-cell lymphoma of MALT type**
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**Background/State of the art.** Approximately 20-35% of Non-Hodgkin Lymphomas (NHL) arise in extra nodal sites and from these about 30-40% are localized in the gastrointestinal tract. There is strong evidence that these lymphomas gradually develop from a polyclonal chronic gastritis in the background of a *Helicobacter pylori* infection. This lymphoma is classified according to the current WHO classification as an extra nodal marginal zone B-cell lymphoma of mucosal associated lymphoid tissue (MALT) type (ICD-O: 9699/32). Due to additional oncogenic events this indolent lymphoma may then progress to a diffuse large B-cell lymphoma (DLBCL; ICD-O: 9680/3). These two lymphomas may co-exist at the same site and are defined as composite lymphomas consisting of a small cell B-cell extra nodal marginal zone B-cell lymphoma of MALT type and the transformed, highly proliferating blastic B-cell lymphoma (Barth et al. 2013).

**Preliminary work:** To understand the transition of the indolent MALT lymphoma into a more aggressive DLBCL, we have analyzed this process of progression of the small cell marginal B-cell lymphoma to its blastic variant by interphase cytogenetics (Barth et al. 1998; Barth et al. 2001), SNP and expression analysis, and could show that this progression is associated with changes on the genomic, transcriptomic and protein level (Flossbach et al. 2013; Flossbach et al. 2012; Barth et al. 2007). We concluded that the aggressive DLBCL phenotype still has many characteristics of the initial indolent lymphoma. This may explain why the aggressive variant still responds well to an eradication therapy of *Helicobacter pylori*. We therefore termed this aggressive lymphoma „blastic marginal zone B-cell NHL of the stomach“. In further expression analyses we could show together with the group of Prof. Hans Kestler from Ulm that on transcriptomic grounds the small cell extra nodal gastro-intestinal marginal B-cell lymphomas (g.i. MZBL), the blastic marginal cell B-cell lymphomas and nodal diffuse large B-cell lymphomas of GCB and ABC type form distinct groups and hence support the standalone concept of blastic marginal zone B-cell NHL of the stomach.

**Overall hypothesis:** The main aims of this project are to identify and to characterize the aberration(s) responsible for this progression using expression profiling and next generation sequencing. Pre-condition for our project is our cryopreserved lymphoma collection, which comprises 7 gastrointestinal marginal zone B-cell lymphomas, 13 blastic gastrointestinal marginal zone B-cell lymphomas, and 5 composite lymphomas with coexisting small and large cell lymphoma compartments including non-neoplastic mucosa with inflammatory infiltrates. This collection originates from the time when gastric resection was regarded as a therapeutic option for these lymphomas and is as such worldwide unique. The combination of already existing expression and SNP data will allow the distinction of the blastic variant of these gastric lymphomas from other extragastric diffuse large B-cell lymphomas and will contribute to further understanding the molecular mechanisms of progression in this context.