ImmunoTools *special* Award 2023

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PATZ1 in MYC-driven B-cell lymphoma

Non-Hodgkin lymphoma (NHL) represents one of the most frequent hematologic malignancies. 85% of all NHL originate from B-lymphocytes (B-cells). B-cells are the center of the adaptive humoral immune system as antibody-producers to combat infectious agents. B-cell lymphomas, including Diffuse Large B cell lymphoma (DLBCL), Follicular lymphoma, Mantle cell lymphoma, and Burkitt lymphoma vary in their clinical features, treatment response, diseases progression, and prognosis. In the late 1990s, the anti-CD20 monoclonal antibody Rituximab was approved for the treatment of B-cell non-Hodgkin lymphomas. Although, further combined with various chemotherapy regimens, Rituximab was associated with significant survival benefits, the fact that the effect of B-cell depletion sometimes worsens the symptoms of the very same conditions asks for a deeper understanding of the underlying molecular mechanisms to better anticipate an impact-forecast of B-cell depletion.

POZ/BTB and AT-hook-containing zinc finger protein 1 (PATZ1 also known as MAZR (Myc-associated Zinc finger related factor, encoded by the Patz1 gene)) is a transcription factor regulating gene expression either as an activator or a repressor depending upon the cellular context. Several studies have reported an important role for PATZ1 in regulating a plethora of cellular functions including stem cell generation and reprogramming, neurogenesis, spermatogenesis, DNA damage response, and cell differentiation. Furthermore, PATZ1 is implicated in tumorigenesis and its overexpression has been described in various human tumor types. In contrast, PATZ1 has been reported as a tumor suppressor in liver cancer, glioblastoma, thyroid cancer, and B-cell lymphomas. Mechanistically, PATZ1 was shown to directly bind and either repress or activate specific oncogenic promoters, such as the MYC promoter. PATZ1 also can orchestrate apoptosis/cell survival by interacting directly with p53 to regulate the expression of p53 target genes or compete with p53 for the binding to DNA. Whether PATZ1 acts as a tumor promotor or suppressor has been proposed to depend on the cellular context and on its protein interaction network. To date, PATZ1 has been claimed as an independent prognostic marker of DLBCL. However, the role of PATZ1 for B-cell lymphoma formation have not been fully understood.

We will perform a CRISPR/Cas9 mediated deletion of *PATZ1* in established human B-cell lymphoma cell lines. These cells will be analyzed *in vitro* for cell growth and chemosensitivity and further characterized by immunophenotyping using classical B-cell differentiation markers including CD45, CD19, CD24, CD21, CD27, CD38, CD34, CD117, CD10 and IgM. To focus on the tumor intrinsic effects, these cells will be transplanted to immunocompromised mice, which allows to investigate the impact of PATZ1 on disease outcome and phenotype of the lymphomas. It is essential to define the exact differentiation status of our PATZ1-deficient B-cells and *ex vivo* lymphomas to be able to associate them with the disease prognosis. ImmunoTools cytometry antibodies would perfectly be suited for this purpose and would essentially push forward our need to determine surface markers on our cells to unravel the specific role of PATZ1 in B-cell lymphoma. As a future prospective, we aim to provide novel aspects for basic research on lymphomagenesis and want to shed light onto the role of PATZ1 during lymphoma development and validate PATZ1 as a prognostic biomarker. We hope you consider our project relevant and are looking forward to your response.

ImmunoTools *special* AWARD for **Bernhard Zdársky** includes 10 reagents

FITC - conjugated anti-human CD10, CD19, CD45, IgM

PE - conjugated anti-human CD24, CD38, CD117

APC - conjugated anti-human CD21, CD27, CD34

DETAILS more AWARDS