Universität Basel

Research Project

Role of the desmosomal adhesion molecule desmoglein-2 in acute lymphoblasic leukemia

Third-party funded project

Project title Role of the desmosomal adhesion molecule desmoglein-2 in acute lymphoblasic leukemia
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Acute lymphoblastic leukemia (ALL) is the most frequent malignancy in childhood with exceptionally high frequency in Mexico City (1, 2). It is characterized by hyper-proliferation and accumulation of lymphoid progenitor cells in the bone marrow and blood with invasion into other tissues during progression of disease (3, 4). Even though pediatric ALL has a high survival rate, relapsed disease, organ infiltration or disease onset during adolescence are challenging to be treated effectively. This highlights the importance of a better understanding of the disease mechanisms. Our preliminary data uncovered a hitherto unknown expression of the desmosomal adhesion molecule desmoglein-2 (DSG2) in two ALL cell lines (Jurkat T-ALL and REH B-ALL), while primary human lymphocytes do not express this protein under baseline condition but during proliferation after PHA stimulation. Importantly, reduction of DSG2 expression by shRNA significantly impaired Jurkat cell viability, suggesting a role of DSG2 in leukemia progression. In the proposed project, the malignant potential of DSG2-deficient ALL cell lines will be clarified by applying these cells in transendothelial migration assays, 3D bone marrow organoid colonization, and in vivo xenograft mouse model. Furthermore, samples from ALL patients affected by different subtypes will be screened for DSG2 expression compared to healthy controls. In these samples, DSG2 protein levels will be reduced by lentivirally delivered shDSG2. The effect of DSG2 depletion on lymphoblast function will be determined with a focus on the contribution to cell proliferation, adhesion and infiltration. With this proposal we will combine the knowledge of a Mexico-based immunobiology laboratory and an associated oncoimmunology group with access to patient samples and expertise in ALL and leukemia mouse models with a Swiss cell adhesion research group with focus on function of desmosomal molecules. This collaboration includes exchange of scientists, samples, material and expertise. We are convinced that the proposed experiments will clarify a possible contribution of DSG2 during ALL progression. Our data may provide novel insights into the mechanisms underlying the pathogenesis of ALL and potentially identify novel treatment approaches.

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