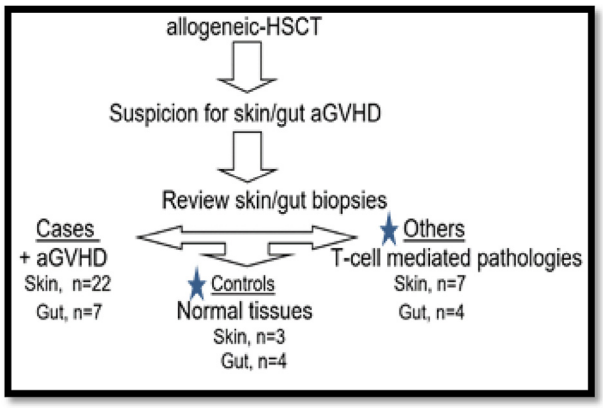

Figure 1. Study design. Samples obtained from University Hospitals Seidman Cancer Center biorepository.

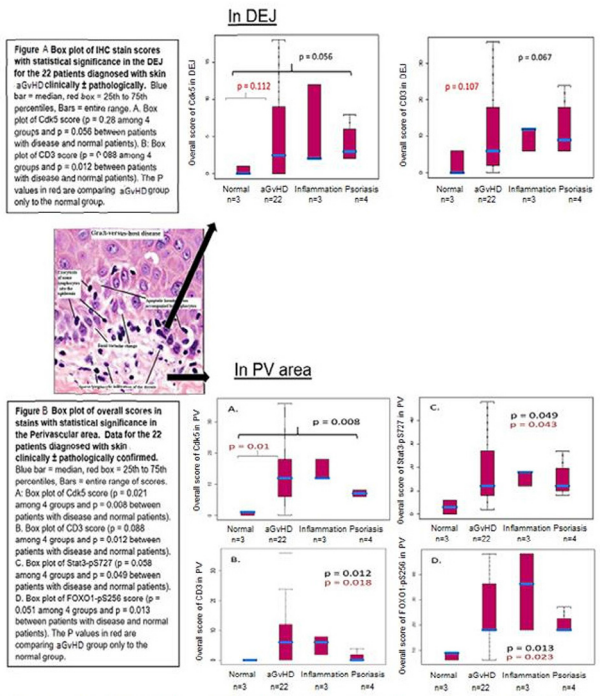

Figure 2. Box plot analysis using Kruskal-Wallis test. Skin overall stain scores with statistical significance at the different areas for the 22 patients with clinical ± pathological skin aGvHD diagnosis A. Dermoepidermal junction B. PV areas.

correlation of Cdk5 in the tissues and peripheral blood leukocytes to aGvHD. The ultimate goal is not only to validate the role of Cdk5 in aGvHD but also to define the potential of Cdk5 as a novel therapeutic target for this disease.

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The Role of S1PR1 Agonism in Thymus-Dependent Generation of Autoreactive T Cells during Experimental Acute Graft-vs.-Host Disease

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Acute graft-versus-host disease (aGVHD) is initiated by alloreactive T cells that attack different host tissues. In clinical allogeneic hematopoietic stem cell transplantation (alloHSCT), the development of aGVHD predisposes to chronic GVHD (cGVHD) with autoimmune manifestations. It is currently unclear, however, how autoimmunity is linked to antecedent alloimmunity. Using murine models of alloHSCT we had previously shown upon transfer the donor T cells gain access not only to the classical target organs of skin, liver and gastrointestinal tract, but also to the thymus, hence causing injury in this primary lymphoid tissue (Dertschnig et al., Blood 2013;122:837 and 2015;125:2720). Thymic aGVHD impaired the compartment of medullary thymic epithelial cells (mTEC) expressing the autoimmune regulator (Aire). Loss of Aire^{+}mTEC was essential for failure to clonally delete self-reactive T cells. In the present work we aimed to test whether continuous blockade of donor T-cell trafficking from activation sites in secondary lymphoid organs would prevent thymic injury and hence prevent the emergence of autoreactive T cells. Using different murine alloHSCT models we analyzed in the present study the effects of pharmacological modulation of the sphingosin-1-phosphate (S1P) signalling pathway interference with the synthetic sphingosin-1-phosphate receptor 1 ($S1PR_1$) agonist KRP203 (a gift from Novartis Inc., Switzerland). We found in unconditioned recipients of haploidentical donor T cells that prophylactic $S1PR_1$ administration (3 mg/kg/day; starting on day -1 before alloHSCT) but not therapeutic administration (starting on day +7) reduced donor T-cell migration to the host thymus, thus significantly attenuating thymic aGVHD. In consequence, the Aire^{+}mTEC pool remained normal with respect to absolute cell numbers. Maintenance of a normal thymic epithelial compartment was indeed associated with the emergence of lower numbers of thymus-dependent autoreactive T cells in the periphery, as assessed by the use of a conditioned OT-II/RIP-mOVA transgenic fully MHC-mismatched alloHSCT model described earlier (Dertschnig et al., Blood 2015;125:2720). We conclude from our study that prophylactic and continuous administration of KRP203 prevents breakdown of thymic central tolerance induction. By blocking thymic autoreactive T-cell production and export, specific $S1PR_1$agonism may hence protect from the development of autoimmune syndromes following alloHSCT.

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A Prospective Trial of Extracorporeal Photopheresis (ECP) in the Modern Transplant Era Reveals Response and Decreased Steroid Doses for Patients with Chronic Graft-Versus-Host Disease

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Background: ECP is often used to treat chronic GVHD (cGVHD) despite an unclear mechanism of action. The NIH Consensus Criteria (2005) addressed grading of cGVHD and response assessment. Provider assessment of response and change in global severity have shown association with survival out-