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Using Protein Simple Nanoimmunoassay (PS-NIA) to Identify High Molecular Weight Isoforms of Thymic Stromal Lymphopoietin (TSLP) as Biomarker in Graft Versus Host Disease

Stanford scientists have discovered novel high molecular weight isoforms of thymic stromal lymphopoietin (TSLP), measured using nanoimmunoassay (NIA), that can serve as a blood-based biomarker for the diagnosis and prognostication of acute graft versus host disease (aGVHD). TSLP isoforms as a biomarker can be transformative for hematopoietic stem cell transplant patients by enabling early therapeutic intervention since TSLP is targetable by Tezepelumab, an FDA-approved anti-TSLP monoclonal antibody.

Hematopoietic stem cell transplant (HCT) is the only curative therapy for bone marrow stem cell diseases such as leukemias, lymphomas, aplastic anemia, and sickle cell disease. Acute graft versus host disease (aGVHD) is a serious and life-threatening complication of HCT that occurs in up to 70% of patients and primarily affects epithelial-lined organs such as the skin, and gastrointestinal tract. Steroid refractory aGVHD of the lower gastrointestinal tract (SR-LGI-aGVHD) carries high morbidity and mortality. Early prognostication with blood biomarkers would allow physicians to modulate therapy early in the course of the disease to improve outcomes. Existing biomarkers such as ST2 and Reg3a are not targetable by therapeutic agents. A biomarker that is both prognostic and targetable could improve outcomes by guiding the early use of directed therapies.

Using NIA, the researchers discovered novel, previously undescribed high molecular weight isoforms of TSLP ranging from 29 to 40kDa. Levels of these HMW isoforms were significantly elevated in patients with aGVHD compared to those without GVHD and increased further in patients with steroid refractory disease. Importantly, this finding was observed across independent patient cohorts from different institutions, which suggests the biomarker is robust across diverse patient populations. Unlike existing biomarkers, TSLP is targetable by Tezepelumab, an FDA-approved anti-TSLP monoclonal antibody currently marketed for severe asthma. Consequently, HMW TSLP isoforms measured by NIA have the potential to serve as both a diagnostic and prognostic biomarker in aGVHD and to guide the use of a targeted therapeutic, which could improve outcomes for HCT patients.

Stage of Development:
Preclinical

Applications

- Blood-based diagnosis and prognostication of acute graft versus host disease in hematopoietic stem cell transplant patients
- Early identification of steroid refractory aGVHD to guide timely therapeutic intervention
- Use as a companion biomarker to guide treatment with Tezepelumab or other anti-TSLP therapies in GVHD
- Potential extension to other TSLP-mediated inflammatory conditions affecting epithelial-lined organs

Advantages

- Non-invasive, blood-based assay that can be integrated into routine post-transplant monitoring
- Identifies novel high molecular weight TSLP isoforms not detectable by conventional ELISA
- Unlike existing GVHD biomarkers such as ST2 and Reg3a, TSLP is targetable by an FDA-approved therapeutic
- Robust across multiple independent patient cohorts, suggesting reliability across diverse patient populations

- Leverages an existing FDA-approved drug (Tezepelumab) which reduces the pathway to clinical translation

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