Docket #: S21-311

CCL5-mediated activation of immune adverse reaction in immune check point inhibitor-treated cancer patients

An increasing number of cancer patients are now receiving immune checkpoint inhibitors (ICIs), which boost the immune system to attack cancer cells. However, this treatment can harm normal cells alongside cancer cells, leading to toxicities in up to 60-70% of patients for skin issues and up to 50% mortality for cardiotoxicities. Identifying the specific cells and pathways responsible for these adverse immune reactions could enable patients to benefit from ICI treatment against cancer without harming normal cells.

Stanford researchers have identified increased clonal cytotoxic Temra CD8+ cells in ICI myocarditis patients. These CD8+ cells exhibit distinct transcriptional changes, notably upregulation of chemokines CCL5/CCL4/CCL4L2. Targeting these chemokines could offer diagnostic and therapeutic avenues to mitigate life-threatening cardiac immune-related adverse events in cancer patients undergoing ICI treatment.

Stage of Development
Preclinical- in vivo studies in mice

Applications

- Immune Checkpoint Inhibitor Toxicity Diagnostic: level of CCL5 in the plasma as a biomarker of toxicity
- Immune Checkpoint Inhibitor Toxicity Treatment: disruption of CCL5 signaling via binding and activation of CCR5

Advantages

- First cell-based biomarker to discriminate immune activation from ICI-mediate toxicity
- Complementary to ICI for Cancer Treatment: Does not affect the therapeutic benefit of ICI on tumor cell killing

Publications

- Zhu, H., Galdos, et al. (2022). Identification of pathogenic immune cell subsets associated with checkpoint inhibitor–induced myocarditis. Circulation, 146(4), 316-335.

Patents

- Published Application: WO2023023269

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