Docket #: S22-499

Lymphocyte trafficking receptor and ligand

Stanford researchers have developed a novel approach to selectively regulate and monitor immune responses in specific mucosal tissues, using the GPCR receptor GPR25 and its ligand CXCL17, which targets lymphocyte localization to non-intestinal mucosal tissues, enabling selective delivery of engineered immune cells for therapy and non-invasive monitoring of mucosal immunity and autoimmune responses.

Current treatments for immune-related diseases in specific tissues like the lungs, airways, GI tract, and glands are often broad-spectrum and lack precision, leading to systemic side effects and limited effectiveness. As a result, there is lingering chronic inflammation and autoimmune responses in these areas leading to tissue damage and a range of debilitating symptoms. There is a clear need for targeted therapies that can modulate local immune activity without suppressing the immune system as a whole. Currently, there is no efficient, non-invasive way to monitor immune responses in these tissues, making it difficult to monitor disease progression and assess treatment efficacy.

To address this issue, Stanford researchers have developed a novel approach to selectively regulate and monitor immune responses in specific mucosal tissues without affecting the entire immune system. By identifying a unique receptor-ligand pair—the GPCR receptor GPR25 and its ligand, chemokine CXCL17, this invention opens new pathways for targeted immune intervention. The receptor GPR25, found on immune cells specific to mucosal tissues offers a direct way to guide immune cells precisely to these areas. This invention provides two primary solutions: targeted immunotherapy and enhanced diagnostics. In summary, this invention introduces a revolutionary tool for selectively controlling and tracking immune responses within specific mucosal tissues, providing a comprehensive solution for managing chronic inflammatory and autoimmune diseases.

Stage of development
Research - Mouse: demonstration that GPR25 expression targets lymphocyte migration to airway, gastric, biliary and GU tract mucosae. Human: in vitro. Initial discovery and validation. The investigators have confirmed expression of the receptor in human lymphocyte subsets implicated in respiratory tract and non-intestinal mucosae, and have shown human in vitro chemotaxis. Genetic. GWAS and eQTL co-localization studies implicate GPR25 dysregulation in autoimmune diseases including multiple sclerosis, inflammatory bowel diseases, uveitis, ankylosing spondylitis, primary biliary cholangitis, and coeliac disease.

Applications

- Targeted Immunotherapy for autoimmune diseases and chronic inflammatory diseases
- Non-invasive immune monitoring
- Vaccine efficacy assessment
- Infection tracking for early detection and intervention.
- Immune response diagnostics

Advantages

- Non-invasive monitoring immune responses in the lungs, airways and other tissues
- Selectively direct immune cells to specific tissues, enabling localized intervention without affecting systemic immunity
- Reduced side effects and complications compared to broad-spectrum immunosuppressants
- Enhanced diagnostic capabilities for monitoring immune responses in specific tissues
- Versatile applications across multiple diseases with improved patient outcomes

Publications

- Ocón B, Xiang M, Bi Y, Tan S, Brulois K, Ayesha A, Kunte M, Zhou C, LaJevic M, Lazarus N, Mengoni F, Sharma T, Montgomery S, Hooper JE, Huang M, Handel T,

Dawson JRD, Kufareva I, Zabel BA, Pan J, Butcher EC. A lymphocyte chemoaffinity axis for lung, non-intestinal mucosae and CNS. *Nature*. 2024 Nov;635(8039):736-745. doi: 10.1038/s41586-024-08043-2. Epub 2024 Sep 18. PMID: 39293486.

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