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Inflammatory Signatures and Human Spleen Organoids for Post-Treatment Lyme Disease and Autoimmune Drug Discovery

Stanford researchers have developed a human spleen organoid platform that models inflammation and autoimmune responses to bacterial peptidoglycans in a physiologically relevant human immune setting. The platform integrates optimized culture conditions with CRISPR/Cas9-mediated FOXP3 knockout in T cells, rendering the organoids susceptible to autoimmune activation. These organoids recapitulate key features of human immunity: monocyte activation, T cell responses, autoreactive B cell expansion, autoantibody secretion, and induction of autoimmune gene programs.

The researchers identified a distinct proinflammatory monocyte signature associated with post-treatment Lyme disease (PTLD) and demonstrated that Borrelia burgdorferi peptidoglycan is a key driver of persistent immune activation. The system is compatible with peptidoglycans from multiple microbial species, including those linked to lupus, rheumatoid arthritis, and inflammatory bowel disease.

The platform supports high-content analytical readouts, including cytokine profiling and single-cell transcriptomics, in scalable multi-well formats suitable for industry deployment.

Stage of Development
Proof-of-concept

Applications

- Preclinical screening of candidate therapeutics (antibodies, enzymes, small molecules) that block peptidoglycan-induced immune activation
- Biomarker discovery and companion diagnostic development for PTLD and autoimmune disorders
- Identification of novel signaling pathways driving peptidoglycan-mediated inflammation and autoimmunity
- Clinical trial stratification using immune signatures and pharmacodynamic biomarkers
- De-risking immunology and inflammation drug pipelines for biotechnology and pharmaceutical companies

Advantages

- Recapitulates human autoimmune responses in a physiologically relevant organoid model
- Scalable and reproducible in multi-well formats suitable for industry-standard deployment
- Compatible with peptidoglycans from multiple microbial species across various autoimmune indications
- Supports high-content readouts such as cytokine profiling and single-cell transcriptomics

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