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Using Mononuclear Phagocyte Markers to Detect Dormant Joint Replacement Infections

Stanford scientists have developed methods to analyze mononuclear phagocyte system markers for detecting prosthetic joint infections that evade conventional neutrophil-based diagnostics. By evaluating the broader immune response beyond neutrophil activity, this novel approach shows promise for identifying biofilm-mediated dormant infections that suppress conventional inflammatory markers, potentially providing a new pathway for early intervention in joint replacement patients.

Current diagnostic methods for prosthetic joint infections rely primarily on identifying neutrophil responses through synovial fluid analysis, acute phase reactants, and inflammatory markers. A key limitation of neutrophil-based diagnostics is that 40% of uninfected joint replacements still show a neutrophil response more than 6 weeks after surgery, making distinguishing between bacterial infection and post-surgical inflammation difficult. However, more concerning are biofilm-resident bacteria on prosthetic surfaces, which can modulate the local immune environment through altered cytokine production and antigen presentation. This modulation can suppress neutrophil recruitment and establish dormant infections that evade conventional diagnostic criteria. The neutrophil response represents only one component of a more complex immune response regulated by the mononuclear phagocyte system, which orchestrates both pro-inflammatory and anti-inflammatory responses through cytokine secretion and immune checkpoint modulation. Analysis of this broader system may provide a more comprehensive and reliable pathway for accurate diagnosis.

This novel diagnostic approach analyzes multiple markers of the mononuclear phagocyte system, including regulatory T-cells, natural killer cells, classical

monocytes, polarized macrophages, and dendritic cells within periarticular tissue samples to create a comprehensive profile of the immune response. Importantly, the method integrates cellular quantification, gene expression analysis, and protein level measurements in both synovial fluid and plasma, which provide several parameters to evaluate immune status. The initial development of standardized protocols for these measurements demonstrates promise for clinical translation and sets the foundation for validation studies. This multi-layered analysis has the potential to distinguish dormant infections from uninfected tissue with greater precision than current neutrophil-based diagnostics, enabling earlier intervention and reducing the risk of infection progression.

Stage of Development:

- Research: in vivo
- Continued research: Development of a proof-of-concept test

Applications

- Detection of dormant prosthetic joint infections that evade conventional diagnostics
- Comprehensive immune response profiling in periarticular tissue
- Early screening for biofilm-mediated infections in joint replacements

Advantages

- Multi-parameter analysis provides independent validation of infection status
- Detects infections that suppress conventional neutrophil response
- Integrates cellular, gene expression, and protein-level measurements
- Distinguishes between post-surgical inflammation and true infections

Patents

- Published Application: WO2026030118

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