Assessment of Implant-Associated Host Cell Response Reveals Distinct Immune Cell Populations

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Purpose: The mechanism by which host cells respond to coated implants in humans is not well characterized. Recent work has established the importance of facilitating a robust host cell response, indicating the first week following implant placement is critical for host cell attachment and protection from biofilm formation. Here, we utilize external fixator (ex-fix) pins as a model of human host cell implant attachment to investigate the effect of localized antibiotics on cell phenotype and inflammatory response toward the goal of preventing implant-associated infections.

Methods: Patients were consented for collection of ex-fix pins and blood samples. Data captured from the electronic health record included demographic, injury characteristics, treatment information, and documentation of complications including infection. All data were entered and stored in REDCap. Upon removal, ex-fix pins were immediately treated with an enzymatic solution for isolation of adherent cells. The resulting implant- adherent cell population was stained for flow cytometric analysis. Cells were separated based on CD45 staining, and then analyzed for surface expression of CD90 (stem cells, fibroblasts), CD11b (monocyte, macrophage), or CD68 (macrophage). Whole blood samples were processed into serum and cryopreserved for further cytokine array analysis.

Results: Using a CD45 parent gating strategy, a predominantly hematopoietic cell lineage response was observed as host cell responder attachment cells. Four distinct cell populations were identified as (1) fibroblasts (CD45–/CD90+), (2) fibrocytes (CD45+/CD90+), (3) innate lymphoid (CD45int/CD90bright), and (4) leukocytes (CD45+/CD90–). The latter group was further assessed to comprise 3 subgroups of monocytes (CD11bbright/CD68–), macrophages (CD11bint/CD68+), and other leukocytes. Of the 4 major cell types identified, leukocytes represented ~75%, followed by fibroblasts (~17%). Leukocytes included ~55% monocytes and 15% macrophages.

Conclusion: The present study observed distinct local immune populations on the surface of orthopaedic implants. Over 75% of the hematopoietic cells on the surface of the ex-fix pins had differentiated into monocytes and macrophages. Toward the goal of preventing orthopaedic implant-associated infections, these data provide further guidance for development of local antibiotic coatings and applications to prevent bacterial attachment and promote host integration.