An Advanced Organotypic Model of the Peri-Prosthetic Microenvironment to Interrogate the Interactions between T-cells and Silicone Shells

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Background

Although BIA-ALCL is a T-cell lineage lymphoma associated with textured breast implants, the etiopathogenesis of BIA-ALCL remains unknown. We engineered an advanced biomimetic (BM) scaffold composed of patient-derived breast tissue that simulates the 3D periprosthetic environment to investigate the interactions between implant shells and primary T-cells.

Methods

Allergan textured (BIOCELL®) and smooth breast implant shells were shaped to line wells in 96-well plates. Mammary tissue was digested to isolate adipocytes, stromal vascular fraction, and epithelial ductal organoids. These components were suspended in 0.3% type I collagen, forming the BM platform, along with patient-derived naïve or activated T-cells (200,000 cells/mL) and cultured with and without implant shell linings in low serum media (0.5% human serum). Additional groups included T-cells cultured in constructs of 0.3% type I collagen only. In parallel, T-cells were cultured in 2D with and without implant shell lining, in both low and full (10% human serum) media.

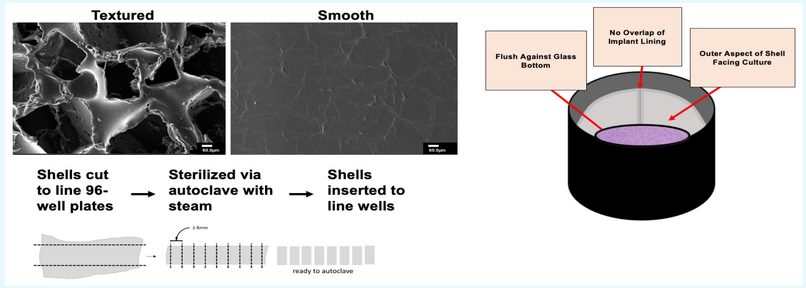


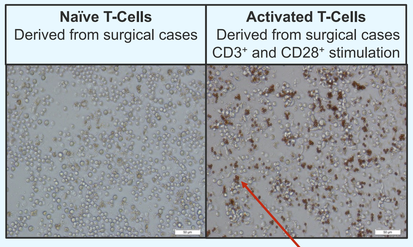
Figure 1. Illustration of our in-vitro model to study cellular behaviors in the peri-prosthetic microenvironment.

Results

In 2D culture, naïve T-cells and activated T-cells showed significant declines in cell number over 10 days across textured, smooth and no implant groups ($p<0.0001$). Full serum groups declined more rapidly than low serum groups. Exposure to textured shells, in both low and full serum, was associated with the greatest decline in T-cell number while cells not exposed to implant shells declined the least. In 3D BM constructs, only activated T-cells demonstrated a slight increase in cell count upon exposure to eithera textured or smooth implant. In contrast, in collagen-only platforms both activated and naïve T-cells decreased in cell count.

Conclusions

When cultured either in 2D or tissue engineered 3D platforms, the lack of proliferation seen upon exposure to implant shells may indicate that silicone surfaces alone are insufficient to induce pathologic transformation and hints at the existence of a potential cofactor playing a role in the pathogenesis of ALCL.



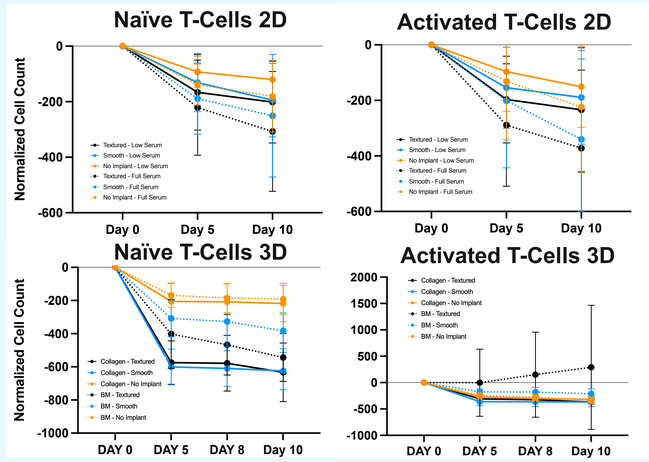


Figure 2. Light microscopy showing naïve and activated T-cells isolated from blood samples (left) and normalized cell counts of naïve and activated T-cells in both 2D and 3D culture models.

Acknowledgments

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