Foreign Body Response to Implanted Human Fascial Lata in a Mouse Model: Implications for Enhancing Pelvic Reconstructive Surgery

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Background

The growing demand for Pelvic Organ Prolapse (POP) repair, driven by an aging population, has highlighted a critical shortage of available surgical grafts [1]. This scarcity is largely due to the commercial withdrawal of all transvaginal mesh products and, more recently, the removal of all mesh for sacrocolpopexy procedures[2].

Human Fascia Lata (HFL) grafts have long been utilized in incontinence procedures and are increasingly used for sacrocolpopexy or graft-augmented vaginal repairs when synthetic mesh is contraindicated or unavailable[3,4]. Despite their usage, there is insufficient data on the Foreign Body Response (FBR), an inevitable process when any material is implanted into the body, especially when compared to synthetic polypropylene (PP) mesh.

Aim

This project aims to directly compare the FBR to HFL and synthetic mesh to better characterize HFL's long-term implications and the mechanisms driving its integration in the body—a necessary step before widespread adoption.

Method

Ethics

Human fascial samples were collected with informed consent, approved by the Cabrini Human Research Ethics Committee. All procedures followed National Health and Medical Research Council guidelines.

qPCR Fluidigm Biomark

Sample Preparation: Animal tissues were stored in RNA later (ThermoFisher) at 4°C for 24 hours, then at −80°C. RNA was extracted using the RNeasy mini kit (Qiagen) and converted to cDNA.

Preamplification: Preamplification was done to increase gene copies, using pooled Taqman assays and Sample Premix. Reactions were preamplified for 14 cycles, then diluted.

qPCR: Samples were analyzed using a 96.96 Dynamic array IFC with Fluidigm Real-Time PCR analysis software (V4.1.1). Target gene expression was normalized to 18sRNA and analyzed using the 2-ΔΔCT method.

Data Analysis and Statistics

Fold changes were calculated against uninjured controls. Statistical analysis was performed using the Mann-Whitney U test in GraphPad Prism v9, with significance at $P \leq 0.05$.

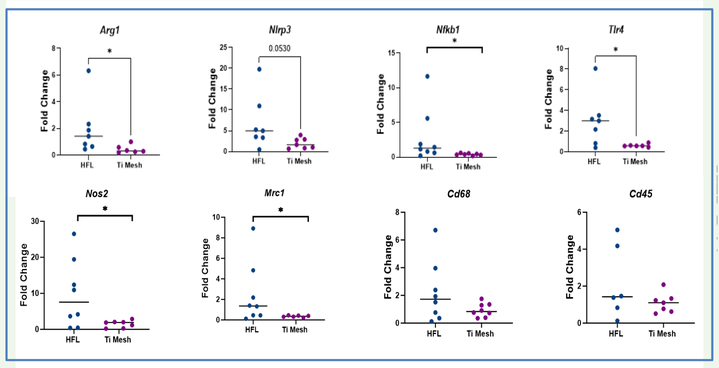
Single Cell Proteomics

Sample Preparation: Fresh frozen mouse skin tissue sections were hydrated, fixed, and stained with PhenoCycler antibodies. Sections were imaged using the PhenoCycler-Fusion system.

Imaging and Analysis: The cyclic process of reporter addition, imaging, and dehybridization was automated. Data were analyzed using Multiplexed Image Analysis (MIA) software. Nuclear and cytoplasm segmentation were performed, and unsupervised clustering with the Leiden algorithm was used for cell phenotyping.

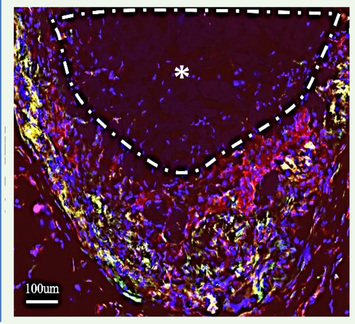
Results

➢ ***Impact of HFL on Chemokine and Cytokine Receptor Profiles***

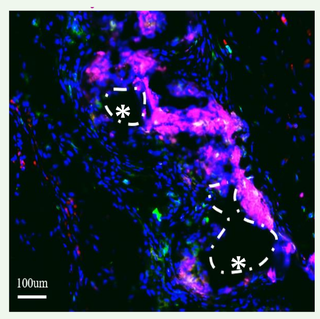


Myeloid marker gene expression: D90

CD31, CD90, CD38

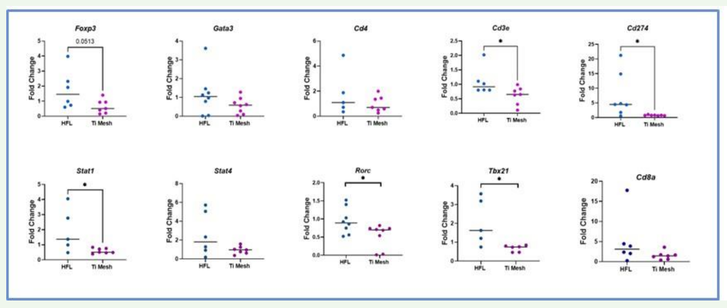


HFL-D90



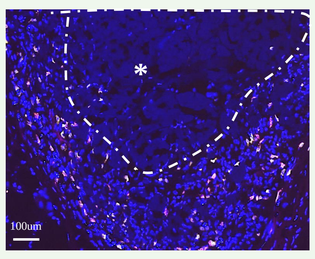
Mesh-D90

➢ ***HFL-Induced Changes in Lymphocyte Recruitment and Activation Pathways***

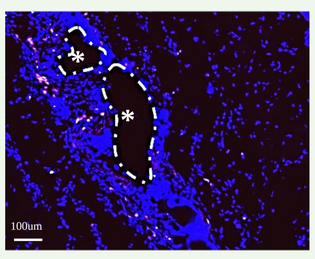


Adaptive immune system activation genes: D90

CD31, CD90, CD38

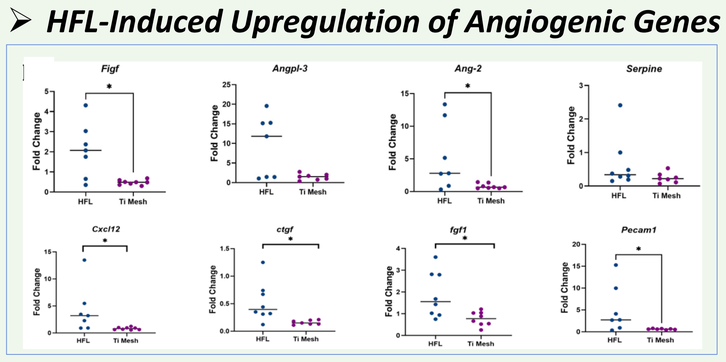


HFL-D90



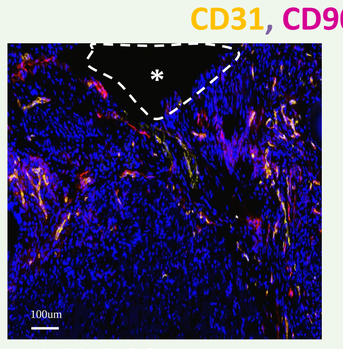
Mesh-D90

➢ ***HFL-Induced Upregulation of Angiogenic Genes***

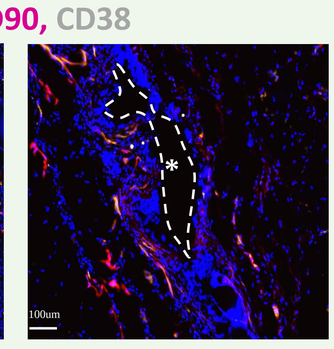


Angiogenesis genes: D90

CD31, CD90, CD38

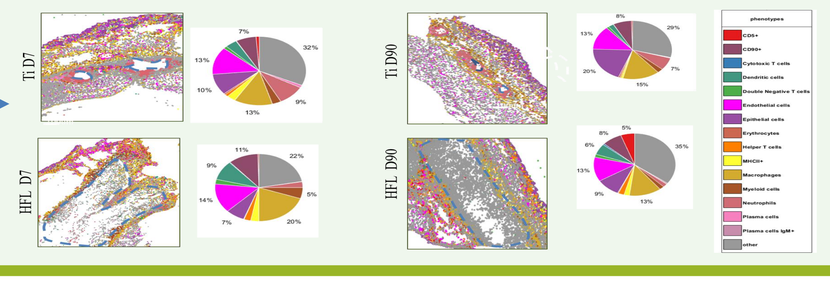


HFL-D90



Mesh-D90

➢ ***Differential Recruitment of Dendritic cells, Macrophages and Helper T cells in HFL after 7 and 90 days***



* HFL or Mesh area

Conclusion

1. HFL grafts triggered a significantly stronger immune response compared to Ti mesh, as seen by increased myeloid-related gene expression and immune cell recruitment at both 7- and 90-days post-implantation.
2. HFL and Ti mesh recruited different immune cell types, shaping the immune response and tissue healing. HFL demonstrated a more dynamic immune profile, characterized by both active inflammatory and anti-inflammatory responses
3. Despite the heightened immune response, HFL grafts also promoted greater angiogenesis and tissue remodeling, underscoring the importance of both inflammatory and anti-inflammatory responses for proper tissue integration and repair.

References

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4. S.B. Tate, L. Blackwell, D.J. Lorenz, M.M. Steptoe, P.J. Culligan, Randomized trial of fascia lata and polypropylene mesh for abdominal sacrocolpopexy: 5-year follow-up, Int Urogynecol J 22(2) (2011) 137-43.

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