

A Preclinical Model of Vocal Fold Tissue Engineering in Pigs Using Human Adipose-derived Mesenchymal Stem Cells

KIRANDEEP KAUR¹, YAZEED ALHIYARI², JENNIFER L. LONG²

¹David Geffen School of Medicine, UCLA, Los Angeles, CA; ²Department of Head and Neck Surgery, David Geffen School of Medicine, UCLA, Los Angeles, CA

INTRODUCTION

- Vocal fold (VF) injuries cause loss of normal voice - healing process involves scar formation that decreases the vibrational ability of vocal folds necessary for voice
- The current traditional treatments such as steroid injections³ and surgical implantation of synthetic fillers or autologous tissue grafts are able to decrease scarring, but not enough to restore normal voicing⁴
- In previous studies, a graft material was developed called cell-based outer vocal fold replacement (COVR)^{12,13}, which mimics the vocal fold ECM and yielded promising results when implanted

OBJECTIVES

- Analyze gene transcripts of pig vocal fold cells after the COVR implantation to identify genomic and extracellular matrix changes in the vocal folds throughout the wound healing process

METHODS

3 pigs (Pig A,B,C) were resected of their vocal folds and hASC-derived COVR graft was implanted. The cell-based outer vocal fold (COVR) is created using a three-dimensional fibrin gel populated with human adipose-derived mesenchymal stem cells (hASC). Tissue samples of the VF were collected and digested in collagenase at different time periods post-implantation to monitor cellular and genomic changes during the healing process. 10,000 cells were analyzed for sing-cell RNA sequencing. Tagged cDNA libraries were created for each cell and sequenced output data from the samples was analyzed using existing software packages, Kallisto and Scanpy. Tissue sample was also collected from Pig A before implantation as a control. Another pig's (Pig D) normal vocal fold was sampled for comparison.

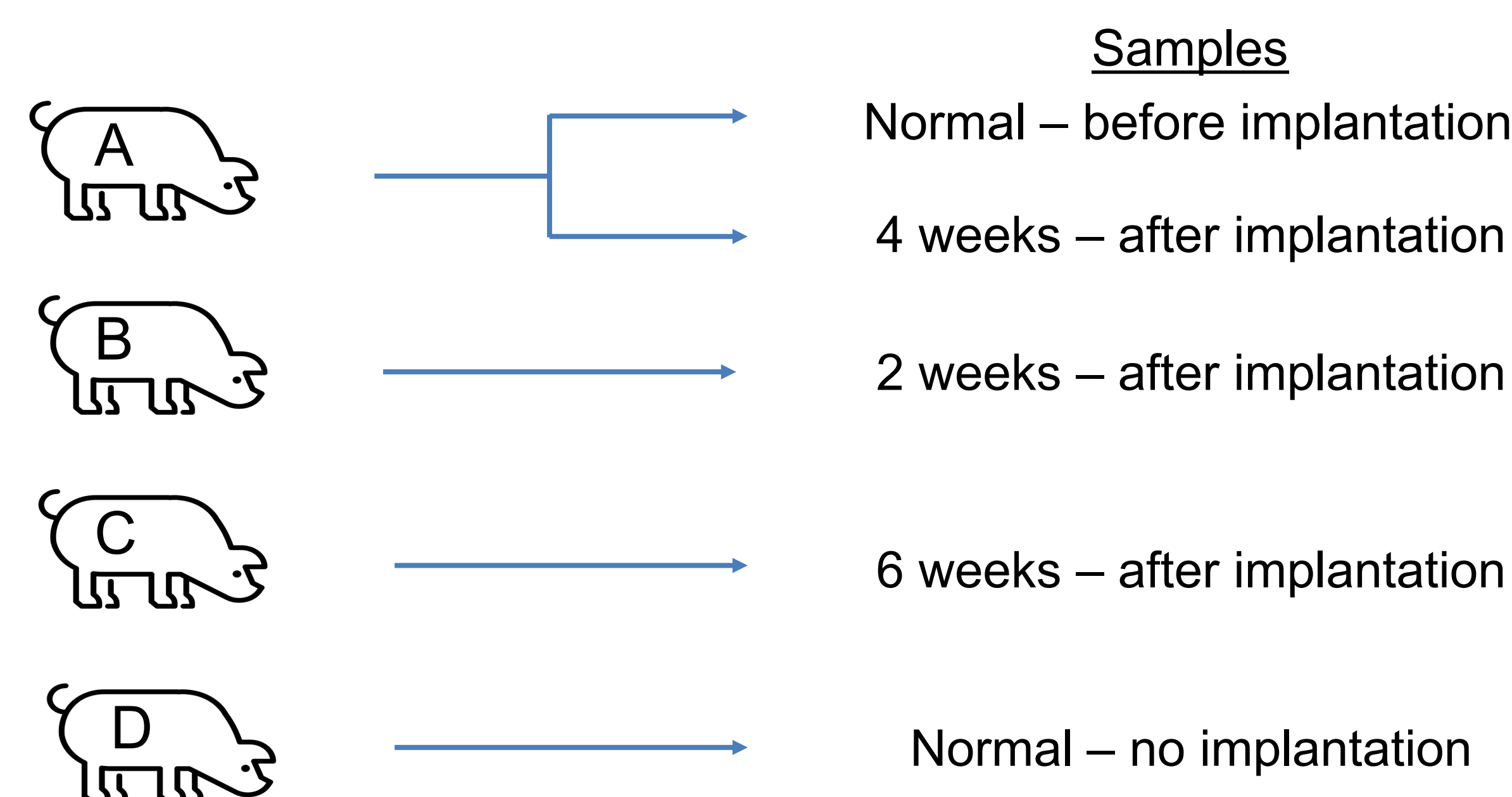


FIGURE 1. Study design

RESULTS

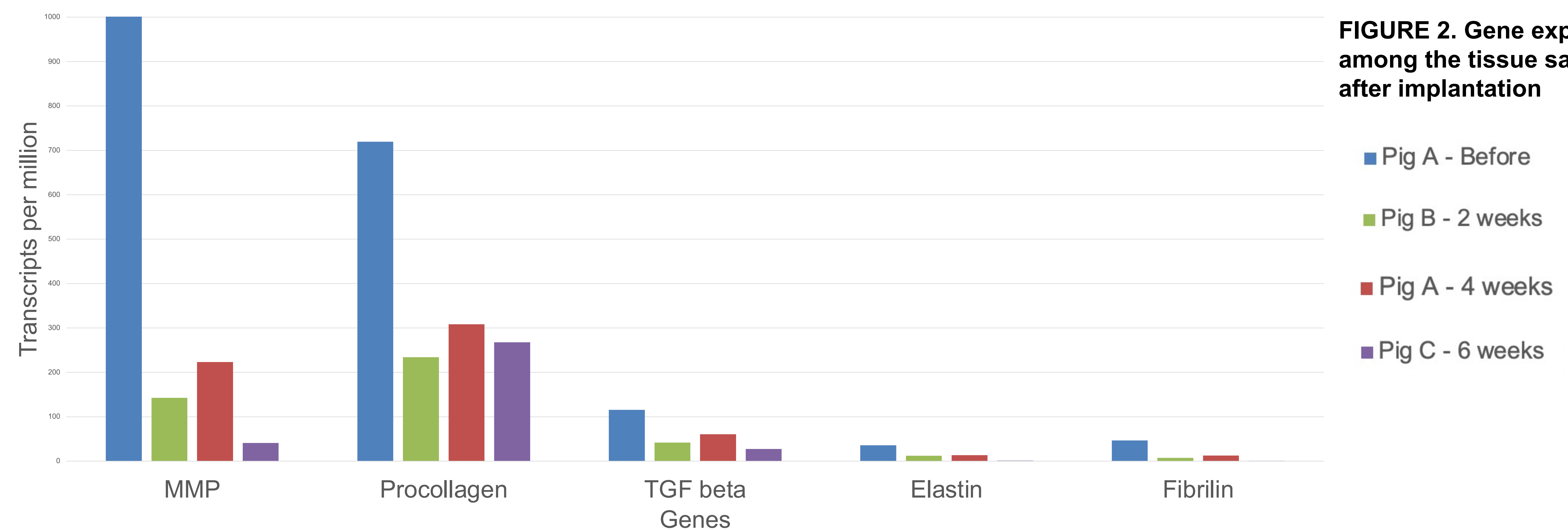


FIGURE 2. Gene expression compared among the tissue samples before and after implantation

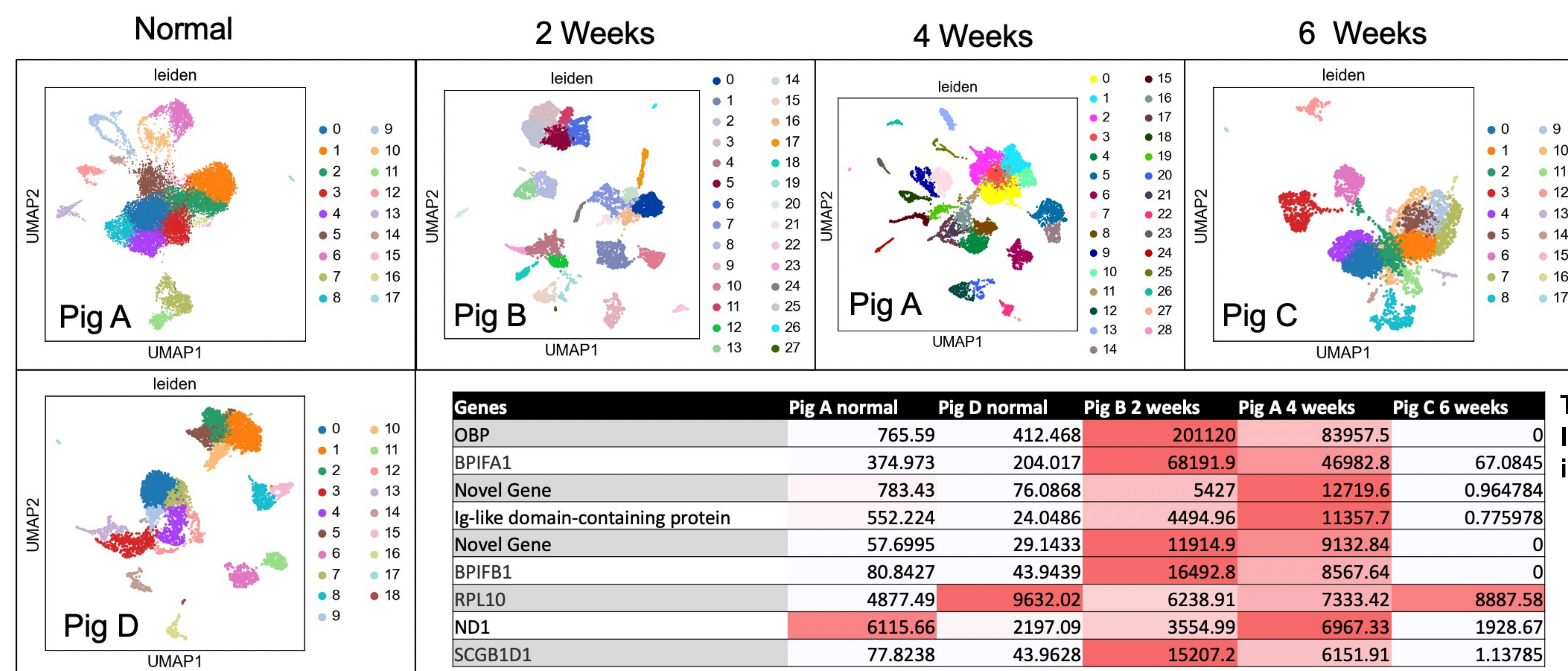


FIGURE 3: Groups by Gene Expression Clusters

TABLE 1: Inflammatory and Immune response post-implantation

Smallest to largest value

CONCLUSIONS

- MMP, procollagen, TGF-beta, elastin, and fibrillin percent composition in overall sample decreased because other genes involved in inflammatory response increased.
- Preliminary data suggests an increase in inflammatory and immune response during weeks 2 and 4 post implantation. Week 6 post-implantation the response decreases to normal conditions
- There is high homogeneity in human and pig genetic composition, therefore further work is necessary to understand if the implanted human cells apoptosed, persisted, or were rejected

ACKNOWLEDGEMENT

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