

## Poster Session 1 (cont.)

### P3

#### ESOPHAGEAL SCAFFOLDS SEEDED WITH EPITHELIAL CELLS FOR ESOPHAGEAL REPLACEMENT THERAPY

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**Purpose:** Esophageal atresia occurs in 1 in 3000 births. Typically, surgical repair includes re-connection of the esophagus or in cases where the esophagus cannot be reconnected, interposition of a piece of stomach or intestine. These surgical options have significant morbidity, therefore, a novel therapeutic option is needed.

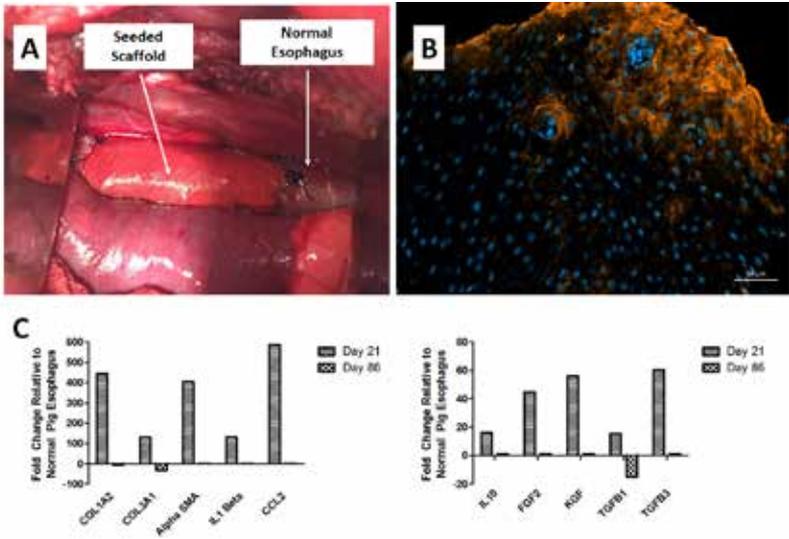
**Methods:** Porcine esophageal epithelial cells were obtained by dissociating esophageal biopsies of normal esophageal mucosa. Cells were allowed to expand for 7-10 days and then were seeded into the lumen of synthetic scaffolds (Biostage) and incubated for 7 days. A 5-8cm section of the thoracic region of the esophagus of a Yukatan pig was removed and replaced with this seeded scaffold. The scaffold was sutured into place and stented. Controls were unseeded scaffolds. Esophageal biopsies were sequentially obtained at different stages of healing and were analyzed via immunofluorescence and qRT-PCR.

**Results:** Initial esophageal biopsies stained positive for pan cytokeratin as well as proliferation marker KI-67. A wound healing qRT-PCR array was used to compare inflammatory and regenerative signals at Day 21 and Day 86. This data demonstrates an upregulation in pro-inflammatory genes IL1 $\beta$  and CCL2 at day 21, but expression that is similar to normal esophagus by day 86. Furthermore, there is a dramatic up-regulation of collagen I, collagen III and alpha smooth muscle actin at day 21, with gene expression being restored to normal by day 86. Growth factors TGFB1, KGF and FGF2 were also up-regulated at day 21, but were restored to near normal levels by day 86.

**Conclusion:** This approach to implanting esophageal scaffolds seeded with autologous epithelial cells demonstrates regeneration over a period of several weeks. The response seen at the tissue level indicates a phased wound healing response- first with inflammation then with regeneration. Continued exploration of the repair mechanisms using this strategy is underway.



## Poster Session 1 (cont.)



- A. Seeded Scaffold Implanted into the thoracic Region of the Normal Esophagus of a Yukatan Mini-Pig
- B. Day 21 biopsy located at the anastomosis stained for pan cytokeratin
- C. Gene Expression Analysis of tissue obtained at Day 21 vs day 86