Histologic characterization of syngeneic orthotopic tracheal transplant in a mouse model

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A mouse model of syngeneic orthotopic tracheal replacement is reliable and reproducible. This model can be used as a surrogate to study histologic changes in the host and graft in tissue engineered tracheal replacement.

Introduction
Failure of the current surgical methods and experimental models in treating life-threatening long segment airway defects has lead to the study of tissue engineered tracheal replacements. An ideal tissue-engineered tracheal replacement would be histologically similar to a syngeneic tracheal transplant. A functional mouse model of orthotopic tracheal replacement would help understand the longitudinal histologic changes at the host and graft.

Methods
Syngeneic orthotopic tracheal transplants were performed on a total of 21 female C57BL/6 mice with pre-determined end-points of 3 (n=5), 7 (n=5), 14 (n=6) and 30 (n=5) days. After euthanasia, the formalin-fixed tracheal samples were analyzed histologically with H&E and basal cells (K5+) were studied using immunofluorescent techniques.

Results
Out of the total 21 mice which underwent the syngeneic tracheal transplant surgery, 16 (76%) survived until their designated end-points whereas, 5 (24%) were euthanized due to signs of severe respiratory distress observed upon daily monitoring. Histological analysis with H&E of the animals that reached their end-points revealed no signs of stenosis, malacia and graft dislodgement; however, disruption of respiratory epithelium was evident at the anastomosis and mid-graft (Figure 2).

Immunofluorescent analysis of the basal cells (K5+) showed a general decrease in the number of K5-positive cells in the 30 day animals on comparison to 3 day animals (Figure 3).

Figure 1: Overview of syngeneic transplant technique

Figure 2: Representative images of H&E stained axial and coronal sections showing disruption of respiratory epithelium (▲). The thin arrow (→) represents the site of anastomosis.

Figure 3: Representative images of K5-positive 3 days and 30 days post-operative syngeneic transplants. (*) represent the inter-cartilaginous respiratory epithelium analyzed, (▲) represents artifact.

We are using this mouse model of tissue engineered tracheal replacement to evaluate various synthetic constructs for tracheal tissue engineering.