5) Both epithelial cells and mesenchymal stem cell–derived chondrocytes contribute to the survival of tissue-engineered airway transplants in pigs

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Abstract

OBJECTIVE:

We sought to determine the relative contributions of epithelial cells and mesenchymal stem cell-derived chondrocytes to the survival of tissue-engineered airway transplants in pigs.

METHODS:

Nonimmunogenic tracheal matrices were obtained by using a detergent-enzymatic method. Major histocompatibility complex-unmatched animals (weighing 65 +/- 4 kg) were divided into 4 groups (each n = 5), and 6 cm of their tracheas were orthotopically replaced with decellularized matrix only (group I), decellularized matrix with autologous mesenchymal stem cell-derived chondrocytes externally (group II), decellularized matrix with autologous epithelial cells internally (group III), or decellularized matrix with both cell types (group IV). Autologous cells were recovered, cultured, and expanded. Mesenchymal stem cells were differentiated into chondrocytes by using growth factors. Both cell types were seeded simultaneously with a dual-chamber bioreactor. Animals were not immunosuppressed during the entire study. Biopsy specimens and blood samples were taken from recipients continuously, and animals were observed for a maximum of 60 days.

RESULTS:

Matrices were completely covered with both cell types within 72 hours. Survival of the pigs was significantly affected by group ($P < .05$; group I, 11 +/- 2 days; group II, 29 +/- 4 days; group III, 34 +/- 4 days; and group IV, 60 +/- 1 days). Cause of death was a combination of airway obstruction and infection (group I), mainly infection (group II), or primarily stenosis (group III). However, pigs in group IV were alive, with no signs of airway collapse or ischemia and healthy epithelium. There were no clinical, immunologic, or histologic signs of rejection despite the lack of immunosuppression.

CONCLUSIONS:

We confirm the clinical potential of autologous cell- and tissue-engineered tracheal grafts, and suggest that the seeding of both epithelial and mesenchymal stem cell-derived chondrocytes is necessary for optimal graft survival.