Abstract

The tongue is a versatile and critical organ. It is instrumental in speech articulation, deglutition, and airway protection. Structural and therefore functional integrity of the tongue may be compromised in head and neck cancer treatment. Surgery, radiation therapy, and chemotherapy all contribute to denervation, fibrosis, and wasting of the lingual muscles. Specifically, weakness and fibrosis of the base of tongue may lead to a disabling dysphagia. Current treatments are highly limited and mainly supportive: tongue-strengthening exercises may slow decline but do not reverse structural changes, and non-oral feeding by gastrostomy tube is often required and life-changing.

Cell-based therapy for the base of tongue is a novel approach to treating the atrophy and fibrosis. In animals, a denervated sheep tongue study found that injected myoblasts from skeletal muscle improved tongue strength (Pisaman, 2014). Myoblasts were also administered in rat tongue hemiglossectomy surgical model paired with improved muscle regeneration and less scar contraction after 6 weeks (Lusamerschomp, 2006). While these studies are promising, a drawback of myoblast therapy is the difficulty in expanding these committed cells to an adequate therapeutic number. Multi-potent stem cells may be more accessible, and may offer greater benefit than myoblasts by acting in other pathways to reduce fibrosis and improve angiogenesis. Here we investigate the application of ischemia-tolerant human bone marrow-derived mesenchymal stem cells (MSCs) and adipose-derived mesenchymal stem cells (ASCs) in a multipotent and myocyte differentiated form (dix) in a novel rodent tongue fibrosis model.

Results

In Vivo

2. IVIS Lumina imaging poses great promise for guiding / dosing therapy
3. Trend toward lesser scar volume with MSC+D treatment arm

Discussion

In this study we develop a reproducible rat model for tongue fibrosis that appears feasible for long-term studies. The rats tolerated partial glossectomy with continued PO intake and weight gain throughout the study in the absence of any signs of distress. Although multipotent stem cells may have broad and life changing therapeutic applications, there is some reserve given their oncopgenic potential, especially if applied to cancer survivors. This model could serve to evaluate therapeutic efficacy of novel therapeutics as well as short and long-term complications. Although a statistically significant difference was not appreciated for our therapeutic arm, this study demonstrates a feasibility of application poised for future studies.

Conclusions

In vivo optical fluorescence detection of administered stem cells using IVIS Lumina II fluorescence and optical imaging hardware. We transfected stem cells with pπRFP, a reporter near-infrared fluorescence protein. Administered these transfected cells to the scarred rodent tongues and used the IVIS Lumina II to detect opalescence as measured by the total radiant efficiency (100% / area [cm²] / 4π) and 44 days after cell injection. (Left) Experimental setup. Rat is under labia anesthesia, while camera is used to withdraw tongue (Middle). (Right) Here we are able to detect a difference in total radiance efficiency that achieves significance at 44 days post injection (P = 0.01). Perhaps this could be the duration it takes for beneficial stem cells to integrate, mature, and begin producing their constituent proteins. (day n = n = 2; b = 1; c = 4; n = 7, 6)

References