The Potential of Tissue Engineering in Maxillofacial Reconstruction Following Oral Cancer Treatment

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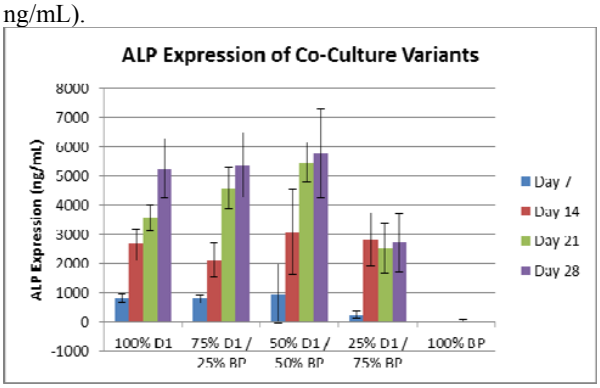
Statement of Purpose: The purpose of this study was to evaluate the use of tissue engineering techniques in patients undergoing maxillofacial reconstruction following oral cancer therapies and to evaluate the potential for the selective incorporation of progenitor cells in tissue engineered implants. Each year approximately 275,000 patients worldwide are diagnosed with oral or pharyngeal cancer, and often require a maxillectomy[1]. Commonly, bone marrow-derived mesenchymal stem cells are used in the reconstruction process, but there are alternatives. The literature indicates that stem cell source plays a significant role in the development of the desired tissue. Periosteal-derived progenitor cells (PDPCs) have demonstrated enhanced bone formation when compared to alveolar and bone marrow-derived mesenchymal stem cells[2]. The goal of this work was to assess the effect of incorporating differing ratios of two progenitor cell types on a ceramic bone graft material.

Methods: Primary periosteal-derived progenitor cells (PDPCs) were isolated from the maxilla of a Holstein cow obtained from Snow Creek Slaughterhouse (Seneca, SC) and expanded *in vitro*. D1 murine mesenchymal stem-like cells (ATCC) and PDPCs were grown in Dulbecco's Modified Eagle Medium supplemented with 10% fetal bovine serum, 1% antibiotic/antimycotic, and 0.2% fungizone. Co-cultures of D1 cells and PDPCs were grown on ChronOS granules (β-tricalcium phosphate) in osteogenic medium with 50μg/mL of L-ascorbic acid 2-phosphate, 3mM β-glycerophosphate, and 20nM dexamethasone (DEX) to evaluate osteogenic potential. The following co-culture ratios were evaluated: 100:0 (D1: PDPCs), 75:25, 50:50, 25:75, and 0:100. Live/Dead staining was performed weekly and images collected. Samples of medium were collected for lactic acid/glucose analysis during every medium change every two or three days. Cells were lysed and stored in -20°C in TE buffer until alkaline phosphatase (ALP) and deoxyribonucleic acid (DNA) concentrations were analyzed. Statistical analysis was performed by creating a model to investigate the covariance from cell concentration and time. Additionally, groups were compared using a pairwise t-test.

Results: The results from this study suggest that all treatment groups maintained high levels of cell viability. Metabolic activity analysis demonstrated that cell ratios of 100:0, 75:25, 50:50 produced elevated levels of lactic acid (>3000 mg/L) by Day 7 with simultaneous decrease in glucose concentration in conditioned medium samples; whereas, levels associated with the 25:75 samples did not reach a peak value of lactic acid until Day 14. The 0:100 test ratio groups resulted in much lower metabolic activities than that of the other groups. Throughout the duration of the study, groups with ratios of 100:0, 75:25, and 50:50 resulted in increased ALP production to maximum activities of 5253±1014, 5374±1101, 5768±1523 ng of ALP/mL, respectively. ALP expression in the 25:75 ratio groups plateaued during Days 14-28 (2720±996 ng/mL). The groups with ratio of 0:100 reached a maximum ALP value on Day 21 (58±33 ng/mL).



Conclusions: Currently, surgical reconstruction techniques or prosthetic rehabilitation techniques need refinement. Future methodologies must restore the ability to masticate, speak, and swallow while minimizing donor site morbidity. Restoration of bodily functions of speaking, swallowing, and chewing is critical for the physical and psychological outcome of the patient. Maxillofacial tissue engineering requires unique insights to maximize clinical results. Traditional cancer treatments can include radiation therapy; thus, defect sites may be hypovascularized and exposed to a variety of environmental conditions. In this preliminary work, metabolic activity varied with cell ratio and therefore can be purposefully modulated. For reconstruction in a hypovascular environment, careful tuning of cell metabolism can be highly desired for long term survival. Co-culture ratios of PDPCs and D1 cells demonstrated significant increases in ALP expression, while remaining viable throughout. Overall, the ratio of 25:75 demonstrated significant ALP expression, while minimizing early metabolic activity, suggesting a ratio more appropriate for a hypovascular environment. Further research is needed to customize maxillofacial tissue engineering options.

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