Compartmentalized Bioreactor for Long-Term Culture of Bone-Cells

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INTRODUCTION: Reducing the profound gap between the physiological environment of the bone cells and in vitro cell culture models is critical for realizing the promise of tissue-engineering strategies to replace, regenerate and restore function to bone lost as a result of disease or injury.

MATERIALS AND METHODS: The transformation of isolated osteoblast inoculum to mineralized, collagenous tissue that simulates native osteoid was followed using optical microscopy and scanning and transmission electron microscopy. Mineralization was assessed using Von Kossa assay and SEM-EDS (Energy Dispersive Spectroscopy.

RESULTS AND DISCUSSION: An advanced bioreactor that mitigates culture shock or the behavioral variations associated with the transition of bone cells from the in vivo to the in vitro environment was developed and tested. The bioreactor based on the principle of simultaneous-cell-growth-and-dialysis, separates a cell growth chamber from a media reservoir by a dialysis membrane, compartmentalizing cell growth and cell nutrition functions. As a consequence of compartmentalization, the pericellular environment is unperturbed by continuous perfusion or punctuated re-feeding schedules and luxury macromolecules synthesized by cells are retained in a manner that more closely simulates the in vivo condition. The stable culture conditions afforded by the bioreactor sustained model cell lines, mouse calvaria-derived MC3T3-E1 (ATCC CRL-2593) and human fetal osteoblasts (hFOB 1.19, ATCC CRL-11372) for extended time periods (30-120 days) without the need for sub-culture.

CONCLUSIONS: Development of differentiated, collagenous bone tissue (biosynthetic osteoid) from disaggregated osteogenic cells over 120 day culture was demonstrated on both 2-D polymer substrates as well as 3-D hydroxyapatite scaffolds. The compartmentalized bioreactor substantially mitigates culture shock and shows promise as an ideal in vitro tool for evaluation of orthopedic biomaterials and development of engineered bone tissue. The bioreactor design is shown to create an extraordinarily-stable pericellular environment that better simulates the in vivo condition than can be obtained using conventional tissue-culture technology.

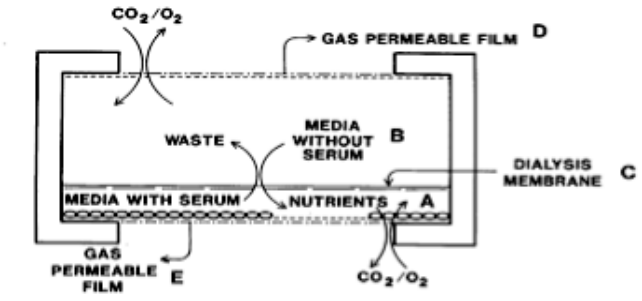

Figure: Design of the Compartmentalized Bioreactor