306d Engineering Functional Myocardium

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Functional engineered cardiac tissue can serve as a model for in vitro pharmacological study and for regenerative medicine concerning congenital and postischemical diseases. We have previously demonstrated that electrical stimulation of myocardiocyte constructs results in tissue with properties similar to that found in vivo (Radisic et al. 2004). However, the conditions of electrical stimulation still need to be optimized (frequency, field gradient, initiation, and duration of stimulation). Furthermore, to engineer fully developed three-dimensional cardiac tissue, medium perfusion is required to satisfy high oxygen demand of the cells.

In this work, we have developed a novel bioreactor to simultaneously electrically stimulate and perfuse cardiomyocytes in a three dimensional scaffold. The bioreactor consists primarily of two perforated parallel sheets of clear, yet conductive, indium tin oxide (ITO) film, separated by a 1 to 3 mm thick silicone membrane. Electrodes are arranged in parallel rows along the x-axis of the bioreactor on the lower surface and in perpendicular columns on the upper surface. Cardiomyocytes are seeded on a collagen scaffold between the electrode array. Electrical current is applied to a single row and only allowed to exit along a single column, thus localizing stimulation to a single node. Repeating this procedure allows us to independently stimulate up to 200 samples in a single bioreactor. Given this capability, experiments were conducted according to a 3-level / 5-component factorial design in order to elucidate complex interactions among the parameters. Expression and presence of cardiac markers were determined by RT-PCR, Western blots and immunochemistry, while ultrastructure was evaluated by morphometric analysis of TEM images.

Radisic M, Park H, Shing H, Consi T, Schoen FJ, Langer R, Freed LE, Vunjak-Novakovic G. 2004. Functional assembly of engineered myocardium by electrical stimulation of cardiac myocytes cultured on scaffolds. Proceedings of the National Academy of Sciences of the United States of America 101(52):18129-18134.