

CYTOMORPHOLOGICAL EVALUATION OF PANCREATIC CELLS IN RESPONSE TO GLUCOSE CHALLENGE

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ABSTRACT

PANC-1 is a human pleiomorphic epithelioid carcinoma of the exocrine pancreas. Previous studies in our laboratory provided evidence that these cells can be manipulated into insulin-producing cells by altering the culture medium with increasing amounts of glucose. There is a paucity in the literature regarding cytomorphologic characteristics of PANC-1 cells under normal culture conditions and when challenged with increased amounts of glucose. The goal of this experiment was to evaluate the nuclear and cytoplasmic characteristics of PANC-1 cells. Initially, cells were grown in flasks with a control medium and then split into four separate groups containing control media or media containing an extra 1%, 2.5%, or 5% glucose. Cells from the three cultures were plated (1 x 10^5 cells/well) and treated with control, 1%, 2.5%, or 5% glucose for 24, 48, and 72 hours. Cells and supernatants were harvested, and cell number and cytomorphology were compared at all phases. Nominal data were analyzed using non-parametric statistics calculating mean ranks to compare all four groups using the Kruskal-Wallace H statistic. While we saw statistically significant differences in most variables by glucose concentration at 24-, 48-, and 72-hours, the most telling was the increased glucose concentration detected by immunohistochemistry at all three phases rising from baseline, peaking at 2.5% glucose concentration, and rapidly declining to baseline levels indicating an inhibiting or toxic effect at 5% extra glucose ($p<.0.05$). This pattern was also consistent in the cytomorphologic changes observed as glucose concentrations increased and were more apparent by the 72-hour phase. This study contributes valuable quantitative data regarding the viability and function of PANC-1 cells as insulin-producing cells with increasing glucose challenge and demonstrates that PANC-1 or similar cells can be further engineered into useful components in drug delivery applications.

Keywords: morphological evaluation, PANC-1, artificial pancreas, tissue bioengineering

INTRODUCTION

Previous studies in our laboratory have demonstrated the effectiveness of several bioceramic-based drug delivery systems integrating various therapeutic agents for controlled and sustained release both *in vitro* and *in vivo* [1,2,3,4]. Further development of these systems for use in human and veterinary applications could have significant implications in treating many chronic conditions by reducing costs, increasing the bioavailability of the therapeutic agents, and restoring lost organ function. One such application is the treatment of diabetes by delivering human insulin at a controlled and sustained rate in response to fluctuating blood glucose levels. While current treatment methods like the use of home glucose testing and insulin pumps have improved patient outcomes over the past 20 years, these are still not ideal and require a great deal of monitoring [6]. Ultimately, our work aims to develop and test drug delivery systems that can contain living cells in a protected environment that can function as physiological demands necessitate.

Prior studies have explored the use of immortalized human cell lines enclosed in a bioceramic reservoir that could allow increased or decreased insulin production as blood glucose levels changed [5]. This type of biocompatible device could be further developed as an artificial organ with living,