

SUNITHA PULIKKOT

Department of Anatomy
College of Medicine and Health Sciences



Dissertation

Title	<i>ESTABLISHMENT OF A 3D CULTURE MODEL OF GASTRIC STEM CELLS SUPPORTING THEIR DIFFERENTIATION INTO MUCOUS CELLS USING MICROFIBROUS POLYCAPROLACTONE SCAFFOLD</i>
Faculty Advisor	Prof Sherif Karam (CMHS), Dr Yaser Greish (COS), Prof Abdel-Hamid Mourad (COE)
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Abstract	

In the stomach, epithelial stem cells are responsible for glandular homeostasis and perpetual production of four main cell lineages secreting mucus, acid, pepsinogen and hormones. These stem cells could represent a source for cell therapy or tissue engineering in cases of gastric mucosal damage. The aims of this study were 1) to manufacture various forms of scaffolds using polycaprolactone, 2) to test the suitability of these scaffolds for growth of mouse gastric stem (mGS) cells, and 3) to evaluate whether this culture system could tolerate exposure to acidic environment for possible future applications. Three forms of polycaprolactone scaffold were fabricated: nonporous, microporous and microfibrillar. Microscopic examination and mechanical testing revealed some similarities between the microfibrillar scaffold and extracellular matrix of the stomach wall. Examination of mGS cells cultured on different forms of scaffold revealed their preferential growth on microfibrillar scaffolds with an initial increase in cell number followed by their differentiation into gland mucous cells after 9 days. Various mechanical, chemical, morphological and molecular examinations revealed that this 3D culture system could partially tolerate a moderate acidic environment. Interestingly, only after 3-day culture at pH 5.5, mGS cells differentiated into mucous cells as demonstrated by binding of N-acetyl-D-glucosamine-specific Griffonia simplicifolia II lectin and significant up-regulation of Spdef mRNA expression. In conclusion, a 3D culture model of mGS cells supporting their differentiation into mucous cells has been established. This study provides the basis for future use of stem cells in gastric tissue engineering for regenerative therapy of some stomach diseases involving mucosal damage.

Keywords: stem cell, gastric mucosa, cell differentiation, tissue engineering

Research Relevance and Potential Impact

Since stomach inflammation leading to ulcers and tumors are common health problems which require new therapeutic modalities, this study will provide the basis for future use of stem cells and microfibrillar scaffolds in tissue engineering for regenerative therapy for some stomach diseases.

Relevant Publications

- Pulikkot P, Greish YE, Mourad AH, Karam SM (2014) Establishment of a three-dimensional culture system of gastric stem cells supporting mucous cell differentiation using microfibrillar polycaprolactone scaffolds. *Cell Proliferation*, 47:553-63.
- Pulikkot S, Greish YE, Mourad A-HI, Thomas SA, and Karam SM (2014) Evaluation of 3D culture model of gastric stem cells for tissue engineering. *Proceedings of the 8th Dubai International Conference for Medical Sciences*, Dubai, UAE.
- Pulikkot S, Saseedharan P, Greish YE, Mourad A, Karam SM (2014) Growth and Differentiation of Gastric Stem Cells on Biodegradable Scaffolds. *Proceedings of the 3rd Biotechnology World Congress*, Dubai, UAE.
- Pulikkot S, Greish YE, Karam SM (2012) Fabrication of nanofibrillar scaffold for gastric epithelial tissue engineering. *Proceedings of the International Workshop on Advanced Material*, Ras El-Khaimah, UAE.

Career Aspirations

This research inspires Sunitha to continue her career as a post-doctoral fellow and then to become an independent stem cell scientist and an academician.