PROJECT TITLE: Fibrosis and Scar Contractures

Latha Satish PhD
Assistant Professor, Educator- Affiliate
Department of Pathology and Laboratory
Medicine, UC College of Medicine
Associate Investigator, Research
Department
Shriners Hospitals for Children–Cincinnati
3229 Burnet Avenue, Cincinnati, OH 45229
lsatish@shrinenet.org; satishla@ucmail.uc.edu
Phone: 513-872-6228
Fax: 513-872-6072

Project Description

1. Characterization of burn eschar derived pericytes
Pericytes are stromal cells, responsible for the maintenance and integrity of capillaries and venules throughout the body. Following an injury to skin, pericytes have the ability to dissociate from these vessels and act as primary contributors to wound healing. In skin, pericytes mediate wound healing by either contributing to fibrosis by becoming myofibroblasts or contributing to angiogenesis by promoting proper growth factors for healing. Our lab studies dermal derived pericytes from burn eschar tissues and from healthy skin. We are interested in the role that pericytes play in scar formation, contraction of wounds, and their abilities to transform to other cell types. It is known that pericytes may share similar functions to another skin cell population called fibroblasts, and we aim to differentiate these two cell populations by determining differences in their genetic profile and their protein expression. Once this is accomplished, differential gene expression will be compared between burn eschar pericytes, healthy skin pericytes, and fibroblasts to determine the impact of burn on pericytes. In doing so, pericytes could be identified as the population of cells that contribute the most to fibrosis following burn injury, and would therefore be a good target to improve wound healing after burn. The WISE student would be assigned various parts of this project and would learn techniques such as western blot, ELISA, RT-PCR, primary human cell culture, immunocytochemistry, and immunohistochemistry. Students would be provided all necessary training and mentoring to support a future as a research scientist.
2. Investigating the pro-healing and anti-microbial effects of probiotics in burn wounds

Following a burn injury, the wound environment can easily become infected with a number of pathogenic bacteria. In burn wounds, the most prominent pathogenic bacterium is Pseudomonas aeruginosa. This gram-negative organism negatively impacts wound healing and creates health complications for a patient. With the rise of antibiotic resistant organisms, there is a need for a means to eliminate pathogenic bacteria without compounding the issues that antibiotic resistance raises. A probiotic strain of bacteria named Lactobacillus plantarum (Lp) is a potential solution to these issues. This probiotic has been shown to eliminate pathogenic bacteria in vitro and in vivo while also promoting proper wound healing. We are interested in understanding the mechanistic signaling pathways by which Lp mediates proper wound healing and the immunological pathways by which its anti-microbial activity is achieved in in vitro and in a mouse burn wound model. The WISE student will be assigned various parts of this project including carrying out the burn wound model on mice, bacterial culture, collection of tissues for: western blotting, ELISA, RT-PCR, immunohistochemistry, and to assist in data analysis. Students would be provided an opportunity to handle animals (if interested) with the necessary training to conduct research for this project, and mentoring to support a future as a research scientist.

3. Anti-fibrotic action of pirfenidone in keloid keratinocytes and hypertrophic scar fibroblasts

Keloid and hypertrophic scarring are both abnormal scarring responses to injury. In both conditions, cells of the skin hyper-proliferate which results in a raised scar. For some these scars can become very large and are a hindrance to everyday life. The drug pirfenidone has been shown to reduce fibrosis and scarring in diseases such as Dupuytren’s disease, a fibrotic condition seen in the palmar fascia of the hand. But the effectiveness of pirfenidone in reducing fibrosis in keloid and hypertrophic scar formation is not yet determined. We recognize a need to understand how pirfenidone alters the genetic expression of these scars in keratinocytes and fibroblasts. We aim to show that pirfenidone prevents this hyper-proliferation and fibrosis seen in these scarring diseases and that pirfenidone could be applied topically to either to reduce fibrosis or prevent the scar from forming entirely. The WISE student would be assigned various parts of this project including human cell culture of keratinocytes and fibroblasts, cellular assays, western blotting, RT-PCR, ELISA, and immunohistochemistry. Students would be provided with training to handle human-derived cell populations, and in developing a novel dermal cream with the required mentoring to successfully complete the assigned projects and consider a future as a scientist.