McGowan Institute for Regenerative Medicine
A program of the University of Pittsburgh and UPMC

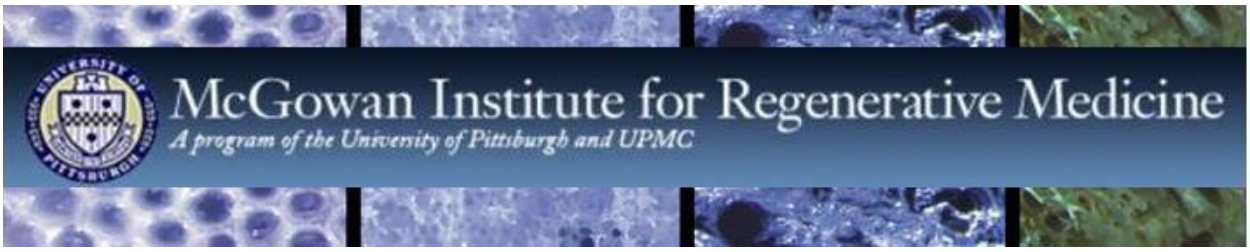
Donor Supports Research Addressing Dupuytren's Disease

The McGowan Institute for Regenerative Medicine recently received a $100,000 gift in support of the vital work being done by affiliated faculty member Latha Satish, MSc, MPhil, PhD. As a Research Assistant Professor in the Department of Plastic Surgery at the University of Pittsburgh, Dr. Satish's research is focused primarily on gaining a better understanding of the pathology and progression of Dupuytren's disease (DD). Dupuytren's disease is a complex, progressive, fibroproliferative disorder of the palmar fascia (a thin sheet of connective tissue in the palm of the hand) that results in the shortening, thickening, and fibrosis of the fascia and aponeurosis of the palm. Dr. Satish's research is focused both at the cellular and molecular level and aims to identify new therapeutic strategies to effectively prevent the progression and recurrence of this disease.

Currently there is no treatment available that can successfully cure or to prevent the recurrence of DD. The development of better therapies has been slowed in part by the lack of an animal model in which candidate therapies may be initially assessed. Unique to humans, DD does not have a counterpart in the animal kingdom, making things much more difficult. Prior to the recent philanthropic gift, Dr. Satish's team attempted a 9-week study to create an animal model of DD by using athymic "nude" rats to investigate the characteristics of human fibroblasts transplanted into an immunodeficient animal host. The goal was to see if these fibroblasts could maintain their distinct disease phenotype compared to control cells harvested from the fascia of individuals undergoing carpal tunnel (CT) release. Through this, DD-derived fibroblasts showed greater persistence over time than control CT-derived fibroblasts and retained a distinct pro-fibrotic physiology.

However, while there was molecular and histological evidence of building fibrosis with DD cells, there was no development of a frank tissue contracture similar to the clinical presentation in humans. This is potentially due to the fact that the model did not completely mimic the human pathophysiology or because more time was required for that degree of fibrosis and contracture to become established. Since Dupuytren's is a disease with a slow and progressive onset, it often takes years to become clinically significant.

Thanks to a generous donor, Dr. Satish can now begin a new, more extensive study. This time, animals injected with the DD cells will be allowed to persist in situ for even longer periods of time. Because even DD cells do show some element of decline over time, Dr. Satish will perform repeated doses of DD cells to achieve frank tissue contracture. Simultaneously, the previous model that showed increased evidence of fibrosis with DD cells in comparison to CT cells will be used to test novel therapeutic test agents. Any agent found to diminish the DD-dependent



fibrotic characteristics (eg, reduction in the levels of ECM proteins, namely collagen; ability to reduce contraction, etc.) will be a potential candidate for clinical translation. To accomplish these goals Dr. Satish collaborates with clinicians Sandeep Kathju, MD, PhD, Department of Plastic Surgery and McGowan Institute affiliated faculty member, and Mark E. Baratz, MD, Department of Orthopedic Surgery, University of Pittsburgh.

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