Establishing an Animal Model of Dupuytren's Contracture by Profiling Genes Associated with Fibrosis

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INTRODUCTION:

Dupuytren's contracture (DC) is characterized by the progressive development of a scar-like collagen-rich cord within the palmar fascia of the hand that results in permanent finger contracture. Currently, DC is incurable and is most commonly treated by surgical resection of the diseased tissue. To date no successful animal model has been described in which, to evaluate potential non-surgical treatments for Dupuytren's contracture.

HYPOTHESIS:

In the present study, we hypothesize that establishing an animal model will ultimately serve as platform to compare variety of treatments for DC.

METHODS:

Fibroblasts derived from carpal tunnel release (CTR) and DC patients were reconstituted in 0.1% low melting point agarose in Hank's Balanced Salt Solution and tagged with Lipophilic Tracer DiR cell-labeling solution; these cells were injected into the forepaw of nude rats. The injected cells were frequently tracked in the forepaw by placing the animal into a Xenogen Ivis Spectrum imaging system for 4 - 8 weeks. At the end of 4 - 8 weeks palmar fascia tissues were harvested from both control (CT –derived fibroblasts) and experimental (DC-derived fibroblasts) animals to perform quantitative real time RT-PCR (qRT-PCR) for candidate genes of interest.

RESULTS:

Our initial studies showed that fibroblast-derived from palmar fascia of carpal tunnel (CT) and DC patients persisted successfully in the forepaws of nude rats. Initial studies with qRT-PCR using RNA derived from four week tissues showed that mRNA levels of alpha-smooth muscle actin and type I collagen were significantly elevated in the forepaws of rats injected with DC-derived fibroblasts but not in the forepaws of rats that received CT-derived fibroblasts. The increase in α-SMA suggests fibroblast to myofibroblast transformation that ultimately may result in scar formation and contracture.

SUMMARY:

Since DC in humans is a slow progressive disease often times requiring years to progress, in order to obtain a successful animal model which recapitulates the actual contractures typical of DC it may be necessary to inject DC-derived fibroblasts into the forepaws of nude rats periodically over months. Future studies will include injecting DC-derived fibroblasts into the forepaws of the rats once every fifteen days for a period of six months to determine if this would result in to the gross phenotypic changes observed in DC. Tissues harvested from these animals at set intervals will be utilized to perform

histology, immunohistochemistry, western blot and qRT-PCR analyses to determine the changes in ECM composition and on specific genes of interest associated with fibrosis in treated vs. control animals.