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Title: Primary Dupuytren's Disease cell interactions with the extra-cellular environment: a link to disease progression?

Hypothesis:
Dupuytren's Disease cells modify their extra-cellular environment to promote a disease-like phenotype in adjacent fibroblasts, promoting disease progression

Methods:
Primary cells derived from Dupuytren's Disease (DD) cord tissue or phenotypically normal palmar fascia from DD patients (PF) are being assessed in novel collagen-based culture systems to assess the ability of DD cells to condition their extra-cellular matrix (ECM). In our sequential collagen culture system, we use transwells to determine whether DD cells, grown on a 0.4μM pore size membrane embedded in a type-I collagen matrix attached to the insert well, can secrete factors that affect the protein expression of PF cells subsequently cultured on conditioned collagen. In our co-culture system, DD cells are seeded onto type I collagen-coated transwell inserts with 0.4μM pores to avoid escape of cells but allowing diffusion of growth factors and other molecules. The insert well is also coated in type I collagen and seeded with PF cells. The co-cultures are maintained for 7 days during which both cell populations can be either left untreated or subjected to exogenous addition of growth factors and cytokines. After 7 days the compartments are separated and the gene expression of the cell cultures assessed by Real Time PCR. T tests and ANOVA analyses are performed using SPSS.

Results:
Preliminary data from our sequential collagen culture indicate that collagen conditioned by DD cells induces β-catenin accumulation in patient-matched PF cells. Collagen conditioned by PF cells does not result in detectable accumulation of cytoplasmic β-catenin. Co-cultures are currently underway to determine if DD cells can induce changes in the expression of *TGFB1* (encoding TGFβ-1), *TGFB2* (encoding TGFβ-2) and *POSTN* (encoding periostin) in PF cells.

Conclusions:
We have previously demonstrated that TGFβ-1-induced β-catenin accumulation in DD cells is modified by Type-I collagen substrate interactions. Our recent data indicate that DD cells can also condition their collagen substrate with factor(s), yet to be identified, that induce PF cells to increase their cytoplasmic β-catenin levels. Increased β-catenin accumulation in PF cells may be indicative of a proliferative response. DD and PF co-culture results are pending. These novel collagen-based culture systems are designed to detect DD cell interactions with the ECM and adjacent PF cells and may allow us to identify that may promote disease progression.