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Inferring the metabolic and transcriptional networks specific to Dupuytren's disease tumours with omics

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Dupuytren's disease (DD) is a fibroproliferative tumour of unknown aetiopathogenesis manifested on the human hand. Studies of genetic abnormalities and environmental factors have provided evidence for a multifactorial nature of DD. The disease progresses with the growth of abnormal fibroblasts and localised ischemia/hypoxia. We speculate that microvessel narrowing preceding localized hypoxia may be one cause of DD, where fibroblast proliferation ensues during perivascular connective tissue damage. Studies of the metabolome and transcriptome of DD-derived fibroblasts (with corresponding control samples) have been performed at normoxic and hypoxic conditions to investigate this hypothesis. The culturing and sampling procedures, including the passage number, were determined that led to reproducible and robust results. The study employed Fourier transform infrared spectroscopy to compare early (primary) cultures to late (n=6) passages. Subsequently, gas chromatography-mass spectrometry combined with microarrays were employed to determine metabolic and transcript profiles of fibroblasts cultured in normoxic and hypoxic conditions from four different DD tissue phenotypes. Carefully controlled culture conditions combined with Principal Component Analysis (PCA) and Discriminant Function Analysis demonstrated early passage (0-4) metabolic differences where a synchronous separation pattern was observed in the PCA scores plots in DD and control fibroblasts. However, subsequent passages (5-6) demonstrated asynchrony, losing distinction between diseased and non-diseased sample phenotypes. Further studies demonstrated metabolic and transcriptional differences between fibroblast cell samples (passage number 4) cultured in normoxic and hypoxic conditions. The metabolic and transcriptional changes related to DD progression are being integrated in a systems-level approach. For the first time, early passage numbers are shown to provide representative metabolic and transcript fingerprinting for investigating DD. We have performed parallel analyses of transcript and metabolic profiles of DD fibroblasts and correlated parameters across the various levels of systemic description. This will now enable us to examine the extent to which systems biology helps investigate pathological mechanisms in tissue fibrosis.

Biography

Samrina Rehman completed her Ph.D in Medical Systems Biology from The University of Manchester (2011). She has since engaged and also initiated a number of challenging collaborative projects to investigate complex human diseases i.e. multifactorial disease requiring systems approaches. Current research interests involve investigation of liver disease including steatosis and steatohepatitis, stem cell differentiation, Dupuytren's disease, scalp disease, chronic myeloid leukemia and also urothelial cancers. Her efforts in bringing together systems biology with medicine to understand complex disease have so far resulted in more than 8 publications in reputable international peer-reviewed journals. Samrina is also serving as an editorial board member for Frontiers in Systems Biology.

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