Reviewer's report

Title: Fibroblasts from phenotypically normal palmar fascia exhibit molecular profiles highly similar to fibroblasts from active disease in Dupuytren's Contracture

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Reviewer: Sandra Kraljevic Pavelic

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The authors present results obtained upon transcriptomic profiling of fibroblasts derived from Dupuytren’s contracture (DC). For that purpose, commercial whole-genome microarrays from Illumina were employed for analysis of gene expression in primary cells derived from affected palmar fascia, adjacent phenotypically normal palmar fascia from same patients, and palmar fascia tissues form patients with tunnel carpal syndrome.

Experimental procedures used by the authors represent standard methods and analyses tools including:
- Primary cell culturing
- Total RNA extraction for microarray analysis
- Microarray assays
- Microarray expression analyses
- Pathway analyses

Conclusions brought by authors may be summarized as following findings:
1. Transcriptomic profiles of DC-disease fibroblasts and fibroblasts from unaffected fascia of DC patients exhibited a much greater overlap than fibroblasts derived from the palmar fascia of patients undergoing carpal tunnel release,
2. Use of collagen-coated culture plates induces changes in gene expression of DC-derived cells at a higher rate in comparison to cells derived from the palmar fascia of patients undergoing carpal tunnel release,
3. Transcriptomic profiles obtained for each DC-derived cell group (each comprising 6 samples) were highly consistent.

Major concerns:

Obtained results are presented reasonably and are of interest to researchers or clinicians with closely related research interests. Even though the methods employed are up to date and represent standard methodology, it should be stated that neither one validation nor functional analysis has been carried out upon microarray results analyses. The authors should note that statements on clinical relevance or functional implications should be validated with at least one
of widely accepted methods (e.g. quantitative reverse transcription-PCR for chosen genes, in vitro models, analysis of targeted miRNAs etc. - please refer to just few randomly chosen articles dealing with microarray studies as a guideline: PLoS One 6 (2011) Tsuge et al. ; Am J Transplant. (2011) doi: 10.1111 Scian et al.; Genomics 97 (2011) De Felice et al.). Indeed, the authors have not succeeded to propose some novel mechanistic interpretation for Duyputren’s contracture pathogenesis due to lack of validation data. They presented a variety of possible cellular processes represented by cluster of expressed genes in Tables 1 and 2 that might be of certain interest. Again, validation data would certainly help in filtering only those processes that are really relevant to disease development or predisposition. For the reader is rather difficult to comprehensively read and interpret the data presented in Tables 1 and 2 as too many possible pathways of common knowledge (more than 30) related even to other specific disorders (e.g. ovarian cancer signaling, acute myeloid leukemia signaling, amyotrophic lateral sclerosis signaling etc.) have been presented.

In conclusion, authors are encouraged to perform validation/functional studies and to compare obtained results not only with their own results but to critically discuss recent papers related to the topic (e.g. data speaking in favor of intrinsically similar characteristic of DC-derived cells from affected and unaffected tissues and some novel, validated signaling pathways implicated in DC have already been reported in literature but are not mentioned by the authors. These data would certainly improve the discussion section).

- Major Compulsory Revisions

Pursuing on the presented study in more details, which include at least validation of most interesting data obtained in microarray assays, would ensure the scientific impact and clinical relevance of presented data.

- Minor Essential Revisions

More comprehensive presentation of data

- Discretionary Revisions

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**Level of interest:** An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests: I declare that I have no competing interests