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LETTER

The importance of verifying the novelty of a finding and the value of combining results

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Dear Dr. Kessler

We have read with great interest the article by Guadagnin et al, "Transcriptome analysis of collagen VI-related muscular dystrophy muscle biopsies."[1] The paper is outstanding being its strengths the number of samples included, complementarity of the methodologies (microarray and RNA-seq), and the functional analyses.

It is compelling that despite differences in methodologies and in the origin of the samples (different disease stage), Guadagnin and co-authors findings are largely coincident with our previous transcriptomics results also on muscle biopsies from patients with Ullrich Congenital Muscular Dystrophy (COL6-RD).[2]

The expression data have been deposited in GEO, but they will not be released until August 2023. Therefore, we do not have access to the complete list of differentially expressed genes. However, if we look at the data available in the manuscript, we find that 50% of the Top 20 upregulated and downregulated genes reported by Guadagnin and co-authors[1] (figure 3) are in common with our dataset and almost one-third of the genes in the list in figure 4 were also found differentially expressed in our study (same direction of change and similar fold change).

The authors claim that **a novel finding of their study was the upregulation of *CILP* and *MGP* genes**. This statement is not correct since in our 2013 publication[2] we described the upregulation of these two genes in the same disease and type of sample using microarrays. These genes are listed in supplementary table 4 in Paco et al, 2013 which can be accessed from the publication and on the GEO database (Ref GSE43698). Therefore, there is no novelty regarding the upregulation of *CILP* and *MGP* genes in muscle from patients with COL6-RD, but rather this result is confirmatory.

Although this is only a specific finding, we think it is important to raise it because it is the responsibility of the authors to check thoroughly previously published work and correctly reflect the state of the art.

The authors could have also drawn conclusions from previous transcriptomic studies on fibroblasts from COL6-RD patients[3,4] which share common gene expression changes with those performed in muscle (e.g., upregulation of *THBS4*).

Overall, the study by Guadagnin et al, together with previous transcriptomic studies reveals a common signature centered around the extracellular matrix that must reflect the driving mechanisms of collagen VI-related diseases. Perhaps, a collaborative meta-analysis could be carried out at this stage.

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