Identification of an organ-independent molecular functional signature representing the active fibrosis process

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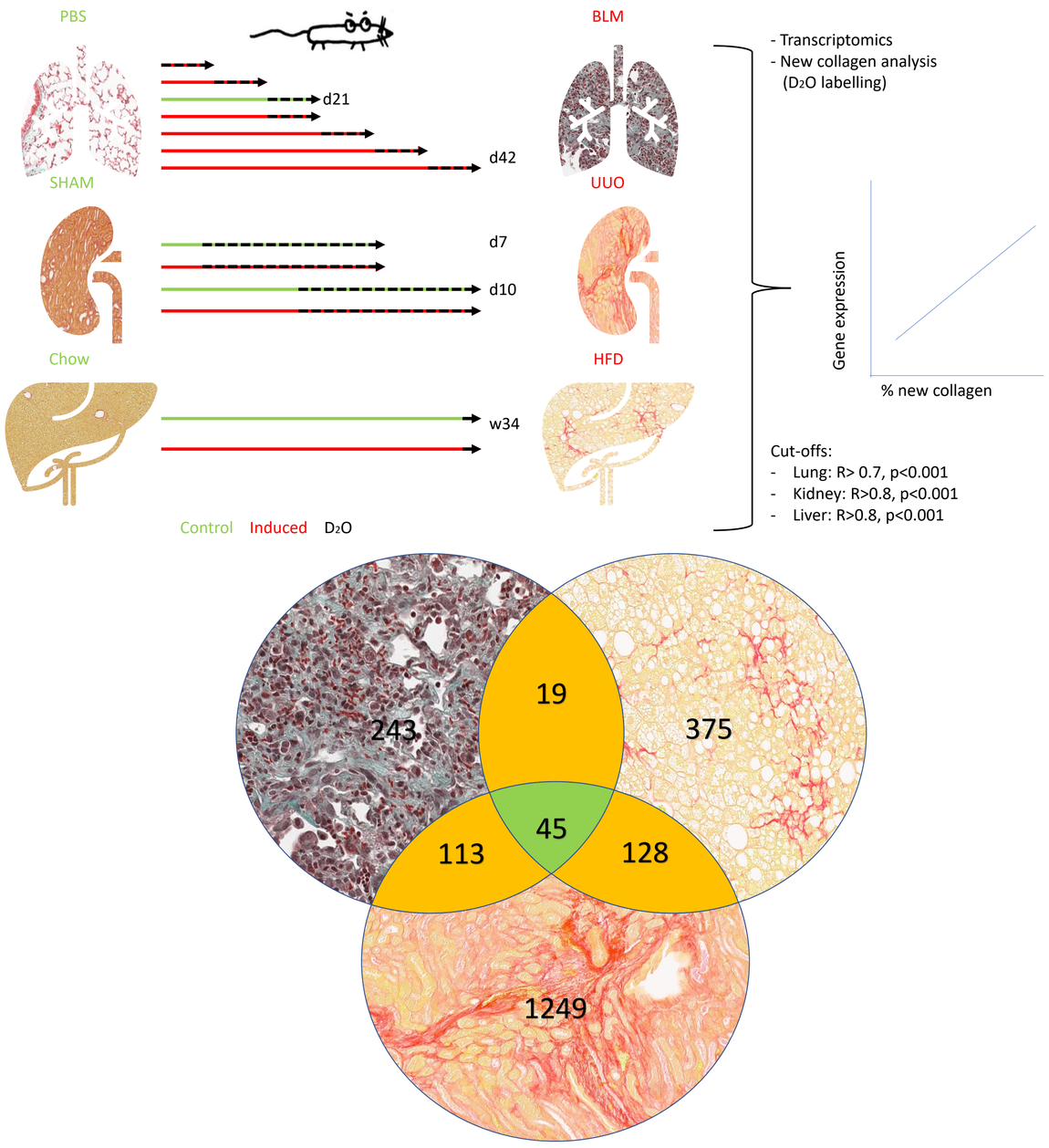
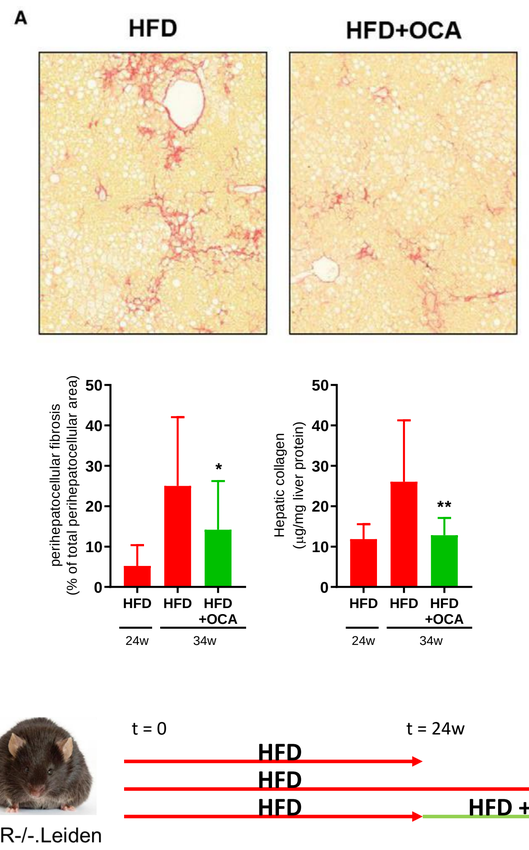
Background

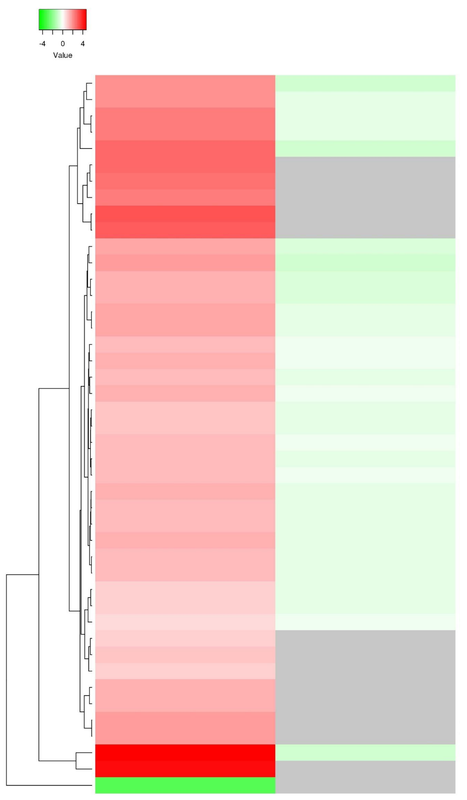
Quantification of active collagen deposition is one of the key parameters determined during the pre-clinical testing of novel therapeutic compounds. mRNA-analysis does not always represent active collagen synthesis well, due to the extensive post-translational modification of collagen. Therefore, we aimed to develop an organ-independent functional molecular signature for newly synthesized collagen by integrating data from deuterium labelled new collagen synthesis with genome wide transcriptome analysis.

Generation of an organ-independent collagen signature

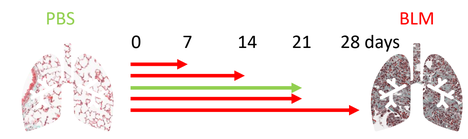


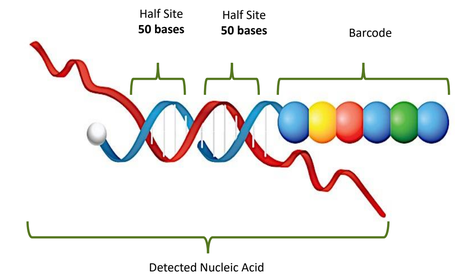
Upregulation of collagen signature is reduced after treatment with obetocholic acid in high fat diet-induced NASH

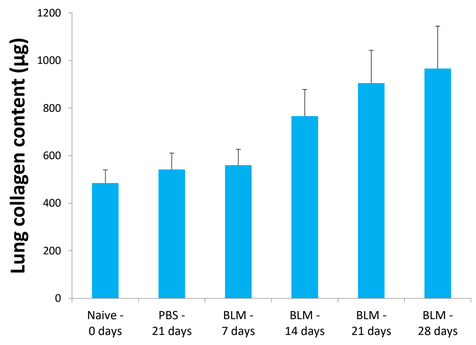


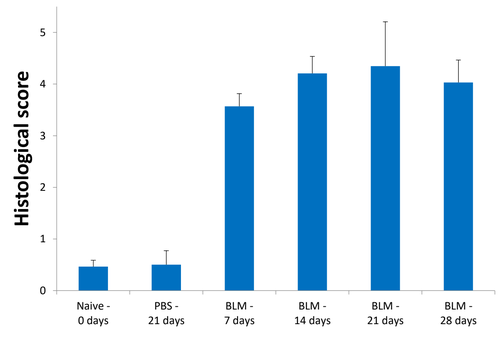


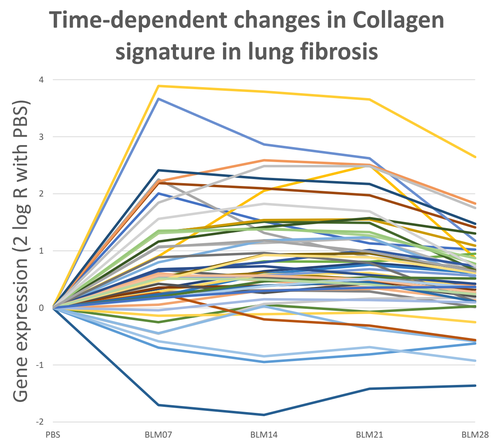
Collagen signature: analysis of time-course bleomycin-induced lung fibrosis using Nanostring

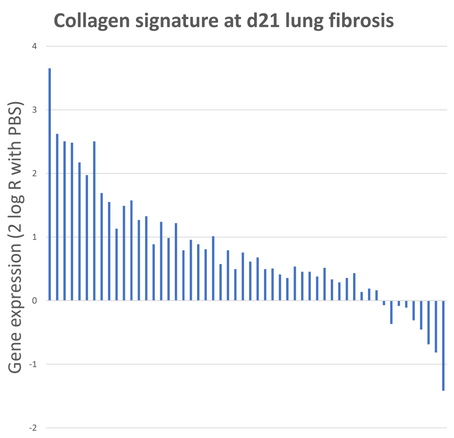




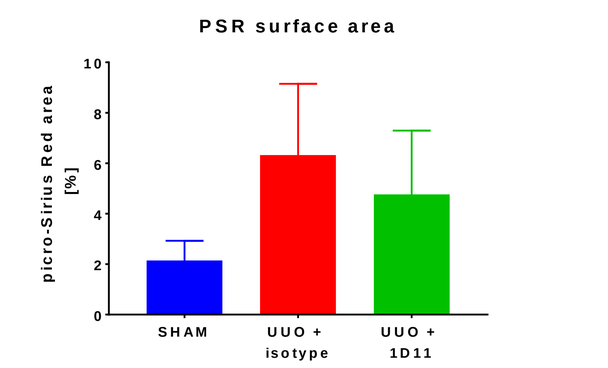


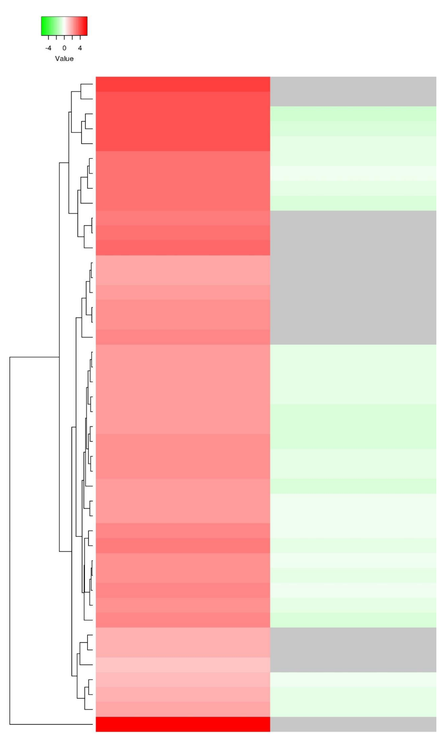






The upregulation of the collagen signature in UUO-induced fibrosis is reduced after treatment with 1D11 (anti-TGFß)





Conclusions

- We have developed a collagen signature signifying active deposition of collagen in experimental fibrosis
- This collagen signature confirmed treatment effects of anti-TGFß and OCA in UUO-kidney fibrosis and HFD-induced NASH
- This signature can be measured easily, quickly and at a lower cost than Next Generation Sequencing using a Nanostring panel