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Abstracts from the 1st World Congress on Epidermolysis Bullosa

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EXTRACELLULAR MATRIX DISTINCT SIGNATURE AMONG DYSTROPHIC EPIDERMOLYSIS BULLOSA VARIANTS

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Introduction & objectives: Mutations in the COL7A1 gene, which encodes collagen VII protein, the major component of the anchoring fibrils in the dermal-epidermal junction, cause all forms of dystrophic epidermolysis bullosa (DEB). Different clinical variants have been described with both dominant and recessive inheritance. However, information regarding the consequences of different COL7A1 mutations in the cell microenvironment, particularly on extracellular matrix (ECM), is still scarce. Moreover, several studies found the spectrum of biologic and clinical phenotypes of DEB to be wider than initially anticipated. Hence, this work aims to unravel the main differences in ECM composition between DEB patients and healthy individuals, as well as between representative variants of the disease. *Materials & methods:* Healthy primary fibroblasts and immortalized cell lines of three DEB variants (generalized DDEB, generalized intermediate RDEB and generalized severe RDEB). The cells were seeded at a density of 50x103 cells per cm^2 for 14 days with 50µg/mL ascorbic acid, in order to promote maximum ECM deposition. Mass spectrometry-based label-free quantification was used to assess changes in the ECM deposited by the different cell populations. Then a combination of western blot, quantitative real-time PCR and histological methods were used to confirm the proteomic results and investigate the biological pathways linked to the obtained results. *Results:* Analysis of the extracellular proteome revealed that fibroblasts from each DEB variant have their own proteomic signature. Independently of the DEB variant – and its associated clinical aggressiveness – the different COL7A1 mutations studied impacted dermal ECM organization through the down-regulation of major ECM players such as collagen XII, decorin, biglycan and lysyl oxidase homolog 2. Furthermore, ECM organization-associated proteins were found to be differently expressed between DEB variants. For the phenotypes associated to increased severity of disease, a down-regulation of proteins linked to ECM structure and remodelling, namely collagens I, III and V and matrix metalloproteinases 1 and 2, was observed. *Conclusions:* Our results corroborate previous studies showing that total loss of collagen VII has an enormous impact on dermal ECM dynamics. Additionally, our results also demonstrated that a partial loss of type VII collagen impacts cell microenvironment, affecting mostly the ECM structural proteins. Overall, our work contributes to the generation of further knowledge on DEB variants molecular features. *Acknowledgements*: The authors would like to acknowledge FCT for grant SFRH/BD/137766/2018 (MDM) and contract CEECIND/00695/2017 (MTC), the ERC Consolidator Grant – ECM_INK (ERC-2016-COG-726061) the European Union for The Discoveries Centre for Regenerative and Precision Medicine (H2020-WIDESPREAD-2014-1-739572).