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Meeting abstract

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Increased levels of large scale deletions of mtDNA of skin fibroblasts result in increased collagen degradation in dermal skin equivalents

BA Schuermann*, M Majora, P Schroeder, H Hajimiragha and J Krutmann

Address: IUF, Molekulare Alternsforschung, Duesseldorf, Germany
* Corresponding author

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Aged tissues contain increased levels of large-scale deletions of the mitochondrial (mt) DNA. Especially extrinsically aged skin has been shown to carry a significant burden of mtDNA deletions along with several other structural and functional impairments. Until now the functional role of mtDNA mutations for functional and structural changes of aged skin is not understood.

Therefore we studied how human skin cells harbouring mtDNA mutations affect their microenvironment by comparing normal human fibroblasts (NHF) to dermal fibroblasts derived from patients suffering from Kearns-Sayre syndrome (KSS) in 3D collagen gels resembling human skin (dermal equivalents, DE). KSS fibroblasts carry a 10,000 fold higher amount of mtDNA deletions exemplified by quantitative measurement of the 4977 bp Common Deletion. We here examined the degradation of components of the extracellular matrix in DE during cultivation.

During six weeks we detected more fragmented collagen measured by the marker hydroxyproline (HYP) via GC-MS. Moreover we observed a less robust collagen lattice structure in dermal equivalents with KSS fibroblasts in comparison to NHF by picrosirius red staining of histological sections. In line with that, we could measure higher mRNA expression levels of the dominant collagen degrading enzyme matrixmetalloproteinase-1 (MMP-1) in KSS DE using realtime PCR and increased MMP-1 protein amounts in histological sections over the whole cultivation time.

We conclude that increased levels of photo-inducible mtDNA deletions are functionally relevant for intensified matrix degradation and are therefore responsible for detrimental changes in photoaged skin.