

Endogenous hyaluronic acid as a putative target to confront skin ageing

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Skin ageing is a multifactorial process consisting of two distinct and independent mechanisms; intrinsic ageing which affects the skin in the same pattern as it affects all internal organs and extrinsic ageing or “photo-ageing”, which is the result of exposure to external factors, mainly ultraviolet (UV) irradiation. Hyaluronic acid (HA) is a major component of the extracellular matrix of the skin. We have recently shown that both intrinsic and extrinsic skin ageing are associated with significant and distinct alterations in HA expression and metabolism.

For the study of intrinsic skin ageing we used photo-protected skin tissue specimens from aged adults (mean age 72 years) and young (mean age 5 years) patients. Extrinsic skin ageing was studied on UV-exposed and UV-protected human skin tissue specimens obtained from the same patient (patients aged 65-85 years). HA was isolated from skin tissue specimens, purified, characterized and quantitated by ELISA. Gene expression of HA metabolizing enzymes such as HA synthases (HAS), hyaluronidases (HYAL) and HA receptors CD44 and receptor for HA-mediated motility (RHAMM) was assessed by RT-PCR.

We found that intrinsic skin ageing is associated with down regulation of HA expression which may be attributed to significant decrease of HA synthases 1 and 2. Furthermore, we found that the expression of the HA receptors CD44 and RHAMM is significantly downregulated in aged as compared to young patients, indicating impair function of HA in adult skin.

Extrinsic skin ageing is associated with a significant increase of HA content in the skin, however, of lower molecular mass, which may be attributed to a concomitant decrease of the expression of HAS1, which is responsible for the synthesis of HA of high molecular mass and an increase of the expression of HYAL1-3. Furthermore, gene expression of CD44 and RHAMM was significantly down regulated in photo-exposed, as compared to photo-protected skin.

These data indicate that skin ageing is related with significant and distinct alterations in HA expression and homeostasis. HA of low molecular mass has been shown to induce inflammatory processes in various tissues whereas HA of high molecular mass plays a protective role against inflammation. Therefore, inducing specific HAS, responsible for the synthesis of HA of high molecular mass or inhibiting HYAL, which degrade HA, may be an alternative way to induce the expression of HA with anti-inflammatory properties in the skin and therefore, to confront skin ageing.