Integratomics of Human Dermal Fibroblasts Treated with Low Molecular Weight Hyaluronic Acid

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Abstract

Hyaluronic acid (HA) is a glycosaminoglycan very common in commercial products from pharmaceuticals to cosmetics due to its widespread distribution in humans and its diversified physico-chemical proprieties. Despite its extended use and preliminary evidence showing even also opposite activities to the native form, the precise cellular effects of HA at low-molecular-weight (LWM-HA) are currently unclear. The 'omics sciences currently in development offer a new and combined perspective on the cellular and organismal environment. This work aims to integrate lipidomics analyses to our previous quantitative proteomics one for a multi-omics vision of intra- and extra-cellular impact of different concentrations (0.125, 0.25, and 0.50%) of LMW-HA (20–50 kDa) on normal human dermal fibroblasts by LC-high resolution mass spectrometry (LC-HRMS). Untargeted lipidomics allowed us to identify 903 unique lipids mostly represented by triacylglycerols, ceramides, and phosphatidylcholines. According to proteomics analyses, LMW-HA 0.50% was the most effective concentration also in the lipidome rearrangement especially stimulating the synthesis of ceramides involved in skin hydration and reparation, cell signaling, and energy balance. Finally, integrative analyses showed 25 nodes covering several intra- and extra-cellular functions. The more complete comprehension of intra- and extra-cellular effects of LMW-HA here pointed out will be useful to further exploit its features and improve current formulations even though further studies on lipids biosynthesis and degradation are necessary.