World Academy of Science, Engineering and Technology
International Journal of Bioengineering and Life Sciences
Vol:9, No:07, 2015

Human Lens Metabolome: A Combined LC-MS and NMR Study

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Abstract : Cataract, or clouding of the eye lens, is the leading cause of vision impairment in the world. The lens tissue have very specific structure: It does not have vascular system, the lens proteins – crystallins – do not turnover throughout lifespan. The protection of lens proteins is provided by the metabolites which diffuse inside the lens from the aqueous humor or synthesized in the lens epithelial layer. Therefore, the study of changes in the metabolite composition of a cataractous lens as compared to a normal lens may elucidate the possible mechanisms of the cataract formation. Quantitative metabolomic profiles of normal and cataractous human lenses were obtained with the combined use of high-frequency nuclear magnetic resonance (NMR) and ion-pairing high-performance liquid chromatography with high-resolution mass-spectrometric detection (LC-MS) methods. The quantitative content of more than fifty metabolites has been determined in this work for normal aged and cataractous human lenses. The most abundant metabolites in the normal lens are myo-inositol, lactate, creatine, glutathione, glutamate, and glucose. For the majority of metabolites, their levels in the lens cortex and nucleus are similar, with the few exceptions including antioxidants and UV filters: The concentrations of glutathione, ascorbate and NAD in the lens nucleus decrease as compared to the cortex, while the levels of the secondary UV filters formed from primary UV filters in redox processes increase. That confirms that the lens core is metabolically inert, and the metabolic activity in the lens nucleus is mostly restricted by protection from the oxidative stress caused by UV irradiation, UV filter spontaneous decomposition, or other factors. It was found that the metabolomic composition of normal and age-matched cataractous human lenses differ significantly. The content of the most important metabolites – antioxidants, UV filters, and osmolytes – in the cataractous nucleus is at least ten fold lower than in the normal nucleus. One may suppose that the majority of these metabolites are synthesized in the lens epithelial layer, and that age-related cataractogenesis might originate from the dysfunction of the lens epithelial cells. Comprehensive quantitative metabolic profiles of the human eye lens have been acquired for the first time. The obtained data can be used for the analysis of changes in the lens chemical composition occurring with age and with the cataract development.

Keywords : cataract, lens, NMR, LC-MS, metabolome
Conference Title : ICMSB 2015 : International Conference on Metabolomics and Systems Biology
Conference Location : Paris, France
Conference Dates : July 20-21, 2015