Proteomic analysis of sub-retinal deposits in age-related macular degeneration

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Introduction

Age-related Macular Degeneration (AMD), one of the major causes of visual loss in Western populations, originates from defects of the retinal pigment epithelium (RPE). AMD affects the macula, the central zone of the retina that is involved in the vision of details and colors. The deposition of cellular debris beneath the retina is well recognized as a key element in the events leading to AMD, by creating a physical barrier between the retina and the vascular choroid. However, the composition of those deposits remains largely unknown. In order to improve knowledge on the pathophysiology of retina aging, we characterized age-related proteome changes in the retina and RPE of the ApoB100$^{+/+}$,LDLR$^{-/-}$ mouse, as a model that develops the main clinical features of human retinal aging.

Material and Methods

Ocular globes of aged and control mice were embedded in OCT, and cryosectioned. Laser Capture Microdissection was used to collect outer segments of the photoreceptors, retinal deposits and RPE samples. After protein extraction and in-gel trypsin digestion, recovered peptides were concentrated and analyzed by nanoLC-MS/MS Data were processed using a set of home-made and open-source software tools. Differentially-accumulated proteins were selected using the MSstats library on R-software with a 5% FDR.

Results and Discussion

From 38 to 96 proteins were identified in the different samples. Lower levels of retinol dehydrogenase and up-accumulation of S-arrestin were found in ApoB100$^{+/+}$,LDLR$^{-/-}$ mice compared to controls. The concomitant up-accumulation of crystallins is consistent with proteomic data in eyes collected from patients with AMD showing increased levels of crystallins.

Conclusions

The proteomic data add possible clues to explain functional changes in the ApoB100+/+, LDLR-/- mouse.

References

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