Common miRNAs in Alzheimer's disease and retinal degenerative diseases

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Purpose: To identify common miRNAs in Alzheimer's disease (AD), age related macular degeneration (AMD) and glaucoma. An important common characteristic to all these three diseases is the amyloid b deposition in the brain of AD patients and in the retina of AMD and glaucoma patients. The pattern of the progression of ocular diseases, from axonal degeneration and progressing through secondary degeneration, is also observed in AD. Interestingly, Aβ and phosphorilated tau (p-tau), proteins that aggregate respectively in plaques and neurofibrillary tangles in the brain of AD patients, have been detected also in glaucomatous patients and have been thought to have a role in progression of visual loss and retinal ganglion cells (RGCs) death.

Methods: Human microRNA Disease Database (HMDD) and mir2Disease databases were used. No validated miRNAs are reported for glaucoma and AMD in HMDD and mir2Disease databses, thus a literature search has been carried out on PubMed and Scopus in order to identify miRNAs putatively involved in glaucoma and AMD. Hence, in order to increase the information available, we analyzed gene association studies on glaucoma and AMD, then the prediction of target miRNAs has been carried out by queries on microRNA.org database (http://www.microRNA.org/). Another enrichment analysis was performed by DIANA-miRPath v.2.0, calculating the probability for each miRNA to be significantly associated to a KEGG pathway.

Results: Twenty-three, eight and nine deregulated miRNAs were found in AD, glaucoma and AMD respectively. In particular, we identified four miRNAs commonly deregulated in AD and AMD, and two miRNAs commonly deregulated in AD and glaucoma. We also identified only one miRNA (miR 23a) commonly deregulated in glaucoma and AMD. None miRNA was found deregulated matching all three neurodegenerative diseases. We enriched the information from literature predicting microRNA from target genes associated to AMD and glaucoma, and we found a number of nine common microRNA matching AD, AMD and glaucoma. We predicted the association of these nine common miRNA to KEGG pathways through TarBase annotation . The most representative KEGG pathways (higher number of miRNA and best p-values) are: 'apoptosis' (hsa04210), 'cytokine-cytokine receptor interaction' (hsa04060) and 'Toll-like receptor signaling pathway' (hsa04620), NF-kappa B', 'HIF-1' and 'neurotrophins'. Incidentally, other pathways are also (well) represented and experimentally identified such, TGF-β, hypoxia inducible factor-1, chemokine signaling, and the pathways related to cell cycle regulation Interesting the NF-kappa signaling pathway is represented by one microRNA miR-146a-5p (p-value 2.6 e-10).

Conclusions: The implications of common miRNAs in the pathogenesis of AD and retinal degenerative diseases offer a novel approach to elucidate unclear molecular mechanisms of these conditions. The findings hereby obtained provide a valuable hint to assess deregulation of specific miRNA, as potential biomarkers and therapeutic targets, in glaucoma and other neurodegenerative diseases by means of preclinical and clinical studies.