

Signaling by extracellular vesicles within the ocular drainage system, a new understanding of glaucoma disease.

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Glaucoma, the second cause of blindness worldwide is a progressive neurodegeneration disease. Elevated Intra Ocular pressure (IOP) is the major risk factor and the only existing treatment target. Crosstalk among the aqueous humor (AH) producing cells the Non-pigmented ciliary epithelium (NPCE) and the AH draining cells, the Trabecular meshwork (TM) contribute to the IOP homeostasis.

Canonical Wnt signaling is associated with glaucoma pathogenesis and IOP regulation. Here we looked for NPCE-derived extracellular vesicles effects on Wnt signaling by TM cells.

Extracellular vesicle extraction and characterization methods were used followed by dose time depended incubation of NPCE derived EVs with TM cells. Canonical Wnt signaling outcomes in TM cells including uptake analysis, proteins and gene expression and matrix metalloproteinase activity were analyzed.

NPCE derived EVs were found to have a significant bi-modal effect on key canonical Wnt proteins, a significant effect on downstream gene expression and increase matrix metalloproteinase activity.

Our data suggest that NPCE derived EVs specifically target the TM cells resulting in changes in the TM extra cellular matrix via the canonical Wnt signaling in TM cells.

These findings may have therapeutic relevance since canonical Wnt pathway is involved in intra-ocular pressure regulation. Further understanding of NPCE-derived EVs-responsive signaling pathways may reveal new targets for pharmacological intervention within the drainage system as a target for glaucoma therapy.