Multifarious Biologic Loaded Liposomes that Stimulate the Mammalian Target of Rapamycin Signaling Pathway Show Retina Neuroprotection after Retina Damage - DTU Orbit (09/08/2019)

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A common event in optic neuropathies is the loss of axons and death of retinal ganglion cells (RGCs) resulting in irreversible blindness. Mammalian target of rapamycin (mTOR) signaling pathway agonists have been shown to foster axon regeneration and RGC survival in animal models of optic nerve damage. However, many challenges remain in developing therapies that exploit cell growth and tissue remodeling including: i) activating/inhibiting cell pathways synergistically; ii) avoiding tumorigenesis and iii) ensuring appropriate physiological tissue function. These challenges are further exacerbated by the need to overcome ocular physiological barriers and clearance mechanisms. Here we present liposomes loaded with multiple mTOR pathway stimulating biologics designed to enhance neuroprotection after retina damage. Liposomes were loaded with ciliary neurotrophic factor, insulin-like growth factor 1, a lipopeptide N-fragment osteopontin mimic and lipopeptide phosphatase tension homolog inhibitors for either the ATP domain or the c-terminal tail.

In a mouse model of N-methyl-D-aspartic acid induced RGC death, a single intravitreal administration of liposomes reduced both RGC death and loss of retina electrophysiological function. Furthermore, combining liposomes with transplantation of induced pluripotent stem cell derived RGCs lead to an improved electrophysiological outcome in mice. The results presented here show that liposomes carrying multiple signaling pathway modulators can facilitate neuroprotection and transplant electrophysiological outcome.