Antioxidant, Nano-in-Micro System for Sustained Erythropoietin Delivery in a Mouse Model of Glaucoma

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GLAUCOMA IS A LEADING CAUSE OF BLINDNESS WORLDWIDE

GLAUCOMA PATHOLOGY

GLAUCOMA IN MICE

ERITHROPOIETIN (EPO) IS POTENTLY NEUROPROTECTIVE, BUT FACES FAST CLEARANCE WHEN INJECTED IN THE EYE

MICROBEAD OCCLUSION MODEL (MOM) OF GLAUCOMA IN MICE

STRATEGY: ANTI-OXIDANT MICROPARTICLES FOR SUSTAINED RELEASE OF EPO IN VIVO

STEP 1: PACKAGE PROTEIN INTO DEXTRAN NANOPARTICLES USING AN AQUEOUS TWO-PHASE SYSTEM TECHNIQUE

Add EPO/dextran nanoparticles to PPSES in DCM to form solid-in-oil emulsion

Add PPSES-dextran-EPO emulsion to aqueous PVA buffer to form solid-in-oil-in-water emulsion

Evaporate organic solvent, wash, and lyophilize

Freeze & Lyophilize

Wash PEG away with DCM

RESULT: EPO-loaded dextran nanoparticles

STEP 2: LOAD EPO-DEXTRAN NANOPARTICLES INTO PPSES MICROPARTICLES USING A SOLID-IN-OIL-IN-WATER EMULSION

Polymer: Poly(propylene sulfide-co-ethylene sulfide) (PPSES)

RESULT: ROS scavenging in vivo, reduced inflammation, disease-responsive drug release

ANTIOXIDANT MICROPARTICLES CHEMICALLY SCAVENGE HARMFUL OXIDATIVE MOLECULES TO COMPLEMENT BIOLOGICAL EPO SIGNALING

RESULT: Increased expression of antioxidant proteins; protection of ganglion cells

RESULT: Clearance from eye in hours to days

PPSES-EPO MICROPARTICLES SIGNIFICANTLY INCREASE EPO RETENTION IN THE EYE AND IMPROVE VISUAL FUNCTION

CONCLUSION: PPSES-EPO MICROPARTICLES SYNERGISTICALLY REDUCE OXIDATIVE STRESS OVER 6 WEEKS TO ALLEVIATE VISUAL IMPAIRMENT IN GLAUCOMA

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REFERENCES


FUTURE WORK

• Further increase EPO loading in microparticles
• Investigate treatment in longer-term disease
• Test PPSES-EPO microparticles in a non-human primate model of glaucoma

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