Methods to Treat and Prevent Post Capsular Opacification Following Cataract Surgery

Dr. A. Sue Menko has invented a novel chick lens capsular bag model for developing new therapies to treat and prevent Posterior Capsule Opacification (PCO), the most common complication of cataract surgery. This elegant, highly reproducible model of lens epithelial proliferation and migration offers many advantages for the analysis of critical signaling pathways, discovery of important new therapeutic targets and discovery of novel drug candidates for prevention of PCO. This invention is the first to identify Src kinase (SFK) signaling as an essential mechanism of PCO development and the first successful demonstration that PCO can be prevented by treatment with small molecule SFK inhibitors.

PCO occurs when myofibroblasts emerge from among the population of lens epithelial cells that remain associated with the lens capsule after cataract surgery, and then persist to develop into this fibroblastic disease which causes visual impairment and blindness. The current treatment for PCO is neodymium (Nd):YAG laser posterior capsulotomy. While widely used and considered low risk, laser treatment nonetheless involves risks to the eye. Far more preferable is to prevent PCO from ever occurring, particularly for use with new focusable lens being developed that preclude the use of laser surgery. This invention provides methods to eliminate the development of PCO by administering inhibitor therapy at the time of cataract surgery.

The chick embryo lens capsular bag model closely mimics human cataract surgery and provides a consistent and reproducible system to elucidate mechanisms and drug leads for PCO therapy. The chick lens capsular bag model has many advantages over existing in vivo and in vitro models because tissue supply is unlimited and large numbers of age-matched capsular bags can readily be prepared for biochemical analysis and drug discovery screening. The invention describes processes for preventing PCO by inhibiting kinase-signaling pathways that are activated as a wound response to the cataract surgery, which in turn lead to the emergence and persistence of disease causing myofibroblasts. The ex vivo mock cataract surgery wound repair model used to identify effective pharmaceutical targets to prevent PCO closely mimics both the lens wound repair process following cataract surgery and the subsequent development of fibrotic disease. The model is well suited for identifying new inhibitor drug candidates and methods for their delivery during surgery.

The most significant mechanistic discovery of the invention relates to the etiology of PCO: the identification of the essential role of Src family kinases (SFKs) in signaling proliferation, migration, and differentiation to a myofibroblast phenotype of cells that modulate the wound repair process. Dr. Menko demonstrated that SFK inhibitors are particularly efficacious in preventing PCO by blocking all three of these major phases that underlie the emergence of the fibrotic-disease causing cell population. By effecting this repair cell population, the pyrazolopyrimidine Src kinase inhibitor PP1 also alters the signals that are responsible to lead the lens epithelial cells across the posterior capsule. The pending patent application identifies a large number of small molecule inhibitor candidates for lead identification. The model can also be used to screen approved drugs that could potentially be repurposed for ophthalmic use.

The invention has important medical significance. The number of people with chronic eye diseases is increasing rapidly as populations in developed countries continue to age. There are more than 20 million cataract cases, more than 2 million open-angle glaucoma cases, and more than 7,600,000 cases of diabetic retinopathy in the US alone. Diabetic patients develop significantly more severe PCO after cataract surgery when compared with nondiabetic patients. Patients with glaucoma are also at increased risk of developing PCO. Nd:YAG laser capsulotomy must be used with caution in glaucoma patients and patients with a history of retinal tears or detachments. Inevitably, the incidence of PCO will continue to rise as the number of patients with chronic eye conditions that require caution, or are contraindicated, for laser treatment, also continue to rise. The invention offers the licensee the means to prevent the development of the PCO fibrotic disease by applying such inhibitors at the time of cataract surgery. The new therapies could include procedures that involve multiple delivery methods for the therapeutics, includings delivery through the intraocular lenses, which would lead to the elimination of PCO and the secondary interventions now required restore sight in PCO patients after cataract surgery.


Follow-up: For further information, please contact Michael Caggiano (michael.caggiano@jefferson.edu, 215-955-6862) in the Office of Technology Transfer and Business Development at TJU, citing TJU docket number MEN_SUE.002.