Retinopathy: Senescence-associated secretory phenotype contributes to pathological angiogenesis

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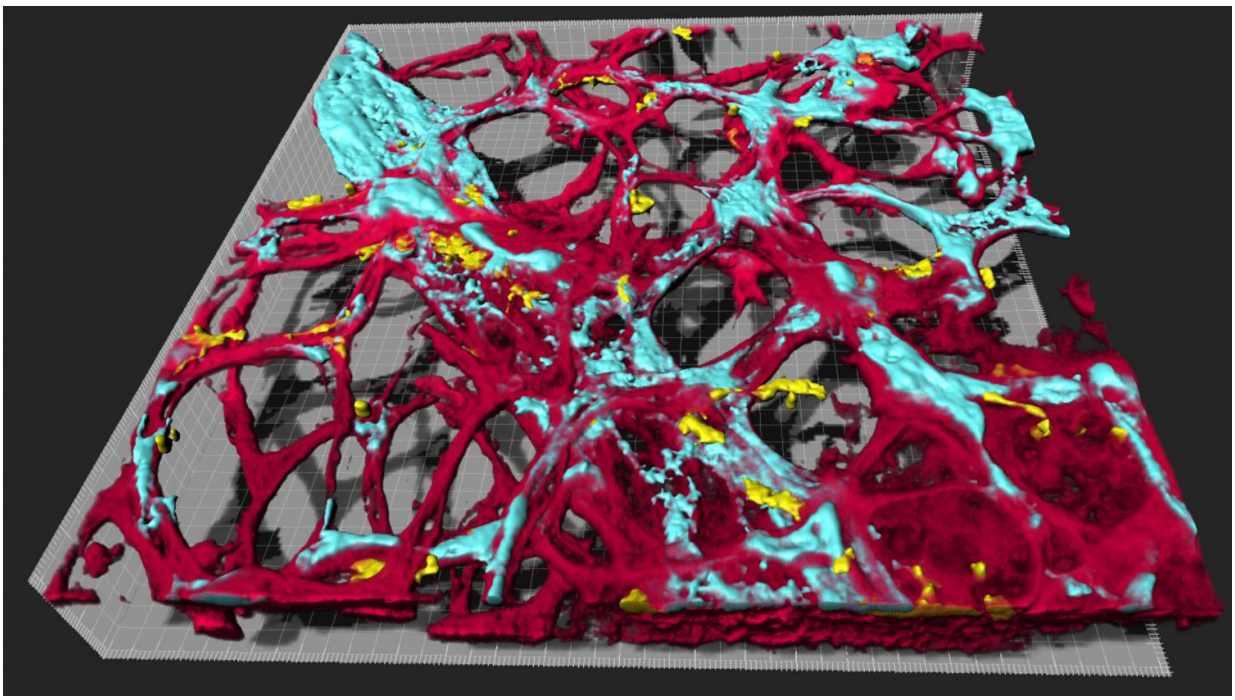

During bouts of neural ischemic such as those occurring in diabetic retinopathy and retinopathy of prematurity, a program of cellular senescence is triggered. Senescent cells then adopt a senescence-associated secretory phenotype that compromises the tissue microenvironment. Pictured is the mouse retinal vasculature (red) that becomes senescent (blue) and contributes to retinal disease progression. Retinal microglia are in yellow. Credit: Sapieha Lab, Maisonneuve Rosemont Hospital, Université de Montréal.

Diabetic retinopathy is the most prominent complication of diabetes and the leading cause of blindness in working age individuals. It is estimated that half a million Canadians are afflicted by diabetic retinopathy and it is predicted that the incidence will double over the next 15 years.

The ability to control and cure this disease has been limited so far. But a study led by Drs. Przemyslaw (Mike) Sapieha and Frédérick A. Mallette, researchers at Hôpital Maisonneuve-Rosemont (CIUSSS de l'Est-de-l'Île-de-Montréal) and professors at the Université de Montréal, sheds new understanding on the mechanisms of the disease as it uncovered a program of accelerated aging of the neurons, blood vessels and immune cells of the retina in areas where blood vessels had been damaged. Dr. Malika Oubaha, postdoctoral fellow in Sapieha and Mallette's group, found that cells of the retina that are cut off from their main source of oxygen and nutrients during disease are resilient and do not die. Instead, they enter a state of cellular senescence (or cellular aging) where they are dormant yet start producing a series of factors that contribute the blinding disease.

Their exciting work lead to the successful mapping and identification of the molecules that are activated during this process of premature aging. Interfering with the early cellular aging process occurring in mouse models of retinopathy with currently available and novel drugs resulted in improved regeneration of blood vessels within the retina and reduced retinal damage.

"Currently available treatments for diabetic retinopathy are either invasive or present adverse side effects when used for long term regimens. Our study does not identify a cure, but by mapping out the events that lead to premature senescence in retinopathy, we are now able to consider novel therapeutic interventions to slow down the disease process and preserve vision", says Mike Sapieha.

The hope

Ultimately, this study identifies potential therapeutic avenues to prevent entry in the dormant senescent state of retina that occurs during diseases such as diabetic retinopathy and help reinstate adequate function of the retina.

The mechanisms of diabetic retinopathy

In the retina (the layer of neurons at the back of the eye that transmits information from light to the brain) of patients suffering from diabetes, there is an initial degeneration of the blood vessels that feed the eye leading to a lack of oxygen and nutrients. This triggers a second phase of deregulated and destructive blood vessel growth within the eye. Given this sequence of events and prominent clinical features, the currently most widely used local ocular therapeutic interventions directly target pathological blood vessel growth, yet present a number of non-desirable off-target effects such as destruction of the retina itself. Overcoming these therapeutic limitations or exploring novel pharmacological avenues is therefore required to ameliorate the safety profiles of current interventions.

The results of this study have been published in *Science Translational Medicine*.

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More information: "Senescence-associated secretory phenotype contributes to pathological angiogenesis in retinopathy," *Science Translational Medicine*stm.sciencemag.org/lookup/doi/ … scitranslmed.aaf9440

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