Centre intégré
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et de services sociaux
de l'Est-de-
l'Île-de-Montréal
Québec

Communiqué de presse

Understanding retinopathy : Senescence-associated secretory phenotype contributes to pathological angiogenesis

Montreal, October 26, 2016 – *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 with 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 Maisonneuve-Rosemont Hospital (CIUSSS de l'Est-de-l'Île-de-Montréal) and professors at the University of Montreal, sheds new understanding on the mechanisms of the disease by uncovering a process of **accelerated aging of the neurons, blood vessels, and immune cells of the retina in areas where blood vessels have been damaged**. Dr. Malika Oubaha, a 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 the disease are resilient and do not die. Instead, they enter a state of cellular senescence (or cellular aging) in which they are dormant yet start producing a series of factors that contribute to the blinding disease.

Their exciting work led to the successful mapping and identification of the molecules that are activated during this process of premature aging. Using currently available and novel drugs to interfere with the early cellular aging process of retinopathy in mouse models, the researchers observed 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", said Sapieha.

Hopeful avenues

Ultimately, the study identifies potential therapeutic avenues to prevent the retina from entering into a dormant senescent state occurring in diseases such as diabetic retinopathy, and to return normal function to the retina.

The mechanisms of diabetic retinopathy

In the retina (layer of neurons at the back of the eye that transmit information from light to the brain) of patients with 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

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deregulated and destructive blood vessel growth within the eye. Given this sequence of events and the prominent clinical features, the most current and widely-used local ocular therapeutic interventions directly target pathological blood vessel growth; however, they present a number of undesirable off-target effects, such as destruction of the retina itself. Overcoming these therapeutic limitations or exploring novel pharmacological avenues is therefore required to improve the safety profiles of current interventions.

The results of this study were published in the journal *Science Translational Medicine.*

The study received funding from the Canadian Institutes of Health Research, the Canadian Diabetes Association, the Foundation Fighting Blindness (Canada), the Natural Sciences and Engineering Research Council of Canada, the Maisonneuve-Rosemont Hospital Foundation, the Fonds de recherche du Québec – Santé, the Canada Research Chairs Program, and the Wolfe Professorship.

About the CIUSSS de l'Est-de-l'Île-de-Montréal

The Centre intégré universitaire de santé et de services sociaux de l'Est-de-l'Île-de-Montréal (CIUSSS-Est) includes Rosement-Maisonneuve Hospital, Santa Cabrini Hospital, the Canadian-Polish Welfare Institute, the Institut universitaire en santé mentale de Montréal, as well as the CSSS de Saint-Léonard et Saint-Michel, the CSSS de la Pointe-de-l'Île, and the CSSS Lucille-Teasdale. Its 43 points of service have nearly 15,000 employees and 580 doctors (full-time equivalent) for a population of 500,000. The centre provides a full range of first-line health and social services; general, specialized, and ultra-specialized hospital care; mental health care; and long-term and residential care. Affiliated with the University of Montreal, the CIUSSS-Est combines its missions of teaching, evaluation, and research with training for doctors and health care professionals. Its two major research centres are nationally and internationally recognized for their expertise in mental health, immunology-oncology, vision health, nephrology, and cell therapy. www.ciusss-estmtl.gouv.qc.ca.

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