DIABETES

Endogenous factor protects vision

The Joslin Medalist study investigates a cohort of patients who have had type 1 diabetes mellitus (T1DM) for 50 years or longer. In this cohort, 35% of patients have no or only mild diabetic retinopathy, a complication in people with diabetes mellitus that can lead to vision loss. A new study in *Science Translational Medicine* has identified an endogenous factor present in the eyes of patients that protects against diabetic retinopathy.

To investigate potential factors, the researchers performed comparative proteomic analysis of eyes donated after death from individuals in the cohort with no retinopathy and individuals with severe retinopathy. Importantly, levels of glycaemic control did not correlate with, and therefore could not explain, the presence of retinopathy.

"From the comparative analysis of the proteomic study, we identified a neuro-retinal protein made specifically in the photoreceptors, retinal binding protein 3 (RBP3), that was elevated in the protected eyes," explains corresponding author George King. "RBP3 has a critical function for vision as it is essential for the regeneration of cis-retinals and trans-retinals, which are factors critical for the photoreceptors (rod and cone cells) to detect light." In addition to detecting RBP3 in the eye, this factor was also detected in the circulation but at ~1,000-fold lower concentrations.

Next, the researchers used mouse and rat models of diabetic retinopathy and showed that recombinant human RBP3 (rhRBP3) could prevent or halt the development of retinopathy when overexpressed in photoreceptor cells or injected directly into the retina.

In vitro and ex vivo studies on retinal vascular cells, Müller cells (a type of retinal glial cell) and isolated mouse retina demonstrated that the mechanism of action of rhRBP3 involves the binding of this factor to glucose transporter 1. This effect slows the uptake of glucose into cells of the eye, which prevents the toxic effects of hyperglycaemia.

"We plan to evaluate the changes in circulatory RBP3 in patients with T1DM or type 2 diabetes mellitus with varying levels of retinopathy, in order to determine its value as a biomarker for retinopathy," concludes King. "We will also perform structural and functional analysis of RBP3 to determine its essential structure, which protects retinal cells from the toxic effects of hyperglycaemia."

Shimona Starling

ORIGINAL ARTICLE Yokomizo, H. et al. Retinol binding protein 3 is increased in the retina of patients with diabetes resistant to diabetic retinopathy. *Sci. Transl. Med.* **11**, eaau6627 (2019)

Images of retina from a cohort member with no retinopathy, even after having type 1 diabetes mellitus for 74 years. Image courtesy of George King/Joslin Diabetes Center.

concentrations in the plasma when leptin levels are low, are the cause of hyperphagia. In addition, the team report that glucocorticoids drive hyperphagia, independent of leptin, during hypoglycaemia. These results are surprising as they demonstrate that the role of leptin in hunger is mediated by an endocrine loop outside of the brain.

The authors now want to find out whether these findings translate to humans. Specifically, they are interested in the extent of the relationship between hypoleptinaemia and hypercorticotesteronaemia.

Alan Morris

ORIGINAL ARTICLE Perry, R. J. et al. Leptin's hunger-suppressing effects are mediated by the hypothalamic–pituitary–adrenocortical axis in rodents. *Proc. Natl Acad. Sci. USA* <https://doi.org/10.1073/pnas.1901795116> (2019)

“in starvation and diabetic ketoacidosis, glucocorticoids ... are the cause of hyperphagia”

Credit: KATERYNA KON/
SCIENCE PHOTO LIBRARY/Getty

and fat mass were slightly reduced in the groups that received *A. muciniphila* supplementation.

The intervention was safe, well tolerated and did not affect the overall gut microbiome structure. "Furthermore, the tests in humans confirm what had already been observed in mice; the pasteurized form of *A. muciniphila* was more efficient than the live bacteria on several parameters," adds Cani. "The most important thing is to confirm the results of this small pilot study in a larger cohort."

Anna Kriebs, Associate Editor,
Nature Communications

ORIGINAL ARTICLE Depommier, C. et al. Supplementation with *Akkermansia muciniphila* in overweight and obese human volunteers: a proof-of-concept exploratory study. *Nat. Med.* **25**, 1096–1103 (2019)

“The most important thing is to confirm the results of this small pilot study in a larger cohort”