

# Protein That Causes Blood Vessel Leakage in DR Found

**R**esearchers from Joslin Diabetes Center have identified a group of proteins present in the vitreous that they believe play a critical role in causing blood vessel leakage among patients with proliferative diabetic retinopathy (DR) and diabetic macular edema (DME).

Edward Feener, PhD, and colleagues, reported in *Nature Medicine*, that their findings could point to potential therapeutic targets for treating DR and DME, as well as cerebral swelling caused by things like head injury and stroke.

"By analyzing the protein composition in the human vitreous, we have identified a new group of molecules that may improve our understanding of the disease processes that contribute to [DR]," said Dr. Feener. "By studying the actions of these proteins in both the retina and the brain, we have shown that our findings may have broad relevance for neurovascular leakage and swelling." Dr. Feener is an investigator in Joslin's Section on Vascular Cell Biology, Director of Joslin's Proteomics Core, which hosted the study, and Assistant Professor of Medicine at Harvard Medical School.

Using cutting-edge mass spectroscopy-based proteomics, the researchers detected 117 proteins in human vitreous and elevated levels of extracellular carbonic anhydrase-I in the vitreous of individuals with diabetic retinopa-

thy. They wrote that this suggests that retinal hemorrhage and erythrocyte lysis contribute to the diabetic vitreous proteome.

Dr. Feener and colleagues injected CA-I into rats and found it increased retinal vessel leakage and caused intraretinal edema. "CA-I-induced alkalinization of vitreous increased kallikrein activity and its generation of factor XIIa, revealing a new pathway for contact system activation," the researchers wrote.

Additionally, they found that CA-I-induced retinal edema was decreased by complement 1 inhibitor, neutralizing antibody to prekallikrein and bradykinin receptor antagonism.

"Subdural infusion of CA-I in rats induced cerebral vascular permeability, suggesting that extracellular CA-I could have broad relevance to neurovascular edema," Dr. Feener wrote. "Inhibition of extracellular CA-I and

kallikrein-mediated innate inflammation could provide new therapeutic opportunities for the treatment of hemorrhage-induced retinal and cerebral edema."

This issue of *RETINA TODAY* takes an in-depth look at the genetics of AMD, as well as the environmental risk factors associated with the disease and racial differences in prevalence.

Finally, we would like to express our appreciation to Genentech for their support of *RETINA TODAY*, and we look forward to a successful 2007! ■



A handwritten signature in black ink that reads "Conni B Koury". The signature is fluid and cursive, with the first letters of the first and last names being capitalized and prominent.

Conni Bergmann Koury  
Editor-in-Chief