Researchers find gene linked to severe diabetic eye and kidney diseases

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Researchers at the John A. Moran Eye Center at the University of Utah and collaborative institutions have identified a gene called erythropoietin (EPO) that contributes to increased risk of severe diabetic eye and kidney diseases, called retinopathy and nephropathy.

The sight-threatening form of diabetic retinopathy, termed proliferative diabetic retinopathy (PDR), is the most common cause of legal blindness in working-aged adults in the United States, accounting for 10% of new onset blindness overall. Diabetes is also the leading cause of kidney disease, called end-stage renal disease (ESRD), in the U.S. and the Western world.

Led by Kang Zhang M.D., Ph.D., Director of the Division of Ophthalmic Genetics at the Moran Eye Center and Associate Professor of Ophthalmology and Visual Sciences at the University of Utah, the study will be published online on May 5, 2008 in the journal *Proceedings of National Academy of Sciences*. Dr. Zhang explains the significance of the discovery: “We know that the development of PDR and ESRD in diabetic patients can be inherited. Although genetic factors are known to be important in the susceptibility (or resistance) to these complications, until now the genes involved have been mostly unknown.”

How did the researchers discover that this gene is involved in PDR and ESRD" In this study the researchers compared 1,618 people with PDR and ESDR, and 954 diabetes patients without any eye or kidney disease in three separate populations. Their studies demonstrate that if a person

has a copy of mutant EPO gene, they have an increased risk of developing PDR and ESRD during their lifetime.

Dr. Zhang explains the current use and cost of EPO for disease prevention and how this discovery may affect its use: “EPO is used extensively to help in the production of red blood cells when treating patients with anemia resulting from renal failure or chemotherapy. In the United States, erythropoietin represents one of the largest single drug expenses for the Center for Medicare & Medicaid Services, approximately $1 billion a year.

Patients with anemia due to chronic renal disease (many of whom have diabetes) who receive frequent dosing of EPO to maintain higher hemoglobin levels have a higher rate of cardiovascular complications than patients who maintain a lower hemoglobin level. A similar effect of EPO on accelerating the decline of kidney function had been suggested by earlier studies. Our study suggests that caution may be warranted when maintaining higher hemoglobin concentration using exogenous EPO treatment in diabetic patients, as it might accelerate progression to PDR and ESRD.”

"Though there is no proven pharmacologic treatment for diabetic vascular eye diseases, inhibiting the growth of unwanted blood vessel growth using antibodies directed against vascular endothelial growth factor (anti-VEGF therapy) has been advocated,” said Dr. Dean Li, who is a co-author from the Program in Human Molecular Biology and Genetics, also at University of Utah, “This genetic study suggests that future therapeutic strategies need to consider blunting the effects of erythropoietin in addition or as an alternative to an anti-VEGF strategy"

Source: University of Utah