FINDING THE GENE RESPONSIBLE FOR KIDNEY FAILURE

TORONTO, ON (EMBARGOED UNTIL NOON, JUNE 21, 2010) – Chronic Kidney Disease affects millions in North America, with persons of African heritage being at a four-fold higher risk, and those of Hispanic heritage having a twoa-fold higher risk compared to the rest of the population. Now, researchers announced at Sunnybrook Health Sciences Centre that they've discovered a gene likely involved in the increased risk of kidney disease in this high-risk population.

Tremendous excitement has been growing in the scientific community worldwide, with an intense race to determine the genetic link responsible for the greatly increased risk many people of African heritage face for End Stage Kidney Disease and the need for dialysis or transplantation. While much of the world has focused on the MYH9 gene, a team from the Rambam Medical Center and Technion in Haifa, led by Toronto's own Dr. Karl Skorecki, has discovered that a neighbouring gene is much more likely to be involved.

Identifying the correct gene that puts people at risk for progressive kidney disease is necessary to understand the underlying reason for the increased risk, and to be able to find strategies to prevent or slow down kidney failure. The team from Israel together with other world class medical research scientists from England, the United States and Africa has made this important advance, which Dr. Skorecki presented for the first time as an invited scientist and lecturer at Sunnybrook Health Sciences Centre.

Tens of costly research studies in the past two years have focused on a particular gene, called MYH9, as being responsible for these population disparities, but no mutations could be identified which might account for the connection. This led Dr. Skorecki's team to look beyond MYH9, by computerized datamining of the recently released 1000 Genomes Project dataset. This datamining, combined with the results obtained from DNA analysis in 955 African Americans and Hispanic Americans and 676 individuals from 12 populations residing in Africa, led Dr. Skorecki's team to conclude that specific genetic variation in the neighbouring genetic region, containing the APOL gene family, is actually much more likely than MYH9 to be responsible for the greatly increased risk for kidney disease in persons of western African heritage. Mutations in the APOL1 member of this family are predicted to change the shape and function of the protein coded by the gene.

A key element in identifying mutations in the APOL1 gene associated with kidney failure was the absence of these mutations in the 306 Ethiopian individuals included in the DNA analysis. Dr. Skorecki's team had already reported that Ethiopians are actually relatively protected from kidney disease and correspondingly do not have the mutations identified as associated with risk for kidney failure.

In a further, fascinating twist of evolutionary medicine, the APOL1 gene in particular is already known to be involved in resistance to African sleeping sickness. African sleeping sickness is caused by an infectious pathogen that attacks the brain and eventually causes coma and death. While it does not occur in North America, it is still prevalent in certain regions of Africa, and it thought to have been a major cause of death in Africa in the past. This led the researchers to postulate that increased susceptibility to kidney failure among persons with African heritage currently living in North America may be related to the protection conferred by genetic variation in the APOL genes, from African sleeping sickness and other tropical diseases in the ancestral past.

The challenge is now to prove the epidemiological, biological and medical relationship between variation in the APOL1 gene and other members of the APOL1 gene family and the risk for kidney disease. Dr. Skorecki and his team plan to pursue these studies in collaboration with Dr. Sheldon Tobe, one of Canada's leading Nephrologists, Associate Scientist with Sunnybrook Health Sciences Centre and Associate Professor in Medicine at the University of Toronto.

Sunnybrook Health Sciences Centre is inventing the future of health care for the one million patients the hospital cares for each year through the dedication of its more than 10,000 staff and volunteers. Internationally recognized leadership in research and education and a full affiliation with the University of Toronto distinguish Sunnybrook as one of Canada’s premier academic health sciences centres. Sunnybrook specializes in caring for Canada’s war veterans, high-risk pregnancies, critically ill newborns, adults and the elderly, and treating and preventing cancer, cardiovascular disease, neurological and psychiatric disorders, orthopedic and arthritic conditions and traumatic injuries.

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