MedicalXpress

Scientists discover unique risk variants of age-related macular degeneration in East Asians

February 25 2015

Age-related macular degeneration (AMD) is a major cause of blindness in the elderly in Singapore and worldwide. By 2040, global projected cases of AMD are 288 million, with the largest number of cases in Asia (113 million).

Currently, intra-vitreal anti-VEGF injection is the main therapy of choice for wet AMD, which generally stabilize vision and are limited in reversing vision loss. Due to their high cost and the large number of retreatments required, there is significant burden on the healthcare system, the patient and society. Importantly, Asians appear to have a distinct clinical presentation of the disease and different responses to treatment. For instance, Asians have poorer response to inhibitors of VEGF compared with patients of European ancestry. Hence, there is substantial interest and clinical need to further understand the pathogenesis of AMD, develop new interventions and identify predictive biomarkers of at risk groups.

Singapore Eye Research Institute, together with Genome Institute of Singapore, performed a comprehensive genome-wide (GWAS) and exome-wide (EWAS) association study for AMD risk genes. The study involved more than 5,600 normal controls and 2,000 East Asians with wet AMD, including a few hundreds of patients from Singapore, with independent replication in 4,000 patients and 10,000 controls from Singapore, Hong Kong, Korea, Japan and China. This project, led by

Prof Wong Tien Yin and the SERI-GIS team, is the largest AMD genetic study in Asia to date.

The investigators found a strong association between an East-Asian specific mutation in a lipid gene (CETP, cholesterol ester transfer protein) and increased risk of wet AMD. The distinct mutation found in Asian patients but absent in European populations is significant and sheds light on the unique pathogenesis of AMD in Asians. This mutation is previously known to increase HDL-cholesterol levels and protect from coronary heart disease. In addition, this research also identified three new genes for AMD for the first time.

The findings clearly implicated HDL metabolism in the pathogenesis of AMD, which may allow the development of new drugs, or the re-purposing of drugs designed primarily for heart diseases, for the treatment and prevention of AMD.

Provided by SingHealth