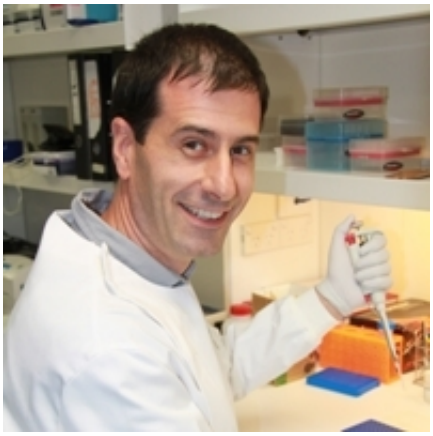
Gypsy study unravels a novel ataxia gene

August 17 2012



A WA study of an isolated population of Eastern European Gypsies known as "Bowlmakers" has unlocked clues about a serious developmental disease - congenital cerebellar ataxia.

Professor Luba Kalaydjieva and Dr Dimitar Azmanov, from The University of Western Australia, say the discovery of an important genetic mutation is likely to inspire other scientific work around the world.

The result of their research for the UWA-affiliated Western Australian Institute for Medical Research (WAIMR) was published online today in the prestigious American Journal of Human Genetics.

It involved working collaboratively with other Australian and European researchers to discover mutations within a gene which has never before been linked to this form of heredity ataxia in humans.

Ataxias are a large group of neurodegenerative disorders that affect the ability to maintain balance, and learn and maintain motor skills. While many genes have already been implicated in hereditary ataxias, understanding their molecular basis is far from complete. New knowledge will help the understanding of normal brain development and function, and the mechanisms of degeneration.

"Gypsies are a founder population," Professor Kalaydjieva said. "They are derived from a small number of ancestors and have remained relatively isolated from surrounding populations. The Bowlmakers - known for their wooden handicrafts such as bowls and spoons - were an ideal group to study because they are a younger sub-isolate, showing limited genetic diversity.

"We studied a novel form of ataxia in 3 families in this ethnic group. Clinical and brain-imaging investigations were done in Bulgaria, in collaboration with radiologists from Sir Charles Gairdner Hospital and Princess Margaret Hospital, and were followed-up by genetic studies at WAIMR and the Walter and Eliza Hall Institute (WEHI), Melbourne.

"Signs of ataxia were detected in early infancy when motor skills like crawling and rolling over did not develop. The affected individuals presented with global developmental delay, ataxia and intellectual deficit. MRI scans showed signs of degeneration of the cerebellum, which is part of the brain controlling motor and learning skills. Overall, the life expectancy is not decreased but the quality of life is severely affected.

"The parents of the affected individuals did not present with any clinical

symptoms of the ataxia, suggesting recessive inheritance," Dr Azmanov said. "Our genetic studies showed unique changes in the gene encoding metabotropic glutamate receptor 1 (GRM1), which is important for the normal development of the cerebellar cortex. The mutations inherited by all affected individuals from their unaffected carrier parents dramatically altered the structure of the GRM1 receptor."

Professor Kalaydjieva said the exact pathogenetic mechanisms leading to the clinical manifestations and cerebellar degeneration are yet to be explained and that this opens novel research avenues for the wider scientific community. "It also remains to be seen if other ataxia patients around the world carry mutations in GRM1," she said.

Provided by University of Western Australia