Australian leads search for genetic risk factors for alcohol-induced liver cirrhosis

A senior scientist at Royal Prince Alfred (RPA) Hospital has received a grant of $2.5 million over five years to undertake groundbreaking international research into Alcohol-induced Liver Cirrhosis (ALC).

Dr Devanshi Seth, at RPA’s Drug Health Services and the Centenary Institute, won the grant from the US National Institute on Alcohol Abuse and Alcoholism (NIAAA), part of the National Institutes of Health (NIH), an agency of the US Department of Health, to look at the genetic risk factors for liver cirrhosis due to alcohol.

Dr Seth said this was the first time such a large scale program, involving thousands of participants across six countries, had ever been undertaken.

“We still do not understand why only a proportion of moderate to heavy drinkers get liver cirrhosis. Nothing so far has been able to explain the unpredictability of why some people get cirrhosis and others who drink equal amounts don’t,” Dr Seth said.

“Apart from alcohol consumption, several contributory factors, including diet, lifestyle, mental health, viral infection and gender, influence the risk of developing cirrhosis.

“We hope that by analysing the genetics in a large international group comprising thousands of drinkers we can detect the genetic risks associated with ALC.”

Like other multi-factorial diseases, alcoholic liver cirrhosis is controlled by a number of genes, each of which makes a small overall contribution. Genetic searches have been inconclusive because the studies performed to date have generally been too small to yield definitive results.

Recent technological advances now enable researchers to simultaneously search for millions of changes in the DNA. By examining a large population with thousands of individuals, the genetic changes linked to cirrhosis can be uncovered.

Dr Seth formed the GenomALC Consortium to conduct this large study with Australian colleagues and clinicians and researchers from the USA, UK, Germany, Switzerland and France.

“I am really excited that some of the most eminent alcohol researchers from around the world are part of this collaboration, including Prof. Paul Haber from RPA, and our former RPA colleague Dr John Whitfield, currently at the Queensland Institute of Medical Research,” Dr Seth said.

“In Sydney, we will recruit 400-500 participants over the next three years through the clinics at four hospitals – RPA, Liverpool, Concord and Fairfield. Half our group will have cirrhosis and the other half, the control group, will have been heavy drinkers for 10 years but be free of liver disease.”
A pilot feasibility study for recruitment at these hospitals has already been undertaken through funding from Lion Nathan's Alcohol Health and Research Scheme.

“Alcoholic liver disease is a hidden epidemic, a silent disease that occurs after a long period of alcohol abuse, costing $3.8 billion per annum in Australia,” Dr Seth said.

“The lack of specific markers for diagnosis and effective treatment compound this burden. That is why this research is so important.”

While the disease has been predominantly seen among men over 50 years of age, it is becoming more frequent worldwide among younger adults and young women earlier.

“Surprisingly, little research has been undertaken in Australia, into the long term damage from alcohol,” Dr Seth said.

“We frequently look at the social costs to the community, such as violence and vehicle accidents, but we are not looking enough at the direct damage to the drinkers themselves. Health problems related to alcohol chronicity are often overlooked because alcohol is so culturally embedded in our society.”

Dr Seth leads several other projects on alcoholic liver disease in collaboration with Professors Paul Haber and Geoff McCaughan at the RPA and Centenary Institute.

Their group is one of few groups comprehensively addressing issues related to alcohol, ranging from genetics, to clinical, biomedical, molecular, mental health co-morbidities through to treatment approaches.

Dr Seth has had a strong and successful collaboration with the Centenary Institute since 2001. The Centenary Institute is an independent leader in medical research, affiliated to RPA and Sydney University. Its dedicated scientists conduct fundamental research to understand the work of the body’s genes, cells and proteins.