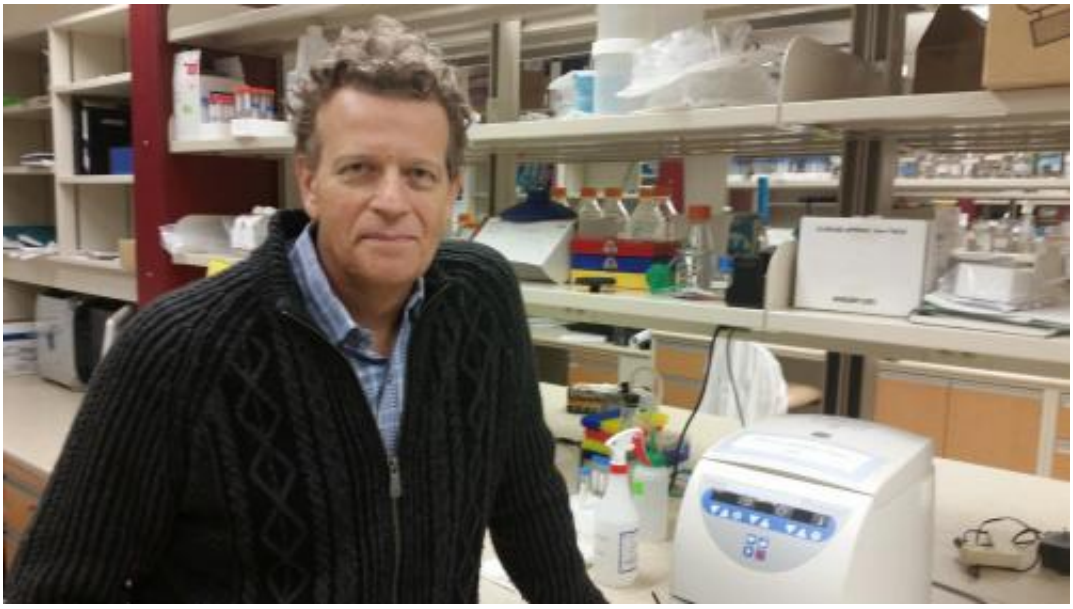
Researchers wind up a 40 year old debate on betaretrovirus infection in humans

February 19 2015, by Ross Neitz



Andrew Mason in his lab. Credit: Faculty of Medicine & Dentistry, University of Alberta

In a new study published in *Alimentary Pharmacology & Therapeutics*, researchers at the University of Alberta's Faculty of Medicine & Dentistry have shown that a betaretrovirus which resembles a mouse mammary tumor virus infects patients with the rare liver disease, primary biliary cirrhosis (PBC).

Using next generation sequencing, the team of scientists at the

University of Alberta along with colleagues at Beijing Genomics Institute, in Shenzhen, China, identified over 2,000 junction regions where the betaretrovirus DNA had inserted into the patient's genome. The demonstration of integration sites is considered a gold standard for detection of retroviral infection and the missing piece of the puzzle in the ongoing dispute of whether humans are susceptible to betaretrovirus infection.

The human betaretrovirus was first discovered in patients with primary biliary cirrhosis by the Andrew Mason laboratory in 2003 at the U of A. This rare form of autoimmune liver disease is found in one in 500 middle aged women and is also responsible for approximately 10 per cent of all liver transplant cases in Canada. PBC is currently considered autoimmune in nature because the majority of patients make antibodies to mitochondrial proteins. The demonstration of viral infection in the bile ducts of patients with PBC adds a new dimension to understanding what may cause the liver disease.

Andrew Mason, a professor in the Department of Medicine working with professor Gane Wong professor of Bioscience and Medicine at the University of Alberta teamed up to find the miniscule amounts of viral genomic sequence using next generation sequencing technology with the Beijing Genomics Institute. They extracted biliary epithelium cells from the liver and derived more than 1 million DNA sequences per sample. The intensive effort was required to prove viral infection in most patients at the site of disease.

"At least we have shown pretty convincingly that a human betaretrovirus infects patients with primary biliary cirrhosis," says Mason. "We had to do this because virologists don't think this betaretrovirus can infect humans due to negative studies in the 1970's when researchers tried to identify mouse mammary tumor virus in breast cancer patients."

Funders of the research believe the findings are encouraging.

"The Canadian Liver Foundation is pleased that its competitive research grant program has supported work that may provide new insights into the cause of autoimmune liver disease, especially primary biliary cirrhosis," says Eric Yoshida, chairperson of the Canadian Liver Foundation's Medical Advisory Committee. "As determining the cause is the key to developing rational new treatments, we hope that this work will translate into improved patient care in the future".

Mason is currently performing patient studies using antiviral therapy to see if it improves clinical outcomes in patients with primary biliary cirrhosis.

"We still have a long way to go to convince the medical community that our virus plays any role in triggering the liver disease process. Some of the anti-viral therapies useful for viral hepatitis and HIV have some effect in our patients with primary biliary cirrhosis but we need to show this in the proper setting of a randomized controlled trial."

Provided by University of Alberta Faculty of Medicine & Dentistry