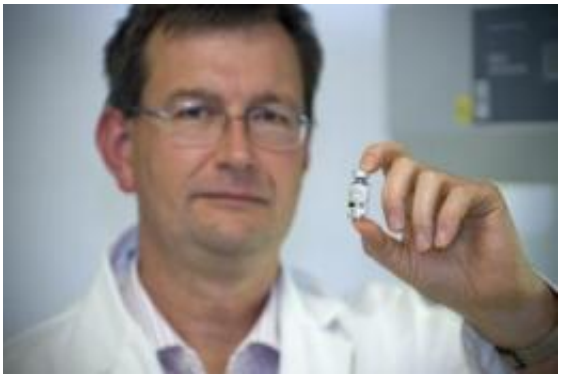
Toxic trio identified as the basis of celiac disease

July 21 2010



Professor Bob Anderson from the Walter and Eliza Hall Institute in Melbourne, Australia, has identified the three protein fragments that make gluten -- the main protein in wheat, rye and barley -- toxic to people with celiac disease. His discovery opens the way for a new generation of diagnostics, treatments, prevention strategies and food tests for people with celiac disease. Credit: Czesia Markiewicz, Walter and Eliza Hall Institute

Walter and Eliza Hall Institute scientists have identified the three protein fragments that make gluten - the main protein in wheat, rye and barley - toxic to people with coeliac disease.

Their discovery opens the way for a new generation of diagnostics, treatments, prevention strategies and food tests for the millions of people worldwide with coeliac disease.

When people with coeliac disease eat products containing gluten their body's immune response is switched on and the lining of the small intestine is damaged, hampering their ability to absorb nutrients. The disease is currently treated by permanently removing gluten from the patient's diet.

Dr Bob Anderson, head of the Walter and Eliza Hall Institute's coeliac disease research laboratory, said it had been 60 years since gluten was discovered to be the environmental cause of coeliac disease.

"In the years since, the holy grail in coeliac disease research has been to identify the toxic peptide components of gluten; and that's what we've done," Dr Anderson said.

The research, done in collaboration with Dr Jason Tye-Din, Dr James Dromey, Dr Stuart Mannering, Dr Jessica Stewart and Dr Tim Beissbarth from the institute as well as Professor Jamie Rossjohn at Monash University and Professor Jim McCluskey at the University of Melbourne, is published in today's issue of the international journal *Science Translational Medicine*.

The study was started by Professor Anderson nine years ago and has involved researchers in Australia and the UK as well as more than 200 coeliac disease patients.

The patients, recruited through the Coeliac Society of Victoria and the Coeliac Clinic at John Radcliffe Hospital, UK, ate bread, rye muffins or boiled barley. Six days later, blood samples were taken to measure the strength of the patients' immune responses to 2700 different gluten fragments. The responses identified 90 fragments as causing some level of immune reaction, but three gluten fragments (peptides) were revealed as being particularly toxic.

"These three components account for the majority of the immune response to gluten that is observed in people with coeliac disease," Dr Anderson said.

This knowledge has already been used by Melbourne-based biotech company, Nexpep Pty Ltd, to develop a 'peptide-based' immunotherapy that aims to desensitise people with coeliac disease to the toxic effects of gluten. Nexpep's Phase 1 trials of the therapy were completed in June and final results are expected in coming months.

The immunotherapy works by exposing people with coeliac disease to small amounts of the three toxic peptides and is based upon the same principles as desensitisation for allergies.

Dr Anderson said although coeliac disease could be managed with a gluten-free diet, compliance with the diet is often challenging and nearly half the people on the diet still have residual damage to their small intestine. "Consequently, the immunotherapy and three other drugs are under development to help people with coeliac disease."

Provided by Walter and Eliza Hall Institute