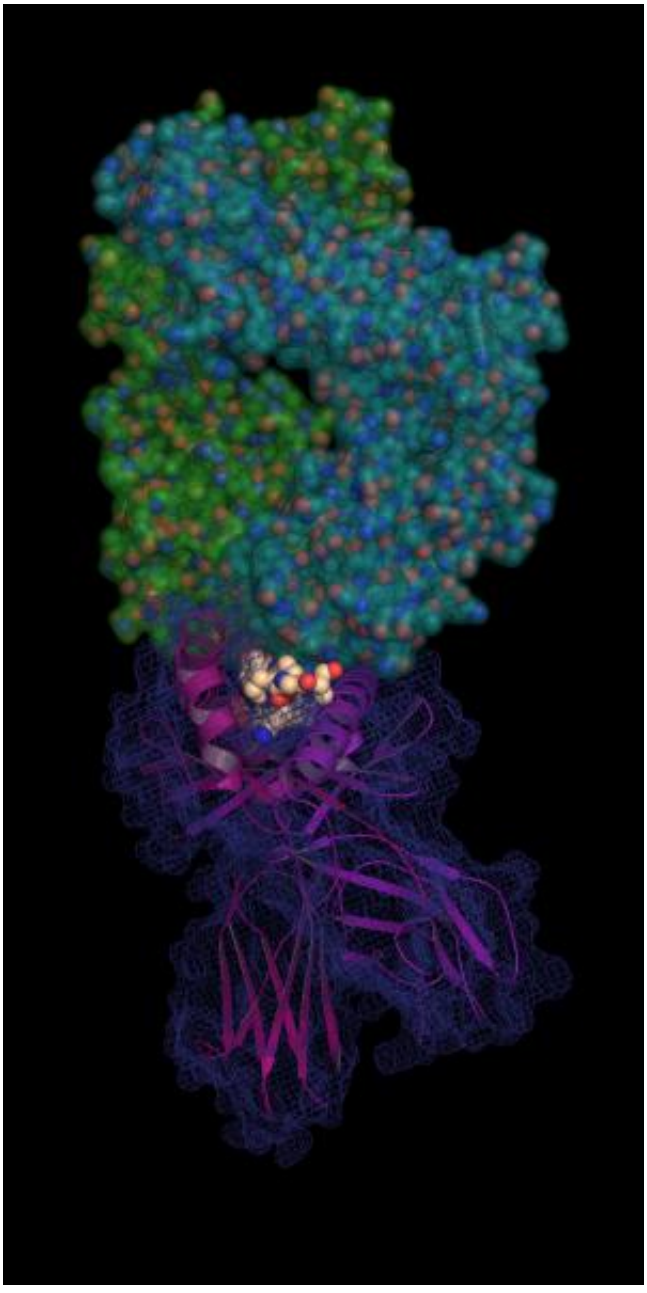
The molecular heart of celiac disease revealed

April 29 2014



Australian, US and Dutch researchers have determined the molecular details of the interaction between the immune system and gluten that triggers celiac disease. Their work opens the way to potential treatments and diagnostics.

Monash, Melbourne and Leiden university researchers, in collaboration with colleagues from a Boston-based company, have described the molecular basis of how most of the immune cells (T cells) that induce celiac disease lock onto gliadin, a component of gluten, thereby triggering inflammation of the lining of the small intestine. This is what gives many celiac sufferers symptoms similar to food poisoning after eating a slice of toast.

"We studied how different T cells bind to gliadin, a component of gluten. And when we looked closely we found the docking mechanism was similar. This provides us with a way to develop drugs that might reduce or turn off the immune response," says Dr Hugh Reid of Monash University. Dr Reid and fellow Australian-based researchers collaborated in the study with Prof Frits Koning from the Leiden University Medical Center in the Netherlands and with US company, ImmusanT.

Celiac disease is an immune system intolerance of gluten, a protein which occurs naturally in grains such as wheat, rye, barley and oats, and therefore is typically found in bread, pastries and cakes. The problem is that certain immune system T cells regard gluten as a foreign and potentially toxic substance, and initiate action against it. This inflammatory process is triggered when these T cells bind to gliadin.

Today's paper, published in *Nature Structural and Molecular Biology*, explains what's happening in the overwhelming majority of celiac

disease sufferers, the ninety-five percent who carry a gene for the particular protein, HLA-DQ2. In 2012, the research team found a similar trigger for the other five per cent who have HLA–DQ8, another celiac disease susceptibility gene.

With the assistance of the Australian Synchrotron, the researchers were able to determine the structure of the molecular complexes that form during the interaction between T cell receptor and gliadin. Armed with this information, they were able to work out what was important in the T cell response.

"This research is a classic example of what the new Australian Research Council Centre of Excellence in Advanced Molecular Imaging strives to achieve," says Prof Rossjohn from Monash University, "Using the latest imaging tools – from microscopes to the synchrotron – we can understand and influence the immune recognition events that trigger immune responses, both good and bad."

Ultimately, the insight provided by the research will assist the development of a blood test and a therapeutic vaccine for patients with celiac disease who carry the gene HLA-DQ2.

More information: "T-cell receptor recognition of HLA-DQ2–gliadin complexes associated with celiac disease." Jan Petersen, et al. *Nature Structural & Molecular Biology* (2014) DOI: 10.1038/nsmb.2817. Received 12 February 2014 Accepted 28 March 2014 Published online 28 April 2014

Provided by Science in Public