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AREA OF EXPERTISE: Molecular immunology, antibody engineering
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DISSERTATION TITLE: *Engineering TCR-like antibodies*

Monoclonal antibodies are widely used research tools and an increasingly successful class of drugs. In this work, Rahel Frick and colleagues engineered “TCR-like” monoclonal antibodies that bind to gluten complexes on the surface of immune cells in celiac disease. A combination of “phage display” technology and computational methods led to the isolation of antibodies that bind strongly and specifically. The antibodies were then used to study the mechanism of celiac disease maintenance and were also found to be promising for therapeutic intervention.

Antigen presenting cells are part of the immune system and display protein fragments (peptides) on their surface for T cells. In celiac disease, the T cells launch an immune response to gluten protein fragments that leads to inflammation of the small intestine. The interaction between T cells and gluten on antigen presenting cells is therefore an important step in celiac disease maintenance. Frick and colleagues used the gluten-specific antibodies to analyze patient biopsies and found that plasma cells are the most important class of antigen presenting cells that display gluten there. This was surprising, as plasma cells are not normally regarded to be antigen presenting cells. Furthermore, these antibodies have shown potential to prevent the activation of T cells, which could be the basis for a new form of treatment. Frick and colleagues also studied the receptors on T cells that respond to the gluten complexes in celiac disease. They found that some of the disease-causing T cell receptors have characteristics that make them bind to gluten complexes particularly well.

In summary, the antibodies engineered in this work, are powerful tools for studies of celiac disease and possibly the basis for a new form of treatment.