Enzyme Allows Those With Celiac Disease To Consume Gluten

University of Washington

While gluten is difficult for all human digestive enzymes to break down, it is especially so for people with celiac disease. For people with celiac disease, gluten catalyzes an inflammatory response, causing symptoms ranging from intense abdominal pain, damage to the intestines, osteoporosis, and nutritional deficiencies to an increased incidence of lymphoma. The chronic condition affects about 2.4 million people in the United States and 1 in 100 people globally, making it more common than inflammatory bowel disease.

Celiac disease is triggered by an autoimmune reaction to the digestion of gluten, a protein found abundantly in wheat, rye, and barley. The only treatment for celiac disease has been a complete exclusion of gluten. For many patients, adopting a gluten-free diet is costly and difficult to maintain given the ubiquity of bread products, which increases the probability of accidental ingestion. Therefore, more than 60% of celiac patients on a gluten-free diet still experience symptoms due to accidental gluten ingestion.

PvP Biologics, a startup from the Institute for Protein Design (IPD) of the University of Washington (UW), began in 2011. A group of undergraduate students used Foldit, an online software, to design proteins with the potential to process gluten in the stomach's highly acidic environment. The team identified a promising protein, redesigning it to target gluten for degradation.

The team developed the protein into an oral enzyme. The enzyme, which PvP Biologics named KumaMax, is a computationally engineered super glutenase that completely breaks down gluten in the stomach. This prevents gluten from entering the intestine altogether, avoiding an inflammatory response.

PvP Biologics was launched through CoMotion, the collaborative innovation hub dedicated to expanding the societal impact of the UW community. By developing and connecting local and global innovation ecosystems, CoMotion assists innovators with achieving the greatest impact from their discovery. The project benefited from several CoMotion resources in its early years; through CoMotion, PvP was able to select a great leadership team with specific experience in developing and partnering gastrointestinal (GI) drugs. As part of that, PvP was able to secure a partnership with Takeda, which provided $35 million in funding for research through Phase 1 clinical studies.

The Phase 1 clinical trial successfully demonstrated safety and tolerability of orally administered KumaMax and confirmed the gluten-degrading activity in participants' GI tracts in healthy patients and those with celiac disease. Takeda, which acquired PvP in 2020 for $330 million, is now conducting a Phase 2 clinical trial, designed to test the enzyme's ability to reduce symptoms and limit intestinal damage against a placebo. This trial involves using KumaMax in patients with uncontrolled celiac disease on a gluten-free diet.

Scientists at IPD believe KumaMax has the potential to provide complete protection from gluten, offering a new treatment for people who have celiac disease. Takeda lists KumaMax as part of its "wave 2" of experimental drug candidates, which it expects to launch in 2025 or after.

This story was originally published in 2024.