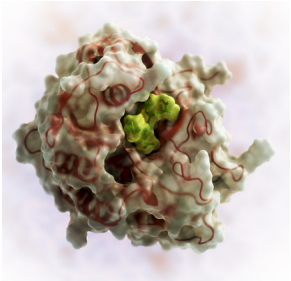
# KUMAMAX AND THE FUTURE OF CELIAC DISEASE

## *At the UW Institute for Protein Design*



A rendering of the KumaMax molecule. Visual: Vikram Mulligan.

### Origin Story: Students and KumaMax

It all started with the 2011 iGEM project — the International Genetically Engineered Machine competition, which attracts academic teams worldwide to design, build and test new biological systems or molecules. Several students on the University of Washington's team had friends with celiac disease, and they decided to build a stomach-active, gluten-busting protease. The students used Foldit, an online game that allows players to manipulate on-screen protein puzzles, to engineer an enzyme known to work at a low pH. They redesigned it to target gluten for degradation, named it KumaMax, produced it in the lab to show it worked, and won the grand prize at MIT in a field of 165 teams.

CELIAC DISEASE (CD), which occurs in genetically susceptible people, prompts the immune system to mount an inflammatory response to dietary gluten. CD is a serious illness: it's characterized by intense abdominal pain and malnutrition-related disorders such as anemia, osteoporosis and infertility, and it afflicts between 1–2 percent of the global population, including 2–3 million Americans. The only treatment is complete exclusion of gluten — a type of protein found in wheat, barley and rye — from the diet.

Excluding gluten from the diet requires intense vigilance, since the protein is ubiquitous in modern food production. Even so, more than 60 percent of celiac patients on a gluten-free diet still experience disease symptoms due to accidental gluten ingestion. And in addition to the suffering inflicted by the disease, it's a costly burden for society to bear. In the U.S. alone, it's estimated that annual healthcare costs related to CD fall between $15 billion to $35 billion, and diagnoses are on the rise.

Despite a clear medical need, no medical therapy for celiac disease is available. However, hope is on the horizon — thanks to researchers at UW Institute for Protein Design, who are advancing a promising new therapy called KumaMax.

### *Finding the Right Route to a Cure*

When food enters the stomach and intestines, digestive enzymes called proteases break down proteins into nutrients that the body can absorb. Gluten is a difficult protein to break down, and human proteases only partially digest it. When incompletely digested gluten fragments enter the intestines of people with celiac disease, the fragments set off an inflammatory immune response.

Many experts believe that the most effective way to treat this disease would be to develop a pill containing proteases that can do what human digestive proteases can't: break down gluten in the stomach before it can enter the intestine and cause an immune response. Taken with meals, this oral protease therapy would break down the gluten before it could cause a chain reaction in people with celiac disease.

### *A More Effective Approach: KumaMax*

Most naturally occurring proteases lack one or both of the two essential characteristics of an optimal celiac therapeutic: effectiveness in the stomach and the ability to break down gluten.

Researchers at the IPD overcame this problem by using a different approach. Starting with a protease that is active and stable in the harsh acidic stomach conditions, they computationally engineered and modified this protease to target the problematic regions of the gluten protein and break it down. **This protease, called KumaMax, is significantly more effective in stomach conditions than the non-engineered protease combination now in clinical trials.**

### *The Next Steps*

Scientists at the IPD think that KumaMax has the potential to provide complete protection from gluten, and their goal is to make this treatment available to people who suffer from celiac disease as quickly as possible.

The next two steps are to assess the efficacy of KumaMax in animal models and to determine its safety profile — both required by the FDA to secure approval for clinical trials in patients with celiac disease. If this research is successful, scientists hope to begin human clinical trials in two years.

### *For More Information*

If you would like to learn more about the UW Institute for Protein Design's work in KumaMax, please contact Katherine Cardinal, MBA, senior director for philanthropy at 206.616.0412 or cardinal@uw.edu.

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