AMYRA Biotech AG
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AMYRA Biotech—Solutions for gluten-related disorders

AMYRA Biotech is ready to partner and scale-up its novel enzymatic treatments for non-celiac gluten sensitivity, and celiac disease.

In recent years, public awareness of gluten-related disorders has become universal. Non-celiac gluten sensitivity (NCGS) and celiac disease (CeD) are two clinically distinct gluten-related disorders that constitute a major public health issue.

During the digestion of gluten, relatively long fragments of digestion-resistant, proline-rich peptides are formed. These peptides, known as gluten immunogenic peptides (GIPs), are resorbed into the body in the gastrointestinal tract. In people who have CeD or are affected by NCGS, however, GIPs trigger inflammatory immune responses that cause a wide array of symptoms.

CeD is the most severe gluten-related disorder, in which GIPs activate the adaptive immune system and trigger autoimmune responses that damage the intestinal villi and cause diarrhea, bloating, vomiting, abdominal pain and other symptoms. If left unchecked, CeD can lead to more severe complications such as malnutrition, osteoporosis, and gastrointestinal cancer.

Although the pathogenesis of NCGS is less well understood, there are significant symptomatic overlaps with CeD. Evidence suggests that GIPs play a major role in triggering NCGS by activating the innate immune system, typically causing gastrointestinal problems, mental fog, chronic fatigue and psychological and neurological disorders.

In western populations, the prevalence of CeD is roughly 1%, and for NCGS between 4% and 6%. Combined, CeD and NCGS are responsible for compromising the health and wellbeing of an enormous segment of the population, yet no effective pharmacological treatments exist for either condition. To date, the only way patients can mitigate their symptoms is via strict adherence to a gluten-free diet. However, the inescapable presence of gluten in food (and even non-food products, such as lipstick) makes gluten avoidance impossible for many people. Unintentional intake through gluten cross-contamination or failure to rigorously follow the gluten-free diet limits the efficacy of the gluten-free 'remedy'.

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> Werner Tschollar, CEO and President, AMYRA

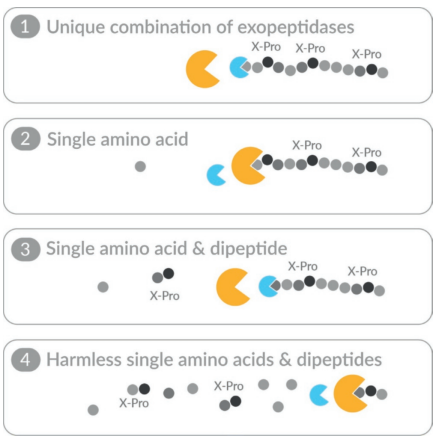

Fig. 1 | The mode of action of AMYRA's exopeptidases. AMYRA's unique and synergistic exopeptidases are able to degrade proline-rich peptides—which are immunogenic for celiac disease and non-celiac gluten sensitivity patients—but remain stable to degradation by naturally occurring digestion enzymes.

Breaking chains of gluten-immunogenic peptides

Enter AMYRA Biotech AG, a private Swiss company that has developed novel enzymatic solutions for both NCGS and CeD via a unique combination of recombinant exopeptidases that destroy the immunogenic structure of GIPs. The proprietary and patented enzymes work synergistically, cleaving GIPs at different motifs and rapidly converting them into harmless single amino acids and dipeptides that do not activate the immune system (Fig. 1). Furthermore, AMYRA has specifically formulated the exopeptidases to maximise their clinical efficacy. "Our data show that it takes just a couple of minutes to entirely destroy the toxic structure of GIPs" said Werner Tschollar, AMYRA's CEO and president.

AMYRA's enzymes—the only known exopeptidases to completely degrade GIPs—were originally identified in a fungus that cleaves proline-rich peptides and the structural proteins of toenails. In collaboration with Lonza, AMYRA created and screened a series of non-toxic production strains to identify combinations of recombinant enzymes capable of degrading GIPs. The results gave rise to the company's two lead products: AMY01, a dietary supplement that should alleviate symptoms of NCGS; and AMY02, a prescription drug candidate for treating CeD. The idea is that both are administered in conjunction with a gluten-free diet, to eliminate the traces of GIPs arising from accidental consumption of gluten.

AMYRA's products have been preclinically validated with promising results. Findings from an extensive in vitro proof-of-concept study show that small amounts of AMY01 degrade GIPs into dipeptides and single amino acids with unprecedented efficiency. This in vitro efficacy has been augmented by extensive toxicology studies showing that the enzymes are neither systemically resorbed nor pharmacologically or metabolically active inside the body. As a result, AMY01 avoids regulatory drug classification and is subject to a faster approval process. AMY01 is currently undergoing an application known as 'generally recognized as safe,' which will significantly accelerate its development as a dietary supplement for NCGS. Testing in healthy volunteers will begin imminently and the product is expected to be on the market in the United States by mid-2021.

Meanwhile, proof-of-concept studies, to evaluate the potential of AMY02 as a prescription drug for treating CeD, is scheduled to begin by mid-January 2021; AMY02 is expected to demonstrate high efficacy, given its favorable GIP cleavage properties.

Open for partnering

AMYRA's dual commercialization strategy significantly mitigates development and investment risks and offers multiple partnership opportunities. In vitro and preclinical data suggest a high probability of development, regulatory and commercial success; the company is open to selling, partnering or out-licensing AMY01 with a global consumer health company or food multinational, and is simultaneously keen to collaborate with a big pharma to finalise the development of AMY02 as a CeD treatment. "CeD and NCGS currently pose a huge medical need" said Tschollar. "AMYRA's products target the trigger of gluten-related disorders and promise to provide safe and effective treatments that can improve the quality of life of millions of people around the world."

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