Mapping of Gluten T-Cell Epitopes in the Bread Wheat Ancestors: Implications for Celiac Disease

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Celiac disease is a multifactorial disorder that affects children and adults with high prevalence. It is characterized by an inflammatory response to ingested wheat gluten proteins. Both classes of gluten proteins, gliadins and glutenins, contain peptides that can bind DQ2 or DQ8 and be recognized by intestinal T cells, but their relative importance differs. Peptides derived from α-gliadins are recognized by T cells from almost all celiac patients, whereas T-cell responses to γ-gliadins and glutenins are much less frequent. This hierarchy probably reflects that certain α-gliadin (αG) proteins contain a stable 33mer fragment that contains a cluster of epitopes. This αG-33mer fragment is naturally formed by digestion with gastric and pancreatic enzymes, it binds well to DQ2 after deamidation by tissue transglutaminase (TG2), and it is recognized much more effectively by intestinal T-cell lines than shorter peptides covering the DQ2-α-I, -α-II, and α-III epitopes. Until now, Celiac disease is treated by excluding all gluten proteins from the diet. Conceivably, a diet based on baking-quality gluten from a wheat species that expresses no or few T-cell stimulatory gluten peptides should be equally well tolerated by the celiac patients and, importantly, also be beneficial for disease prevention.

To identify baking quality, harmless wheat, the authors followed the evolution of the wheat back to the species that most likely have contributed the AA, BB, and DD genomes to the bread wheat. Gluten were extracted from a large collection of these ancient wheat species and screened for T-cell stimulatory gluten peptides.

The authors found, that the relative contribution to the overall immune reactivity of gluten differs widely between the AA, BB, and DD genome-encoded gliadin proteins. Especially the fragments identical or equivalent to the immunodominant 33mer fragment are encoded by α-gliadin genes on the wheat chromosome 6D and thus absent from gluten of diploid einkorn (AA) and even certain cultivars of the tetraploid (AABB) pasta wheat. Furthermore, pronounced differences in the expression of the various γ-gliadin T-cell epitopes are noted between individual AA genome cultivars.

These findings have implications for celiac disease because they raise the prospect of identifying or producing by breeding wheat species with low or absent levels of harmful gluten proteins.