larger proportion of patients than just those who carry a genetic variant," said Hakonarson.

For their studies, the researchers will use automated technology from Illumina Inc, in San Diego, that can process more than 200 patient blood samples per day and simultaneously analyze more than 550 000 genetic variants for each sample. Once this "BeadLab" is installed this summer, the hospital will have one of the largest genotyping programs in the world, said Hakonarson. He added that other collaborations will be sought once the project gets under way. "We would obviously want to make sure that whatever we generate, if it's new, novel, and could constitute a better therapy or better diagnostic, that somebody then takes that forward."

LONG-TERM GOALS

In studying the genes involved in complex diseases, Hakonarson sees a considerable benefit in studying children, as opposed to adults. "The key benefits are that the traits that you're studying are cleaner in children because they haven't had that age-dependent effect over time," he said. "So from that standpoint, we will have more power to detect genetic variants that contribute to conditions."

Ultimately, the investigators hope to identify predictive diagnostic markers that can be applied to all children. In addition, the findings could lead to the development of diagnostic and therapeutic agents for both children and adults.

Tailoring treatments to individuals' genetic profiles is still in the early stages of development, said Hakonarson. It is hoped that such targeted therapies will lead to customized treatments based on genetic information from each individual patient. While ethical issues arise when banking genetic information about patients, many note that such data are critical to improving medicine and that proper safeguards can protect individuals' rights and privacy. □

Enzymes Might Cut Celiac Symptoms

Bridget M. Kuehn

PATIENTS WITH CELIAC DISEASE MAY one day have a treatment that will help them digest hidden gluten in foods or allow them to enjoy a somewhat less restrictive diet.

Between 0.5% and 1% of individuals in the United States and Europe are believed to have celiac disease, and their inability to digest gluten protein in wheat and other grains may lead to serious gastrointestinal tract complications (van Heel DA and West J. *Gut*. 2006;55:1037-1046). Complications of celiac disease may include malnutrition, anemia, cancer, osteoporosis, and poor pregnancy outcomes.

Currently, the only treatment for patients with celiac disease is complete exclusion of foods such as breads, pastas, and many processed foods that contain gluten. Doing so is difficult, however, because gluten is ubiquitous and may not be listed as an ingredient in many food products. But recent research suggests that oral formulations of enzymes that are able to break down gluten may be a useful adjunct treatment to dietary restriction or may allow a somewhat less restrictive diet for patients with the disease.

In a trio of articles published in June, Chaitan Khosla, PhD, at Stanford University in Palo Alto, Calif, and colleagues presented evidence that suggests that a cocktail of enzymes might be a useful therapy for celiac disease. The scientists targeted components of gluten, structures consisting of proline and glutamine, that gut enzymes are unable to break down. Previously, scientists had identified bacterial prolyl endopeptidases (PEPs) as enzymes that might be useful in reducing the toxic effects of gluten because they cleave proline structures and can function in the duodenum.

Khosla and colleagues identified a second enzyme EP-B2, a glutamine-specific cysteine protease found in barley that is active under gastric conditions and could complement the activity of a PEP by cleaving glutamine (Bethune MT et al. *Chem Biol*. 2006;13:637-647). They demonstrated that the combination of EP-B2 and a PEP in concert with gut enzymes could break down the problematic components of gluten under conditions mimicking those of the gastrointestinal tract (Siegel M et al. *Chem Biol*. 2006;13:649-658). Finally, they demonstrated the ability of EP-B2 to help break down gluten in the rat gut (Gass et al. *J Pharmacol Exp Ther*. doi: 10.1124/jpet.106.104 [published online ahead of print June 6, 2006]). The group had previously shown that PEP could help break down gluten in the rat gut (Piper JL et al. *J Pharmacol Exp Ther*. 2004;311:213-219).

"By adding glutamine- or proline-specific enzymes to the existing protease armamentarium [of the gut] you could make gluten as easy to digest as milk or meat," Kola said.

Khosla said the next step will be launching clinical trials of EP-B2 in humans to understand how it would function in the human gastrointestinal tract, whether it would be safe, and how much it might help patients with celiac disease.

Currently, the physician's role in managing celiac disease often ends when they provide a diagnosis and refer the patient to a dietician, Khosla explained. However, an oral therapy that would be used in combination with dietary restriction could give physicians a tool to help improve outcomes for patients, he said. □