Mining the 'wisdom of crowds' to attack disease

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Crowdsourcing, the act of contracting out problems to large groups rather than tapping individual experts, has solved puzzles in fields such as marketing, engineering and computer software. But can the wisdom of crowds help cure disease?

A large, multidisciplinary panel has recently selected 12 pioneering ideas for attacking Type 1 Diabetes, ideas selected through a crowdsourcing experiment called the Challenge in which all members of the Harvard community, as well as members of the general public, were invited to answer the question: What do we not know to cure Type 1 Diabetes?

"We wanted to ask the entire Harvard community—faculty, students, and administrators and staff of all levels and specialties—to share their 'out of the box' questions and proposals for this challenge, regardless of whether they had the expertise or resources to answer the question," said Harvard Catalyst Director and HMS Dean for Clinical and Translational Research Lee Nadler. "We wanted the participants to apply their insights to a problem that may not have been in their academic or intellectual domain."

Among these winners are a patient, an undergraduate student, an MD/PhD student, a human resources representative, and researchers who are not experts in the field.

Out of 190 entries, 12 were chosen. Each of the winners, who will be formally announced in a ceremony held at Harvard Medical School on

September 28, will receive a prize of $2,500. Working with the Leona M. and Harry B. Helmsley Charitable Trust, Harvard Catalyst plans to solicit research proposals from within the Harvard research community on some or all or the winning questions.

In a letter to the Harvard University community at the Challenge's launch in February, Harvard President Drew Faust expressed her hope that "such broad outreach, will help stimulate innovative thinking and potential new understandings and therapies," wishing that "in the spirit of this novel project, we will continue to multiply the means to connect the remarkable people and ideas across Harvard in imaginative and powerful ways."

Apart from the potentially revolutionary submissions from the community, the Challenge, in which Harvard collaborated with InnoCentive, provides evidence that finding new and innovative ideas for tackling disease is itself an act of innovation. "The Challenge was an exercise in tapping the knowledge of the widest possible community and encouraging the formation of new teams and new forms of collaboration around a specific topic area," says Dana-Farber Cancer Institute's Eva Guinan, MD, director of the Harvard Catalyst Linkages program and one of the Challenge's co-leaders.

According to research by Challenge co-leader Karim Lakhani, PhD, an assistant professor at Harvard Business School, innovation contests like this one can help reveal and foster unexpected and novel solutions to vexing scientific problems. "Open innovation is an effective way to solve scientific problems in the business world."

The Challenge was part of an American Recovery and Reinvestment Act (ARRA)-funded effort by Harvard Catalyst and InnoCentive to investigate whether new approaches employed in the private sector for sparking new research directions and collaborations might be useful in

the academic healthcare community.

The winners and their ideas

- Anonymous: The Diabetes Triangle: A systematic approach to align diabetes classification with diabetes management
  A new way of looking at diabetes by the numbers. Is there a better way of classifying diabetes than "type 1" and "type 2?" This winner, a patient with an uncommon form of diabetes and who wished to remain anonymous, thinks there is: A new scale—the Diabetes Triangle—that would use three simple measures to classify diabetes in a much more fine-grained, personalized way. This easy-to-use scale would help patients, and their doctors, better understand their disease and the steps they need to take to control it.

- Megan Blewett: Lipid Autoreactivity in Type 1 Diabetes: Clue to Etiology, Co-Occurrence, and Drug Discovery
  Diabetes chemistry 101. Even though diabetes medications are essentially chemicals, we don't know much about the chemistry underlying the development of diabetes. Harvard College undergraduate chemistry major Blewett suggests that studying diabetes diabetes - and in particular how, in the context of diabetes, the immune system interacts with molecules called lipids - from a chemical perspective could yield new insights into the diabetic process and new strategies for treatment.

  "I first heard about the Challenge through the campus-wide email sent by President Faust," said Blewett. "I was drawn to the fact that the challenge promised to create a dialogue spanning scientific disciplines and based on the merit of people's ideas. Opportunities like this are extremely rare."

- Kevin Dolan, MS: Type 1 Diabetes, Patient Maintenance and Care
  Keeping a constant eye on blood sugar. The current crop of implanted insulin pumps do their job by keeping constant track of the amount of glucose in the fluids that bathe our cells, a kind of proxy method for tracking blood sugar. Dolan, who works in Human Resources at HMS and who has Type 1 Diabetes, suggests that a new generation of pumps that sample blood sugar directly could help improve patients' quality of life and blood sugar control, consequently bringing overall health care costs down.

  "Type 1 Diabetes is a complicated disease that requires one to be thinking constantly about what he/she eats, what his/her exercise level has been or needs to be, what his/her blood sugar level is at, and knowing if it rising or falling," said Dolan. "Despite all that, it is not a disease that prevents someone from being successful in whatever endeavor they choose to pursue. I felt providing the perspective to Challenge of someone who deals with Type 1 Diabetes on a daily basis would help researchers as they pursue improved diabetes care management and eventually a cure."

- Mark Feinberg, MD: Synergistic System Targeting for Type I Diabetes
  Taking a multi-pronged approach. Which is better: to treat the root causes of diabetes from one direction at a time, or from multiple directions at once? Feinberg favors the latter. He suggests that a better understanding of how different parts of the immune system affect the pancreas in diabetes would allow for the development of tools capable of targeting those parts simultaneously.

"I had two recent 'jolts' that motivated me to take part in the contest," said Feinberg, a cardiologist at Brigham and Women's Hospital. "First, I recently had a patient with long-standing Type 1 Diabetes who, despite his and his doctors' best efforts, was suffering the end-stage effects of his disease. The second was the news that a very young family member of mine had just been diagnosed with Type 1 Diabetes. This prompted me to think about my own research endeavors and whether some of the things I've been studying could be applicable to this disease."

- David Friedman, MD: A Quiet Role for Platelets and Eosinophils in Pathogenesis of Type 1 Diabetes?
  Roles for other immune cells in diabetes? The discussion about immunity in Type 1 Diabetes usually focuses on T-cells. But the immune system has many, many more components. Beth Israel Deaconess Medical Center nephrologist Friedman wants to know whether these other parts, including, for example, cells and proteins involved in the body's response to allergens and parasites, might also play roles in the development of diabetes.

  "In thinking about the Challenge, I wanted to connect immunity and autoimmunity through the lens of genetics," Friedman explained. "There are ideas that would generally be considered too speculative for funding through typical channels."

- Jason Gaglia, MD: In depth analysis of T cell repertoire during the development of type 1 diabetes in pancreatic islet infiltrating and peripheral CD4 T cells
  The T-cell as a window on diabetes development. What can immune system T-cells tell us about the origins of diabetes? Gaglia, an endocrinologist in the Pathology Department at HMS,

suggests quite a bit. He proposes using T-cells in the blood as a view into what's going on in the pancreas of patients with diabetes. This approach could help lead to new, targeted treatments, or to ways of measuring whether treatments are working.

"The Challenge gave me an opportunity to think globally about approaches to diabetes, as opposed the niche my research has focused on," Gaglia commented. "It has helped me explore aspects of my field and related fields that are removed from my current research."

- Danwei Huangfu, PhD: A cell-electronic approach to insulin therapy
  Merging Biology and Engineering. Where should we look for the next generation of blood sugar monitors? Our own bodies. Eons of evolution have fine-tuned our beta cells to sense blood sugar levels and secrete insulin accordingly, in precisely the right amounts. Huangfu, a postdoctoral fellow at Harvard University, proposes linking beta cells of the pancreas to an electronic insulin pump, establishing a new paradigm for diabetes control.

  "I am preparing to start my own laboratory, and looked at the Challenge as an opportunity to identify novel research directions," said Huangfu. "But I realized that my own research had become more focused on the cells destroyed by diabetes than on the disease itself. Thinking through my submission has, in the end, made me more conscious of Type 1 Diabetes as a disease."

- Carols Mendivil-Anaya, MD: Integral treatment of type 1 diabetes using smart liposomes

Make "smart" treatments for diabetes. The current methods of taking diabetes medications—by mouth or by injection—allow these drugs to spread throughout the body. Mendivil-Anaya, an endocrinologist from Colombia in a doctoral program at Harvard School of Public Health, suggests using microscopic spheres (called "smart liposomes") studded with proteins that can dial down the immune attack against the beta cells in people with Type 1 Diabetes to carry drugs directly to the pancreas, giving them extra targeted punch.

"I have seen the trials and tribulations of many Type 1 Diabetes patients as they moved from childhood into adolescence and adult life," said Mendivil-Anaya. "This has made the human face of diabetes is very familiar and very close to my heart."

- Dirk Moore, PhD: Family-based Association Studies to Identify Gene-Environment Interaction and Genomic Imprinting in Type 1 Diabetes (T1D)
  Probing the "nature vs. nurture" question. How do genes and environment mix in the development of diabetes? A biostatistician at the University of Medicine and Dentistry of New Jersey, Moore believes that by re-analyzing genetic studies using new statistical techniques, it may be possible to tease apart their relative roles in ways that lead to better tools for controlling or preventing diabetes.

  "I have taken part in InnoCentive challenges in the past," said Moore, "and when I saw the Ideation Challenge posting, I realized that some of the family-based population study designs that I have worked with in other fields could be applicable to important questions in Type I diabetes."

- Matthew Meyerson, MD, PhD; Sally Kent, MD, PhD; David Hafler, MD; Joonil Jung PhD; Alex Kostic; and Akinyemi I. Ojesina, MBBS, PhD: Hunting for microbial genomes in type 1 diabetes by next-generation sequencing
  A germ theory for diabetes. Viruses like to leave little bits of genetic baggage behind. This team of researchers from the Broad Institute of MIT and Harvard, Dana-Farber Cancer Institute, the University of Massachusetts Medical Center, and Yale School of Medicine to find out whether viruses or other microbes might play some part in triggering diabetes by looking for signs of this baggage in the genes of people with diabetes.

- James Mulvihill, DMD: Development of a non-invasive blood glucose monitor
  Measuring blood sugar without the blood. For patients with diabetes, keeping close track of their blood sugar means a lifetime of painful needle pricks or an implanted glucose pump. Mulvihill, a former president and CEO of both The Forsyth Institute and the Juvenile Diabetes Research Foundation, wants to know whether it's possible to develop a blood glucose sensor that works without actually having to break the skin.

  "My motivation to respond to the challenge came from my knowledge of what an important advance it would be in the care of individuals of all ages with both Type 1 and Type 2 diabetes, if a reliable methodology to monitor blood glucose non-invasively could be developed," Mulvihill said. "My knowledge comes from having a child who 20 years ago was diagnosed with Type 1 diabetes, as well as meeting thousands of individuals with Type 1 diabetes and their families."

- Srinivas Viswanathan, PhD: Post-Gastric Bypass Nesidioblastosis

as a Model for Understanding Beta-Islet Cell Neogenesis
Turning up the volume on beta cell replacement. Why do beta cells undergo an explosive period of growth in the wake of gastric bypass surgery? We don't know, but Harvard MD/PhD student Viswanathan thinks this phenomenon could provide new insights into ways of replacing lost beta cells in patients with Type 1 Diabetes.

"I'd not considered doing any work on diabetes before, but happened to be on my Surgery Rotation at the time the challenge was announced, and at the time I had contact with many patients who had undergone gastric bypass procedures," said Viswanathn. "I was intrigued by the observation that many of these patients were no longer diabetic after having the surgery, and read about this phenomenon wherein gastric bypass surgery could alter the pancreas's insulin-producing capacity."

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