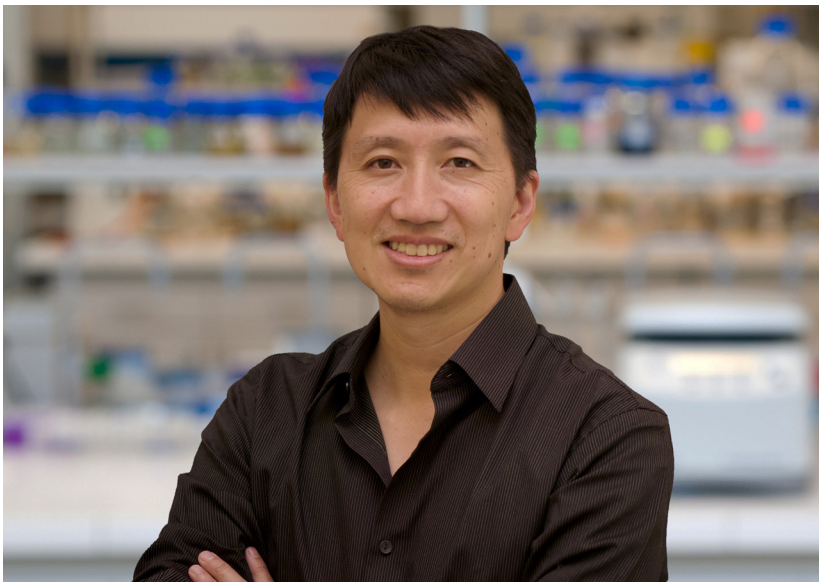

TIMOTHY YU, MD, PhD
Attending Physician, Division of Genetics and Genomics
Boston Children's Hospital
Associate Professor of Pediatrics
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"Harrington Discovery Institute is an exemplar of what's needed to jumpstart the development of medicines for rare diseases."

BREAKTHROUGHS,
INDIVIDUALIZED

FOCUS: Personalized oligonucleotide therapy for Niemann-Pick disease.

Dr. Yu is responsible for developing what is considered the world's first example of individualized genomic medicine—a drug customized solely for a single patient, designed on the basis of that patient's specific pathogenic mutation.

This remarkable achievement was made possible by the relatively new antisense technology, wherein small pieces of DNA or RNA, called antisense oligonucleotides (ASOs), are used to precisely target splice-altering mutations (genetic alterations in the DNA sequence) at the RNA level, restoring proper gene assembly and rescuing gene function.

Niemann-Pick type C (NPC) is a rare inherited disease that affects the body's ability to metabolize cholesterol and lipids within cells, which in turn malfunction and eventually die. NPC can affect the brain, nerves, liver, spleen, bone marrow and in severe cases, lungs. The condition is commonly fatal within the first two decades of life. Current treatments are focused on helping people live with their symptoms.

With help from Harrington Discovery Institute, Dr. Yu and his team are designing personalized ASO therapy for NPC. "In some cases of this disease, a mutation alters RNA splicing of the NPC1 gene, resulting in loss of function," Dr. Yu says. "We have generated ASOs targeting these mutations, screening them for their ability to restore normal NPC1 splicing in patient-derived cell models."

"Beyond Niemann-Pick disease, this work has the exciting potential of fulfilling a longstanding dream of using genetic tools not just to diagnose but to accelerate the development of drug treatments, rapidly get them FDA-approved, and made available to children with rare conditions."

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