Accelerating rare disease drug discovery by combining research and therapeutics development

Rare disease research and drug discovery requires collaboration between patients, organisations, researchers and clinicians. Only then can treatments for the millions of people with a rare disease become a reality.

INTERVIEW WITH **Professor Matthew Wood** Director, Oxford-Harrington Rare Disease Centre

INTERVIEW WITH **Jonathan S. Stamler, MD** President, Harrington Discovery Institute

Only a small percentage of people living with a rare disease have an approved therapy for their condition, presenting a great challenge to global health.

Turning promise into action

Most rare diseases have a genetic cause, resulting from variations in a person's DNA. With recent developments in genomics and the ability to quickly and cost-effectively sequence patients' DNA, there is now the exciting opportunity to design personalised medicines for rare diseases.

The Oxford-Harrington Rare Disease Centre (OHC), a partnership between the University of Oxford and Harrington Discovery Institute, is combining world-leading research with expertise in therapeutics development to accelerate the discovery and delivery of new treatments for rare diseases.

New hope for patients with Duchenne muscular dystrophy

Duchenne muscular dystrophy (DMD) is a rare neuromuscular disease characterised by progressive muscle degeneration and weakness. DMD is caused by a defect in a gene that makes dystrophin, which acts like a shock absorber when muscles contract. Without dystrophin, muscles progressively become damaged and weakened. People with DMD typically do not live past their 30s.

Angela Russell, Professor of Medicinal Chemistry at Oxford, has been working on a protein called utrophin, which was found to function similarly to dystrophin in protecting muscle. Her group has discovered new classes of molecules that increase utrophin production. Her project was recently selected by the OHC for further drug development and commercialisation support.

Innovative technologies: DNA repeat expansion disorders

Huntington's disease (HD) is a fatal disease that causes certain brain cells to degenerate. Symptoms include uncontrolled movements and difficulty walking. HD results from a disease-causing DNA repeat expansion, wherein a segment of DNA within the huntingtin gene expands.

Edward Grabczyk, Professor of Genetics at Louisiana State University and Harrington Rare Disease Scholar, identified that the genetic mutation underlying DNA repeat expansion in HD is driven by the protein MLH3. He designed novel oligonucleotide drugs to decrease MLH3 activity, which in turn should slow or stop the progression of the disease. Grabczyk's approach may enable the treatment of other related disorders, and today, his technology is licensed with Takeda Pharmaceuticals.

The OHC has a philanthropically funded programme focussed on Friedreich's ataxia, a neurodegenerative rare disease with a related disease mechanism. It works with an international network of patients, foundations, researchers and clinicians towards developing new therapies for the one in 40,000 people affected by this disease.

Advancing treatments towards patients

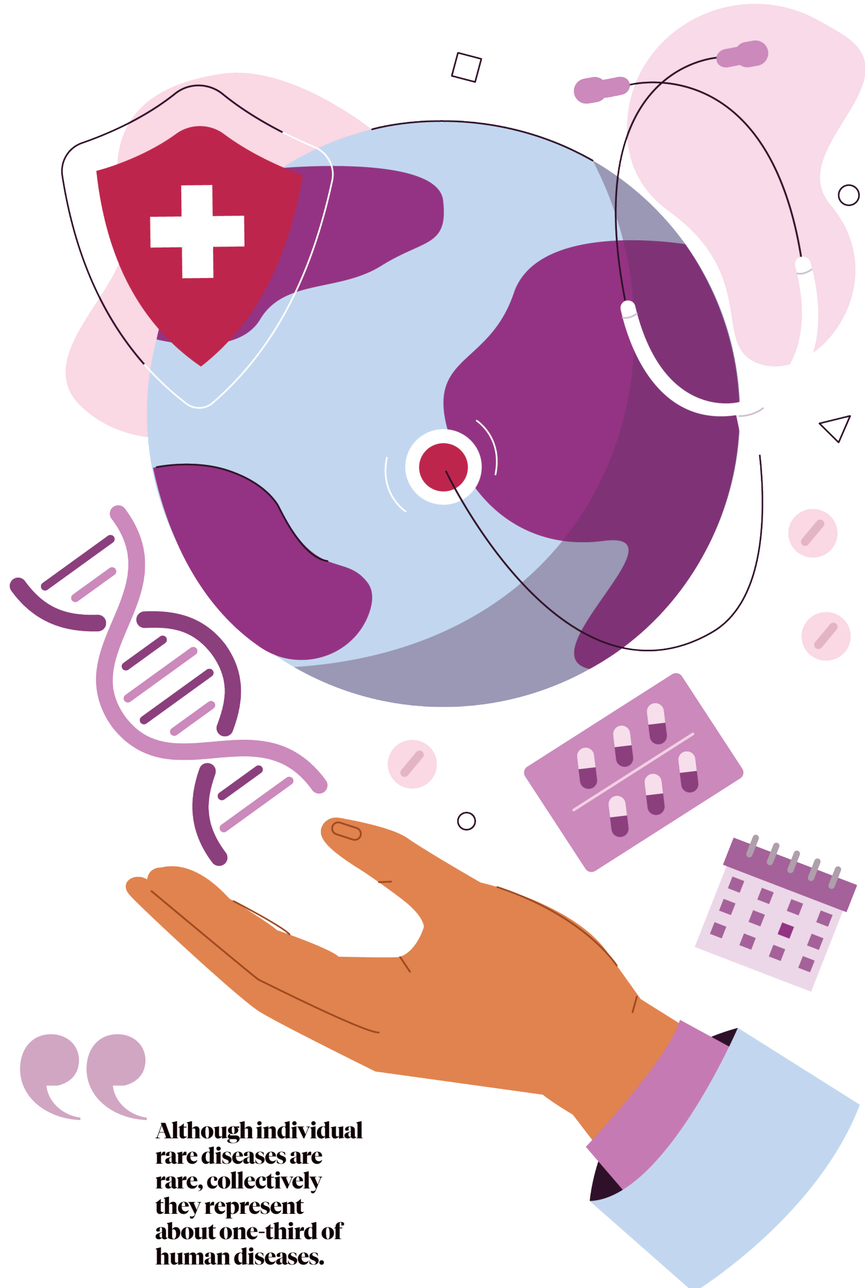
Harrington Discovery Institute is an international drug discovery and development organisation established to address unmet therapeutic needs. It provides comprehensive support to leading scholars and entrepreneurs across academic centres in the US, UK and Canada. The focus is on medical breakthroughs that show great promise but would not otherwise advance to clinical trials.

By concentrating on philanthropic, scientific and business development resources during the early, high-risk stage of drug discovery and creating pathways toward commercialisation, Harrington drives the progress of therapeutic candidates towards further investment and clinical trials.

Partnering for cures

The University of Oxford has hundreds of researchers working on a range of rare diseases and cutting-edge therapeutics. Its new Institute of Developmental and Regenerative Medicine (IDRM), where the OHC is based, aims to develop new drugs and therapeutic strategies for neurological, cardiovascular and immune diseases.

Matthew Wood, Director of the OHC, Professor of Neuroscience at Oxford's Department of Paediatrics, and Director of the MDUK Oxford Neuromuscular Centre, recognises the need for partnership with the global rare disease community in achieving the goal of accelerating rare disease therapeutic development. Wood explains: "There are significant challenges in meeting the needs of rare diseases. With advances in genomics and drug development and delivery, we are now in a position to make a difference for people who have had little hope of finding a treatment."



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Finding hope in a global movement to cure rare diseases

Global collaborations are needed to meet the challenges of rare disease and to drive progress in scientific research towards delivering therapies for people living with rare diseases.

INTERVIEW WITH **Christian Lantz** DPhil Candidate in Biomedical Sciences, NIH-Oxford

INTERVIEW WITH **Sophie New, Jordan New and Cooper New**

SPREAD WRITTEN BY **Dr Julie Stevens** Programme Manager, Oxford-Harrington Rare Disease Centre, University of Oxford

Individuals with rare diseases and their families typically have a long journey to a diagnosis with little hope for a cure. The Oxford-Harrington Rare Disease Centre, a partnership between the University of Oxford and Harrington Discovery Institute, brings together the resources and capabilities needed to accelerate novel treatments for patients living with a rare disease.

Individually rare, collectively common

There are 400 million people across the globe living with a rare disease, affecting 1 in 17 people during their lifetime. Although individual rare diseases are rare, collectively they represent about one-third of human diseases. Fewer than 5% of rare diseases have approved treatments.

The Oxford-Harrington Rare Disease Centre (OHC) was established to accelerate treatments and cures. Its work supports the drug development life cycle from early drug discovery to preclinical studies, clinical development, regulatory approval and ultimately through to commercialisation.

"This affiliation represents a commitment to patients first and a tremendous opportunity to improve the health and outcomes of those living with a rare disease," says Jonathan S. Stamler, MD, President of Harrington Discovery Institute.

I feel very fortunate to be involved in rare disease research having experienced living with a rare disease.

Finding hope and community

Sophie and Jordan New learned through genetic testing that their young son, Cooper, has FBXO11, an intellectual developmental disorder. This ultra-rare disease occurs in less than one in a million people.

Cooper's parents, and grandparents Rusty and Liz Cooper, set out to learn as much as possible about FBXO11 and any potential treatments. Rusty, a financial advisor at Morgan Stanley, learned about Harrington Discovery Institute at University Hospitals in Cleveland, Ohio through Morgan Stanley GIFT Cures℠ powered by Harrington Discovery Institute. This programme provides opportunities for philanthropists to combine their resources to magnify the impact of their medically related giving, whether on a specific disease or across a broader spectrum.

"For the first time in Cooper's life, someone understood our son. Not only did they understand our medical mystery, but they also provided us with the most impactful gift we could've imagined, hope. Harrington turned on the lights in our blacked-out world," says Jordan New.

From diagnosis to doctorate

Christian Lantz was diagnosed at age eight with the rare neuromuscular disease, limb-girdle muscular dystrophy. His diagnosis inspired his interest in science and the ambitious decision to pursue a doctorate in neuromuscular disease research.

Lantz, now a doctoral student in the National Institutes of Health (NIH) Oxford-Cambridge Scholars Program, researches a group of rare diseases originating from mitochondria, causing amyotrophic lateral sclerosis (ALS), a form of dementia, and a form of spinal muscular atrophy (SMA). He is mentored by the OHC Director, Professor Matthew Wood, at the University of Oxford.

His project links the immense resources of the NIH and National Center for Advancing Translational Sciences (NCATS) in the US with disease-specific expertise and UK institutions with a shared mission. These invaluable projects create the global networks that will bring together the funders, researchers, drug development experts, foundations and regulatory bodies that will drive rare disease drug delivery.

"I feel very fortunate to be involved in rare disease research having experienced living with a rare disease. The rate of advancements in gene therapy and research gives me hope that many more rare diseases will be addressed with treatment options in the future," says Lantz.

Help us cure rare diseases

We invite you to join us in supporting the OHC and its mission to advance cures for rare diseases. Your support will help us to continue to fund drug discovery and development and provide the resources needed to advance promising scientific breakthroughs into treatments for patients. Together, we can make a difference in the lives of those living with rare diseases and their families.

Find out more at **oxfordharrington.org**