RAREBASE

Reimagining rare disease research: The science & technology behind Rarebase

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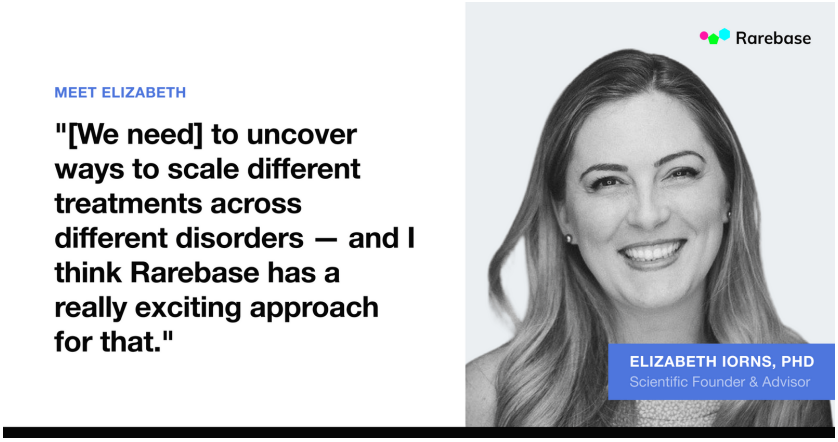

Introduction

Rare disease research is undergoing a transformation — one powered by the evolution of innovative technologies and forward-thinking

investment from the traditional biopharmaceutical industry. Now, the ability to harness biotechnology in collaboration with the rare disease community promises to change the face of rare disease research, according to Rarebase Scientific Founder and Advisor Dr. Elizabeth Iorns.

Our team sat down with Dr. Iorns, whose scientific expertise includes high-throughput screening approaches, to discuss the realities of discovering therapies for rare diseases — and how Rarebase provides a path forward for individuals affected by rare genetic conditions. Read on to learn more about advances in science and technology that have reshaped the landscape for patients today and enabled new approaches to drug discovery for rare diseases.

Advances in the clinic empower people living with rare diseases

“We’re in this era of biology,” says Dr. Iorns, “All kinds of really interesting technology that’s actually being brought forward into the clinic to help patients.” Physicians now have the tools — like next-generation sequencing — to identify the genetic mutations that cause patients’ rare diseases, according to Dr. Iorns. “Our ability to sequence the genome at scale…and find the genes that are causing disease…that’s routinely done in the clinic.” Such progress equips more patients with essential knowledge about the root cause of

The pros and cons of different treatment modalities

Many approaches exist for developing therapies that target the genetic root cause of a rare condition. One option has emerged as a novel treatment for rare disease patients: gene therapy. This umbrella term encapsulates various techniques for correcting a genetic mutation. For example, scientists can engineer a virus to shuttle a non-diseased copy of a gene into the patient's cells — thus combating the underlying genetic mutation.

There are some drawbacks, Dr. Iorns cautions, and patients only get one shot at this type of treatment. "At Rarebase, we see this a lot, where our [collaborators] are funding gene therapies… I'm always very careful to say: A gene therapy for an individual child, if you are just starting that journey today, is going to take years and millions of dollars of investment." Using a viral approach can also hold significant unforeseen risks of adverse events for patients, particularly because gene therapies currently used in the clinic are not reversible.

> **"[Almost] everything that you take that's not injectable is a small molecule," says Dr. Iorns, "All the pills you take as drugs, those are**

> **what we have in our arsenal of therapies. And for all of these patients, they are the most practical path."**

Other avenues are available to patients that do not require the same amount of risk and investment. Small molecule therapeutics can target gene expression, rather than attempting to correct a causal mutation — and can, for example, adjust the expression of the diseased gene back to healthy levels in a reversible manner. "[Almost] everything that you take that's not injectable is a small molecule," says Dr. Iorns, "All the pills you take as drugs, those are small molecules." Opting for a small molecule approach over gene therapy can mean fewer barriers to patient care and can reduce some of the risks incurred during the treatment process. Prescription drugs are also easier to manufacture and distribute to the broader patient community than gene therapies.
"Sometimes I think people overlook that small molecules still are the mainstay of what we have in our arsenal of therapies. And for all of these patients, they are the most practical path."

Scaling small molecule drug discovery for rare diseases

We use high-throughput screening in control brain cells — called neurons — and treat them with a battery of drug candidates to understand how each drug impacts the expression of nearly 15,000 genes. As Dr. Iorns explains, “I think the way to think about [the Rarebase drug discovery platform] Function™ is — we are screening every drug against every gene. So that way we can, in one experiment, know which drug might work for [a patient’s] specific genetic mutation.”

> **“That’s the tipping point we’re in right now,” says Dr. Iorns, “That transition from, ‘We can understand what's causing your disease. Now let's try to find ways where we can scale different treatments across different disorders.’ I think Rarebase has a really exciting approach for that.”**

In this way, we have identified potential therapeutic candidates for each of the 28 diseases in our research portfolio. These candidates are specific to the genetic root cause of each rare disease — and in some cases, may target shared biology across multiple disorders. “That’s the tipping point we’re in right now,” says Dr. Iorns, “That transition from,

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Contact us to learn more.