Rarebase

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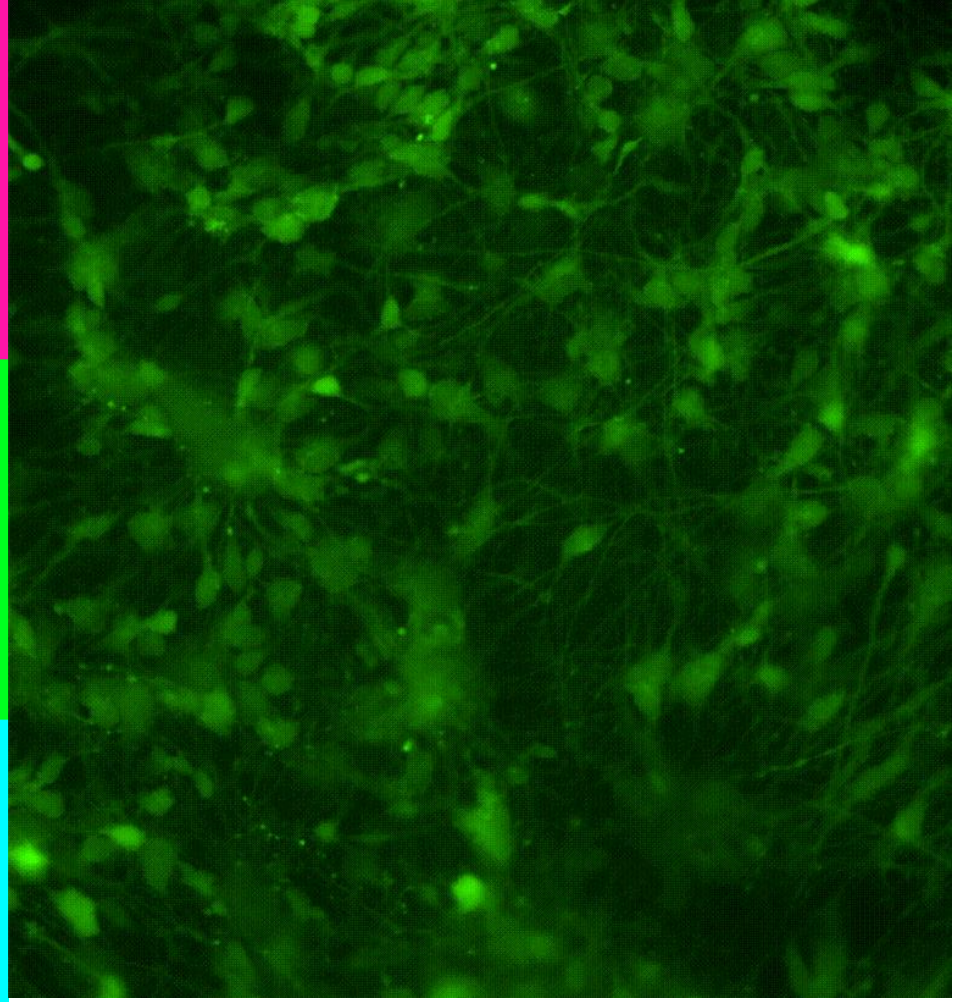
At Ultragenyx Bootcamp
4/28/2023

The hard things about drug development and why we should never give up.



Human biology is complex, humanity doesn’t fully understand it yet

- We can't fully predict yet how drugs interact with our body, which is why we still need clinical trials
- We're making technological progress, e.g. Alphafold, but even with current state of AI, predictions are limited
- It's hard to test anything in humans quickly, because of safety concerns

High costs

- **Cost to drive a new therapy to the clinic is exponential**
- **Large, complex operations involved**
- **Regulatory landscape to ensure proper process**
- ***Most of funding has come from “the market”***

It takes a long time

- Many steps need to be performed serially
- Speed of biology is a limiting factor
- Science = two steps forward, one step back (or sometimes, the other way around)

No silver bullets

- **Nothing is going to be perfect (most likely)**
- **Tweaking our biology typically comes with a price (side effects)**
- **Perfect is the enemy of good ("*what does it mean to find a Cure*")**

If it'd be easy it may already have been done

- **Pharma is a big industry >100 years old**

However!

- ***We haven't done everything we can, especially in rare diseases***
- ***New technologies open new pathways***

Fostering strong hope for the future: feeling good about what we do

- **What is your end goal?**
  - Don't make it too difficult for yourself to succeed (also don't make it to easy)
  - Careful gearing towards "therapeutic success"
- **We have to accept this is going to be a lot of work, with statistically little chance to impact ourselves**
- **Connect with others who're in the same boat**
- ***Remember, it's a marathon: find collaborations, don't try to do everything on your own***

What Rarebase does differently

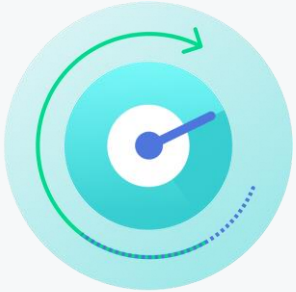
- Working relentlessly on cost and speed efficiency at scale
- Involving community to de-risk programs/therapeutic candidates
- Bringing together the community, drug hunting and engineering
- We are a learning organization, and we are learning with you

What we've done so far

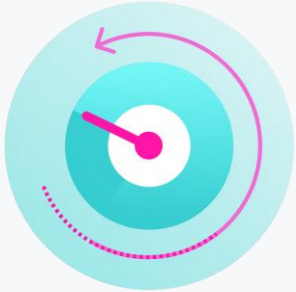
With our platform, we are turning drugs into a “dial” to turn a gene up or down

~4,000 FDA-approved and experimental drugs

Gene expression on 15,000 genes



Drugs that dial a gene “up”



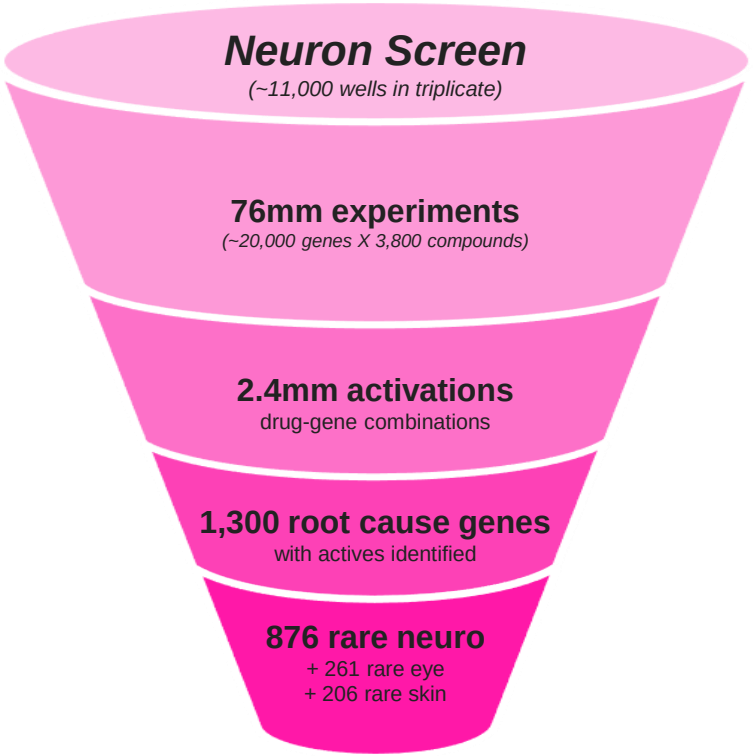
Drugs that dial a gene “down”

Our solution: discover small molecules that regulate the genes responsible for rare diseases

Biological effect or genetic mutation		Therapeutic approach
Not enough functional protein e.g., haploinsufficiency		Increase expression
Too much functional protein e.g., Gain of Function (GOF)		Decrease expression
No functional protein e.g., Loss of Function (LOF)		Increase expression of a paralog
Altered protein function		Alter expression of pathway genes

Rarebase

We have implemented the Function platform and identified hundreds of potential treatments.



Opportunities for >90% of rare neuro root cause genes

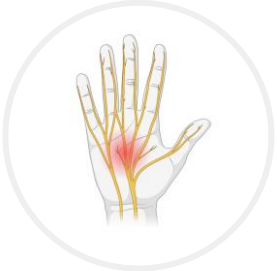
Active compounds identified for over 1,300 root cause genes in a single shot

Rarebase is poised to have *significant impact* across therapeutic areas in rare disease

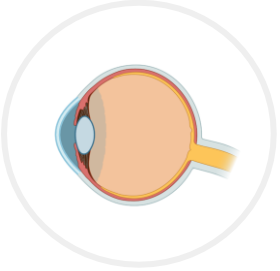
Central nervous system

1373 genes

Peripheral nervous system

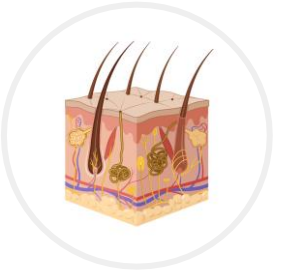


Ophthalmology



415 genes

Dermatology



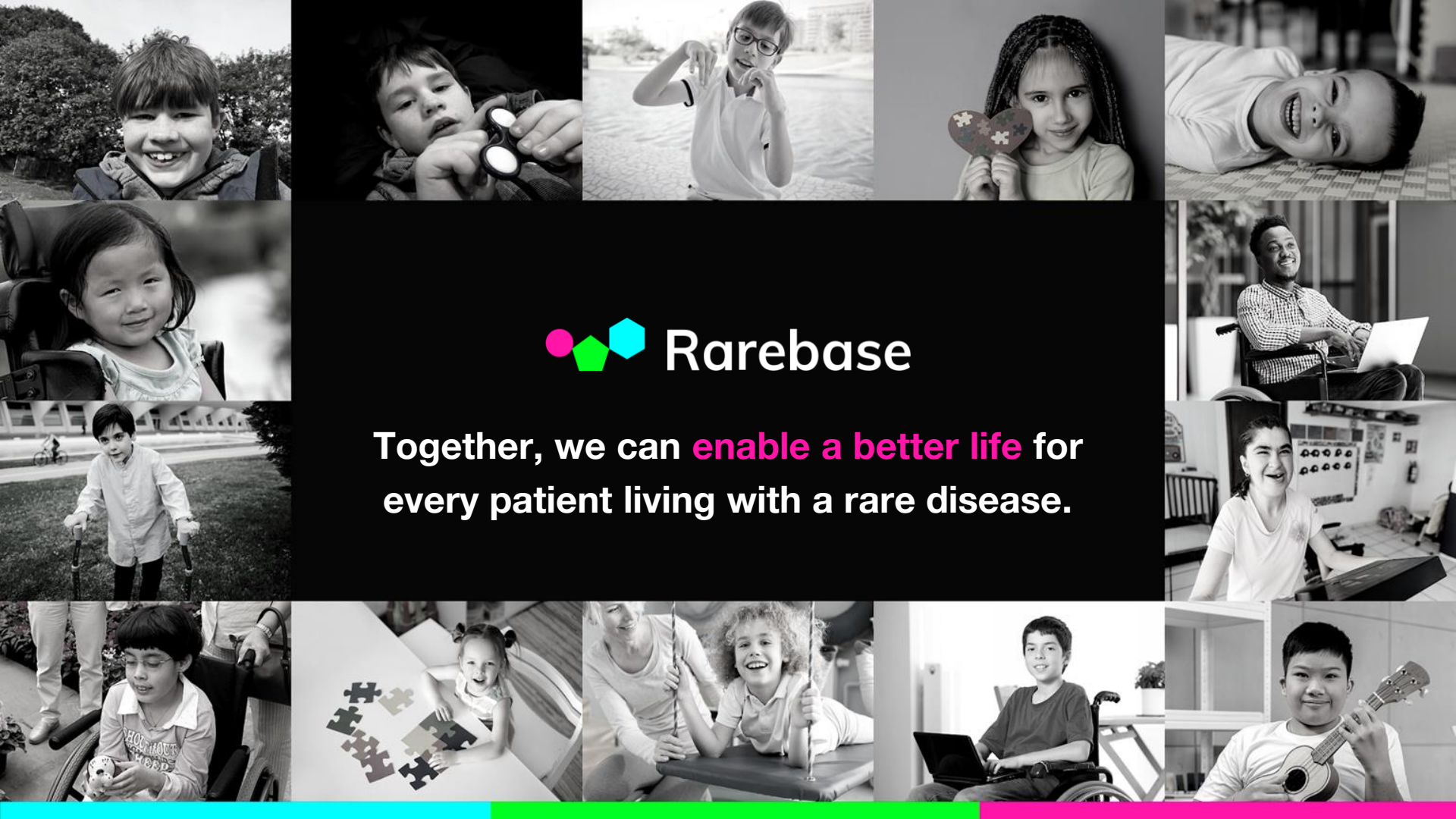
322 genes

Musculoskeletal

120 genes

Rich datasets detailing millions of connections between compounds, genes, cell types

- Repurposing opportunities
- In-licensing opportunities for novel indications
- Novel, drug development


Rarebase
Together, we can enable a better life for every patient living with a rare disease.