Patient-centered outcomes

Matt Might | matt.might.net | @mattmight

I’m here to make your life more difficult.

A complete definition for *patient-centered outcome* is hard.

What is a “*patient-centered outcome*”?

“meaningful and important to patients and caregivers”

Not strictly a function of clinical utility.

What is “actionable”?

To patients, *everything* is actionable.

That makes measuring outcomes hard.

The Genetic Counselling Outcome Scale (GCOS-24)

Using the scale below, circle a number next to each statement to indicate how much you agree with the statement.
Please answer all the questions. For questions that are not applicable to you,
please choose option 4 (neither agree nor disagree).

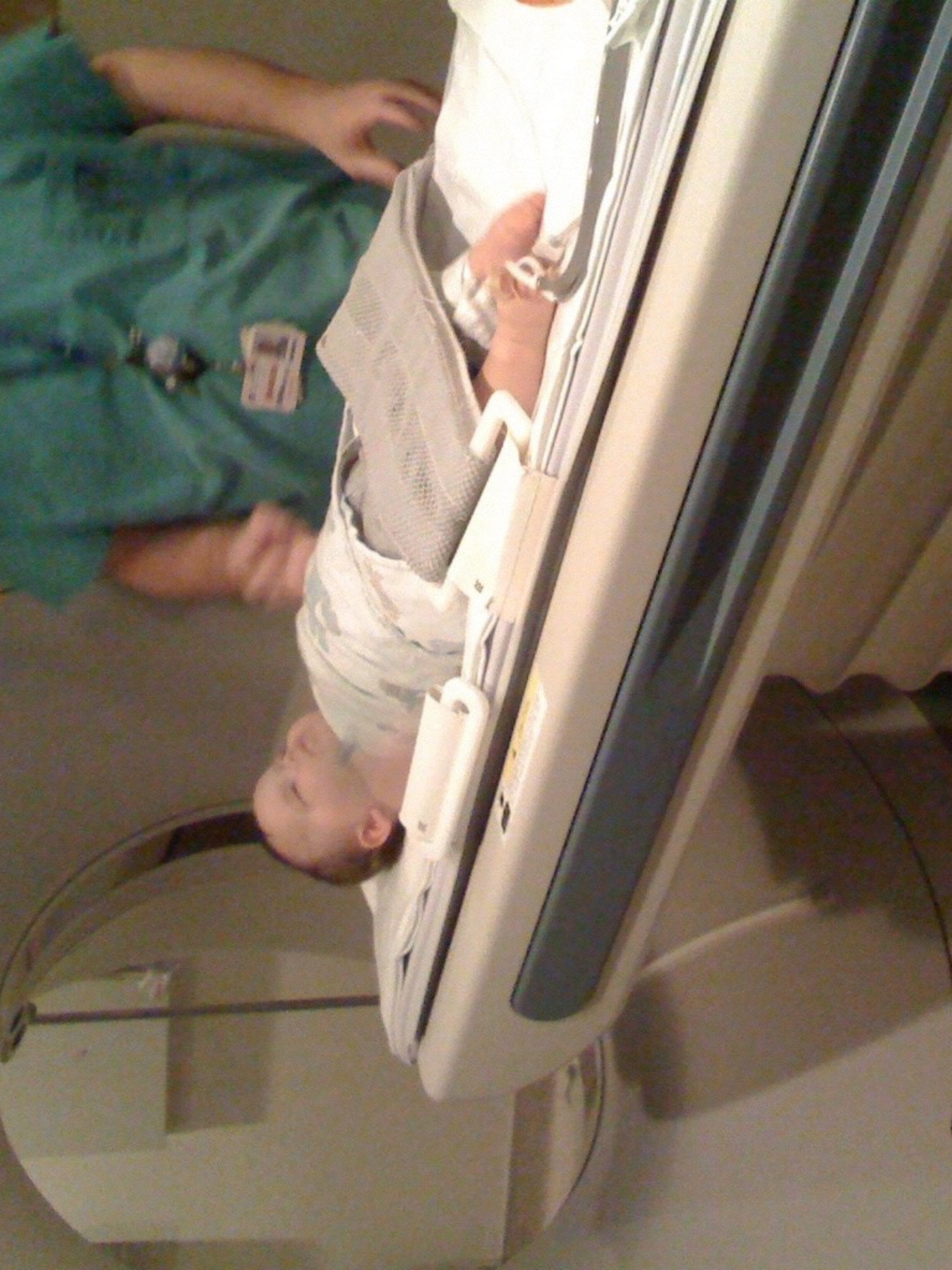
1 = strongly disagree
2 = disagree
3 = slightly disagree
4 = neither disagree nor agree
5 = slightly agree
6 = agree
7 = strongly agree

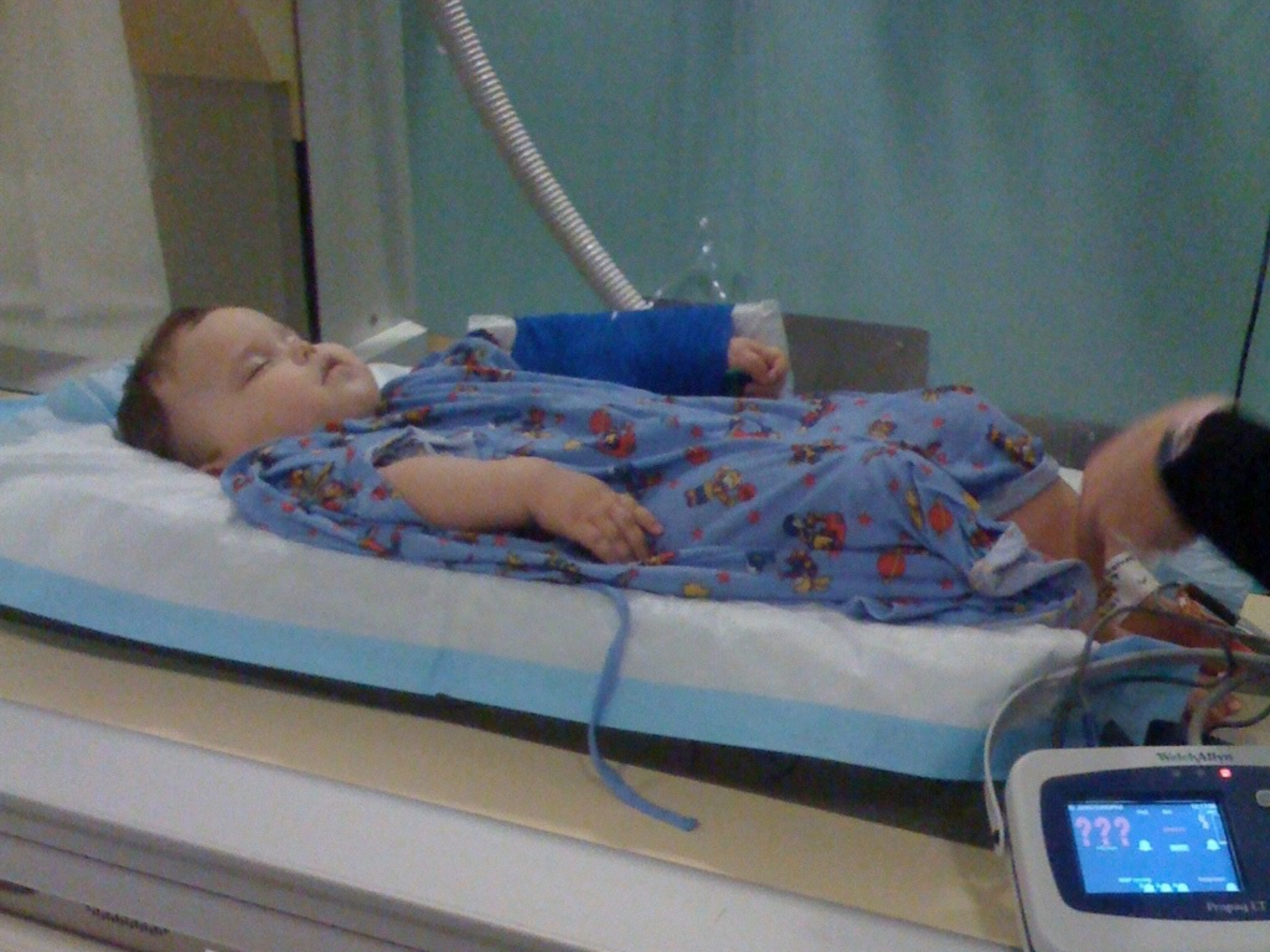
		strongly disagree	disagree	slightly disagree	neither agree nor disagree	slightly agree	agree	strongly agree
1	I am clear in my own mind why I am attending the clinical genetics service.	1	2	3	4	5	6	7
2	I can explain what the condition means to people in my family who may need to know.	1	2	3	4	5	6	7
3	I understand the impact of the condition on my child(ren)/any child I may have.	1	2	3	4	5	6	7
4	When I think about the condition in my family, I get upset.	1	2	3	4	5	6	7
5	I don't know where to go to get the medical help I / my family need(s).	1	2	3	4	5	6	7
6	I can see that good things have come from having this condition in my family.	1	2	3	4	5	6	7
7	I can control how this condition affects my family.	1	2	3	4	5	6	7
8	I feel positive about the future.	1	2	3	4	5	6	7
9	I am able to cope with having this condition in my family.	1	2	3	4	5	6	7
10	I don't know what could be gained from each of the options available to me.	1	2	3	4	5	6	7
11	Having this condition in my family makes me feel anxious.	1	2	3	4	5	6	7
12	I don't know if this condition could affect my other relatives (brothers, sisters, aunts, uncles, cousins).	1	2	3	4	5	6	7
13	In relation to the condition in my family, nothing I decide will change the future for my children / any children I might have.	1	2	3	4	5	6	7
14	I understand the reasons why my doctor referred me to the clinical genetics service.	1	2	3	4	5	6	7
15	I know how to get the non-medical help I / my family needs (e.g. educational, financial, social support).	1	2	3	4	5	6	7
16	I can explain what the condition means to people outside my family who may need to know (e.g. teachers, social workers).	1	2	3	4	5	6	7
17	I don't know what I can do to change how this condition affects me / my children.	1	2	3	4	5	6	7
18	I don't know who else in my family might be at risk for this condition.	1	2	3	4	5	6	7
19	I am hopeful that my children can look forward to a rewarding family life.	1	2	3	4	5	6	7
20	I am able to make plans for the future.	1	2	3	4	5	6	7
21	I feel guilty because I (might have) passed this condition on to my children.	1	2	3	4	5	6	7
22	I am powerless to do anything about this condition in my family.	1	2	3	4	5	6	7
23	I understand what concerns brought me to the clinical genetics service.	1	2	3	4	5	6	7
24	I can make decisions about the condition that may change my child(ren)'s future / the future of any child(ren) I may have.	1	2	3	4	5	6	7

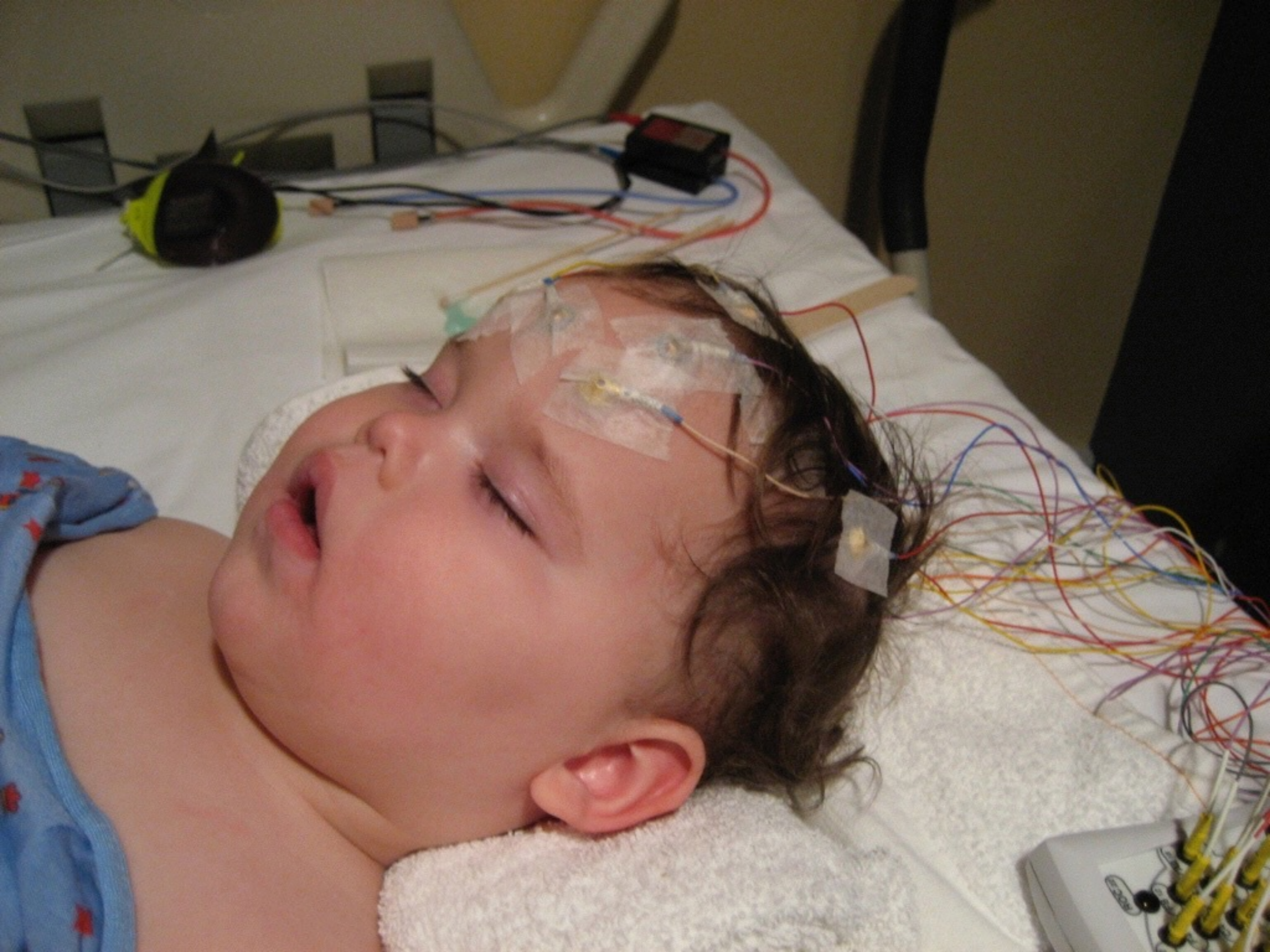
Six data points

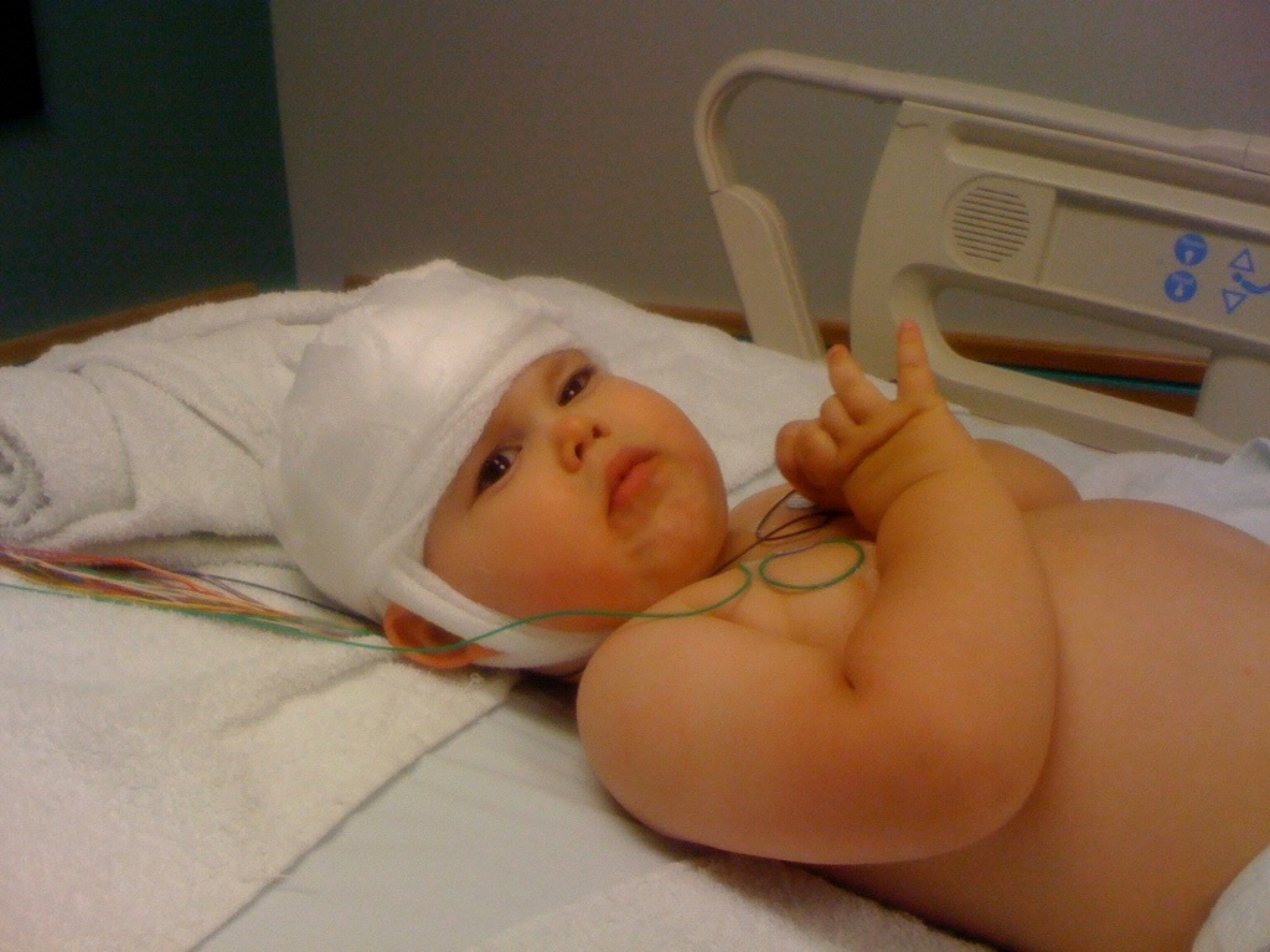
Bertrand

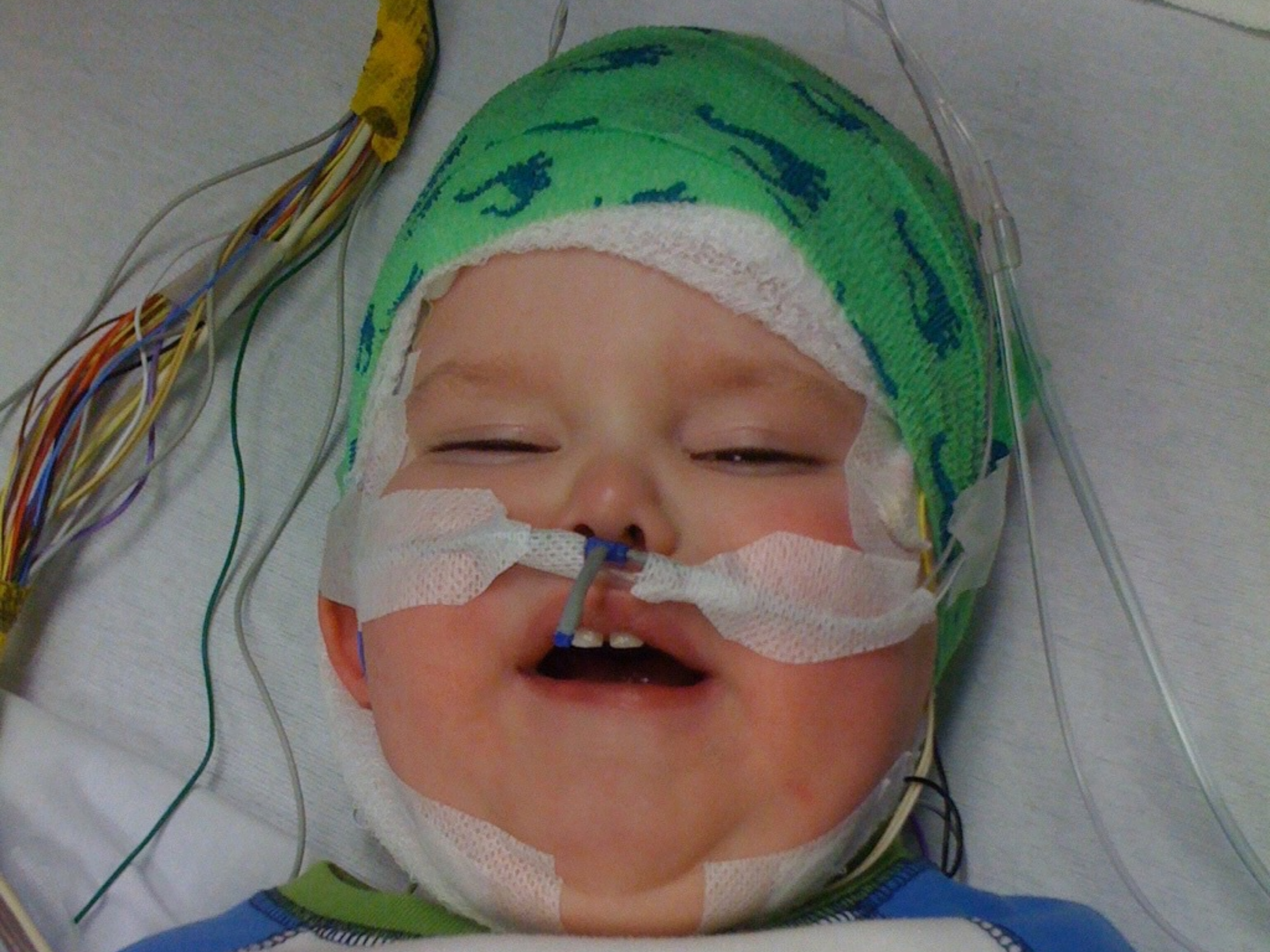
“undiagnosed island”

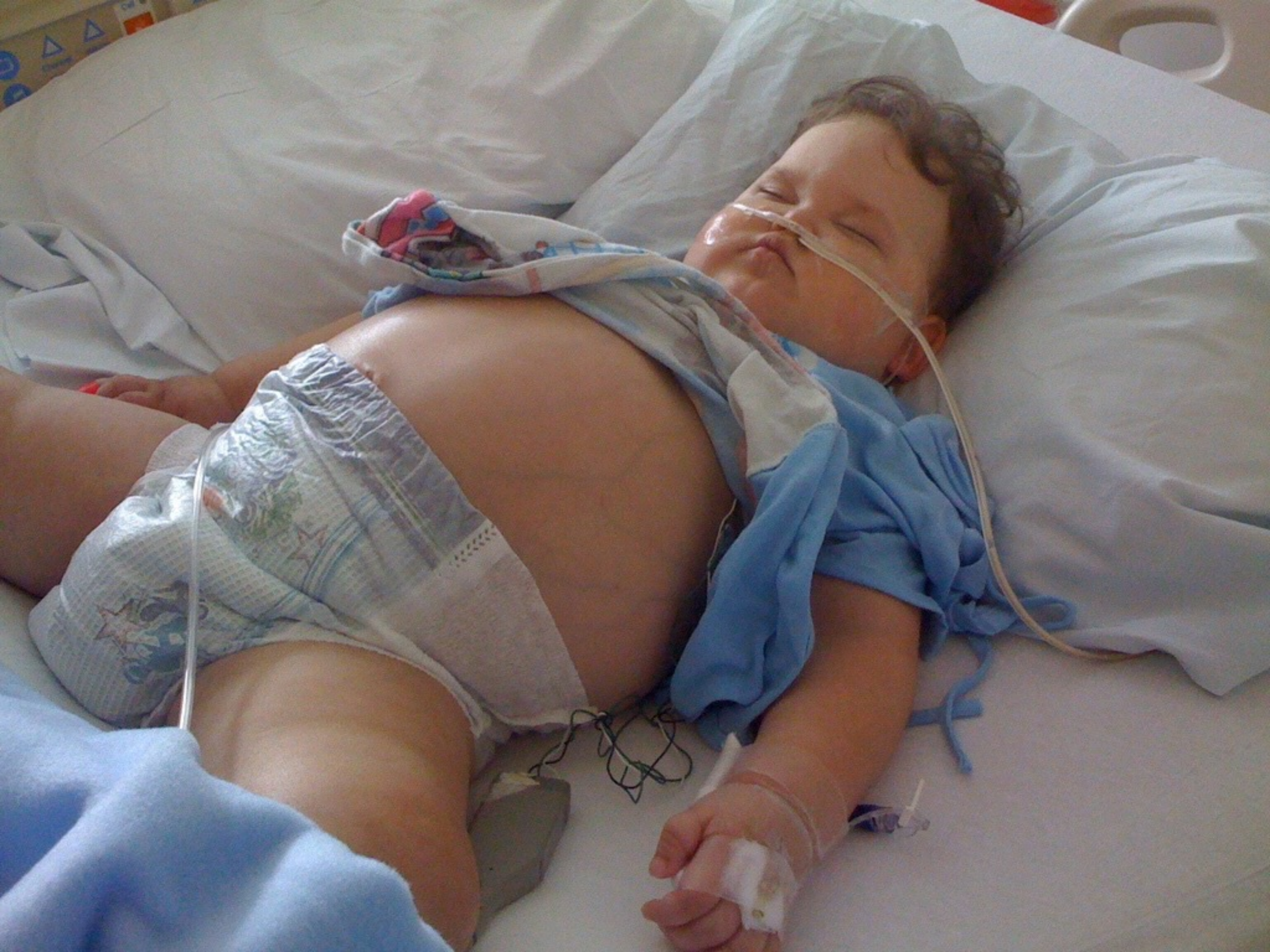


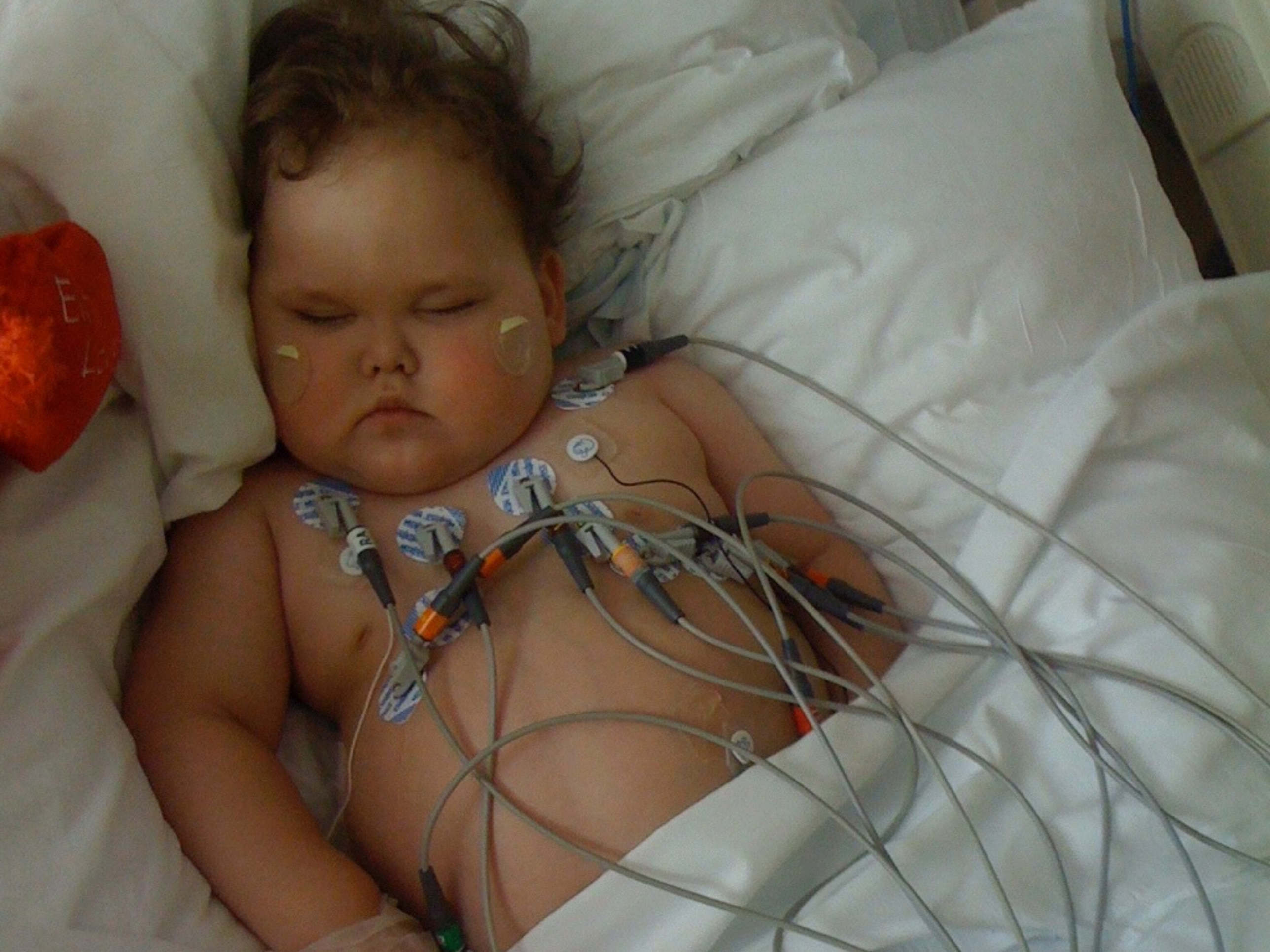


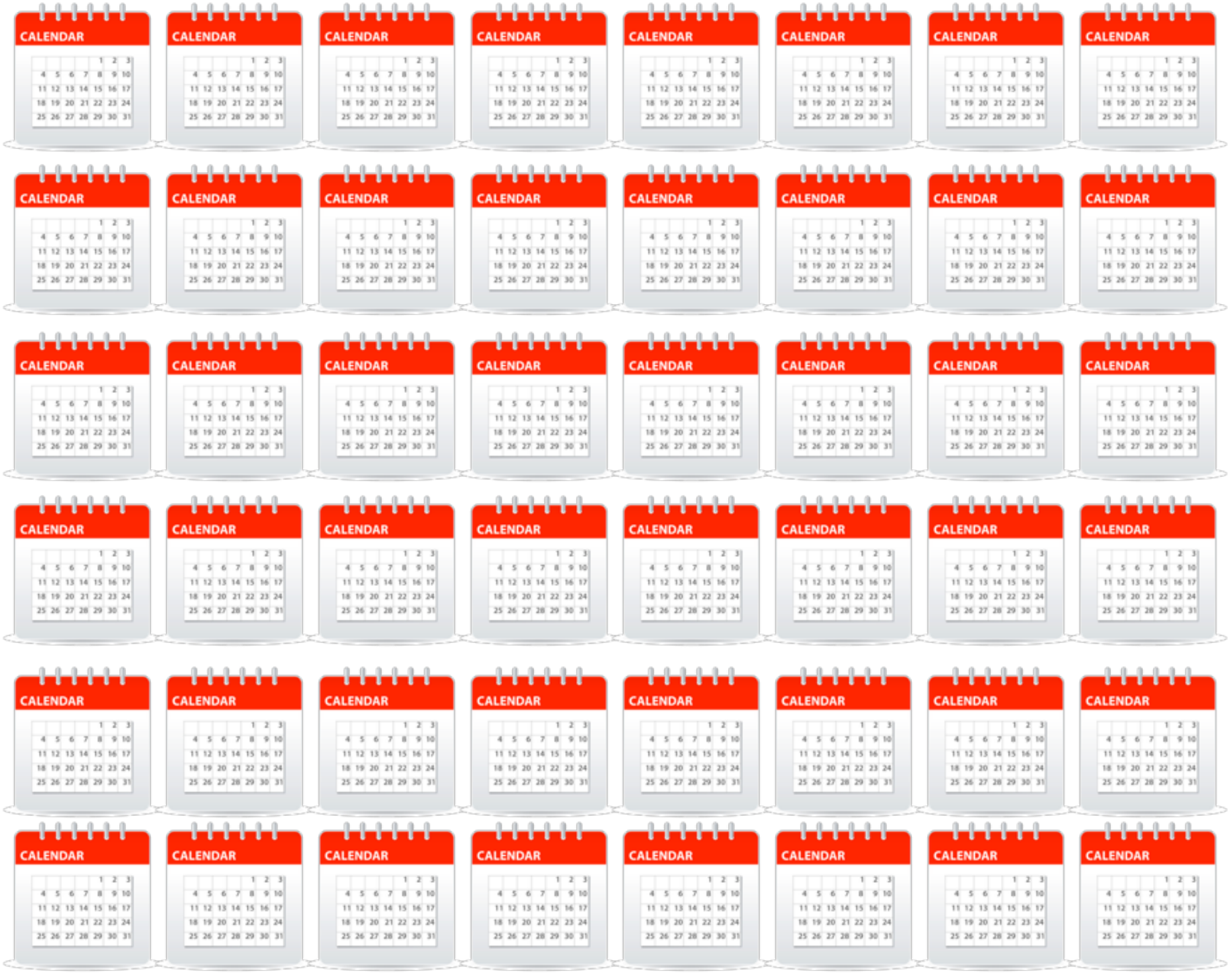








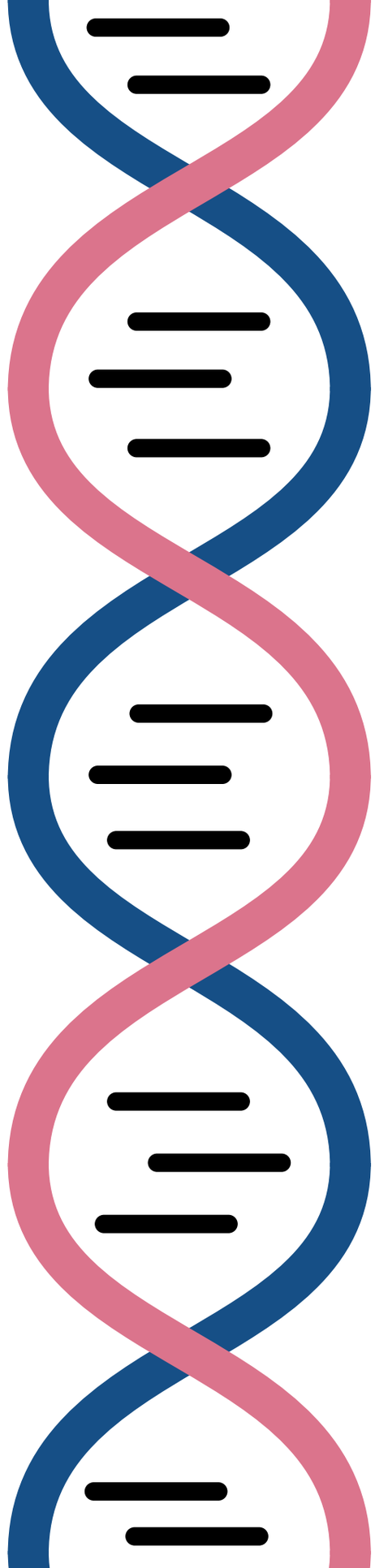


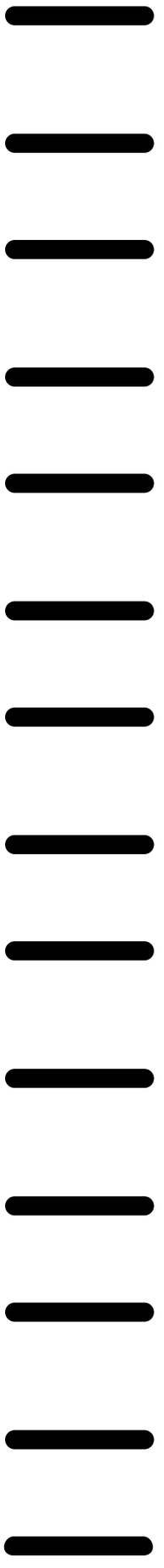

CALENDAR

David Goldstein

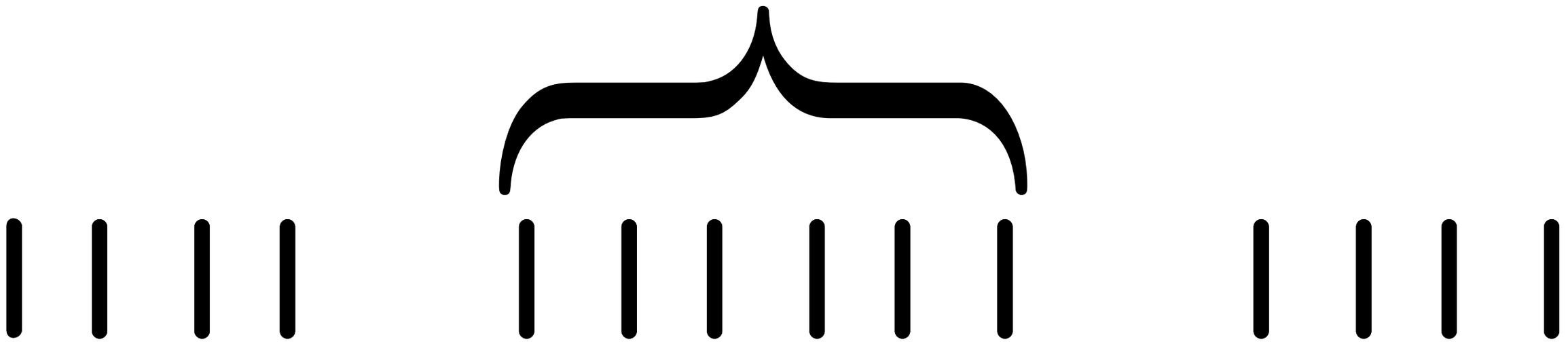
Kelly Schoch

Vandana Shashi

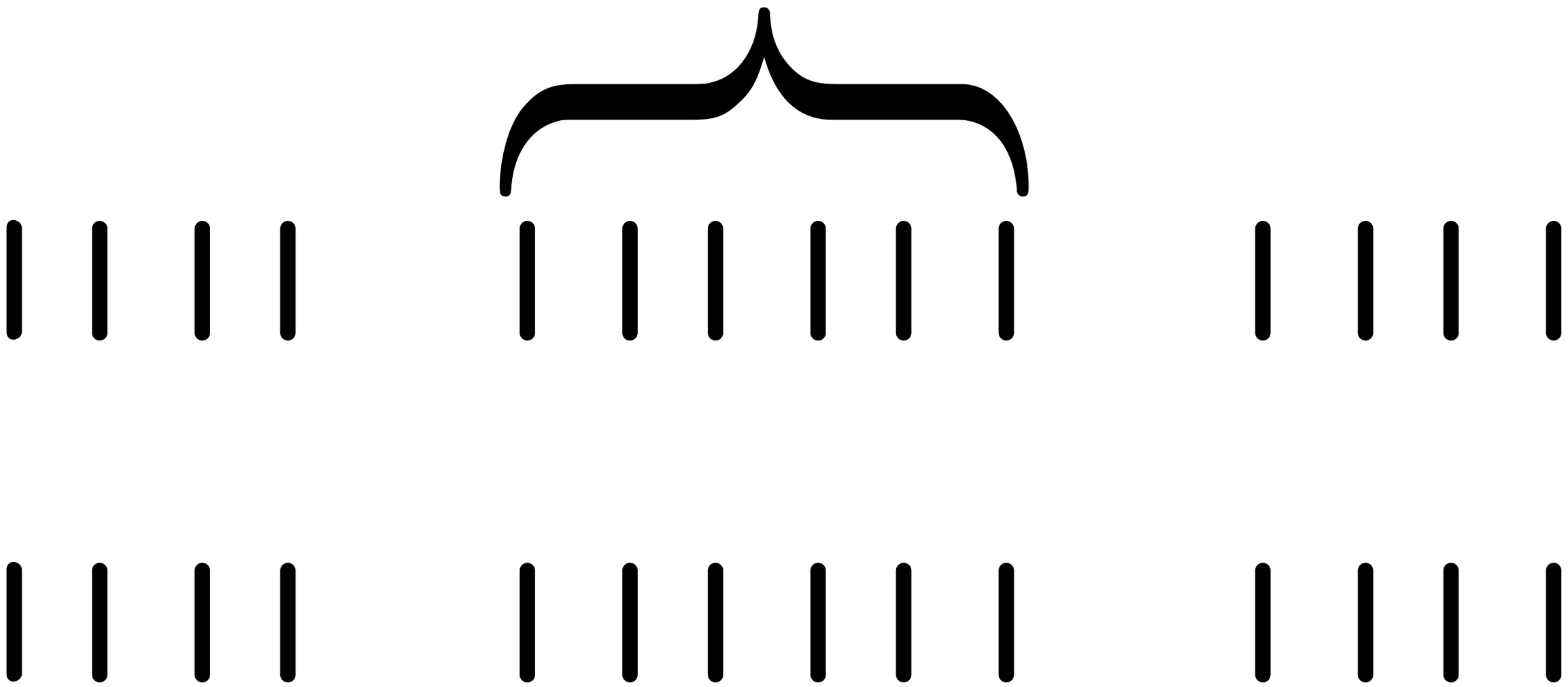




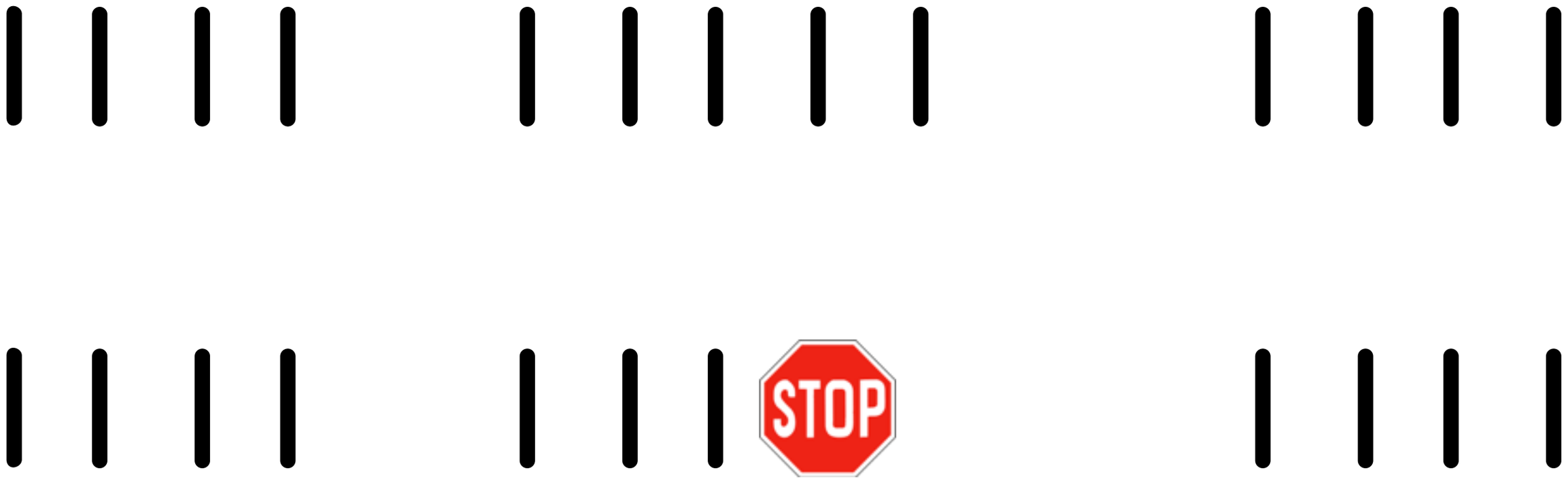
NGLY1



NGLY1



NGLY1



“first”

“only”

a “VAKS”

“not actionable”

ExAC Browser Beta | Gene, transcript, variant, | About | Downloads | Terms | Contact | FAQ

Gene: NGLY1

NGLY1 N-glycanase 1
Number of variants 562 (Including filtered: 633)
UCSC Browser 3:25760435-25831530
GeneCards NGLY1
OMIM NGLY1
Other External References

Transcripts

Gene summary

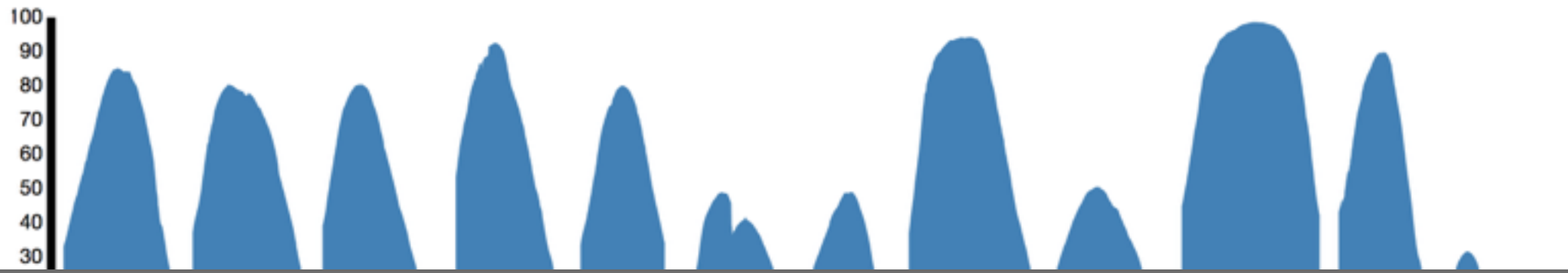
(Coverage shown for canonical transcript: ENST00000280700)

Mean coverage 56.11

Display: Overview | Detail | Include UTRs in plot

Coverage metric: Average | Individuals over X

Metric: mean



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“Let’s find the others.”

So, I wrote a blog post.

Hunting down my son's killer

I found my son's killer.

It took three years.

But we did it.

Not quite like this.

reddit

GIZMODO

Hunting Down My Son's Killer

Hacker News

Google NGLY1

Web Maps Images Shopping Videos More Search tools

About 12,000 results (0.43 seconds)

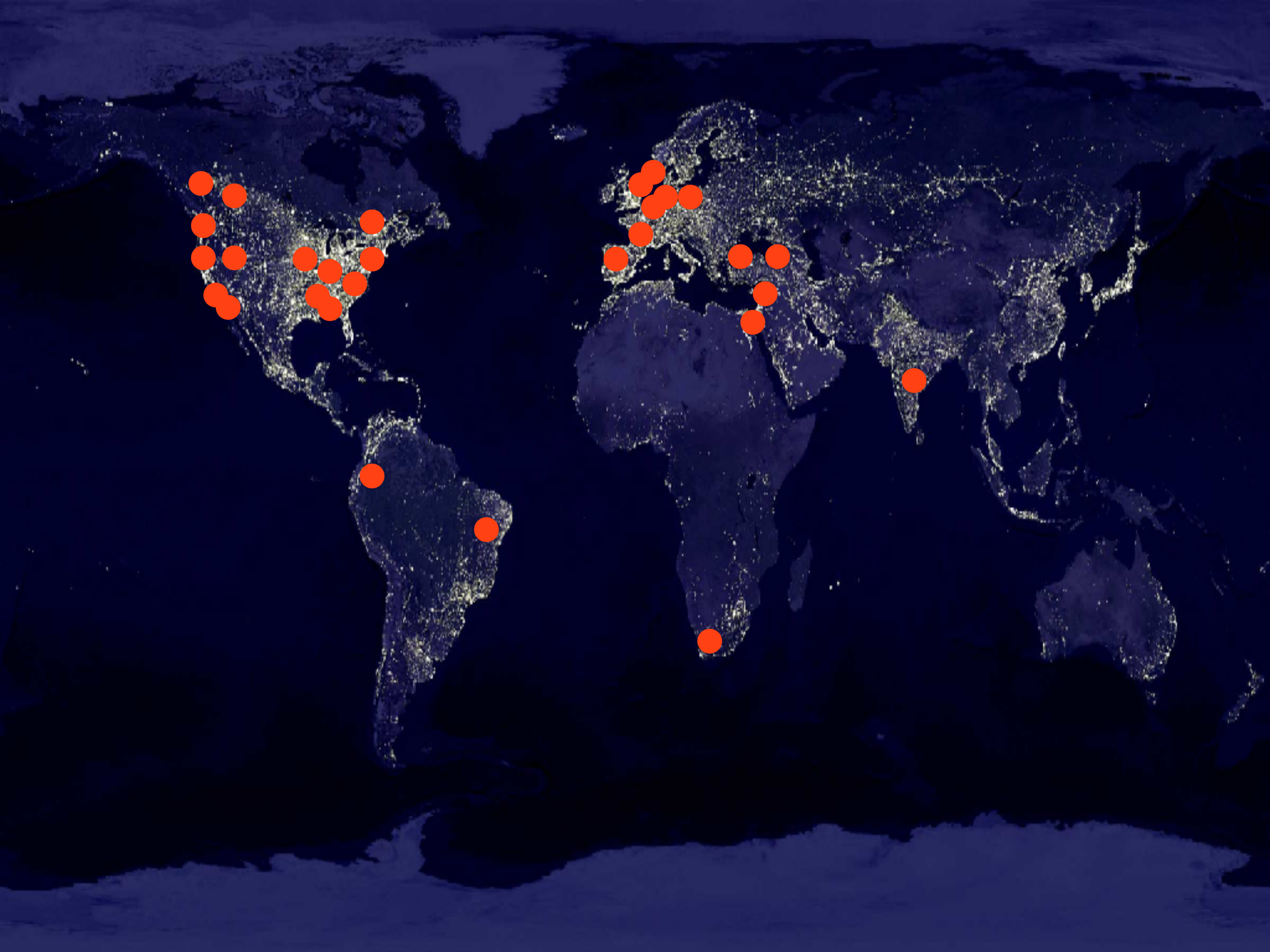
NGLY1 Gene - GeneCards | **NGLY1** Protein | **NGLY1** Antibody
www.genecards.org/cgi-bin/carddisp.pl?gene=**NGLY1**
Complete information for **NGLY1** gene (protein-coding), N-glycanase 1, including: function, proteins, disorders, pathways, orthologs, and expression.

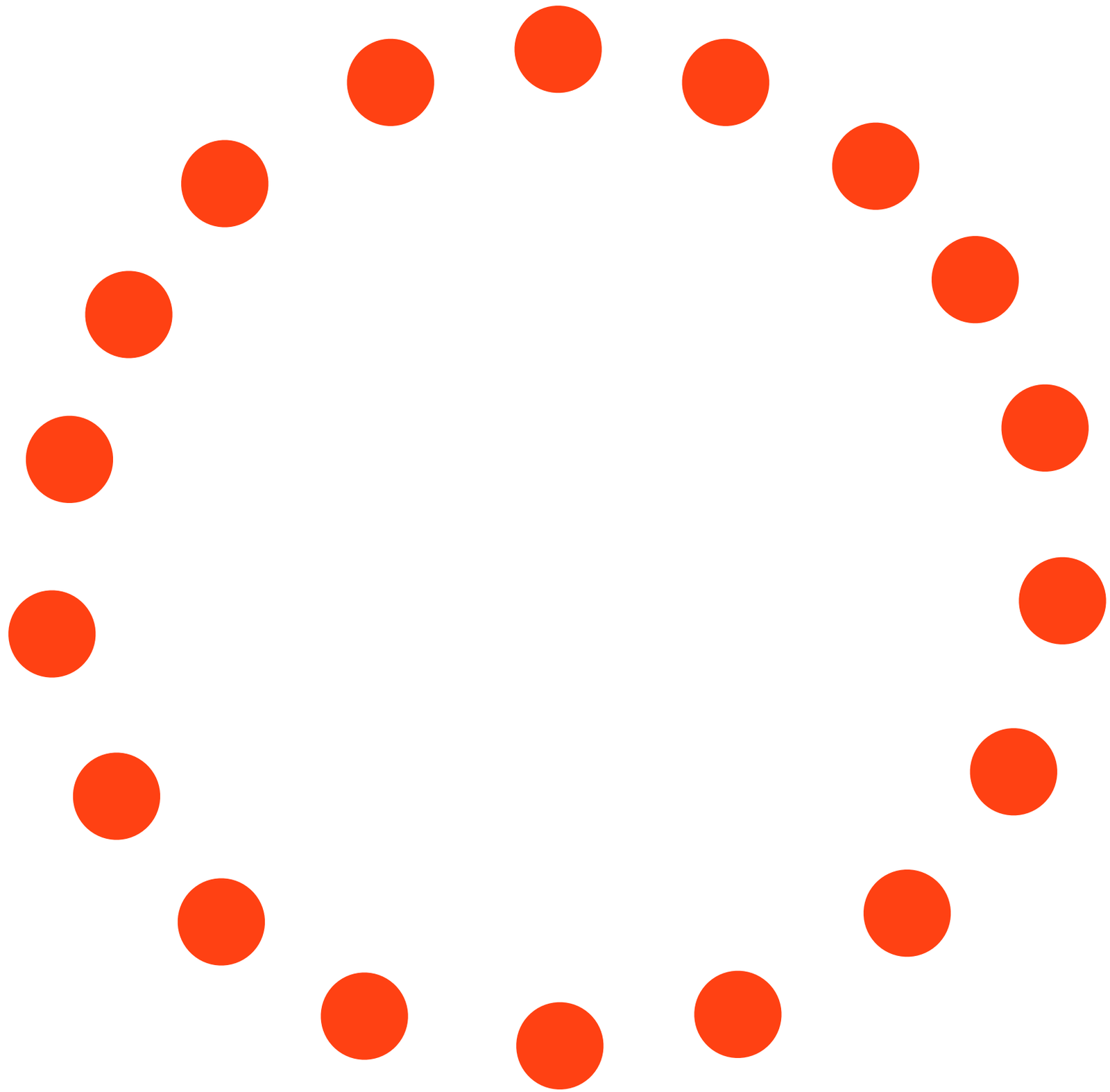
NGLY1 - Wikipedia, the free encyclopedia
en.wikipedia.org/wiki/**NGLY1** Wikipedia
Peptide-N(4)-(N-acetyl-beta-glucosaminyl)asparagine amidase is an enzyme that in humans is encoded by the **NGLY1** gene.

NGLY1 N-glycanase 1 [Homo sapiens (human)]
www.ncbi.nlm.nih.gov/gene/55768 National Center for Biotec...
5 days ago - This gene encodes an enzyme that catalyzes hydrolysis of an N(4)-(acetyl-beta-D-glucosaminyl) asparagine residue to ...

OMIM Entry - * 610661 - N-GLYCANASE 1; **NGLY1**
www.omim.org/610661 OMIM : Online Mendelian...
Jun 12, 2013 - (2000) identified several homologs of yeast Png1, including human **NGLY1**. In yeast, Png1 was expressed in both the cytoplasm and nucleus.

Hunting down my son's killer - Matt Might
matt.might.net/articles/my-sons-killer/
We discovered that my son inherited two different (thus-far-unique) mutations in the same gene--the **NGLY1** gene--which encodes the enzyme N-glycanase 1.





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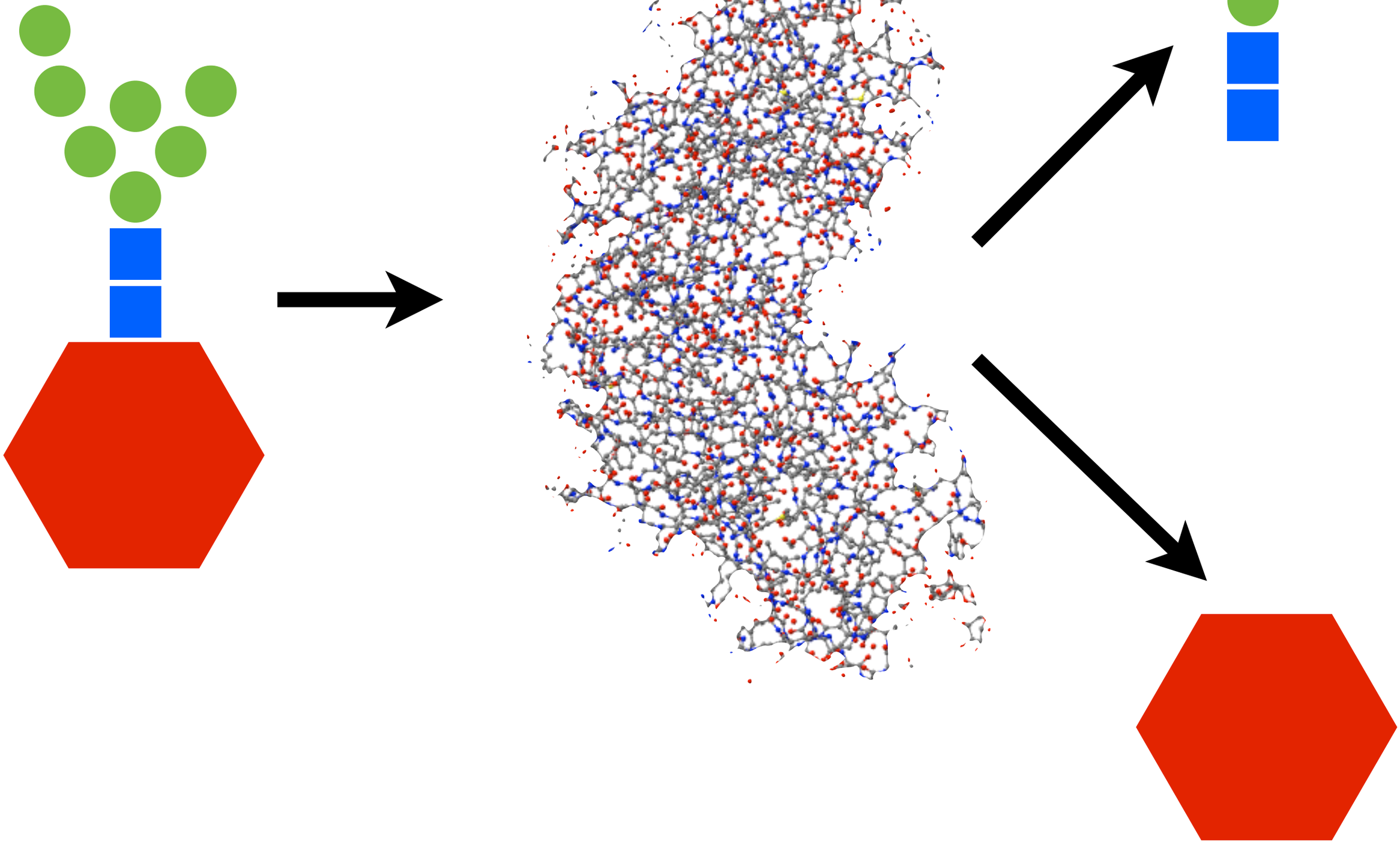
Natural History Study for Disorders of Glycosylation

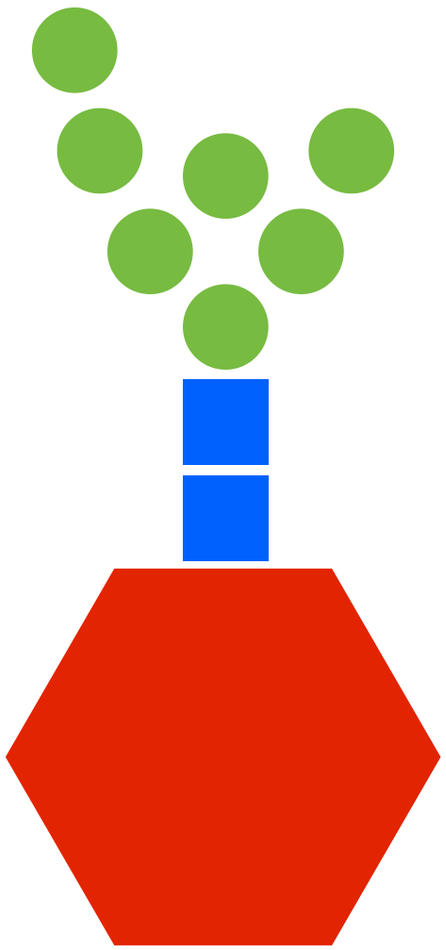
National Institutes of Health

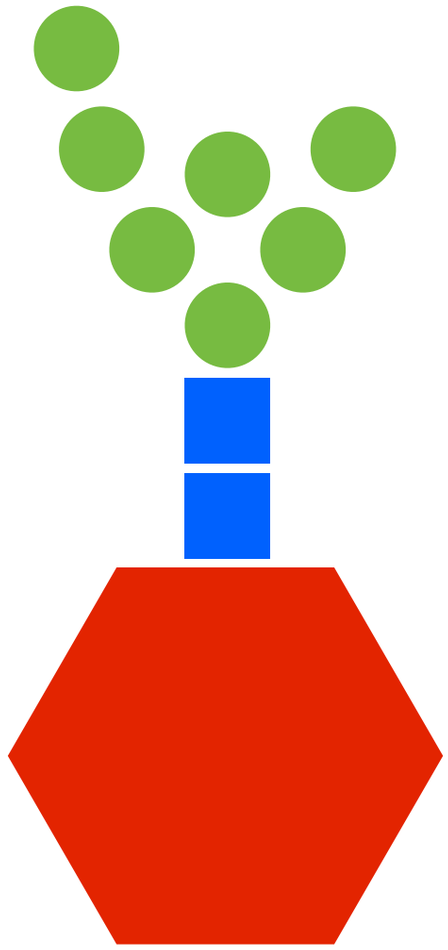
Bill Gahl

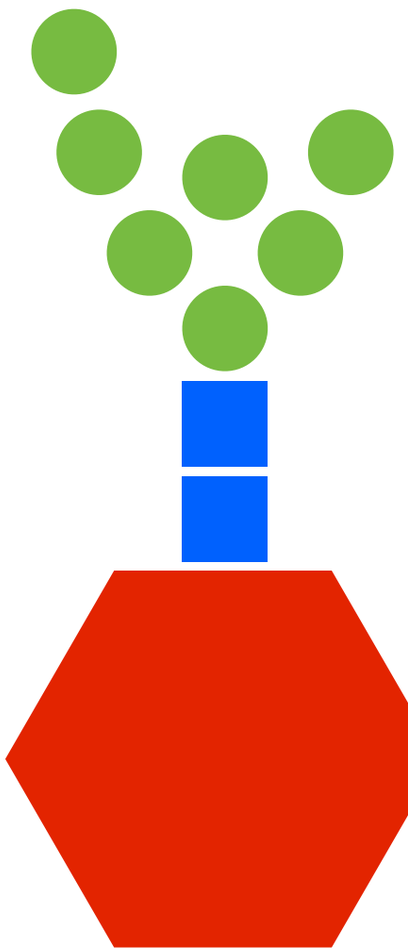
Biomarkers!

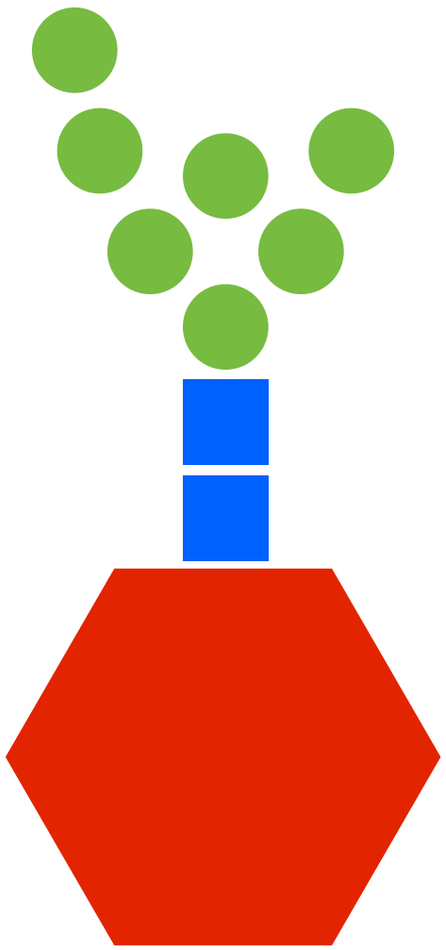

John "Rocket" Williams IV

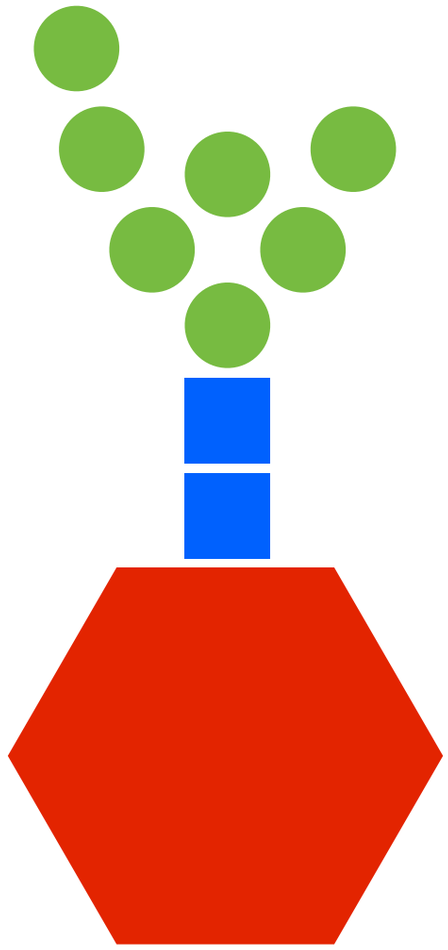


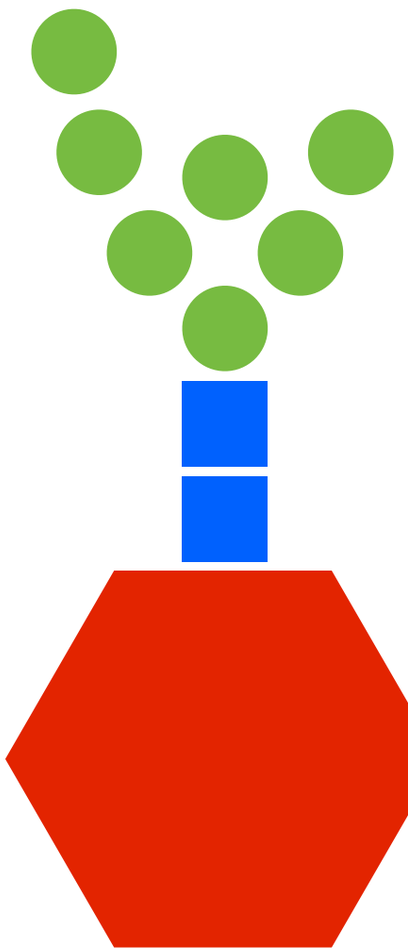


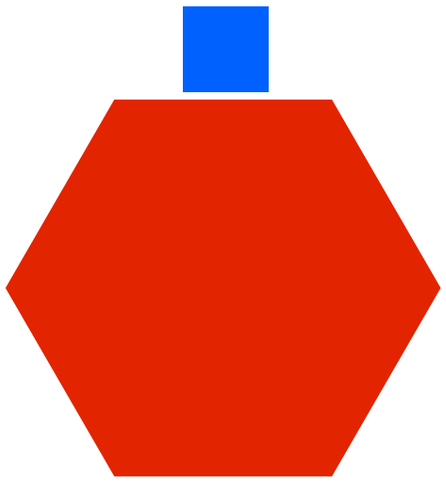


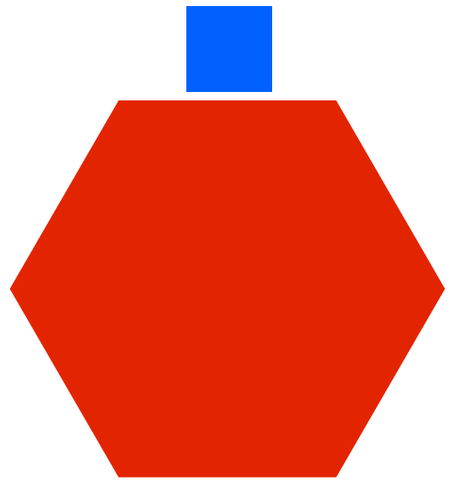


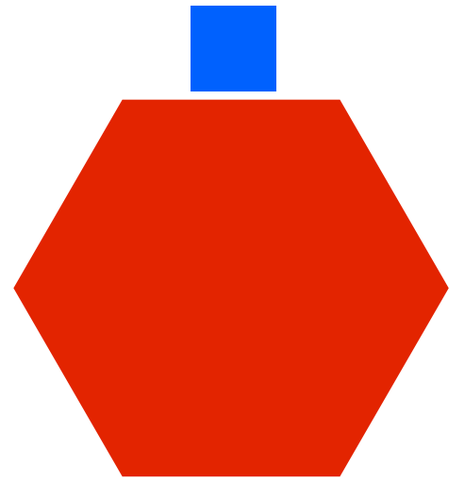


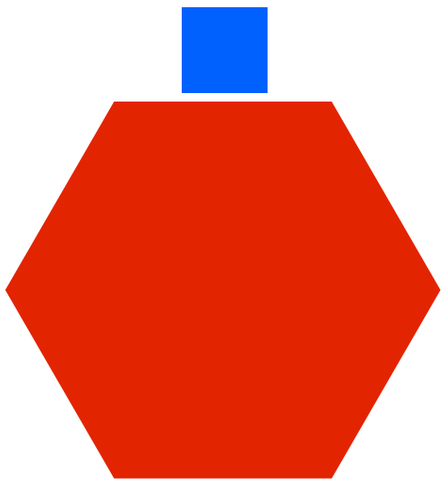


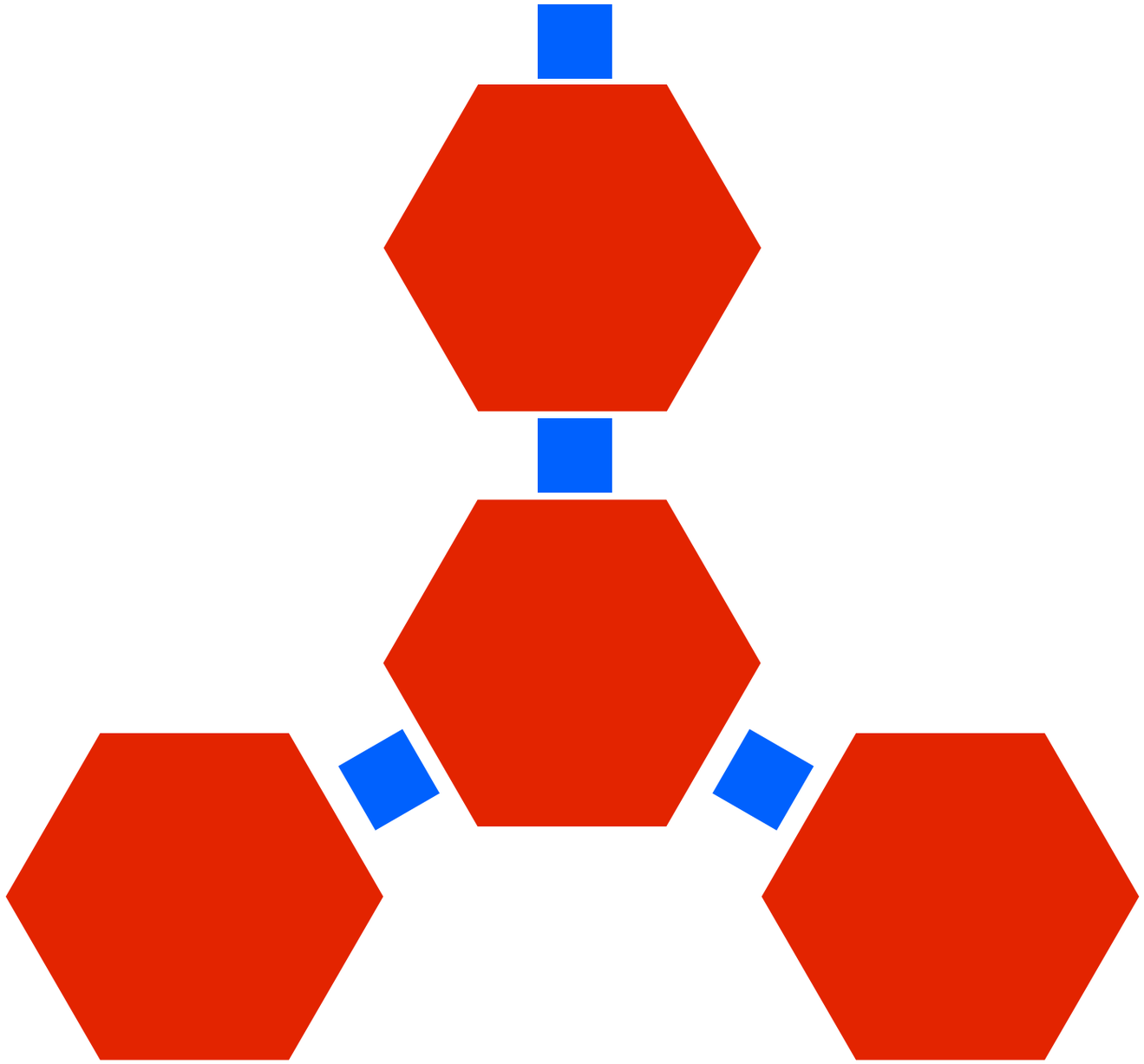


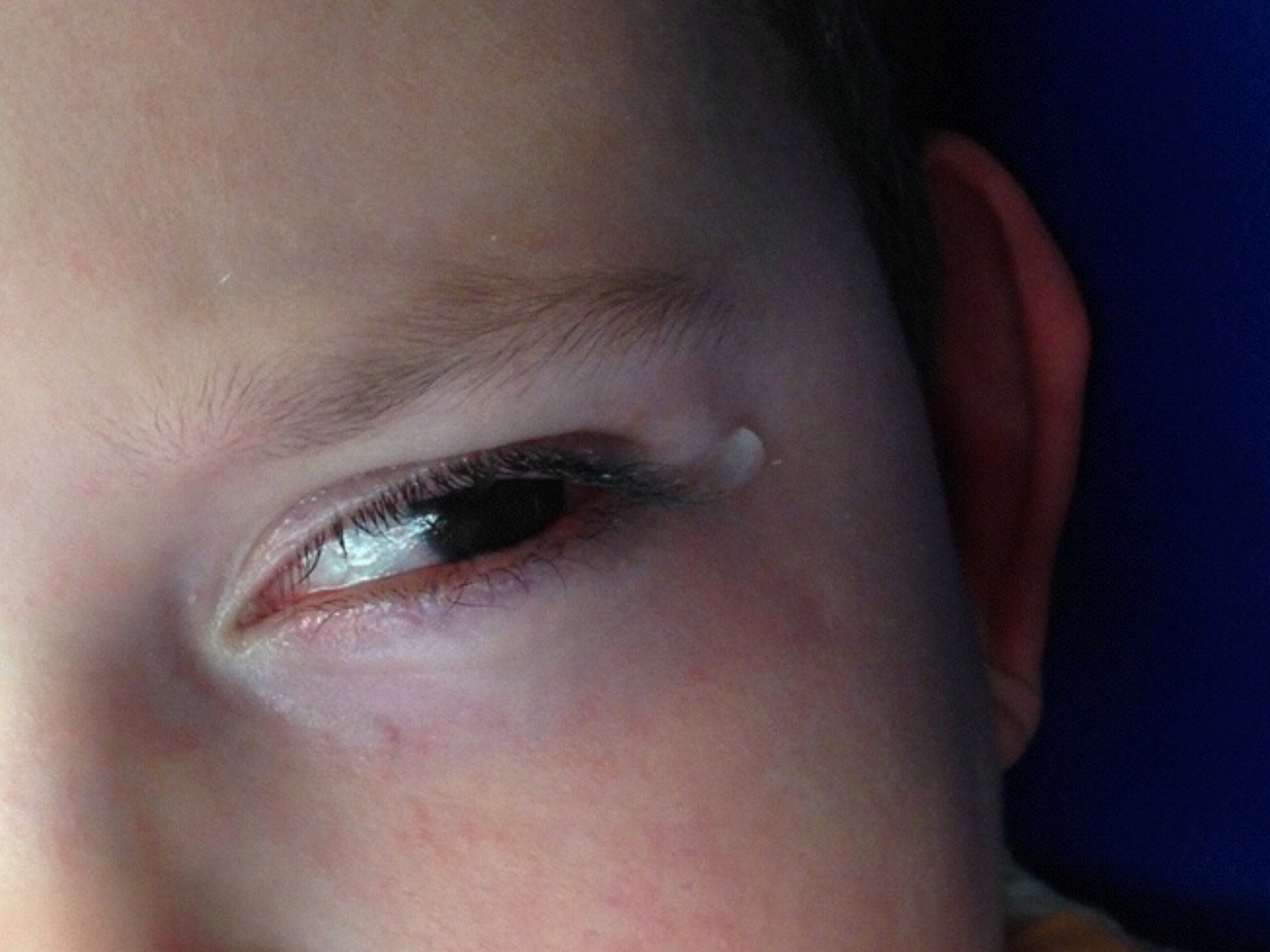






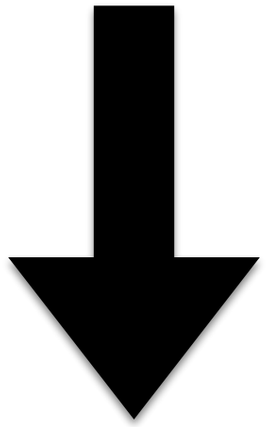






computer science

computer science



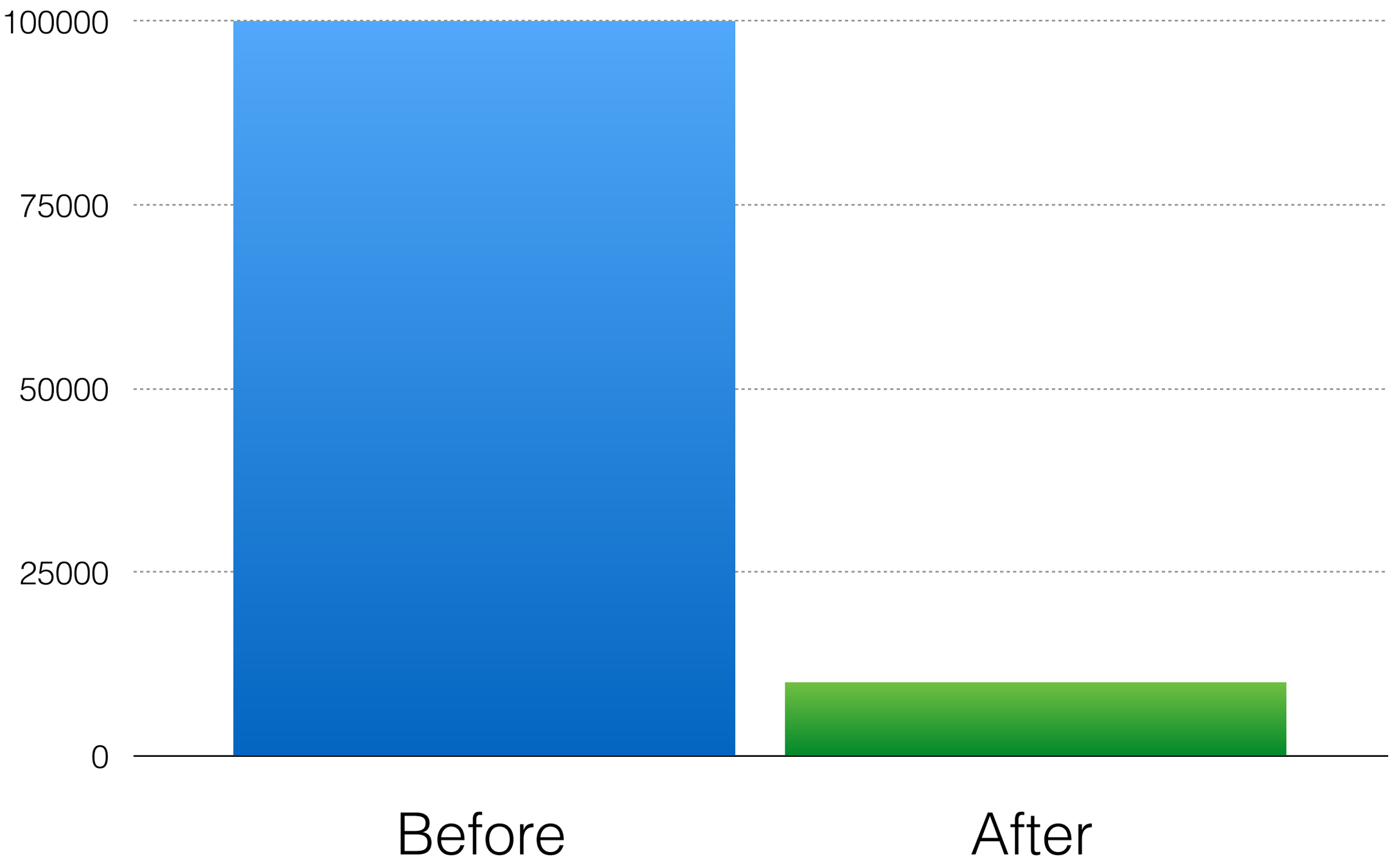
biology & medicine

Toward therapeutics for NGLY1 deficiency

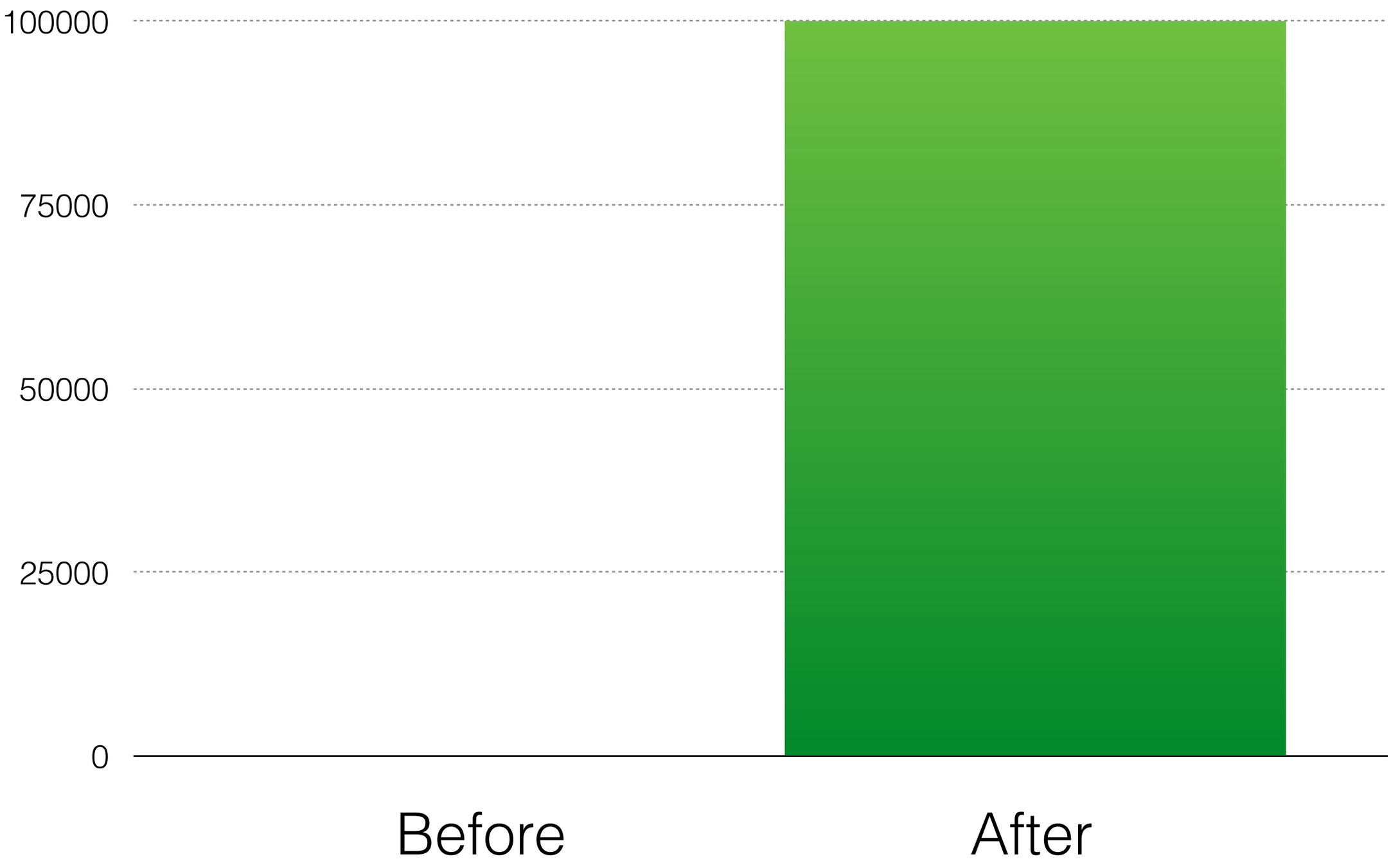
THE UNIVERSITY OF UTAH

Is that “action”?

Annual medical bills



Annual spending on postdocs



Yes

Replicable?

Milo’s family

MILO'S JOURNEY

....looking for companions

Reaching out

This page is for parents, doctors, or researchers who may know of other children like our son, Milo. If you know of a similar case, please get in touch with us. The more cases we have, the more opportunities we will have to improve our understanding of his condition and facilitate research that can help him and others.

Find out more

- What this site is for
- Case study:

Finding others like our Milo

Currently, at age 3, Milo's primary challenges are global developmental delay and significant hypotonia. He has had surgical repairs for a minor cleft in his soft palate, for ptosis, for C1 stenosis, for a tethered

Mother added as co-author on research paper.

Aiden’s family

The Stop Sign in Aidan's Genes (PURA GENE)

I have something special to show you, a little piece of yourself.

But first let me tell you why it's so incredible to me.

My son Aidan was born 13 years ago with an undiagnosed developmental disability so for 13 years I've been watching human development in slow motion. The strength of our muscles, the authority of the brain, the power of the body to heal. The same brain that's made it difficult for him to walk and impossible for him to speak, has also given him the cognitive ability and dexterity to drive a power wheelchair and find other ways to communicate.

For 13 years Aidan's medical team has been searching for a cause of his medical issues. For 13 years we've come up empty handed.

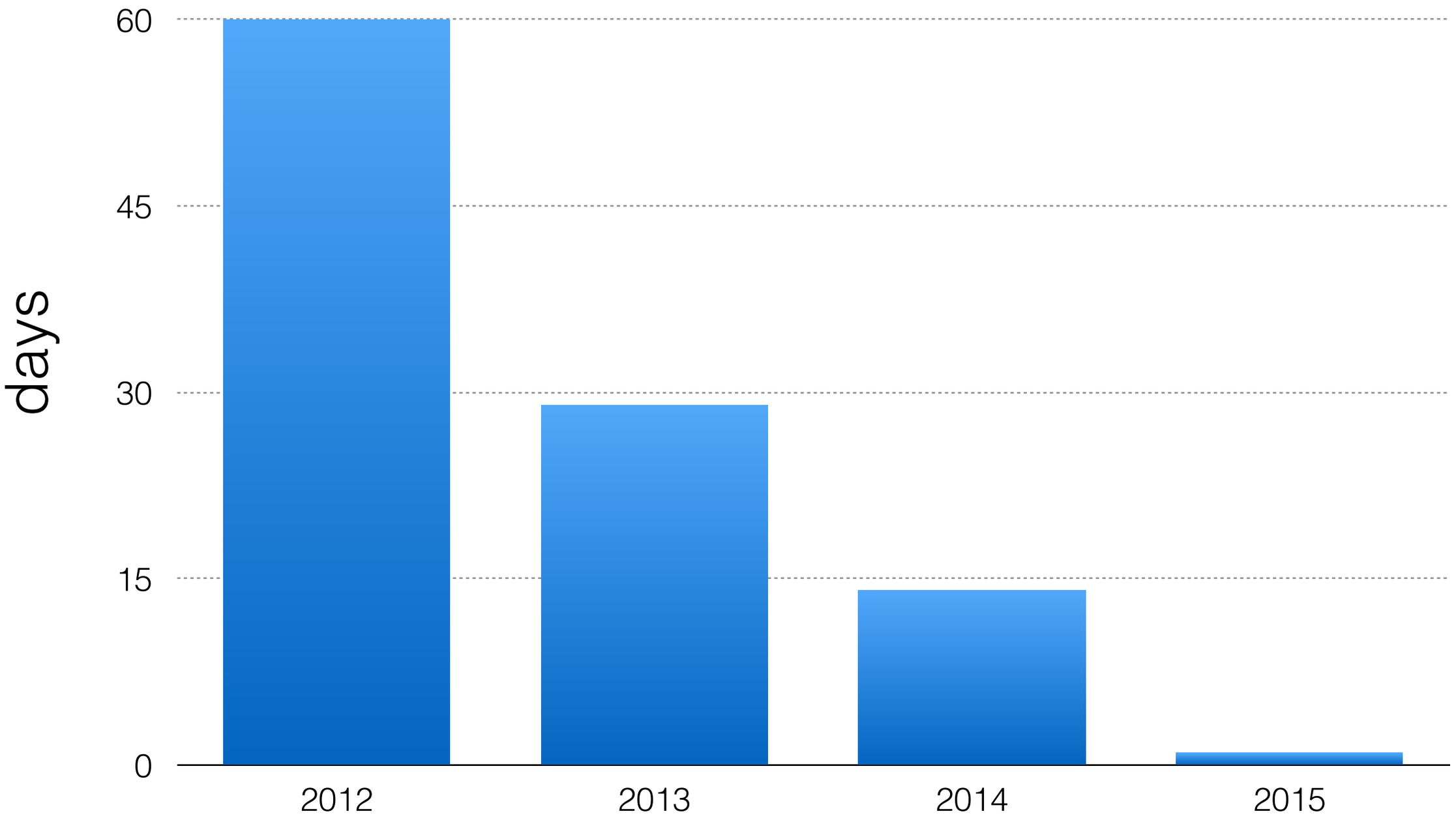
Until now.

Six months ago Aidan's whole exome was sequenced and we found two genetic mutations.

Tess’s family

Help Us Find Others Like Tess

Time to find a matching patient with social media



Overview of NUBPL Mutations

GeneDx (USA): c.166G>A (maternal); c.815-27T>A (maternal); and c.693+1G>A (

Ambry 1 & 2 (USA): c.311T>C (maternal); p.L104P (maternal); and c.815-27T>C (

Kevelam 1 (Arg.): c.166G>A (unknown); and c.815-27T>C (unknown) (older resu

Kevelam 2 (

Kevelam 3&

The p

Kevelam 6 (

Kevelam 7 (
duplication

Big news: This year Aidan was able to have his Whole Exome sequenced. It was covered by insurance at a reduced cost by the lab. It was discovered that he has two genetic variants on his PURA gene on his 5th chromosome. While it is not officially a diagnosis because it has not been thoroughly studied, there is enough information to conclude that it is causative in nature. Aidan's clinical information will be presented in a genetics

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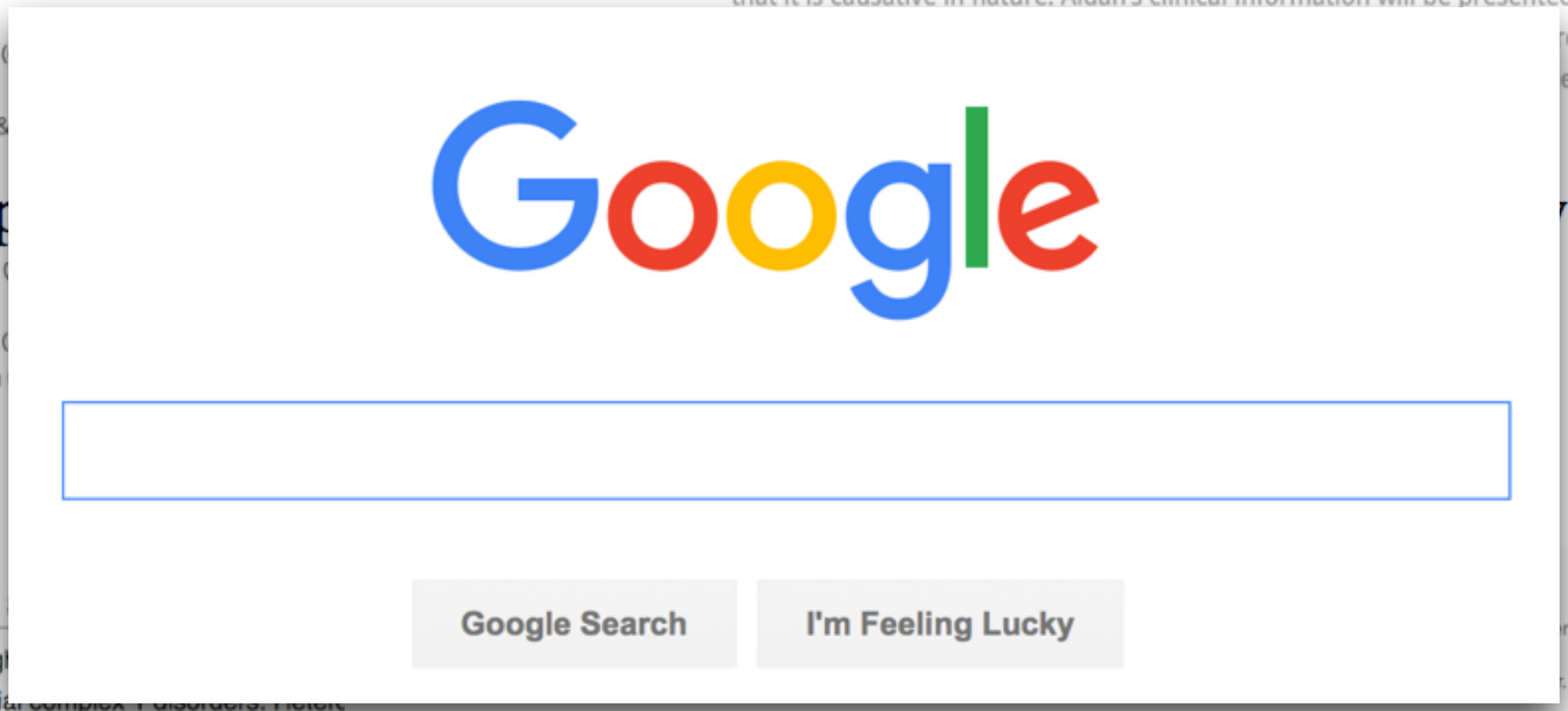


Clinical

High-throug

mitochondria

complementation studies showed that the

consistent with autosomal recessive inher

pathogenicity of the variants that were ide

Complex compound heterozygous variant

mutation (c.166 G>A) resulting in missens

T>C) that caused a splicing error and a co

Two of 232 (1%) control chromosomes we

nt.

We created this page **in order to find other people like Tess**. If we can find even one more person with the same mutation or symptoms, it'll be easier for us and Tess's doctors to figure out what is happening to her and how to help her.

Her symptoms and her specific mutation are set out below.

To read about her journey so far, check out the blog posts "Gene Genie" (**click here**), "This Isn't Over" (**click here**), "Not Giving Up" (**click here**), and "Answers" (**click here**).

To listen to podcast episodes about her genetic journey, check out "Label My Kid Please" (**click here**), "The Dark Night of Uncertainty" (**click here**), and "The Genetic Mystery Continues" (**click here**).

UPDATE: I have amazing news: all your sharing about Tess worked. We found a match!

Tracy Dixon-Salazar


CURE
EPILEPSY
CURE
EPILEPSY

Seizures began 17 years ago

High school diploma

Associate’s degree

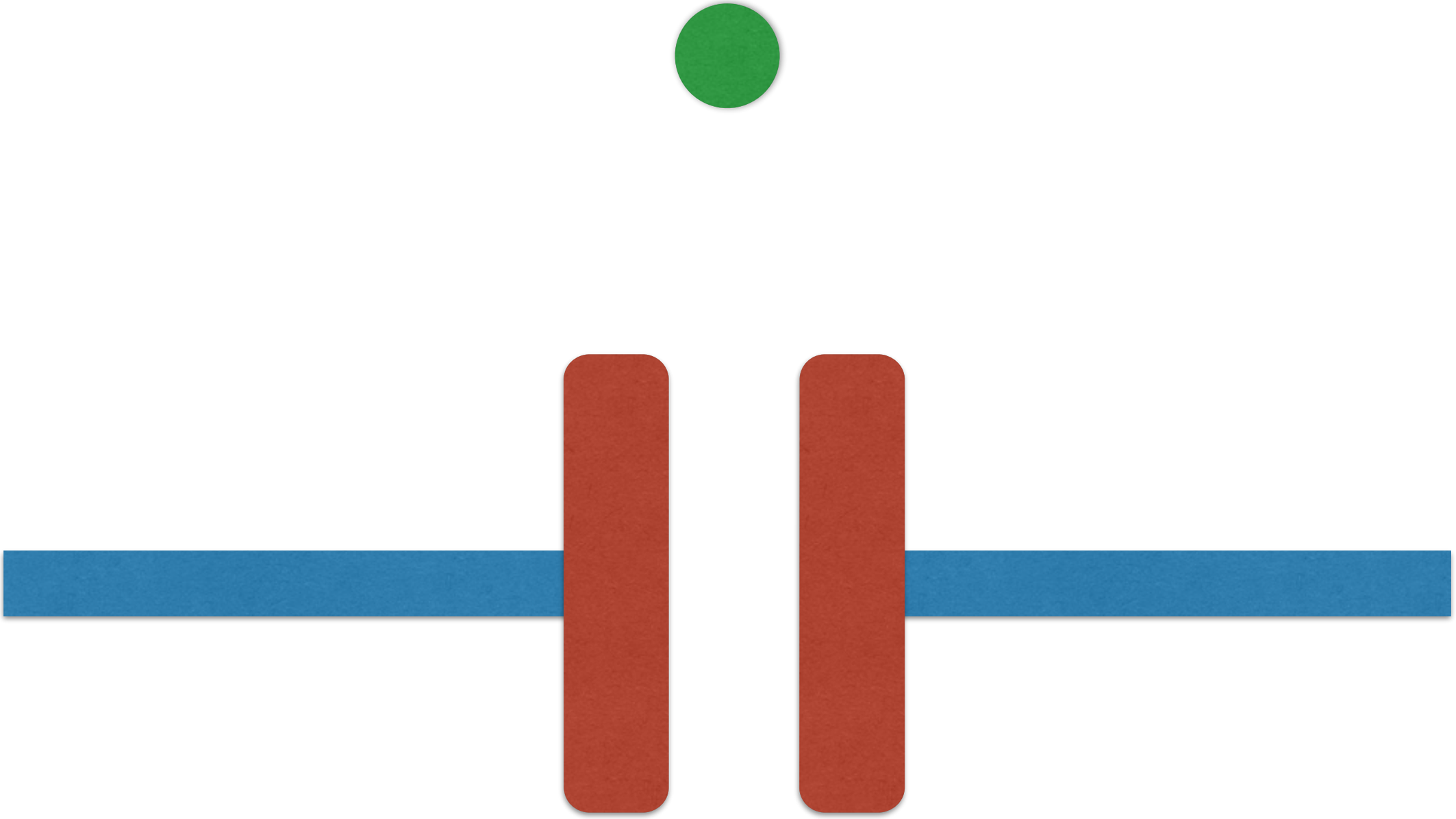
Bachelor’s degree

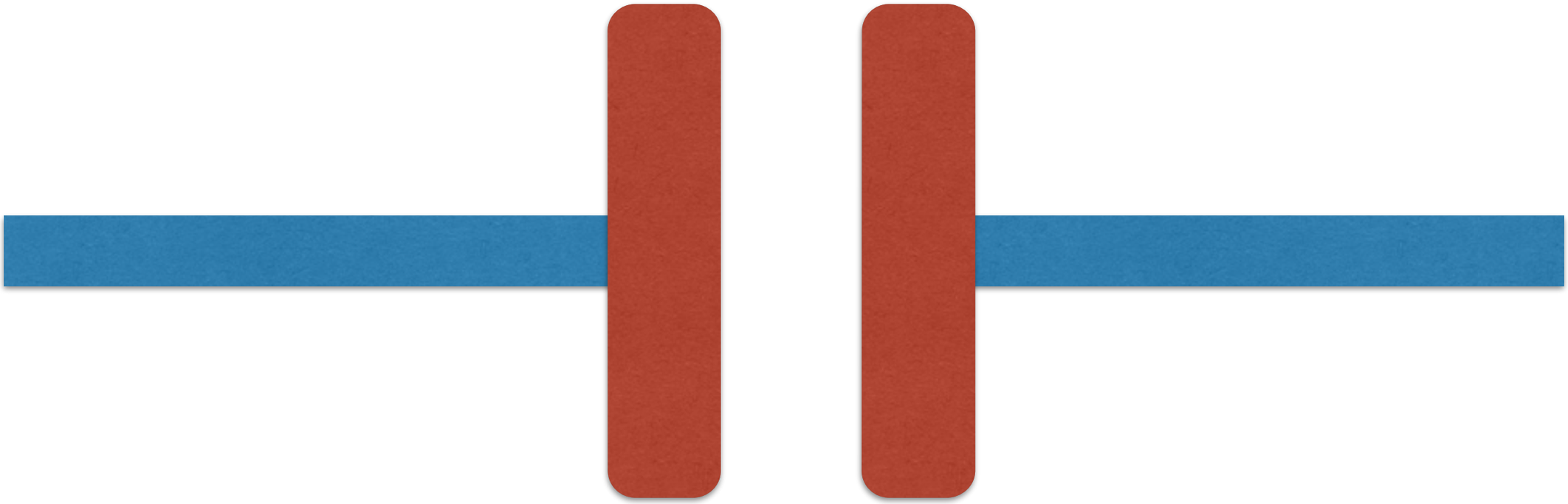
Master’s degree

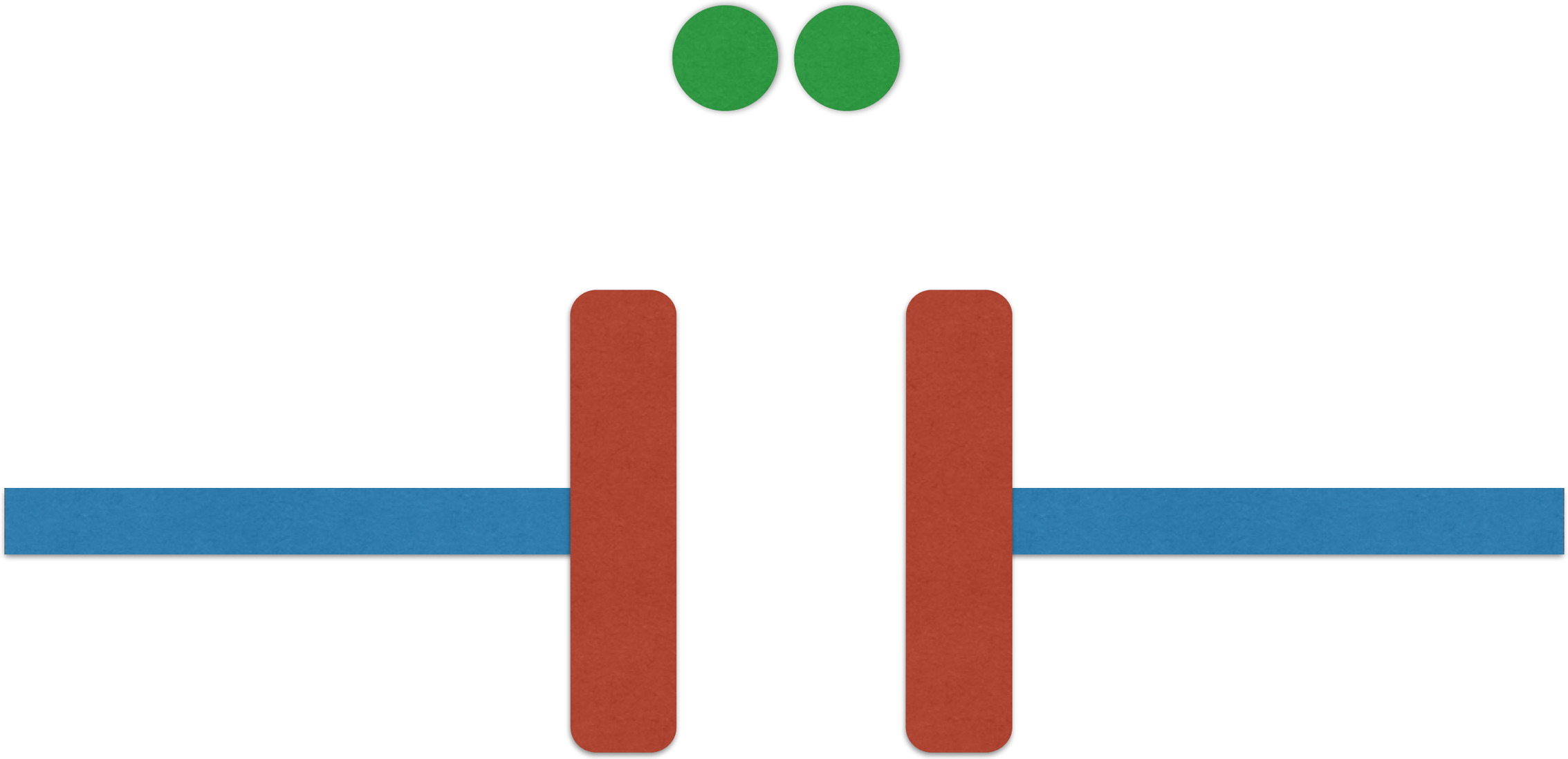
Ph.D. in neurogenetics

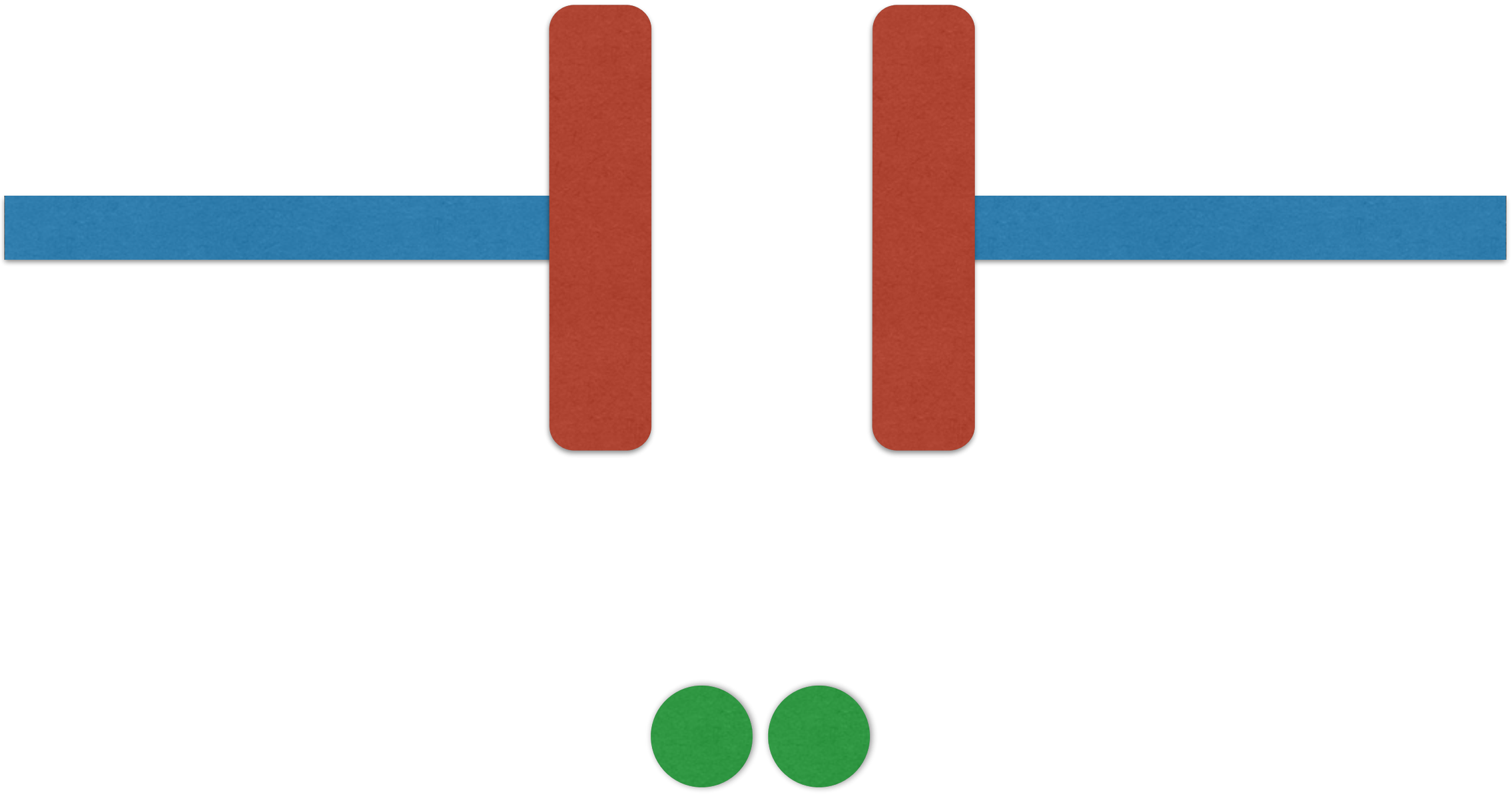
Postdoc doing variant analysis for exomes

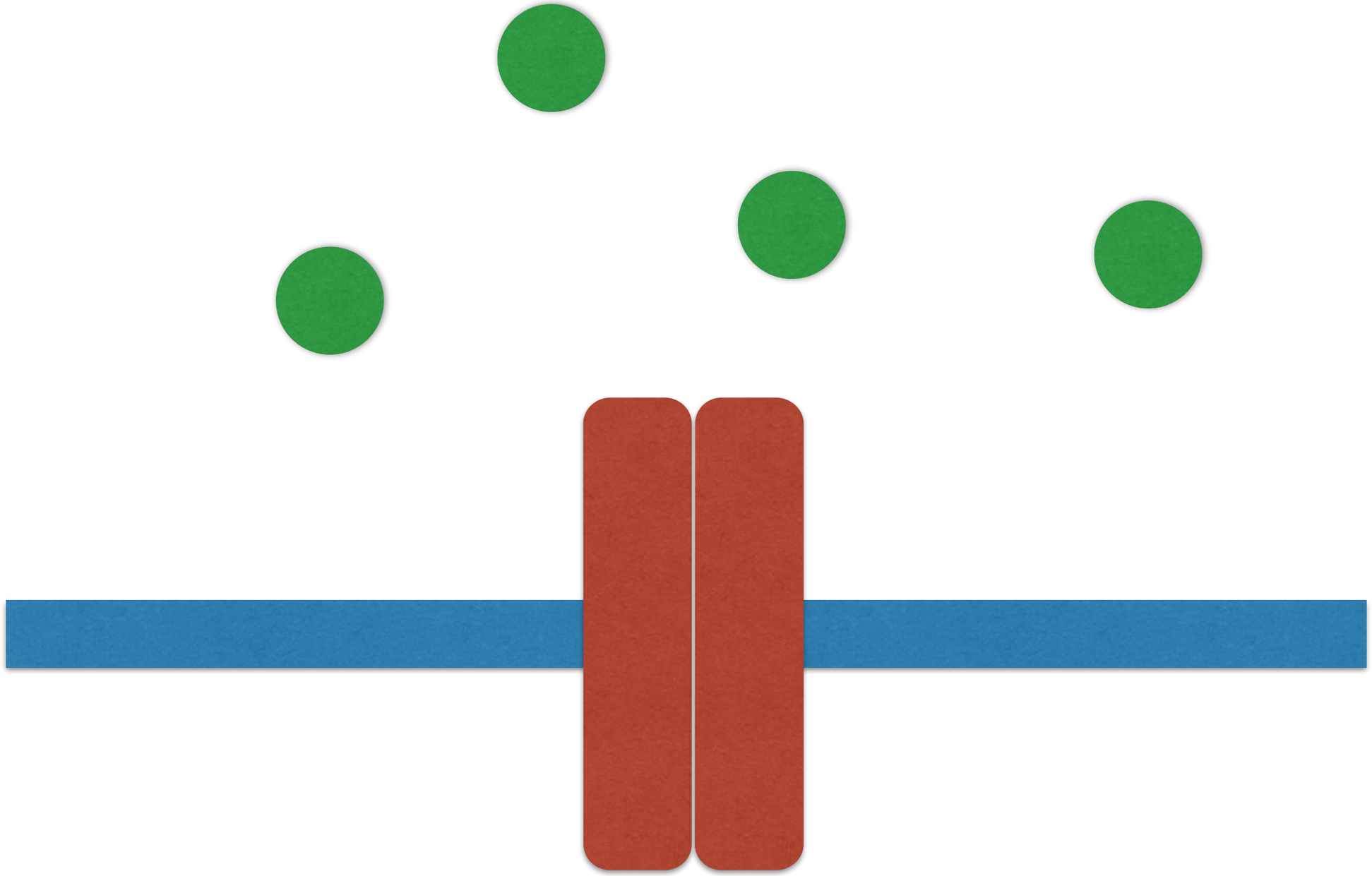
multiple VUSs in L-type calcium channel genes







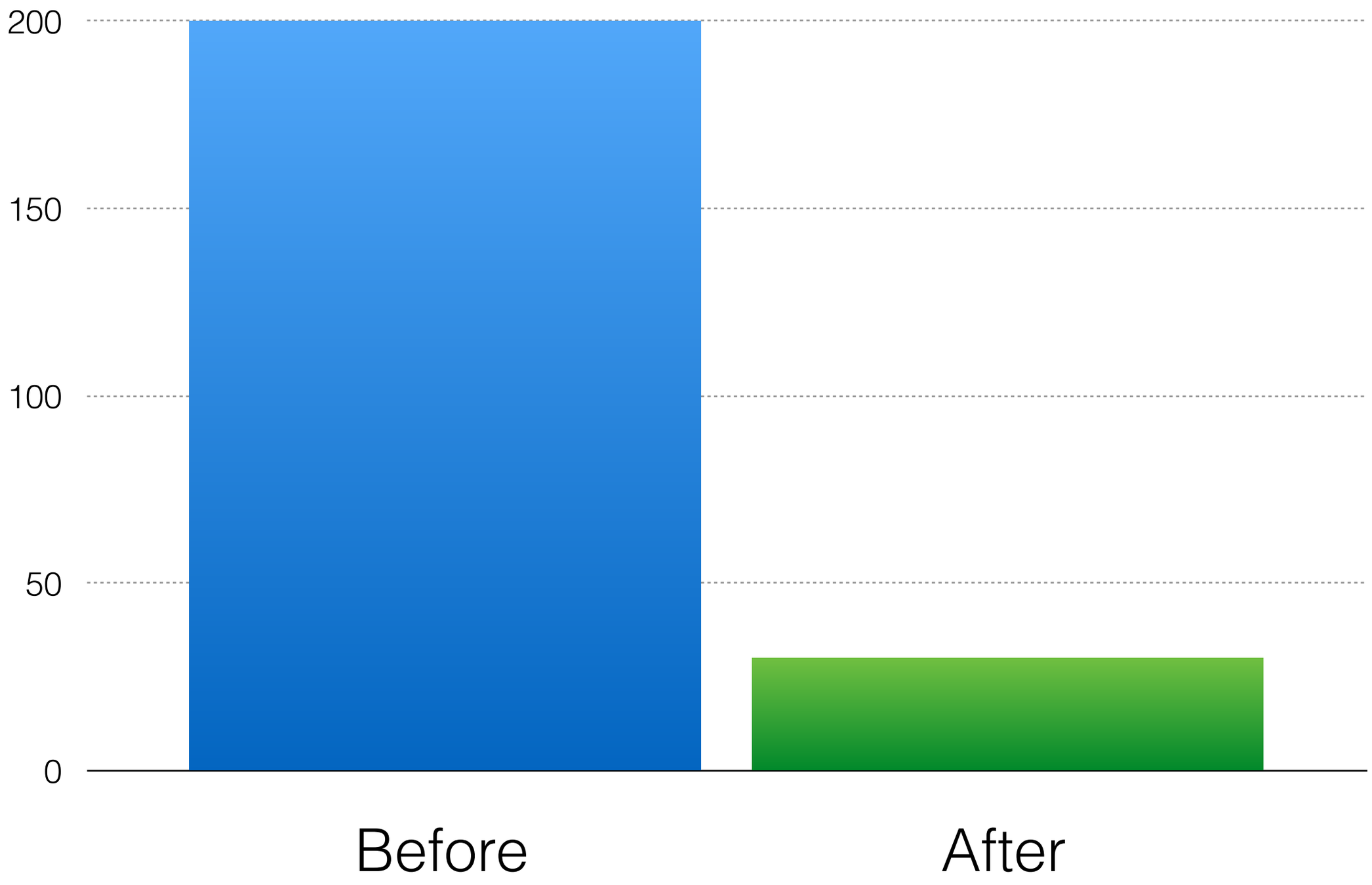




“likely gain of function in L-type calcium channels”

verapmil: L-type calcium channel blocker for arrythmias

Seizures per month



If the only thing we're going to act on are genes known to be linked to diseases or drugs, then we're not going to get very far as when we're willing to take risks.

Tracy Dixon-Salazar

https://www.youtube.com/watch?v=k2zD2MuQsQE

Sonia & Eric

THE NEW YORKER

SEPTEMBER 27, 2013

A PRION LOVE STORY

BY D. T. MAX

Not long ago, I got an e-mail that began this way: "I am writing to introduce myself and my wife and our quest to cure fatal familial insomnia." The writer had found me because, in 2006, I published a book called "The Family That Couldn't Sleep." It's the story of a remarkable family in the Veneto who, for two hundred years, have had a hereditary insomnia that leads to death, usually in their fifties. No one escapes the fate. The

The Genetic Counselling Outcome Scale (GCOS-24)

Using the scale below, circle a number next to each statement to indicate how much you agree with the statement.
Please answer all the questions. For questions that are not applicable to you,
please choose option 4 (neither agree nor disagree).

1 = strongly disagree
2 = disagree
3 = slightly disagree
4 = neither disagree nor agree
5 = slightly agree
6 = agree
7 = strongly agree

		strongly disagree	disagree	slightly disagree	neither agree nor disagree	slightly agree	agree	strongly agree
1	I am clear in my own mind why I am attending the clinical genetics service.	1	2	3	4	5	6	7
2	I can explain what the condition means to people in my family who may need to know.	1	2	3	4	5	6	7
3	I understand the impact of the condition on my child(ren)/any child I may have.	1	2	3	4	5	6	7
4	When I think about the condition in my family, I get upset.	1	2	3	4	5	6	7
5	I don't know where to go to get the medical help I / my family need(s).	1	2	3	4	5	6	7
6	I can see that good things have come from having this condition in my family.	1	2	3	4	5	6	7
7	I can control how this condition affects my family.	1	2	3	4	5	6	7
8	I feel positive about the future.	1	2	3	4	5	6	7
9	I am able to cope with having this condition in my family.	1	2	3	4	5	6	7
10	I don't know what could be gained from each of the options available to me.	1	2	3	4	5	6	7
11	Having this condition in my family makes me feel anxious.	1	2	3	4	5	6	7
12	I don't know if this condition could affect my other relatives (brothers, sisters, aunts, uncles, cousins).	1	2	3	4	5	6	7
13	In relation to the condition in my family, nothing I decide will change the future for my children / any children I might have.	1	2	3	4	5	6	7
14	I understand the reasons why my doctor referred me to the clinical genetics service.	1	2	3	4	5	6	7
15	I know how to get the non-medical help I / my family needs (e.g. educational, financial, social support).	1	2	3	4	5	6	7
16	I can explain what the condition means to people outside my family who may need to know (e.g. teachers, social workers).	1	2	3	4	5	6	7
17	I don't know what I can do to change how this condition affects me / my children.	1	2	3	4	5	6	7
18	I don't know who else in my family might be at risk for this condition.	1	2	3	4	5	6	7
19	I am hopeful that my children can look forward to a rewarding family life.	1	2	3	4	5	6	7
20	I am able to make plans for the future.	1	2	3	4	5	6	7
21	I feel guilty because I (might have) passed this condition on to my children.	1	2	3	4	5	6	7
22	I am powerless to do anything about this condition in my family.	1	2	3	4	5	6	7
23	I understand what concerns brought me to the clinical genetics service.	1	2	3	4	5	6	7
24	I can make decisions about the condition that may change my child(ren)'s future / the future of any child(ren) I may have.	1	2	3	4	5	6	7

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1	I am clear in my own mind why I am attending the clinical genetics service.	1	2	3	4	5	6	7
2	I can explain what the condition means to people in my family who may need to know.	1	2	3	4	5	6	7
3	I understand the impact of the condition on my child(ren)/any child I may have.	1	2	3	4	5	6	7
4	When I think about the condition in my family, I get upset.	1	2	3	4	5	6	7
5	I don't know where to go to get the medical help I / my family need(s).	1	2	3	4	5	6	7
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“not actionable”

Thank you!

Matt Might | matt.might.net | @mattmight