Community

What do you do when you’re the first?
What can a Community of one do?
How do you create a Community?
What can a Community do?
“Undiagnosed island”
NGLY1
NGLY1
What if \( n = 1 \)?
“Not actionable.”
Aftermath
The science is the medicine.
“We can’t do this alone.”
“Let’s find the others.”
Hunting down my son's killer

I found my son's killer.

It took three years.

But we did it.

Not quite like this.
2,000,000
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
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)]
National Center for Biotech...
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.
MEDICAL DISPATCH

ONE OF A KIND

What do you do if your child has a condition that is new to science?

BY SETH Mnookin

MATT MIGHT and Cristina Casanova met in the spring of 2002, as twenty-year-old undergraduates at the Georgia Institute of Technology. Cristina was majoring in chemistry, and Matt was majoring in math; both were also pursuing minors in biochemistry. They were drawn to each other by their shared interest in science and medicine. They quickly discovered that they had a lot in common: both enjoyed playing video games and both were members of the university’s science club. Their friendship blossomed over the next few years, and eventually they decided to get married in 2006.

City, and the first available appointment fell on the same day as a mandatory faculty retreat. That afternoon, when Matt was able to check his phone, he saw that Cristina had left several messages. “I didn’t listen to them,” he told me in an e-mail. “I didn’t have to. The number of them told me this was really bad.”

Bertrand had brain damage; at least, that was the diagnosis until an MRI revealed that his brain was perfectly normal. After a new round of lab work was done, Bertrand’s doctors concluded that he likely had a rare, inherited movement disorder called ataxia-telangiectasia. A subsequent genetic screening confirmed their suspicions.

Dr. David Goldstein to direct Institute for Genomic Medicine at Columbia University

Open science and social media were key in the discovery and growth of the NGLY1 rare disease community. Article by Seth Mnookin.

NGLY1 in The New Yorker!

Do you know a NGLY1 patient?

If you know a patient with NGLY1-deficiency, or think you do, please contact us immediately.

You can reach us directly at info@ngly1.org

NGLY1 Symptoms

Global Developmental Delays

Movement Disorder

Hypotonia
Communities can push science!
Clinical research
Biomarkers!
High-throughput drug screening
Transgenics
KAL

NUTRITIONAL

INNOVATIVE QUALITY

Since 1932

Yeast Flakes

PREMIUM • UNSWEETENED • FORTIFIED

Gluten Free

Wonderful Nutty Flavor
Non-GMO

NET WT. 22 oz. (624 g)
Biologics
Human NGLY1 full length protein (ab163212)

Overview

Product name: Human NGLY1 full length protein

Description

Nature: Recombinant
Source: Wheat germ
Amino Acid Sequence
Species: Human

Ship in: 10 μg
Price: $402

Order now and get it on Tuesday, February 10, 2015

ADD TO BASKET
Or
Request quote for bulk purchase

Shipping info

$60.00 to United States
Same day delivery on Boston area
PEG polymer

TAT peptide
When suddenly...
a breakthrough
Endo-β-N-acetylglucosaminidase forms N-GlcNAc protein aggregates during ER-associated degradation in Ngly1-defective cells

Chengcheng Huang1,2, Yoshito Hanada3, Akira Hosomi3, Yuki Masahara-Negishi4, Junichi Seino5, Haruhiko Fujibayashi1, Yoko Funakoshi1, Takehiro Suzuki1, Naoshi Dohmae1, and Tadashi Suzuki1,2*

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Edited by David W. Russell, University of Texas Southwestern Medical Center, Dallas, TX, and approved December 30, 2014 (received for review August 1, 2014)

The cytoplasmic peptide:N-glycanase (PNGase; Ngly1 in mice) is a deglycosylating enzyme involved in the endoplasmic reticulum (ER)-associated degradation (ERAD) process. The precise role of Ngly1 in the ERAD process, however, remains unclear in mammals. The findings reported herein, using mouse embryonic fibroblast (MEF) cells, that the ablation of Ngly1 causes dysregulation of the ERAD process (manuscript not only delayed degradation but also the occurrence of protein aggregates) strongly suggested the existence of an ERAD system dedicated to N-linked glyco- proteins; in this system, specific N-glycan structures dictate the efficiency of proteasomal degradation. Moreover, this study may also provide a potential mechanism underlying the pathogenic consequences of a newly emerging genetic disorder caused by mutation of the human Ngly1 gene.


Significance

In the endoplasmic reticulum (ER), N-glycans on glycoproteins play important roles in dictating the folding status of proteins by a sophisticated N-glycan-dependent protein quality control system. This ER-associated degradation (ERAD) in cells that were defective in ERAD dysregulation was caused by an unexpected deglycosylating activity of endo-β-N-acetylglucosaminidase, another cytosolic deglycosylation enzyme, and this action resulted in the intracellular formation of protein aggregates. Our results clarify why the critical role of Ngly1 may be evident in cytosolic event of the ERAD process by controlling the conformation/status of proteins. This study may also provide a potential mechanism for explaining the pathology of a human genetic disorder caused by mutations in the Ngly1 gene.

Author contributions: C. and T. S. designed research; C. performed research; C., T., Y., A., K., S., H. F., Y. F., T. S., N. D., and T. S. analyzed data; and C. and T. S. wrote the paper.

The authors declare no conflict of interest.

Endo-β-N-acetylglucosaminidase forms N-GlcNAc protein aggregates during ER-associated degradation in Ngly1-defective cells.
“Community breakthroughs”
Yes Repeatable?
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
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.
All knowledge is actionable.
The knowledge enables community.
The community drives action.
Thank you!
matt.might.net