New Research Discoveries Benefiting People with Down Syndrome and Opportunities for Participation

November 4th, 2025

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ANSCHUTZ MEDICAL CAMPUS

LINDA CRNIC INSTITUTE for DOWN SYNDROME

GLOBAL DOWN SYNDROME FOUNDATION

Anschutz School of Medicine

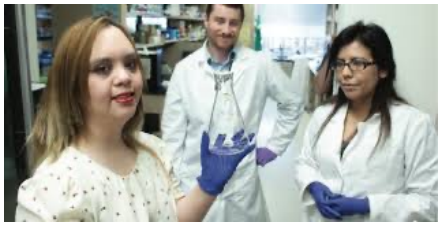
INCLUDE Data Coordinating Center

DS-Connect® The Down Syndrome Registry

The Crnic Institute is the largest center for Down syndrome research in the world

Serving people with Down syndrome through advanced biomedical research leading to improved medical care

70+ research teams



200+ scientists

250+ scientific publications since 2012

GLOBAL DOWN SYNDROME FOUNDATION

Anschutz School of Medicine

2017: an inflexion point

Congressional hearing on Down syndrome research

U.S.A. House of Representatives

October 25th, 2017

Michelle Sie Whitten, Dr. Joaquin Espinosa, Dr. William Mobley, Frank Stephens

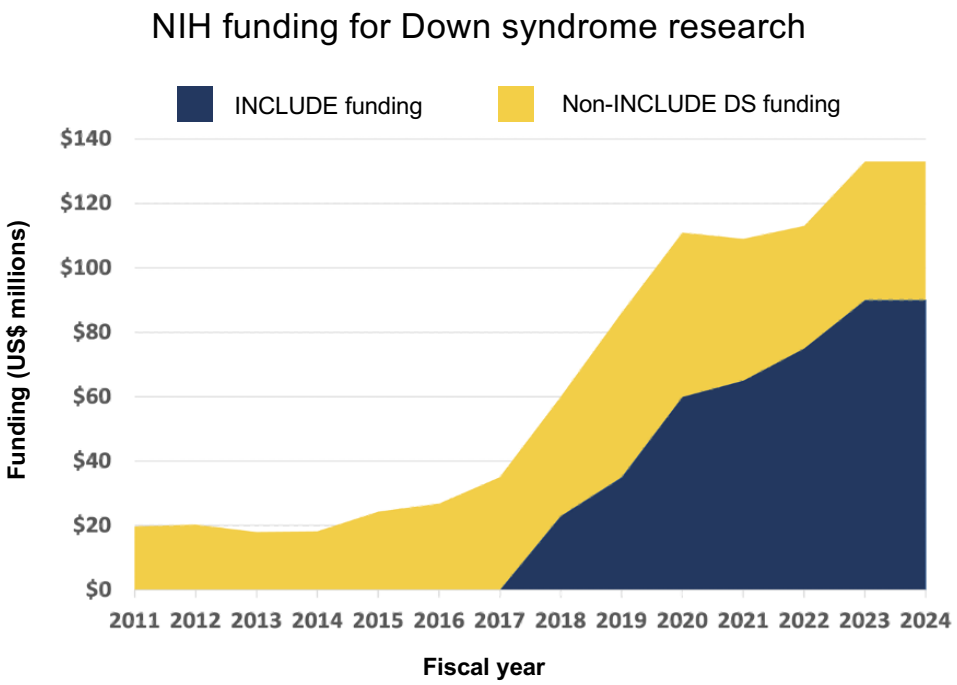
Frank Stephens:
'I am a man with Down syndrome, and my life is worth living'

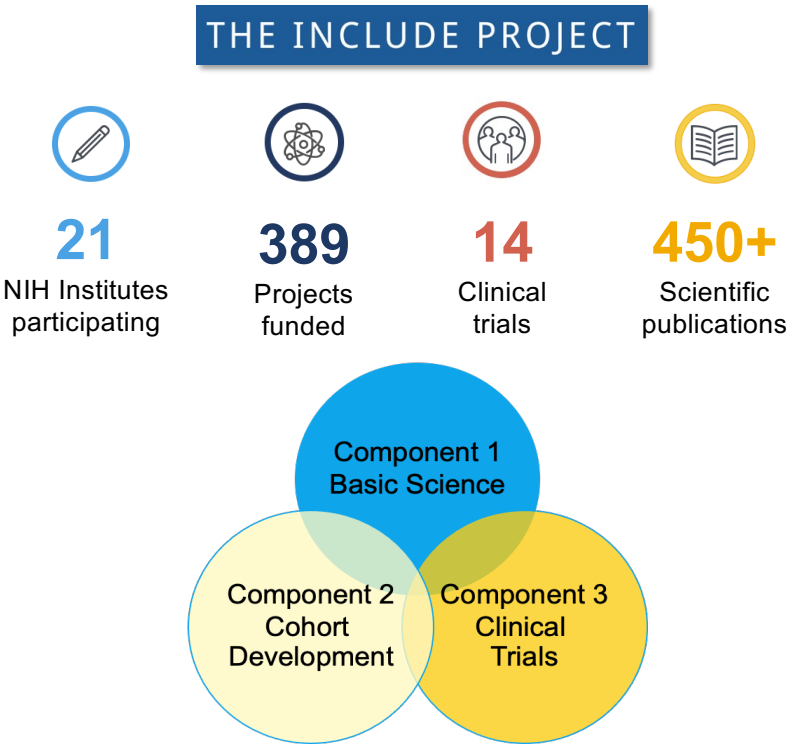
Dr. Francis Collins, Frank Stephens

A productive collaboration between self-advocates, members of Congress, the GLOBAL Down Syndrome Foundation, scientists, and NIH officers, leading to creation of the NIH INCLUDE Project

2018: NIH launches the INCLUDE Project

A trans-NIH project to increase research in Down syndrome





Advocacy efforts leading to the INCLUDE project

Congressional hearing on Down syndrome research

Labor HHS & Education Subcommittee, House of Representatives

October 25th, 2017

Rep. Cathy McMorris Rodgers and family

Rep. Rosa DeLauro and constituents

Rep. Tom Cole and constituents

Strong bipartisan support for more Down syndrome research

People with Down syndrome have a different ‘clinical risk profile’

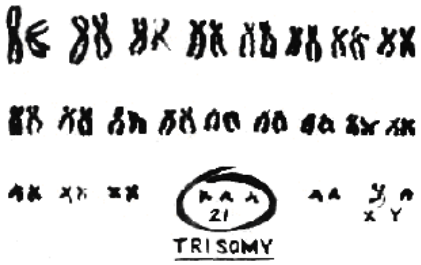
Cancer

Atherosclerosis

Hypertension

Allergies

Common (but variable) traits:
Stunted growth
Neurodevelopmental delays
Early aging



Autoimmunity

Alzheimer’s

Leukemias

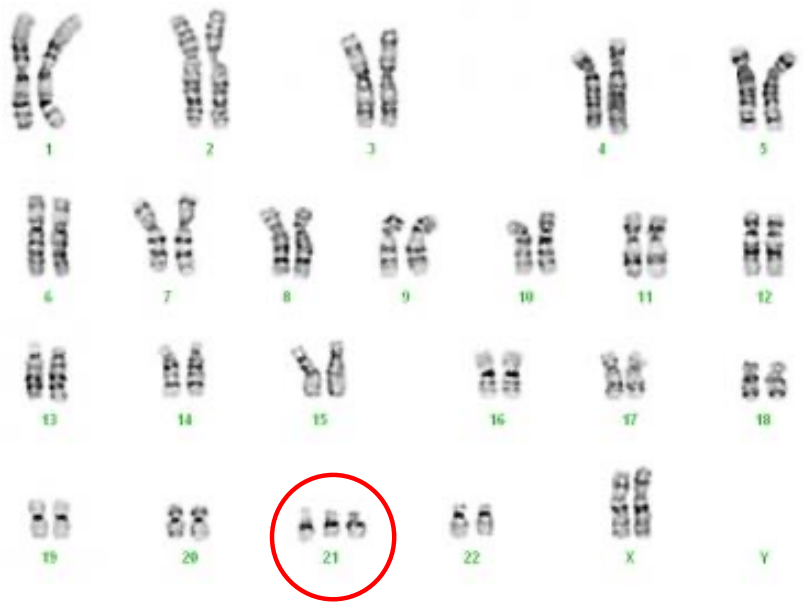
COVID-19

Congenital heart disease, autism spectrum disorders, seizures disorders, and more…

To help people with Down syndrome live longer and healthier lives, we must study the **co-occurring conditions** of Down syndrome

An extra copy of chromosome 21 modulates the appearance and severity of major medical conditions

Human chromosomes: the karyotype



How does an extra copy of this little piece of DNA cause the developmental and clinical hallmarks of Down syndrome?

Which exact genes (out of ~200) encoded on chromosome 21 cause the various features of Down syndrome?

How could we counteract the undesired effects of chromosome triplication and gene overdose to benefit people with Down syndrome?

Diversity = Discoveries

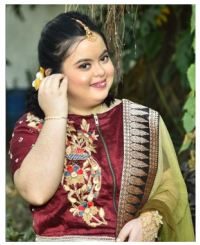
Persons with Down syndrome will teach us how to help them











They are dealing with the trisomy in their own unique personal way

Not two of them are the same, each of them can teach us something new

What factors define the ultimate clinical impacts of the extra chromosome?

The Human Trisome Project (HTP)

A large **cohort study** with deep clinical data,
a multidimensional biobank, and -omics datasets

>1,600 participants
recruited since 2016

LINDA CRNIC INSTITUTE
HUMAN TRISOME PROJECT™
GLOBAL DOWN SYNDROME FOUNDATION

GLOBAL
DOWN SYNDROME FOUNDATION

trisome.org

Thousands of biospecimens collected
and 'omics datasets generated

- Clinical histories
- Genomes
- Transcriptomes
- Immune maps
- Metabolomes
- Microbiomes

Data shared through the
INCLUDE Data Hub

INCLUDE Data Hub

includedcc.org

50+ research projects supported

30+ publications

Funded by:

NIH *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

NIH National Heart, Lung, and Blood Institute

NIH National Institute on Aging

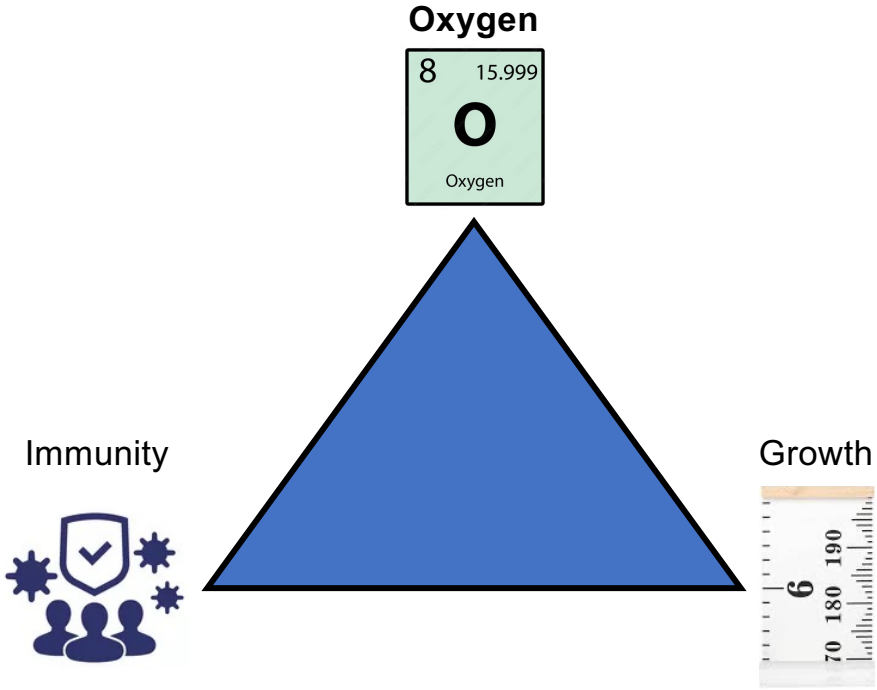
NIH National Institute of Allergy and Infectious Diseases

NIH National Institute on Deafness and Other Communication Disorders

NIH National Center for Advancing Translational Sciences

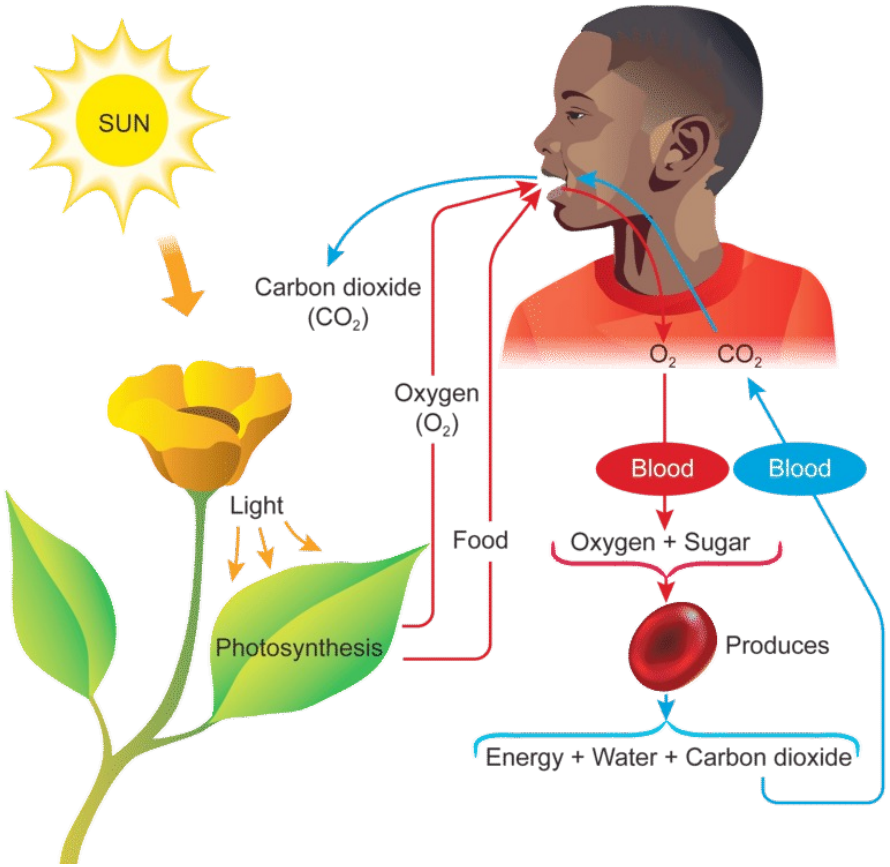
Three pillars of health:

Oxygen, growth, and immunity



Breathe, grow, and be yourself

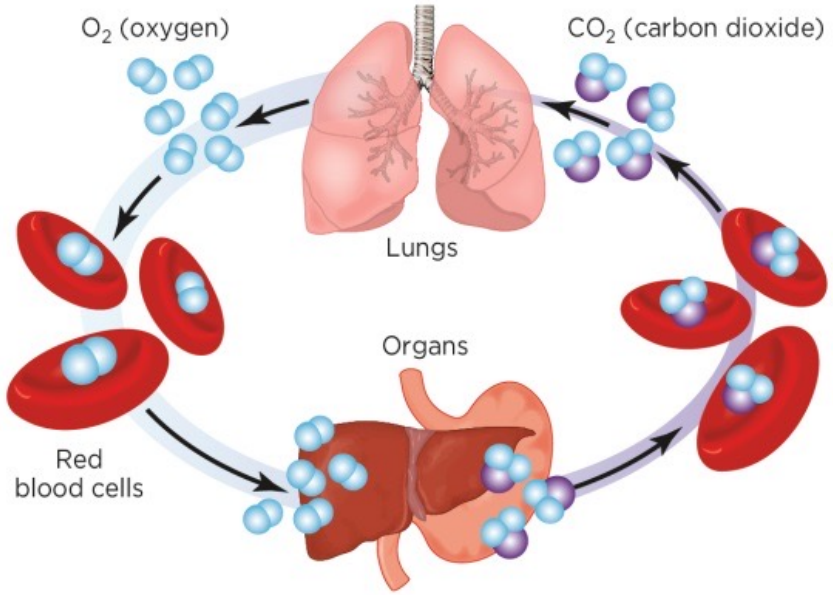
Oxygen is important



Life on Earth:

1. The Sun shines
2. Trees, plants, and algae use sunlight and carbon dioxide (CO_2) to grow and produce di-molecular oxygen (O_2)
3. We breathe in air, which is ~21% O_2, to stay alive.
4. Our cells employ the oxygen we breathe, along with a carbon source (such as sugar), to create energy.
5. We breathe out CO_2

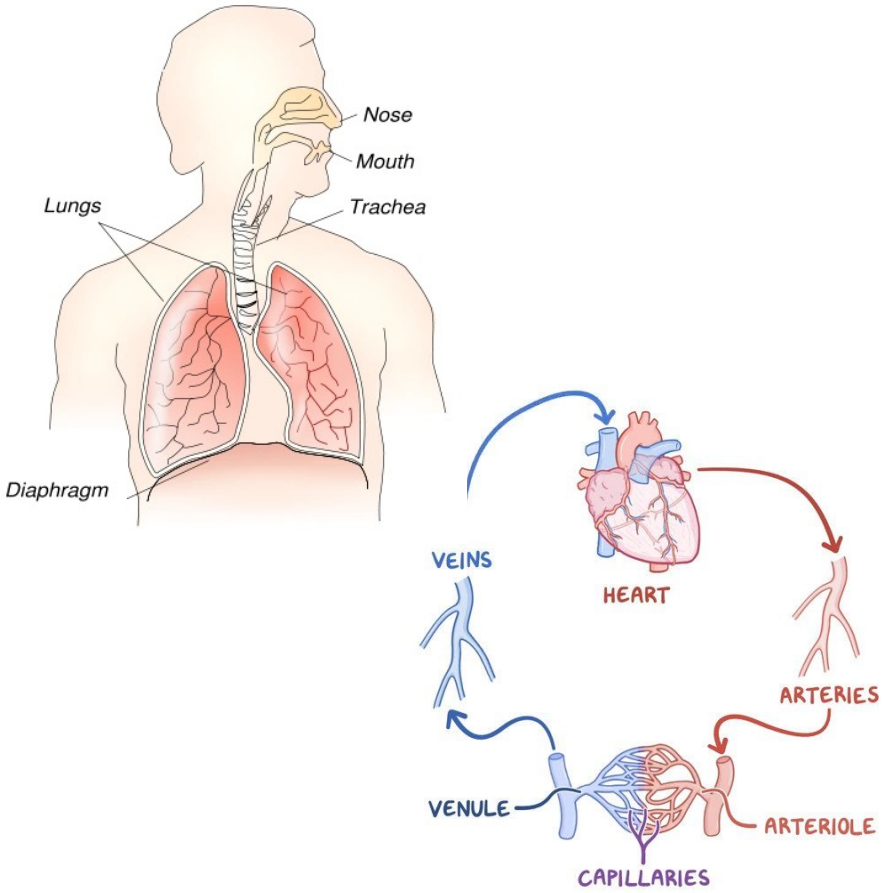
Breathing is important



Breathe in, breathe out:

1. Air goes in through our nostrils (ideally).
2. Once in the lungs, oxygen is loaded into red blood cells.
3. Red blood cells deliver oxygen to all other parts of the body.
4. Red blood cells take up the carbon dioxide (CO_2) back to the lungs.
5. We breathe out the excess CO_2.

Other important things:



1. Air must flow freely through the ‘upper respiratory tract’ into the lungs.
2. Lungs must be free of other things (such as water, food) to take air.
3. The heart should pump blood efficiently in and out of the lungs.
4. The heart should pump faster when we need more oxygen (such as during exercise).
5. Red blood cells, which are the most abundant cells in the human body, should be in good shape too.

Scientific fact:

On average, individuals with Down syndrome have less oxygen in the blood

Individuals with Down syndrome display '**hypoxemia**' or '**hypoxia**'

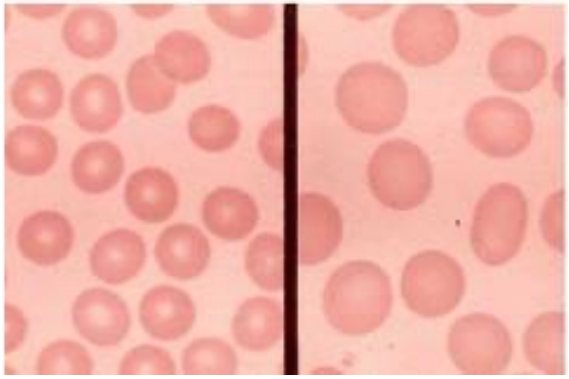
What are ‘normal’ oxygen levels?

Blood oxygen saturation (SpO_2)

100 - 98 %		Normal
97 - 95 %		Insufficient Tolerable, patient hardly notices any influence
94 - 90 %		Decreased Immediate intervention (eating, exercise)
< 90 %		Critical Referral to specialist
< 80 %		Severe hypoxia Hospitalization
< 70 %		Acute danger to life

It is unusual for people with Down syndrome to display 98-100% oxygen saturation

People with Down syndrome tend to be ‘hypoxemic’



Key scientific observations:

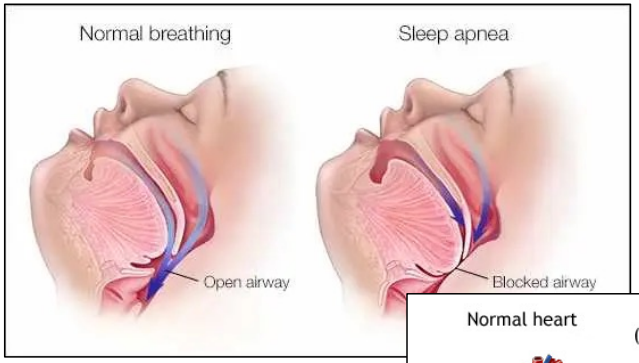
1. On average, individuals with Down syndrome have less oxygen in the blood.

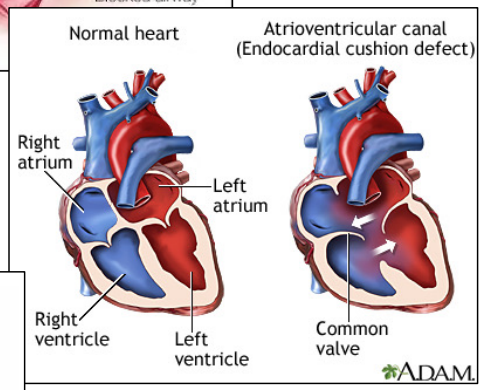
2. Individuals with Down syndrome do more breaths per minute, that is, they are breathing harder.

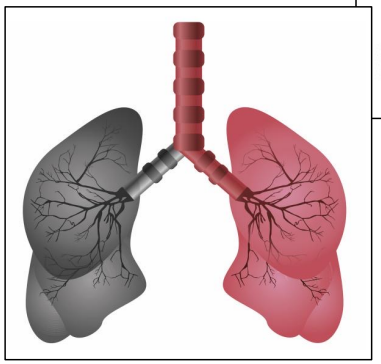
3. People with Down syndrome are constantly making new red blood cells (a.k.a. erythropoiesis).

4. Red blood cells of people with Down syndrome are fewer in number but bigger in size, a sign of ‘young’ red blood cells (a.k.a. macrocytosis).

Why do persons with Down syndrome experience hypoxia?



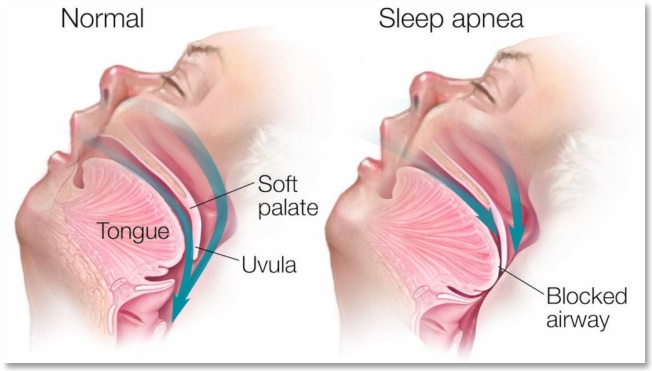


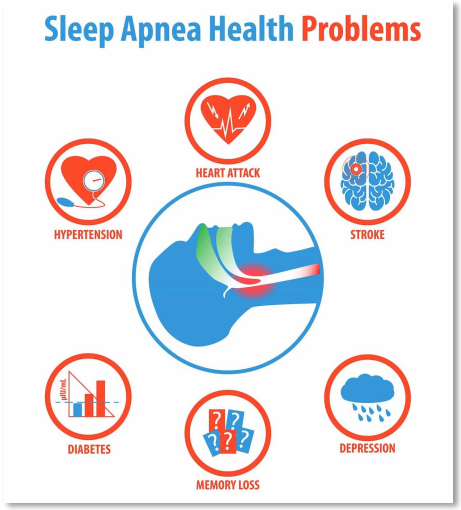


There could be several causes:

1. Obstructive sleep apnea (OSA).
2. Inadequate heart function.
3. Decreased lung function.
4. Decreased ‘adjustment’ (sympathetic response).
5. Other causes.

OSA: Obstructive Sleep Apnea





OSA in Down syndrome:

1. Studies indicate up to 85% prevalence in Down syndrome.
2. If untreated, can increase risk of many other conditions.
3. It is exacerbated by obesity.
4. Treating OSA improves neurodevelopmental outcomes.

Hypoxia is no fun

Hypoxia can lead to:

1. Decreased brain activity, including poor reflexes, decreased memory recall, decreased attention, impaired judgment, decreased motor coordination.

2. Decrease muscle work capacity, contributing to a lethargic or fatigued state.

3. If more severe, hypoxia can cause seizures and other neurological complications (e.g., **nystagmus**).

4. Over time, hypoxia could impair growth and normal organ function.

Call to action:
How to help our loved ones with Down syndrome?

- Be aware of hypoxia!
- Complete a sleep study.
  - AAP: polysomnography before the age of 4
- Consult with your doctor about therapeutic options for OSA: tonsillectomy, adenoidectomy, CPAP, hypoglossal stimulation.
- Track oxygen levels at home: knowledge is power!

Call to action:
How to help our loved ones with Down syndrome?

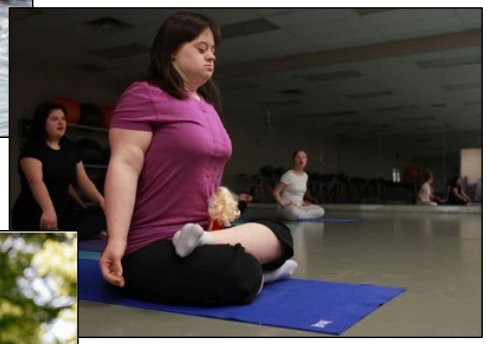
Beyond congenital heart defects:

- Continue to monitor for good heart function during annual health check ups (such as electrocardiograms).
- Don’t leave heart issues ‘unattended’.
- Keep a healthy heart through good diet and exercise.

Call to action:
How to help our loved ones with Down syndrome?

- Watch out for ‘dysphagia’: food and water going into the lungs.
- Complete a swallow study if recommended by your doctor.
- Engage in feeding therapy as needed.
- Stay clear of lung infections!: use masks, get vaccines, and use distancing as needed.
- Watch out for **vitamin D deficiency**: vitamin D is important for lung development and function.

Call to action:
How to help our loved ones with Down syndrome?



- Learn to breathe properly!
- Start a yoga practice
- Walk in green spaces, get out in the Sun, and hug a tree as often as possible!
- Keep a healthy weight

Clinical trial for oxygen supplementation

There are **many clinical trials for OSA** funded by the INCLUDE Project

DOSA

Oxygen Therapy in Children and Adolescents
with Down Syndrome and Obstructive Sleep Apnea

https://www.dosatrial.org

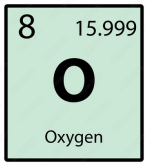
Dr. Raouf Amin
Cincinnati Children's Hospital

Funded by: THE INCLUDE PROJECT

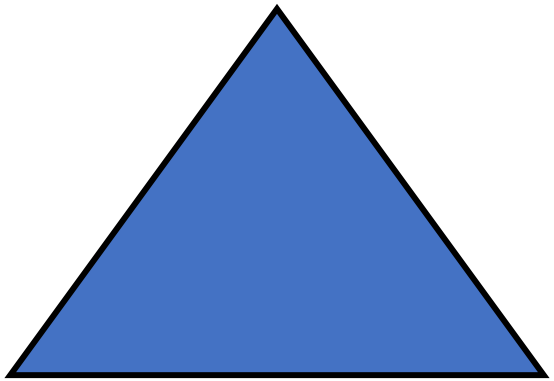
Three pillars of health:

Oxygen, **growth,** and immunity

Oxygen



Immunity

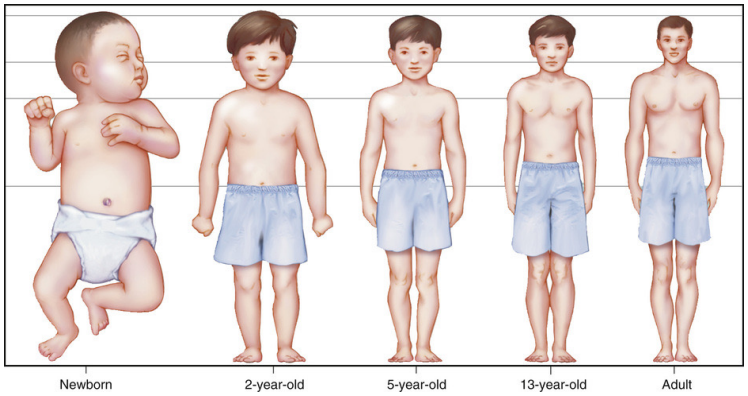


Growth

Breathe, **grow**, and be yourself

Growth and regeneration in human health

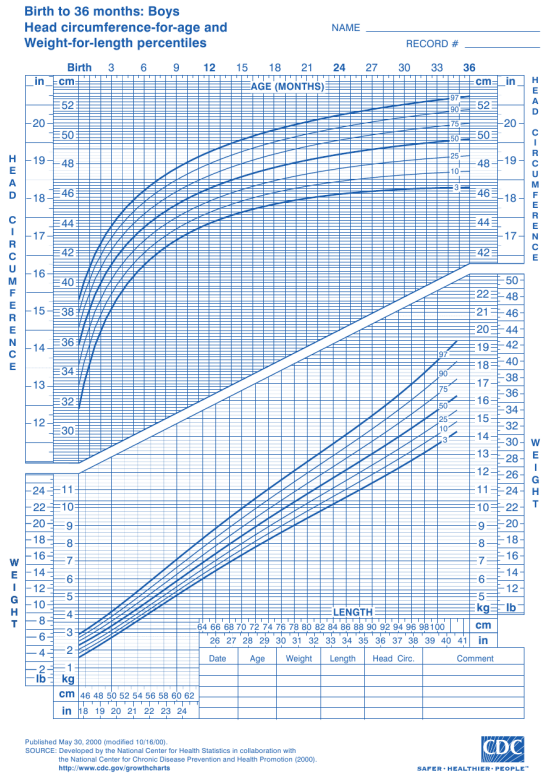
Human development involves coordinated growth of various body parts, organs and tissues



- Human development involves not only growth in size, but also increase in the number of cells and harmonic changes in the proportions of various body parts.
- Coordinated changes in body size and body composition are key for healthy human development.
- Proportional growth of muscles and bones is needed for muscle strength, psycho-neuro-motor development, social adjustment, well being, and quality of life.

Growth and regeneration in human health

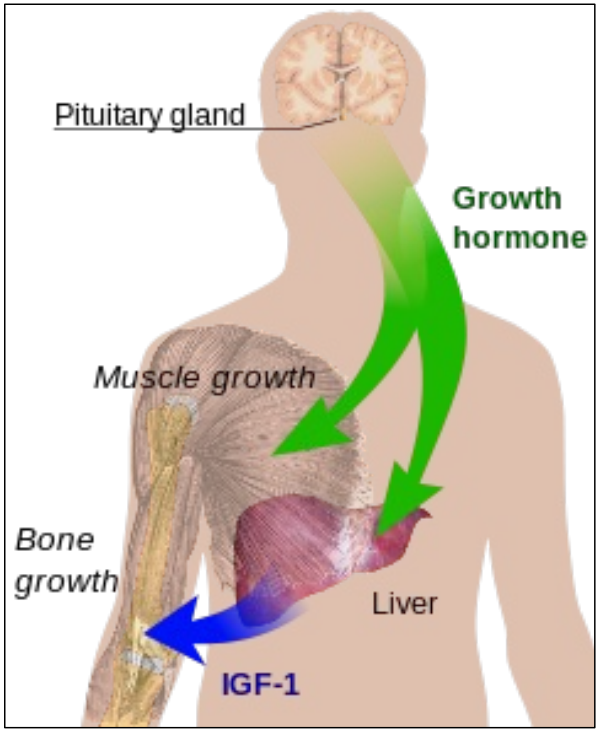
Human development involves coordinated growth of various body parts, organs and tissues



- The coordinated growth and shift in proportions during early childhood is captured by growth charts.
- Head circumference grows exponentially during the first year of life.
- Weight and height increase more linearly during early childhood.

Growth and regeneration in human health

Human development involves coordinated growth of various body parts, organs and tissues



- Human growth is driven by the pituitary growth hormone and the insulin-like growth factor 1 (IGF1).
- Growth hormone is produced by the pituitary gland, IGF1 is produced mostly (~75%) by the liver.
- Deficiencies in either growth hormone or IGF1 impair human growth and development.

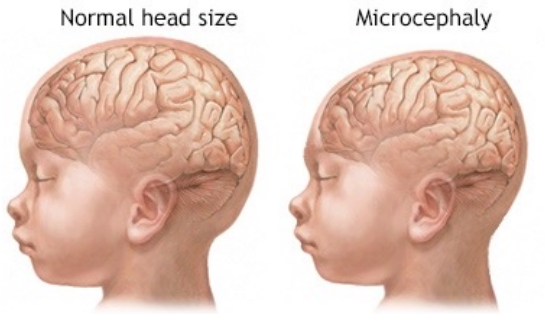
Growth and Down syndrome

Persons with Down syndrome display stunted growth and differences in body proportions

- It is estimated that persons with Down syndrome are, **on average**, 20% shorter than they would otherwise be if they did not have trisomy 21.
- Persons with Down syndrome have, on average, increased ‘body mass index’ (BMI), that is, more pounds per inch.
- **Adults with Down syndrome have higher rates of obesity not because they are heavier, but because they are shorter…**

Growth and Down syndrome

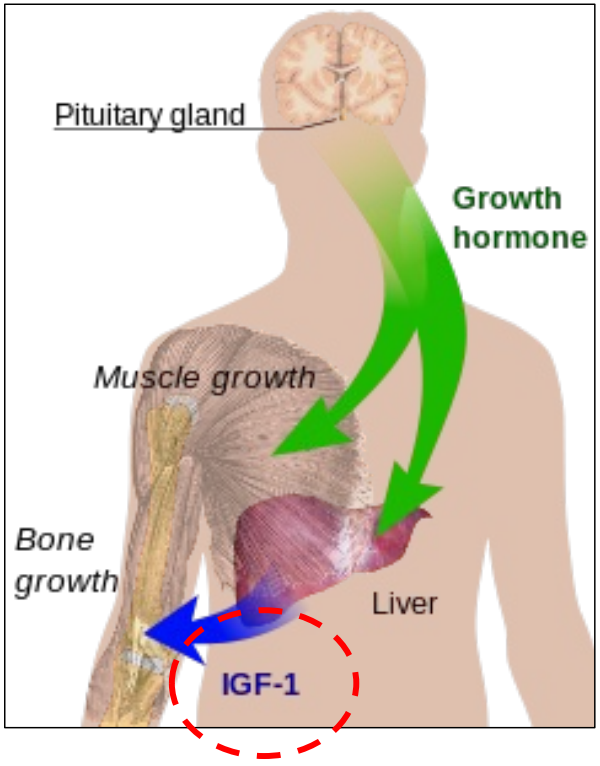
Persons with Down syndrome display smaller head circumferences and decreased brain volume



- On average, individuals with Down syndrome have decreased brain volume, with some brain regions being more affected than others.
- Decreased brain volume is likely to contribute to the neurodevelopmental differences characteristic of Down syndrome.
- **Disclaimer:** although brain size is modestly correlated with IQ, **there is much more to intelligence than just brain size!!**

Growth and Down syndrome

Why are persons with Down syndrome smaller?



On average:

Persons with Down syndrome make the right amount of growth hormone

However:

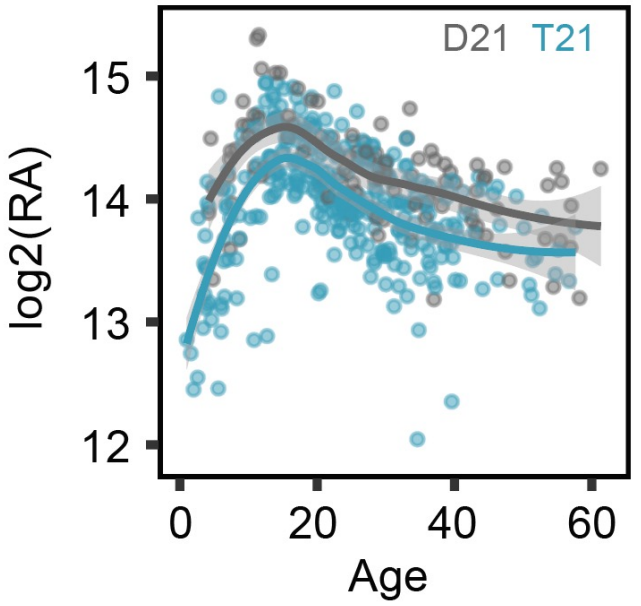
Individuals with Down syndrome make less IGF1!

IGF1 deficiency and Down syndrome

What could be the impacts of IGF1 deficiency?

Lifelong physiological properties of IGF-I	Growth	Bone metabolism	Lipid and glucose metabolisms	Neuroprotection
	Neurogenesis and synaptogenesis	Anabolizing	Antioxidant and antiinflammatory	Antiapoptotic
	Genital development	Proliferative	Hepato- and cardioprotection	Mitochondrial protection

IGF1: Insulin-Like Growth Factor 1



D21: controls T21: trisomy 21

IGF1 deficiency and Down syndrome

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	Neurogenesis and synaptogenesis	Anabolizing	Antioxidant and antiinflammatory	Antiapoptotic
	Genital development	Proliferative	Hepato- and cardioprotection	Mitochondrial protection

IGF1 deficiency could contribute to:

- Stunted growth
- Poor bone health
- Accelerated aging
- Decreased brain health
- Alzheimer's disease

Disclaimer: a lot more research is needed to decipher the exact effects of IGF1 deficiency in Down syndrome.

IGF1 deficiency and Down syndrome

What could be the impacts of IGF1 deficiency?

Lifelong physiological properties of IGF-I	Growth	Bone metabolism	Lipid and glucose metabolisms	Neuroprotection
	Neurogenesis and synaptogenesis	Anabolizing	Antioxidant and antiinflammatory	Antiapoptotic
	Genital development	Proliferative	Hepato- and cardioprotection	Mitochondrial protection

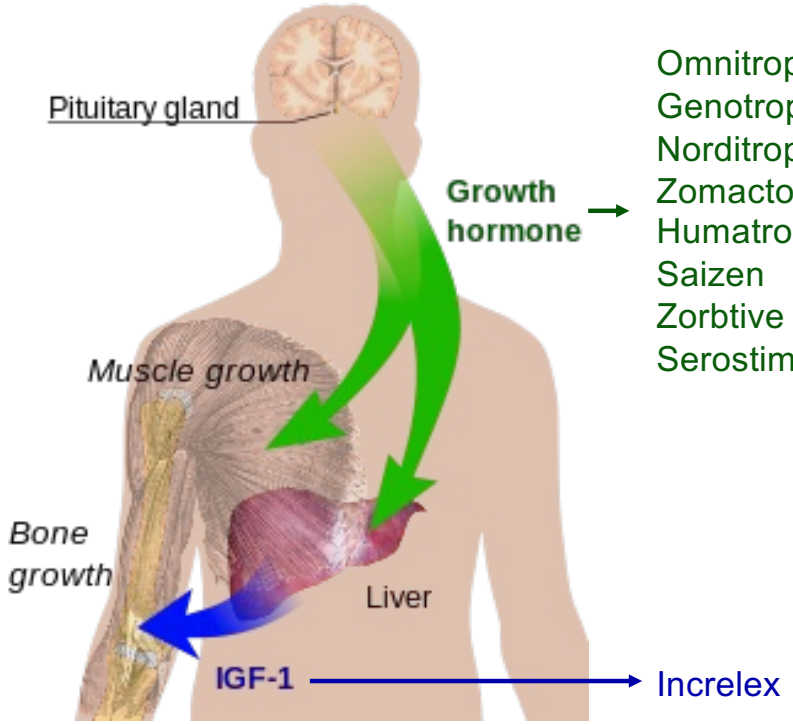
Stunted growth in Down syndrome is associated with higher risk of:

- Autism dual diagnosis
- Some forms of lung disease
- Some autoimmune disorders

One study found a significant association between stunted growth and lower intelligent quotient (IQ):

Klosowska et al, Translational Pediatrics 2022

What could be the benefits of growth hormone therapy (or IGF1 therapy) in Down syndrome?



Both growth hormone and IGF1 exist as FDA-approved therapies for some forms of growth disorders.

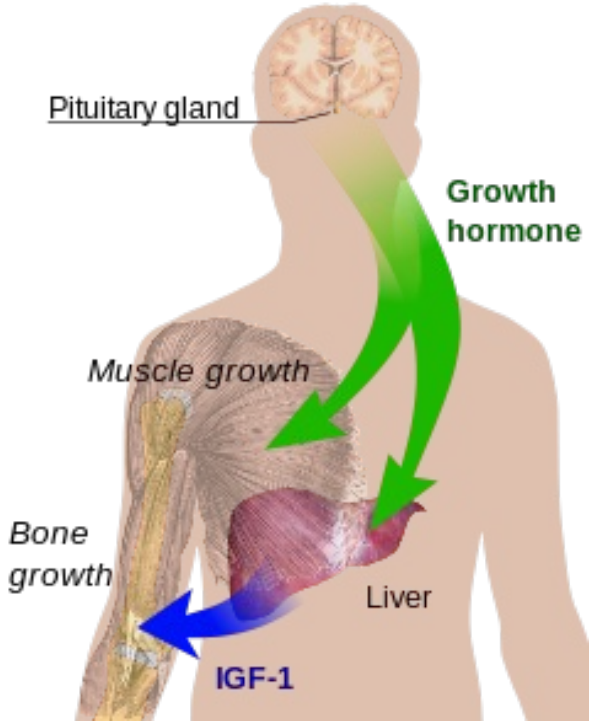
Growth hormone is approved for:

- Growth Hormone Deficiency
- Short Bowel Syndrome
- Prader-Willi Syndrome
- Other conditions…

IGF1 is approved for:

- Severe Primary IGF1 Deficiency (SPIGFD)

What could be the benefits of growth hormone therapy (or IGF1 therapy) in Down syndrome?



- Growth hormone therapy has been tested in Down syndrome but IGF1 therapy has not been tested (to the best of our knowledge)
- Growth hormone treatment was shown to 'boost' IGF1 production in Down syndrome, thus alleviating IGF1 deficiency
- **What were the benefits (and side effects) of growth hormone treatment in persons with Down syndrome?**

What could be the benefits of growth hormone therapy (or IGF1 therapy) in Down syndrome?

GH treatment in pediatric Down syndrome: a systematic review and mini meta-analysis

David Shaki[1,2], Eli Hershkovitz[1,2*], Shai Tamam[3], Arkadi Bollotin[2], Odeya David[1,2], Guy Yalovitsky[2], Neta Loewenthal[1,2], Lior Carmon[1,2], Dganit Walker[1], Raphael Nowak[2] and Alon Haim[1,2]

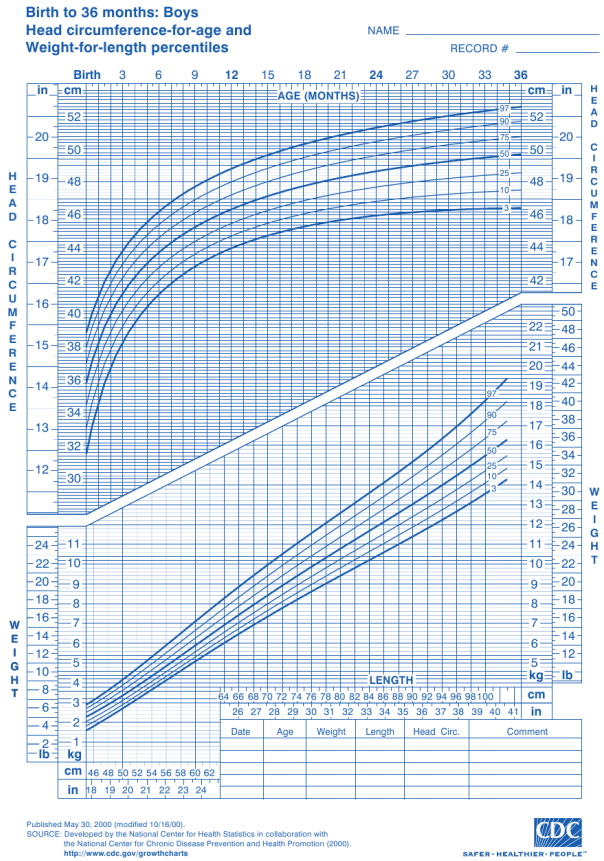
[1]Pediatric Endocrinology Unit, Soroka University Medical Center, Beer Sheva, Israel, [2]Faculty of Health Sciences, Ben-Gurion University, Beer Sheva, Israel, [3]Library of Life Sciences and Medicine, Tel Aviv University, Tel Aviv, Israel

frontiers | Frontiers in Endocrinology

2022

- Sixteen studies reported the medical use of growth hormone in children with Down syndrome.
- Growth hormone was found to be safe and effective for 'short-term' height growth.
- Other potential benefits (e.g., cognition?) remain undefined and would require more research.
- ***Author's conclusions:*** *"As GH treatment is safe and effective for short-term height growth, GH therapy should be considered in long-term treatment (of children with Down syndrome)".*

The big question: are we ‘overshadowing’?

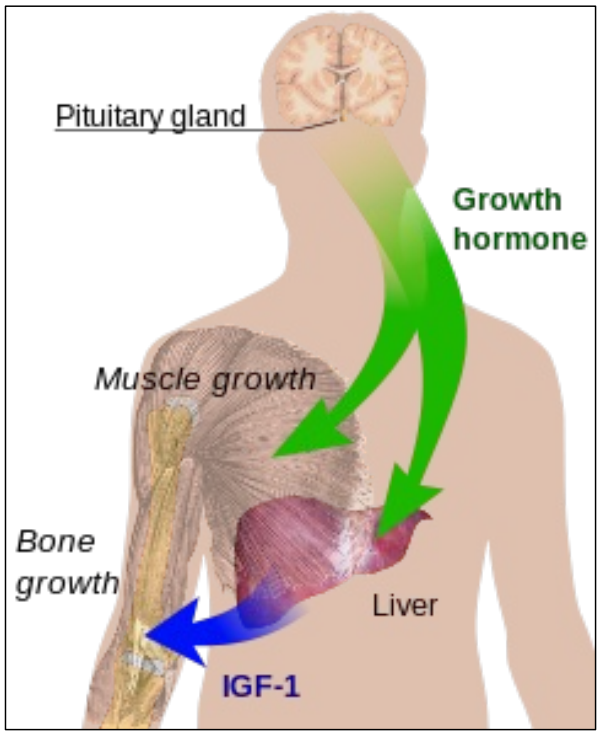


- **Diagnostic overshadowing**: when a medical condition is dismissed as the ‘normal presentation’ of another medical condition without exploring alternative causes.

- What is the value of the CDC growth charts ‘customized’ for children with Down syndrome?

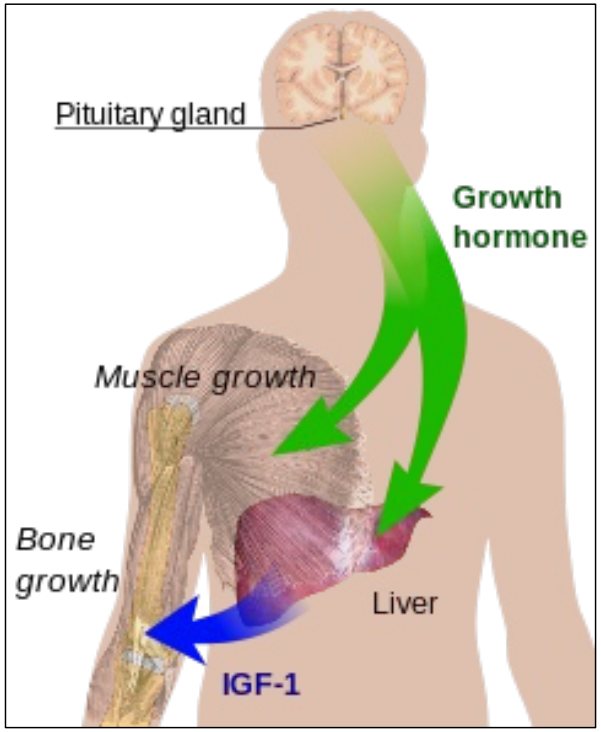
- Are we collectively dismissing stunted growth, IGF1 deficiency, and the potential interventions (e.g., growth hormone, IGF1)?

Calls to action



- **More research is needed!**
- Start a collective dialog about the impact of stunted growth and ‘dysmorphogenesis’ (i.e., abnormal formation of organs and tissues)
- Engage endocrinologists and rheumatologists in the ‘medical care team’ (i.e., specialists who understand growth hormone and IGF1)

Calls to action

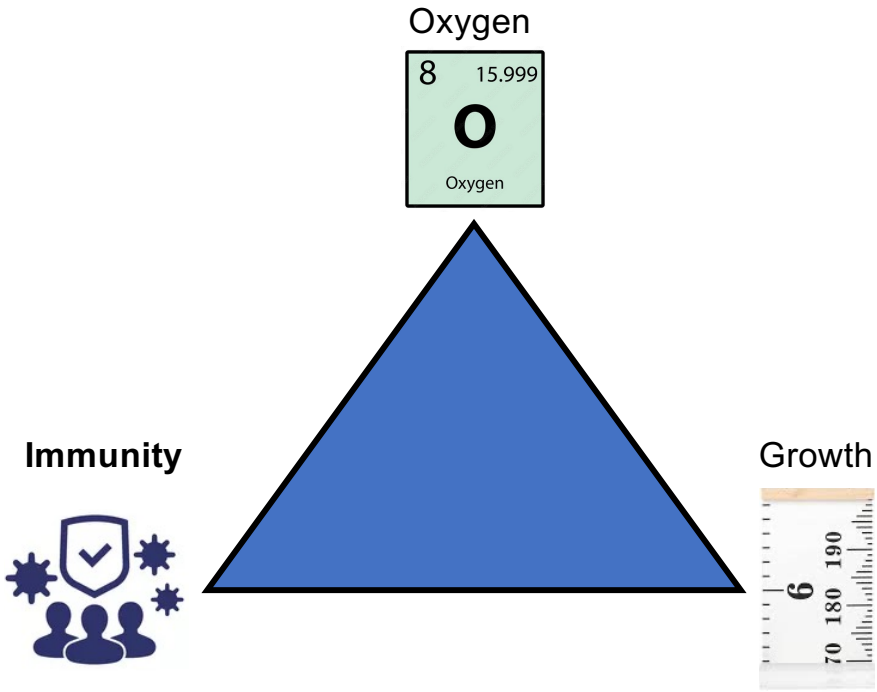


- **Take care of the liver!:**

- No booze
- Balanced, **low fat diet**, keep a healthy weight
- Watch out for signs of **liver dysfunction** during health check ups:
  - Alanine transaminase (ALT)
  - Aspartate transaminase (AST)
  - Alkaline phosphatase (ALP)
  - Albumin
  - Bilirubin
  - Gamma-glutamyltransferase (GGT)
  - Other tests

Three pillars of health:

Oxygen, growth, and **immunity**



Breathe, grow, and **be yourself**

Clinical trial pipeline for immunomodulatory therapies in Down syndrome:

First trial completed, second trial nearing completion, third trial within sight

Idea

Basic Research
- Identify Target

Pre-Clinical Research
- Validate Target
- Develop Therapeutic

Clinical Trials
- Test Safety
- Test Efficacy

Regulatory Approval & Medical Care

2016 → 2020 → 2023 - - - - - - - - ▸

Trisomy 21 consistently activates the interferon response

Kelly D Sullivan[1,2,3,4]*, Hannah C Lewis[1,2], Amanda A Hill[1,2], Ahwan Pandey[1,2,3,4], Leisa P Jackson[1,3,4], Joseph M Cabral[1,3,4], Keith P Smith[1], L Alexander Liggett[1,5], Eliana B Gomez[1,3,4], Matthew D Galbraith[1,2,3,4], James DeGregori[1,5,6,7,8,9], Joaquín M Espinosa[1,2,3,4]*

eLIFE elifesciences.org

NCT04246372 **Completed**

Tofacitinib for Immune Skin Conditions in **Down Syndrome**

Conditions

Down Syndrome | Alopecia Areata | Atopic Dermatitis / Eczema | Hidradenitis Suppurativa | Psoriasis | Vitiligo

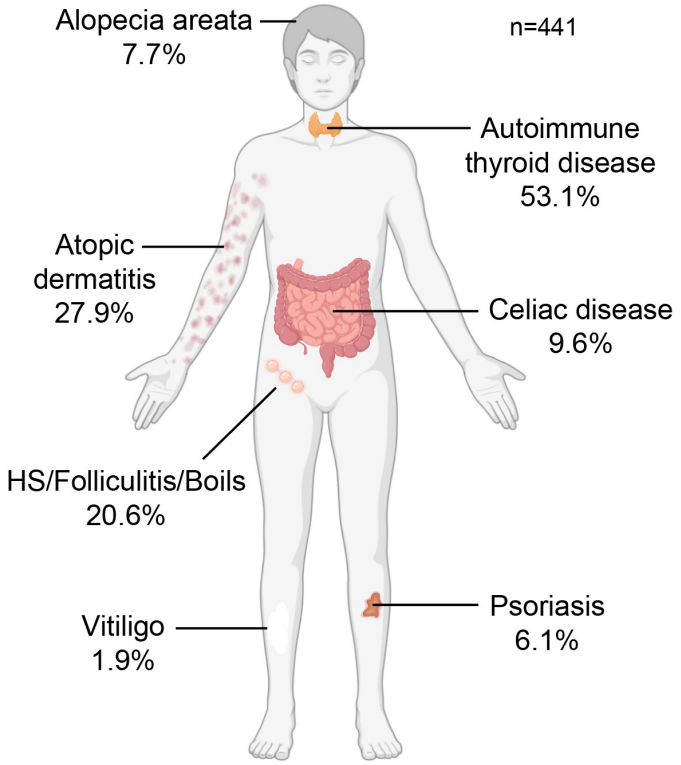
NCT05662228 **Recruiting**

Therapies for **Down Syndrome** Regression Disorder

Conditions

Down Syndrome | Regression

Key observation: widespread autoimmunity in Down syndrome



HTP data

>75% of adults with Down syndrome have been diagnosed with at least one autoimmune condition

>50% of people with Down syndrome have autoimmune thyroid disease (AITD), leading to **hyper**thyroidism or **hypo**thyroidism

>35% adults with Down syndrome have been diagnosed with one or more autoimmune skin conditions

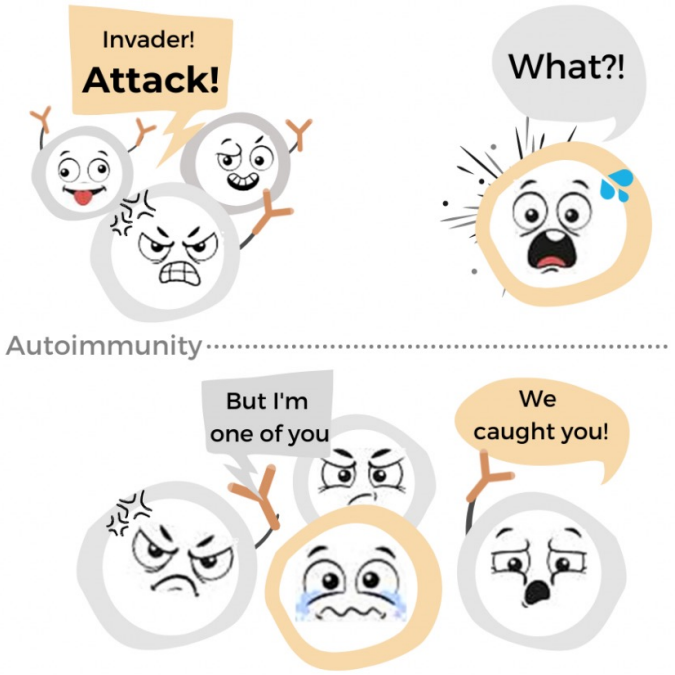
~10% of adults with Down syndrome have been diagnosed with celiac disease

Type I diabetes, 'Down syndrome arthropathy', and other, more rare autoimmune conditions, are also more common

Autoimmunity in a nutshell:

Good: self-tolerance

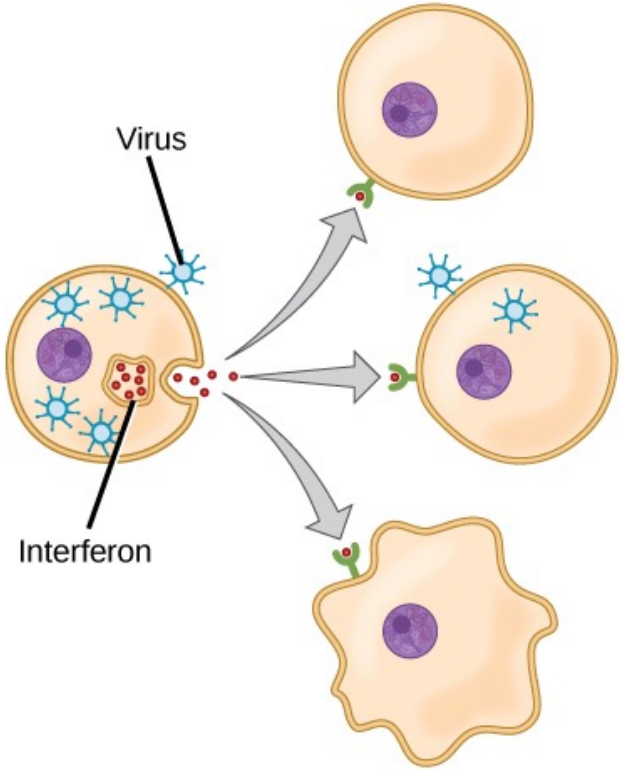
Bad: self-harm



Adapted from Advanx Health blog

People with Down syndrome have hyperactive interferon signaling

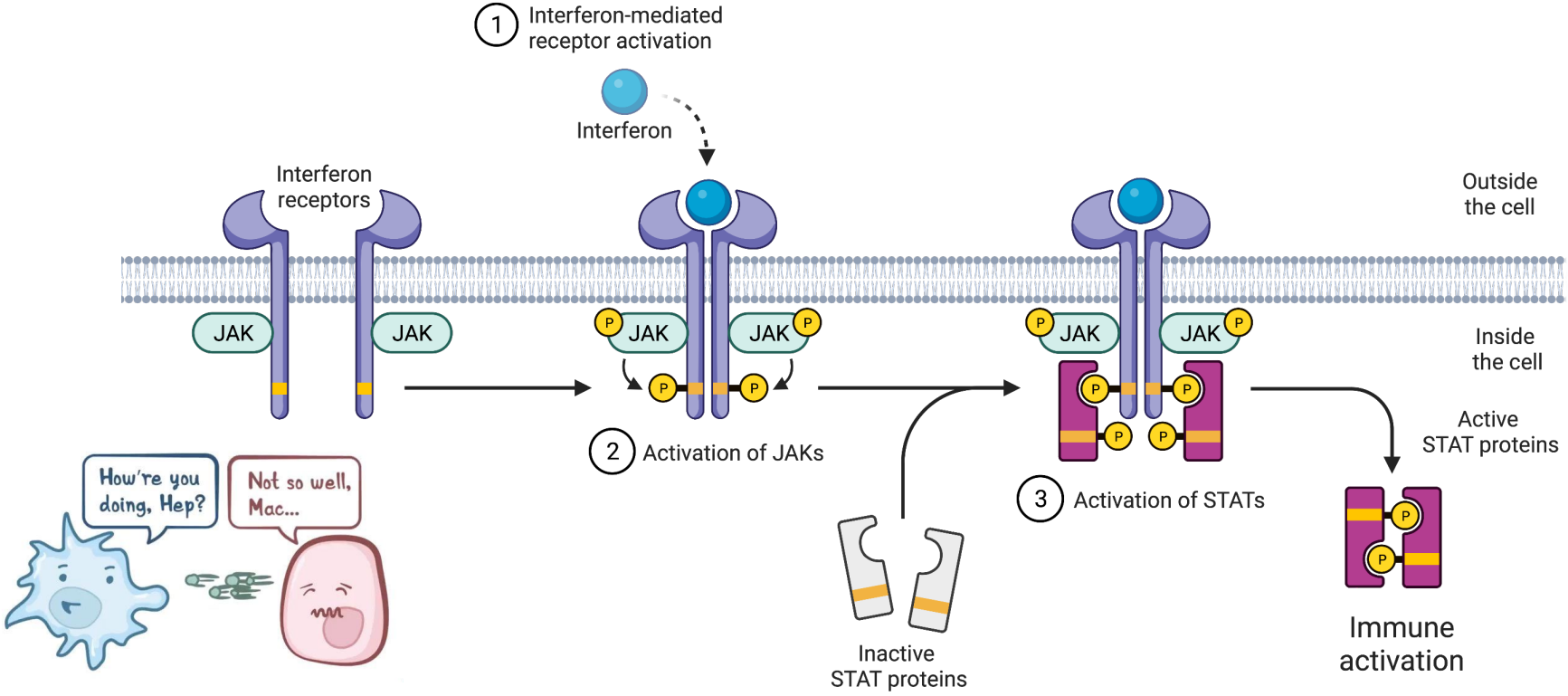
What is interferon signaling?



- Interferon signaling is an important part of the immune system involved in the anti-viral defense.
- Interferons are ‘cytokines’ that activate many different types of immune cells.
- Interferon hyperactivity is a known risk factor for autoimmunity.

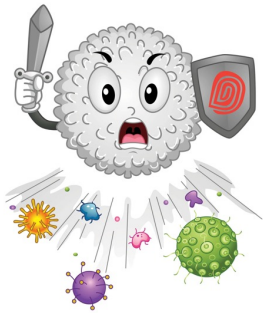
Why do people with Down syndrome have hyperactive interferon signaling?

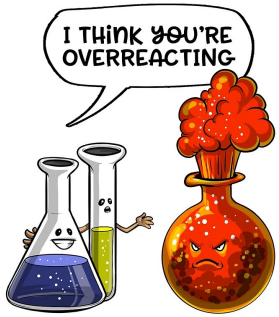
The interferon receptors are encoded on chromosome 21!
People with Down syndrome 'over-produce' interferon receptors

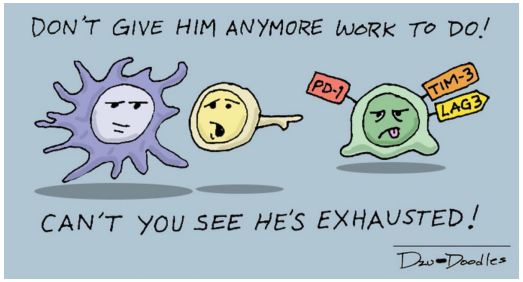


Interferon receptor ‘overdose’ is not good

- An extra copy of the interferon receptors leads to ‘over-reaction’ throughout the immune system.
- Interferon hyperactivity can cause the immune system to make mistakes and attack healthy tissues.
- Chronic interferon hyperactivity could lead to exhaustion of the immune system later in life.



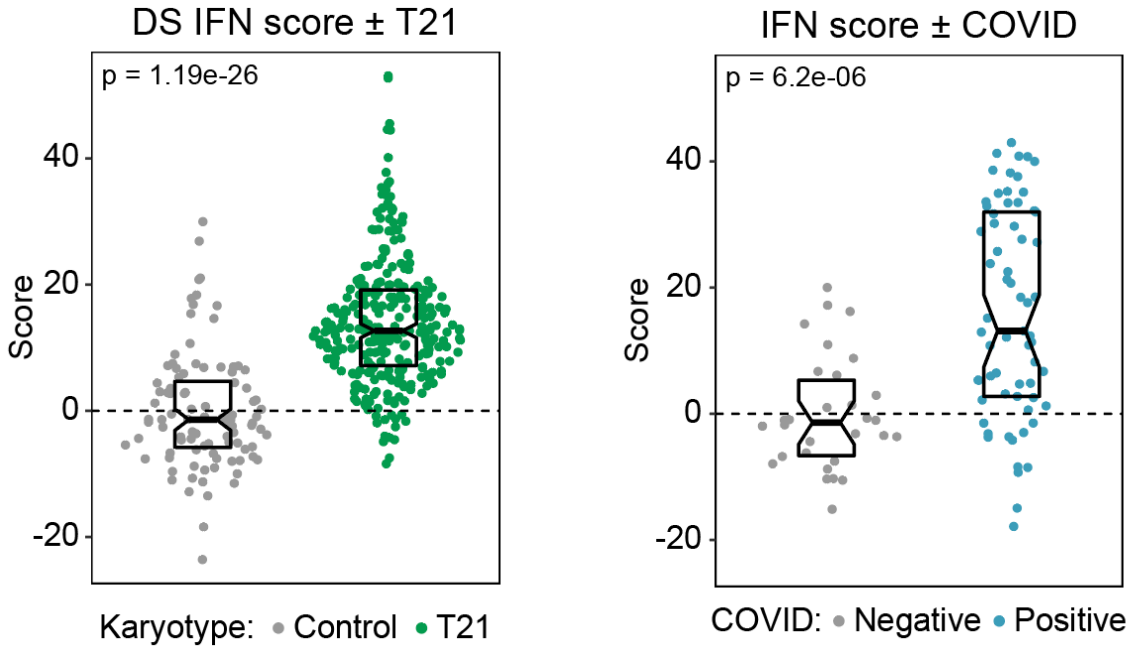




Too much of a good thing sometimes is bad…

The blood of people with Down syndrome looks like is fighting a viral infection

The hyperinflammation observed in Down syndrome is on par with that observed during a COVID-19 infection



IFN scores are commonly used to monitor the degree of IFN activity

T21: trisomy 21

Galbraith et al, Science Advances 2023

Would drugs that decrease the interferon response improve the health of persons with Down syndrome?

Approved therapies that decrease the interferon response: JAK inhibitors

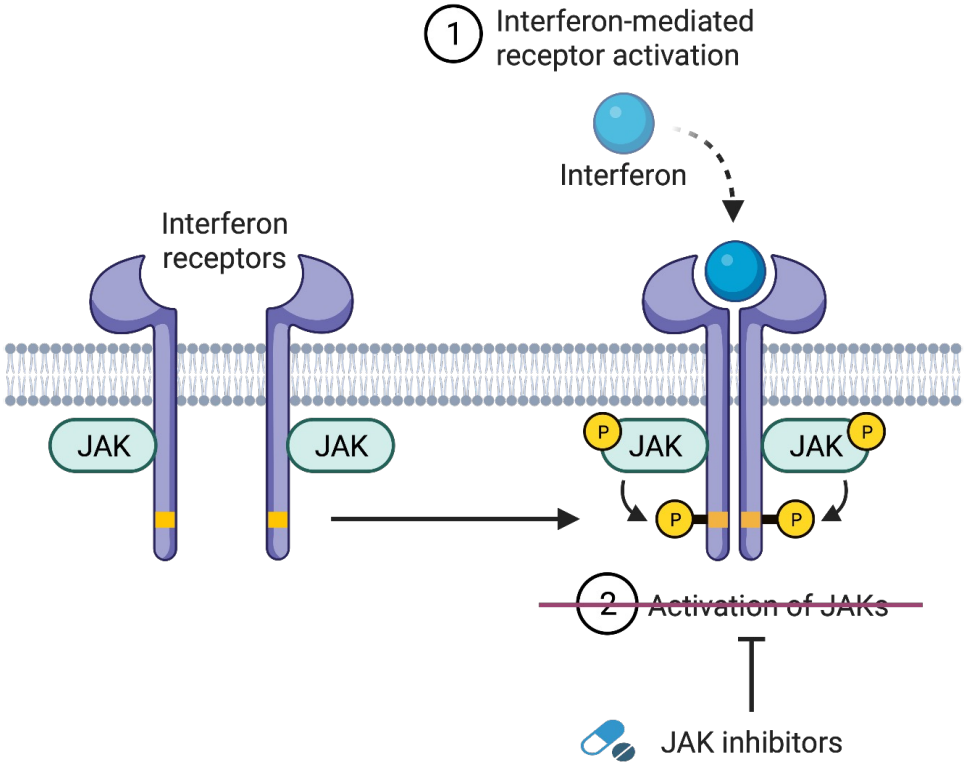
Target	JAK1/3	JAK1/2	JAK1	JAK1/2	JAK1
Rheumatoid arthritis	+	+	+		
Psoriatic arthritis	+		+		
Polyarticular course JIA	+				
Ulcerative colitis	+		+		
Atopic dermatitis			+		+
COVID-19		+			
Alopecia areata		+			
Chron's disease			+		
Polycythemia vera				+	
Ankylosing spondylitis			+		
Myelofibrosis				+	
GVHD				+	
Axial spondylarthritis			+		

There are many JAK inhibitors approved for 13 different indications!

These medicines are used by rheumatologists, dermatologists, gastroenterologists, hematologists and more!

Could JAK inhibitors 'normalize' the immune system in Down syndrome?

JAK inhibitors could attenuate the ill effects of interferon receptor overdose



JAK inhibitors are small molecules designed to inhibit the JAK enzymes acting ‘downstream’ of the interferon receptors.

JAK inhibitors are taken daily orally as pills and have a short ‘half-life’ in the body.

The action of JAK inhibitors is fully reversible, as they are rapidly cleared from the human body within hours.

First clinical trial for JAK inhibition in Down syndrome

Treating five autoimmune skin conditions in one trial

Alopecia areata (patchy hair loss)

Hidradenitis suppurativa (boils)

Atopic dermatitis (eczema)

Psoriasis

Vitiligo

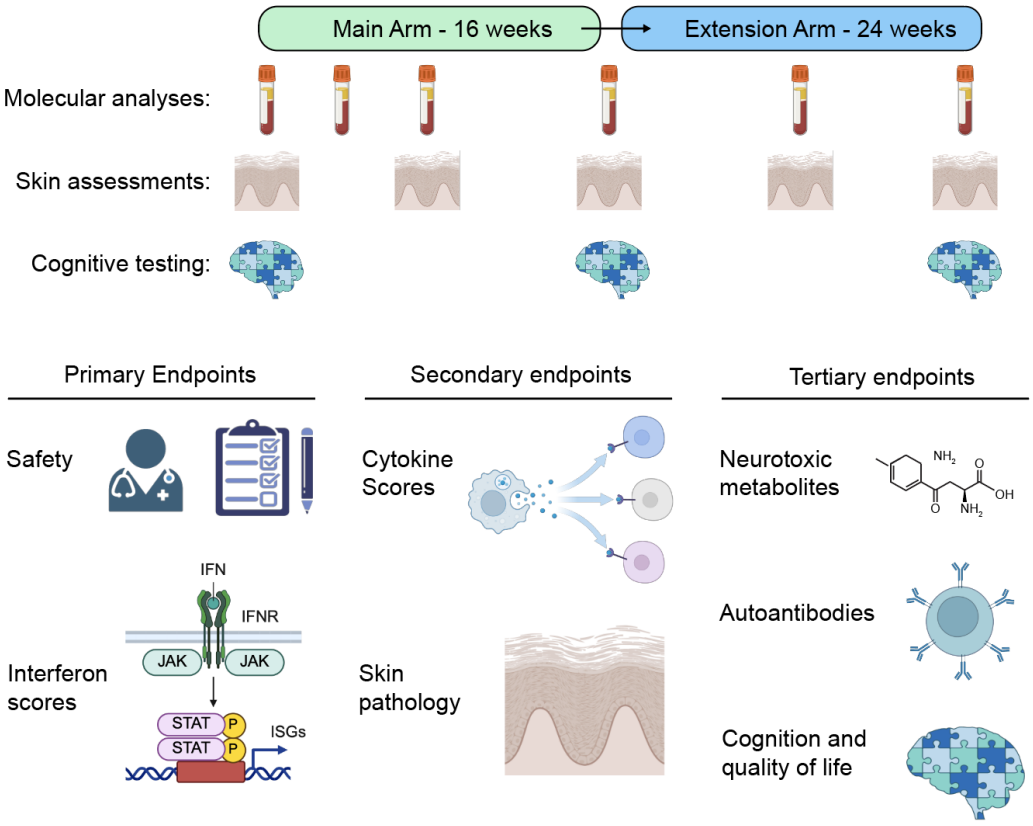
All five conditions are more common in people with Down syndrome

More than 35% of adults with Down syndrome have been affected by one of these conditions

4-9 months of treatment with the FDA-approved JAK inhibitor Tofacitinib (Xeljanz)

Funded by: NIH THE INCLUDE PROJECT NIH National Institute of Arthritis and Musculoskeletal and Skin Diseases

First clinical trial for JAK inhibition in Down syndrome



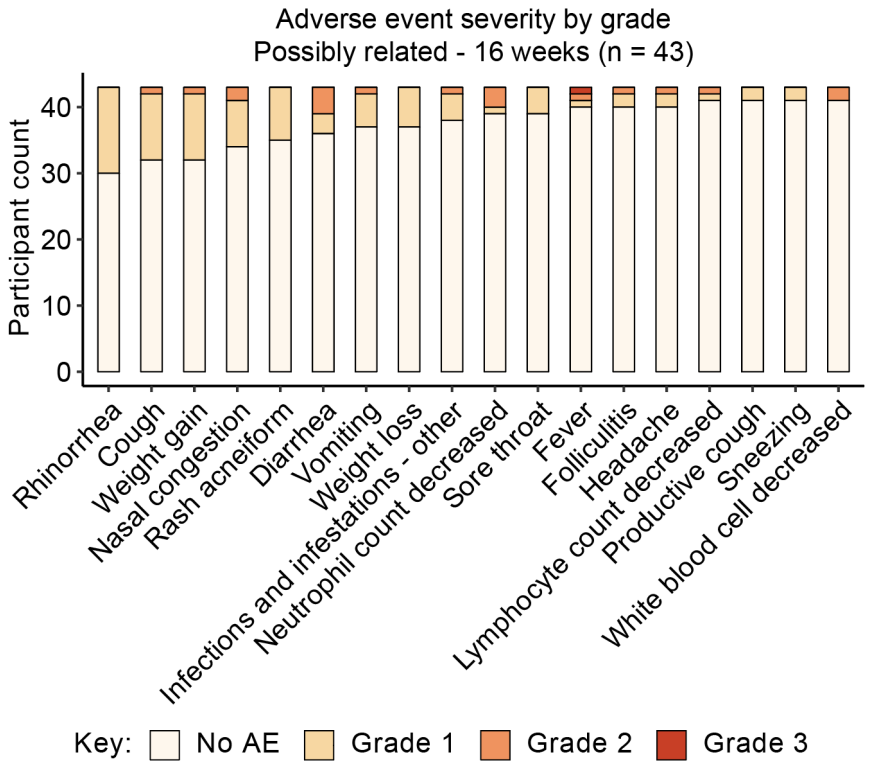
- ✓ Phase II, open label
- ✓ Ages 12-50
- ✓ 40 participants completing 16 weeks of treatment
- ✓ JAK inhibitor: tofacitinib

Key endpoints:

- Safety
- Immune markers
- Skin pathology
- Cognition

JAK inhibition is safe in Down syndrome

Safety endpoint was met!



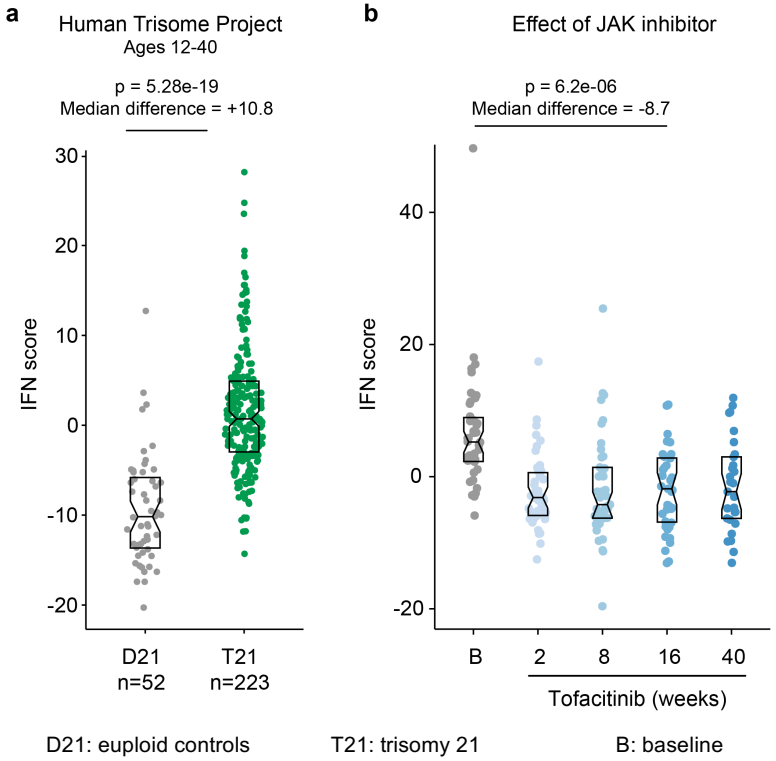
Safety profile reminiscent of that observed in the general population:

- Symptoms of upper respiratory infection
- Weight change
- Skin rash
- Mild clinical lab abnormalities

A single serious adverse event documented over 27.7 years of observation: an episode of thromboembolism in a participant taking oral contraceptive pills, which are known to increase risk of thromboembolism. Participant recovered favorably.

JAK inhibition reduces interferon scores and other biomarkers of autoinflammation

Normalization of IFN scores without overt immune suppression



D21: euploid controls T21: trisomy 21 B: baseline

The JAK inhibitor reduces IFN scores down to the range observed in the general population, not any lower.

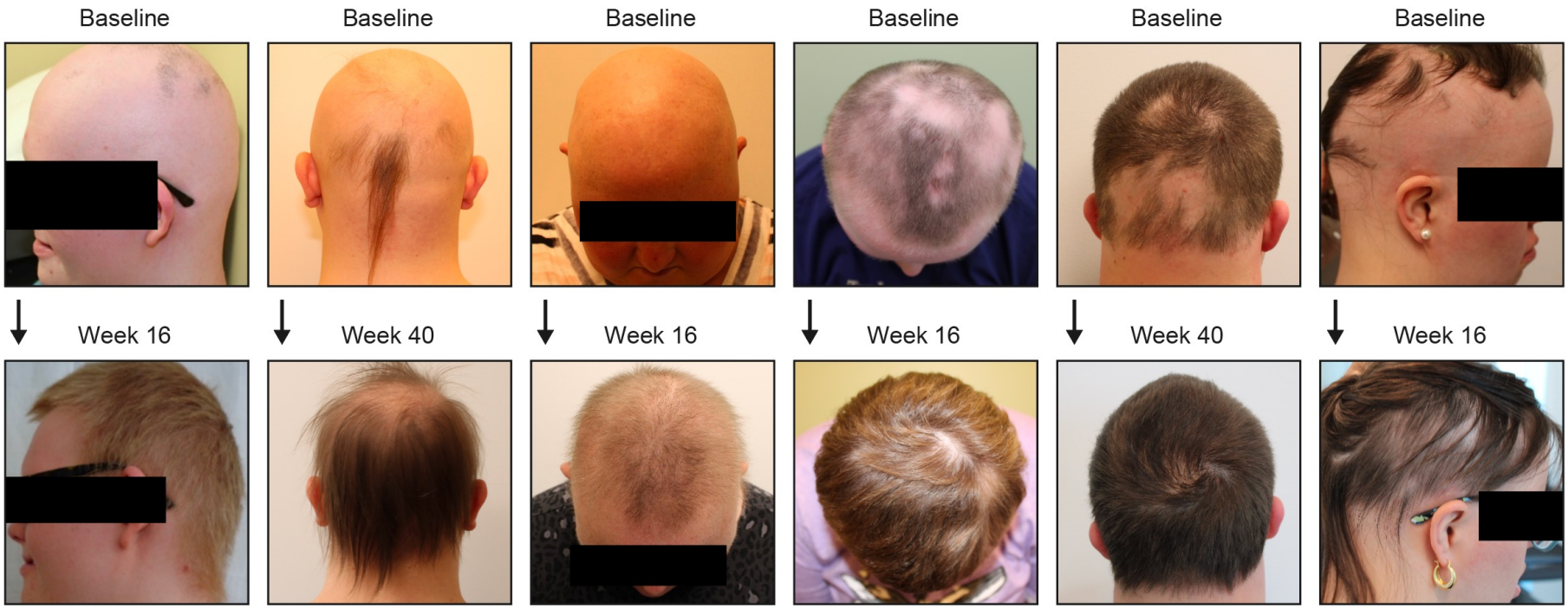
The JAK inhibitor also reduces cytokine scores and kynurenine pathway metabolites.

Endpoints met!

Galbraith et al, *Science Advances* 2023
Rachubinski et al, *eLIFE* 2024

JAK inhibitors can be used safely in Down syndrome to treat many different autoimmune skin conditions

Alopecia areata:



Male, 40 years old – Psoriatic arthritis

When a picture is worth a thousand words

Before

After

Participant monitored outside of the trial at the University of Vermont Medical Center

Benefits of JAK inhibitors go much deeper than the skin…

Down syndrome Regression Disorder (DSRD)

- A rare but devastating condition characterized by catatonia, loss of speech, depersonalization, loss of ability to perform activities of daily living, hallucinations, delusions, and aggression.

- A subset of DSRD cases are associated with signs of immune dysregulation affecting the central nervous system (CNS), often associated with preceding immune trigger events.

- Is DSRD an autoimmune condition, akin to autoimmune encephalitis?

When the families drive the research

Story behind the design of the first randomized clinical trial
for Down Syndrome Regression Disorder

Well+Being

A mystery illness stole their kids' personalities. These moms fought for answers.

Their children's decline was dramatic, with patients losing function in days or weeks, including the ability to talk, move or take care of themselves.

May 12, 2024

The Washington Post

Clinical trial for mechanistic investigation of therapies for Down syndrome Regression Disorder

A collaboration between the Crnic Institute, Children's Hospital Colorado, and Children's Hospital Los Angeles.

Principal Investigators:

Santoro

Sannar

Espinosa

Co-Investigators:

Rachubisnki

Patel

Kammeyer

Galbraith

Consultants:

Sanders

Tartaglia

Charoensook

Funded by: NIH THE INCLUDE PROJECT NIH *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

Recruiting now!

Clinical trial for mechanistic investigation of therapies for Down syndrome Regression Disorder

Three goals:

1. To define the relative **safety** profile of Lorazepam, IVIG, and Tofacitinib in DSRD.

2. To compare the **efficacy** of Lorazepam, IVIG, and Tofacitinib in DSRD.

3. To investigate potential **mechanisms** underlying DSRD and its response to therapies.

Is it safe? Is it effective? What is the mechanism?

Clinical trial for Down Syndrome Regression Disorder (DSRD)

Scientists and physicians have teamed up to identify potential treatments for DSRD.

Why participate?

- Examine the safety and effectiveness of different potential treatments for DSRD: lorazepam, IVIG or tofacitinib

Who can participate?

- People with Down syndrome between 8-30 years old who have symptoms or a diagnosis of DSRD. Additional participation criteria apply.

Email DSresearch@cuanschutz.edu or scan the QR code to learn more.

Scan code or learn more at bit.ly/DSRDStudy

Conclusions

- Interferon hyperactivity could cause many health issues in individuals with Down syndrome, such as autoimmune disorders, severe complications from lung viral infections (e.g., COVID19), and neurological disorders.

- Research into immune system dysregulation in Down syndrome has illuminated therapeutic strategies being tested in first-in-kind clinical trials (e.g., JAK inhibition).

- Restoring immune balance could have multidimensional benefits in Down syndrome, even perhaps from early development.

Understanding Down syndrome as an interferonopathy

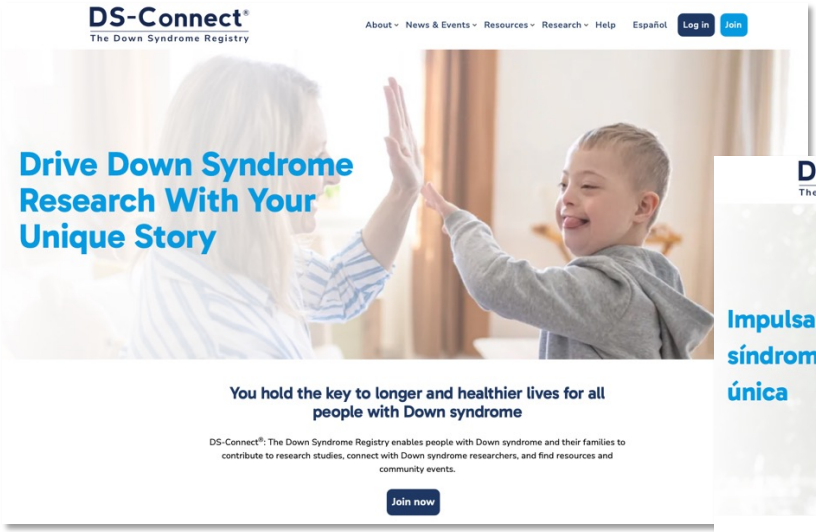
Outstanding questions

- What is the long-term safety profile of JAK inhibition in people with Down syndrome?
- What are all the possible benefits of immunomodulation in Down syndrome?
- How early could treatment start? Is pre-natal treatment even possible?
- Should everyone with Down syndrome be treated or only those with clinically evident autoimmunity?

Understanding Down syndrome as an interferonopathy

DS-Connect®
The Down Syndrome Registry

DS-Connect® is back!

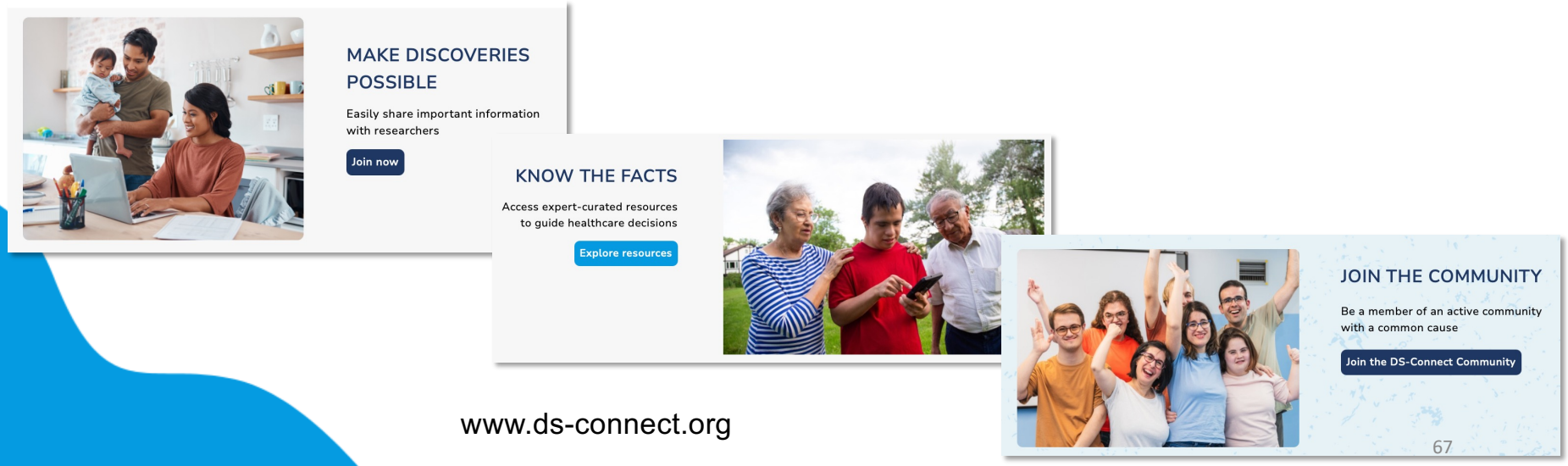


www.ds-connect.org

DS-Connect®

The Down Syndrome Registry

- Collaborative effort between NIH and the Crnic Institute.
- Secure platforms for families to contribute their knowledge.
- New website, fresh design and branding.

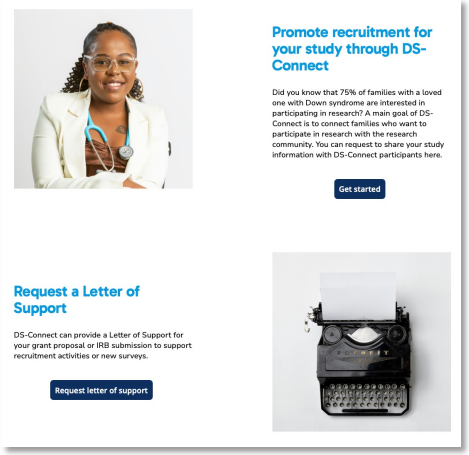


www.ds-connect.org

DS-Connect®

The Down Syndrome Registry

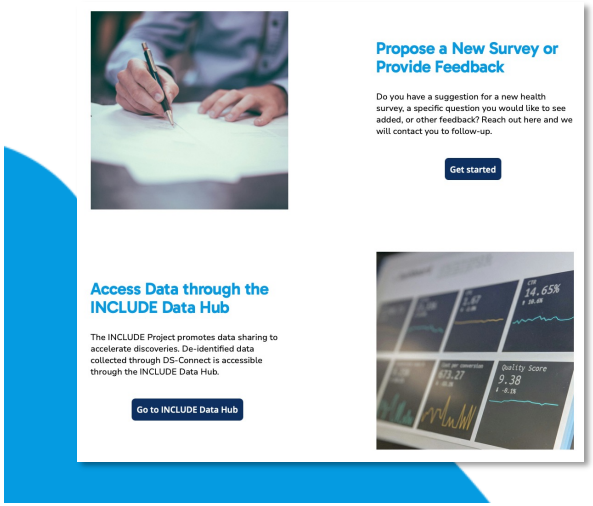
- New and improved features
- Modern and secure cloud environment
- Fully translated to Spanish
- Updated tools for researchers

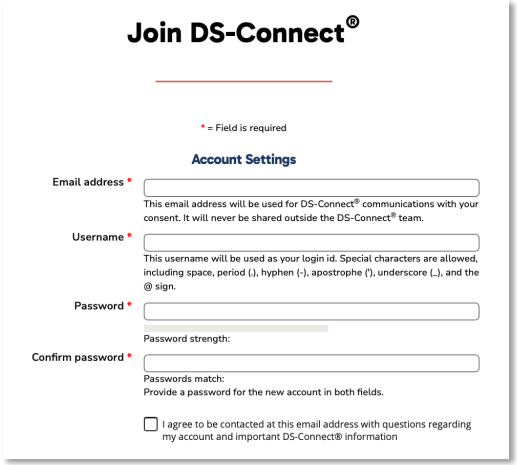


www.ds-connect.org

DS-Connect®
The Down Syndrome Registry

- User-friendly data visualization dashboards
- Improved surveys and new surveys
- Quarterly webinars and newsletters
- Goal: 100,000 participants





DS-Connect®

The Down Syndrome Registry

MAKE DISCOVERIES POSSIBLE

Easily share important information with researchers

KNOW THE FACTS

Access expert-curated resources to guide healthcare decisions

JOIN THE COMMUNITY

Be a member of an active community with a common cause

Join our nearly 6,000 registrants today!

ds-connect.org

Scan to Learn More and Register

DS-Connect®
The Down Syndrome Registry

Free Webinar

Dr. Daniel Combs

Emerging Obstructive Sleep Apnea Treatment Options for People with Down syndrome

December 10, 2025
1 - 2 pm MT

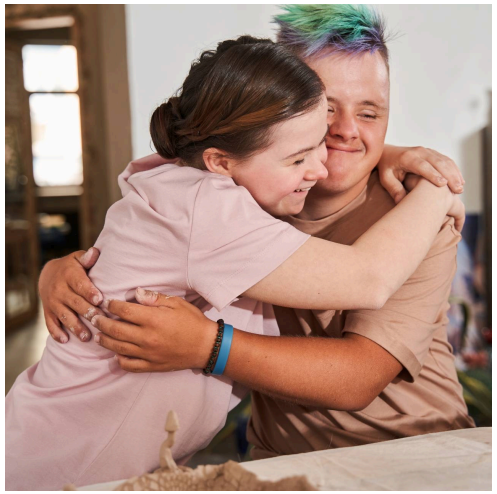
Trial Ready – Cohort Down Syndrome TRC-DS

Enroll in TRC-DS to participate in upcoming clinical trials for Alzheimer's disease

INCLUDE
INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndromE

Dr. Mike Rafii
Alzheimer's Disease Therapeutics Institute
University of Southern California

ABATE STUDY



- ABATE Trial **www.abate-study.com**
- Participants 35-50 years old with DS
- The study is specifically designed for people with DS and is testing a potential treatment for Alzheimer's disease
- We have 2 goals:
  - To learn more about the study treatment's safety
  - To see if it slows down memory loss and thinking problems

ALADDIN study coming soon…

	ABATE	ALADDIN
Study Sponsor	AC Immune	Alzheimer's Clinical Trials Consortium - Down Syndrome (ACTC-DS)
Name of Therapy	ACI-24.060	Donanemab (Kisunla)
Therapy Being Tested	Active Immunotherapy	Antibody Immunotherapy
Phase	Phase 1b/2	Phase 4
Route of Delivery	Intramuscular Injection	Intravenous Infusion
Placebo Controlled?	Yes	Yes
Age	35 – 50 yo	35 – 50 yo
Expected Enrollment	80	60
Participation Duration	2 years	2 years
Active Locations	USA, UK, Spain	USA

ALADDIN will test a medicine that is already approved in the general population

Acknowledgements

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Matthew Galbraith
Data Sciences Program

Lyndy Bush
Administrative and Outreach Program

THE INCLUDE PROJECT

NIH *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

GLOBAL DOWN SYNDROME FOUNDATION®

ANNA & JOHN J. SIE FOUNDATION

NIH National Heart, Lung, and Blood Institute

NIH National Institute of Allergy and Infectious Diseases

NIH National Center for Advancing Translational Sciences

NIH National Institute on Aging

NIH National Institute of Arthritis and Musculoskeletal and Skin Diseases

NIH National Institute on Deafness and Other Communication Disorders
Advancing the science of communication to improve lives

School of Medicine
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

INCLUDE Data Coordinating Center

Many many wonderful collaborators

The research participants and their families

Michelle Sie Whitten and the amazing team at the Global Down Syndrome Foundation