PRF By The Numbers

Progeria
Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Please Do Not Reproduce Children's Photographs Without Express Permission From PRF

Produced by Leslie B. Gordon, MD. PhD; Medical Director

March 31, 2025

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PRF By The Numbers: A Data Sharing Tool

- PRF By The Numbers is a **data sharing tool** originating from The Progeria Research Foundation's programs and services.

- We translate information collected within our programs and services, and develop charts and graphs which track our progress from year to year.

- This allows you to assess where we've been, and the improvements we've made for children with Progeria.

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Why Sharing Data Is Essential

- According to the National Institutes of Health:

  "data sharing is essential for expedited translation of research results into knowledge, products, and procedures to improve human health."

  http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html

- In other words, everyone benefits by knowing and learning as much as possible about Progeria - the scientific and medical communities, the public, and the children.

NIH National Institutes of Health
Turning Discovery Into Health

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PRF By The Numbers…Here's How It Works

➢We take raw data collected through our programs and services, remove any personal information to protect the participant, and present it to you in a format that is engaging and informative.

➢ PRF programs and services include:

- The PRF International Registry
- The PRF Diagnostics Program
- The PRF Cell & Tissue Bank
- The PRF Medical & Research Database
- PRF Research Grants
- Scientific Workshops
- Clinical Trial Funding and Participation
- Progeria Connect

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Our Target Audience

- PRF By The Numbers is intended for a broad array of users
  - Families and children with Progeria
  - The general public and nonscientists of all ages
  - Scientists
  - Physicians
  - The media
- This means that different types of slides will be of interest depending on who is looking at the information. We have designed this slide set so that you can pull out what is most important to you.
- We love suggestions - if you don't see some facts and figures here that you think would be informative, please let us know at

info@progeriaresearch.org

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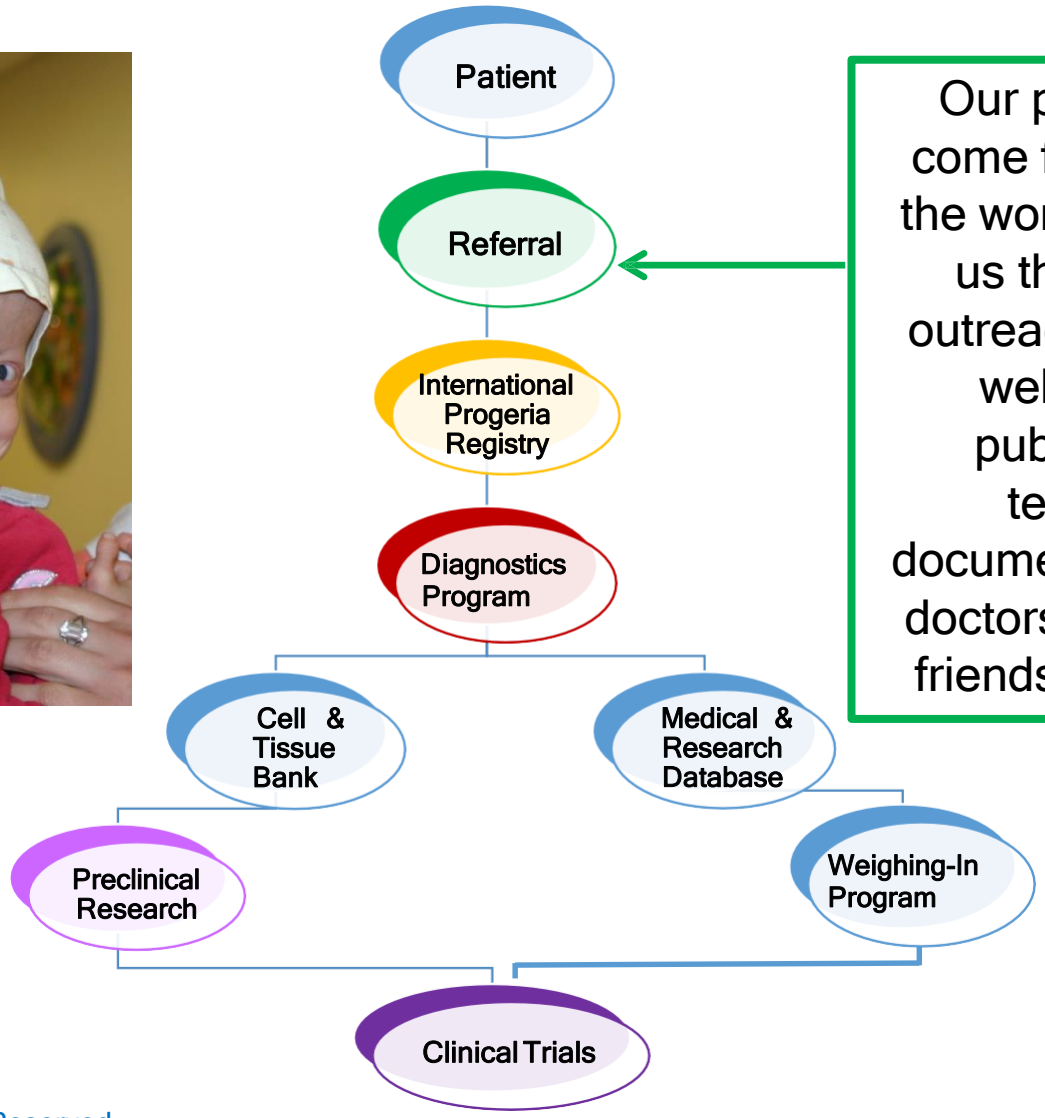
PRF Programs: It All Starts With The Children



Our participants come from all over the world. They find us through our outreach – the PRF website, our publications, television documentaries, their doctors, neighbors, friends and family.

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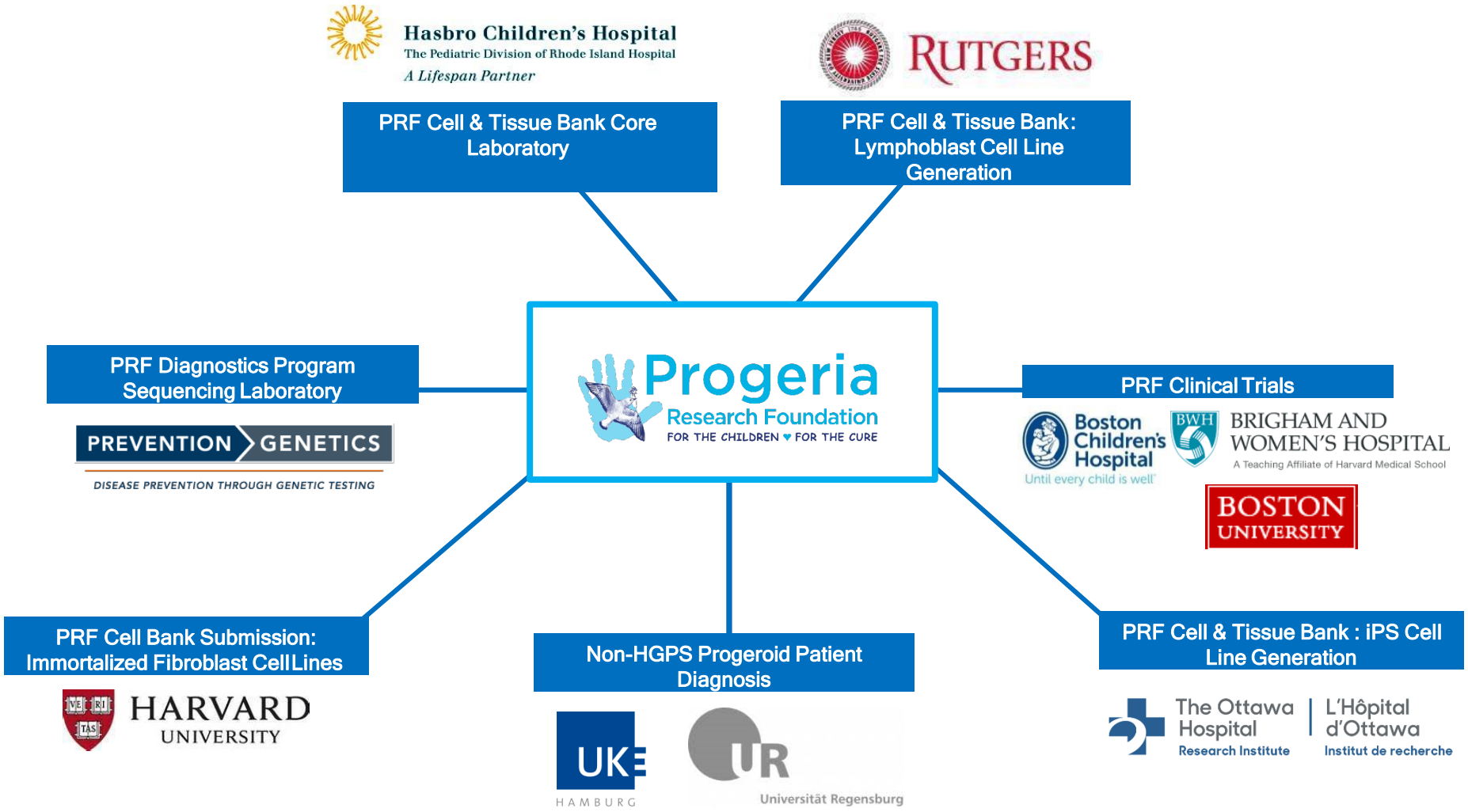
Program Collaborations for Success



Our Program Collaborators

Our collaborating institutions are crucial to our ability to help children with Progeria. We are extremely grateful for these ongoing partnerships:

- Hasbro Children's Hospital
  - Location of The PRF Cell & Tissue Bank
  - Program IRB approval

- PreventionGenetics
  - CLIA*-approved genetic sequence testing

- Ottawa Hospital Research Institute
  - Induced Pluripotent Stem Cell (iPSC)
  - CLIA*-approved generation and distribution

Our Clinical Trial Collaborators

Our collaborating institutions are crucial to our ability to help children with Progeria

- Harvard University – Associated Hospitals:
  - Boston Children's Hospital
  - Brigham and Women's Hospital
  - Dana Farber Cancer Institute

Boston Children's Hospital
Until every child is well™

PRG Science & Technology

BWH BRIGHAM AND WOMEN'S HOSPITAL
A Teaching Affiliate of Harvard Medical School

- NIH – funded Clinical and Translational Study Unit at Boston Children's Hospital
- Sentynl Therapeutics, Inc.

NIH National Institutes of Health
Turning Discovery Into Health

SENTYNL THERAPEUTICS, INC.

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Number of Living PRF-Identified Cases

March 31, 2025

Total Number of Children with HGPS* and PLs** Worldwide: 203

HGPS* Worldwide: 149

HGPS* in the United States: 15

Progeroid Laminopathies** Worldwide: 54

Progeroid Laminopathies** in the United States: 11

*Children in the HGPS category have a progerin-producing mutation in the LMNA gene

**Those in the Progeroid Laminopathy category have a mutation in the lamin pathway but don't produce progerin
**Cases of PL do not include those identified solely from published scientific journal articles

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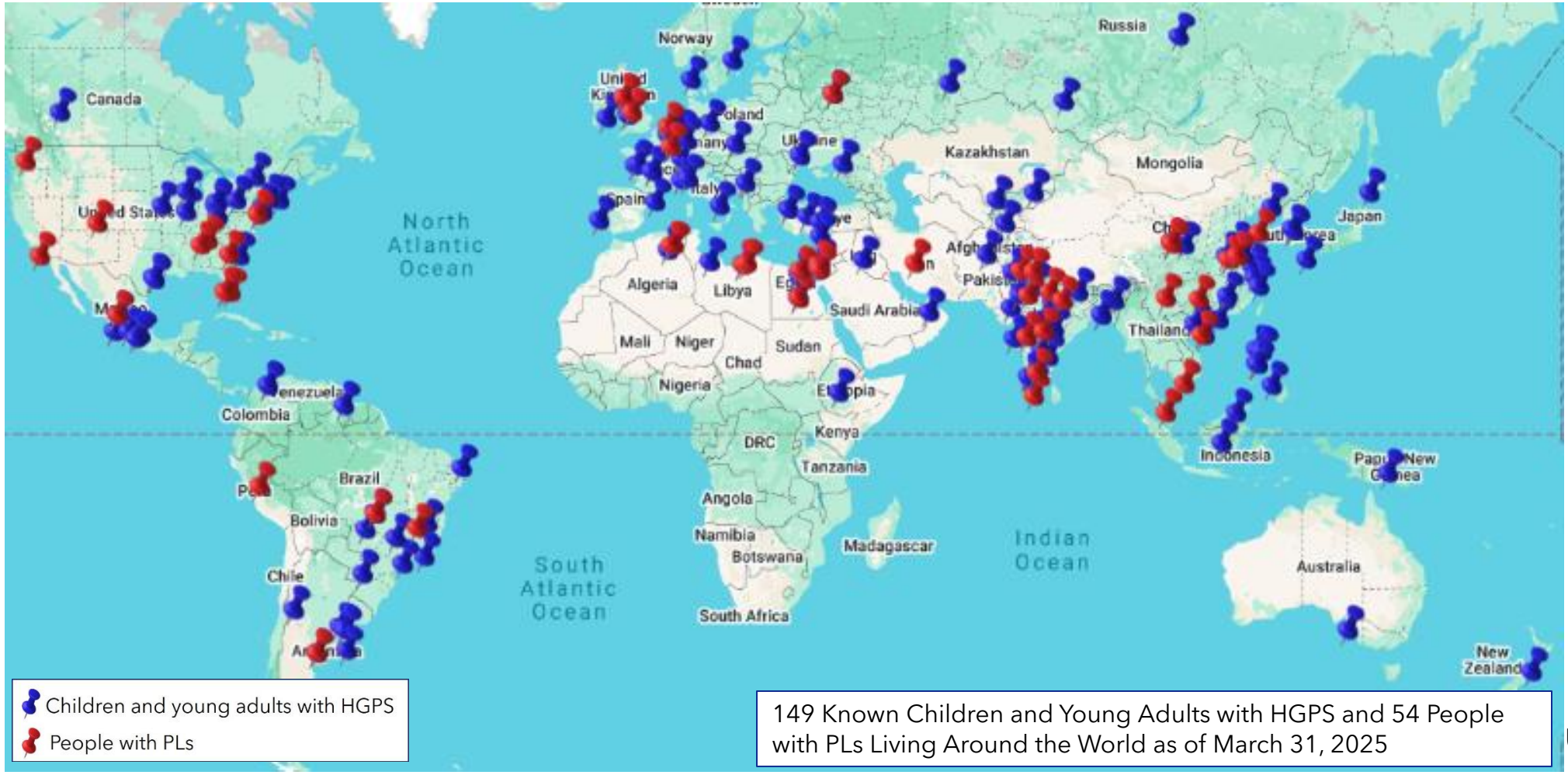
Living PRF-Identified Cases Reside In 51 Countries Today

Afghanistan
Algeria
Argentina
Australia
Bangladesh
Belgium
Brazil
Canada
China
Colombia
Czech Republic
Denmark
Egypt
Ethiopia
France
Germany
Guyana
India
Indonesia
Iran
Iraq
Ireland
Israel
Italy
Japan
Kazakhstan



Libya
Luxembourg
Malaysia
Mexico
Nepal
Netherlands
New Zealand
Oman
Pakistan
Palestine-Gaza
Papua New Guinea
Peru
Philippines
Portugal
Russia
Serbia
South Korea
Spain
Sweden
Tajikistan
Turkey
Ukraine
United Kingdom
USA
Vietnam

...and Speak 37 Languages

Amharic	Czech	German	Japanese	Marathi	Russian	Telugu	Vietnamese
Arabic	Danish	Hebrew	Kannada	Nepali	Serbian	Tok Pisin	Yiddish
Bengali	Dutch	Hindi	Korean	Pashto	Spanish	Turkish	
Cebuano	English	Indonesian	Malay	Portuguese	Tagalog	Ukrainian	
Chinese	French	Italian	Malayalam	Punjabi	Tamil	Urdu	

прогерии исследовательский фонд

خيشلا ثاحبأ ةسسؤم

조로증 연구 재단

早衰症研究基金會

Progeria Araştırma Vakfı

Progeria रिसिच फाउंडेशन

早老症研究財団

బాలుడ బాలికవయస్సుముదరుకండానే వృద్ాాప్యరూప్ంలోనికిమచ్చటరోయుచ్చు ండేటున్

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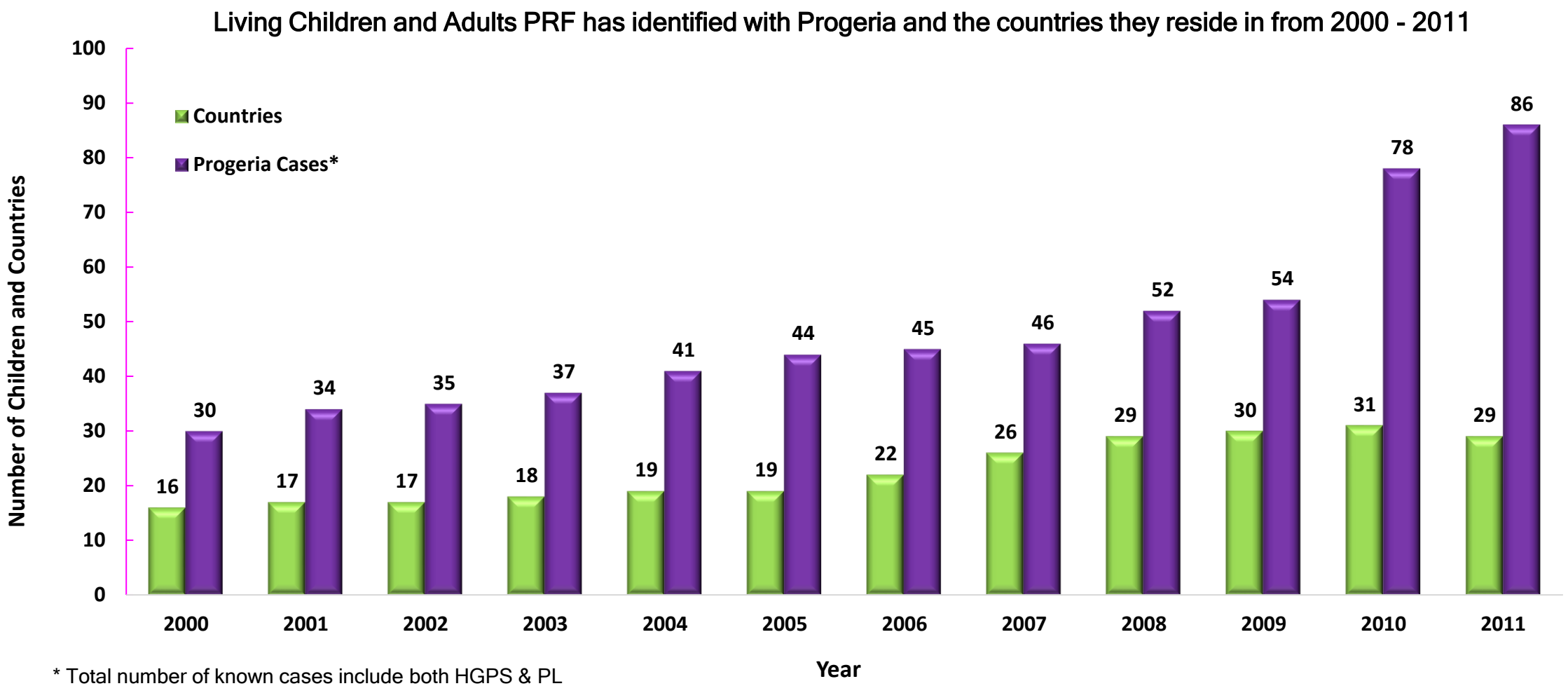
Every Year Our Numbers Grow



* Total number of known cases include both HGPS & PL
* When a child passes away, numbers are decreased

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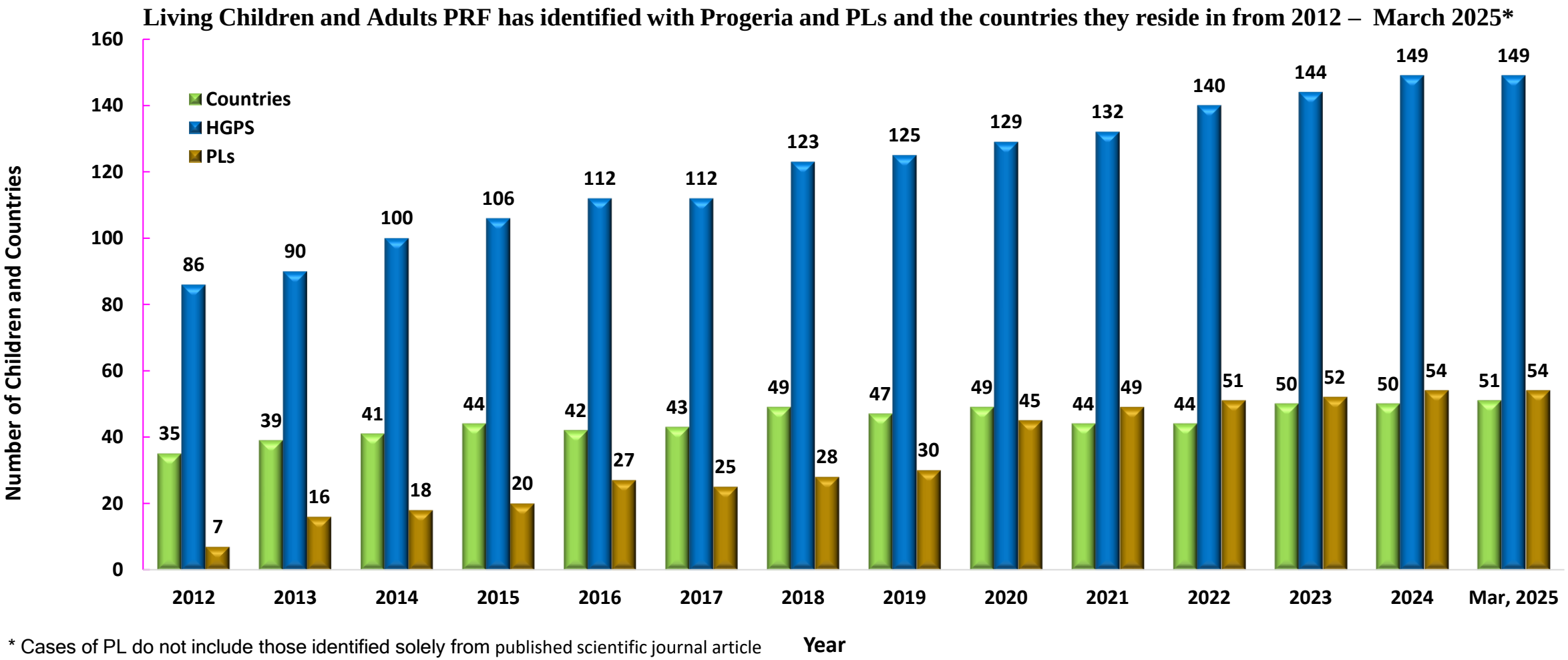
Every Year Our Numbers Grow



* Cases of PL do not include those identified solely from published scientific journal article
* When a child passes away, numbers are decreased

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Tracking Children with Progeria Through Prevalence

- How does PRF estimate how many children we are searching for, and in what countries? We use ***population prevalence***.

- Prevalence is the proportion of children with Progeria per total population.

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How Prevalence Is Estimated

- At PRF, we use a formula based on the number of children we've identified in the US. We then expand that out to the world population.
- We do this because we have the most complete reporting for the US and since Progeria has no gender, ethnic, or other biases, we assume that the prevalence in the US is the same prevalence in other countries.
- PRF calculates prevalence for the US based on *Worldometer* population estimates.

USA Prevalence of Progeria

March 31, 2025 population statistics:

- The US population is:

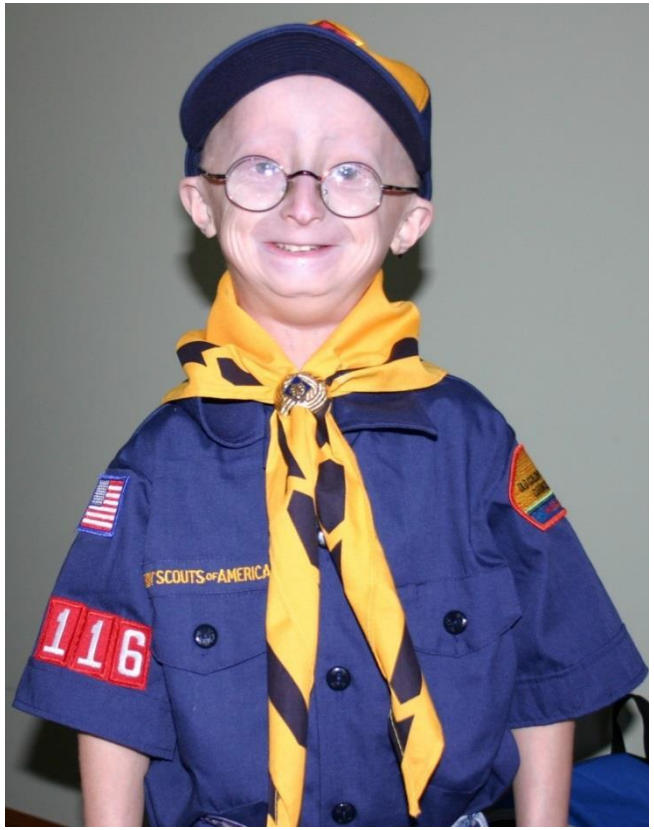
  346,812,230 people

- Number of PRF-identified children with HGPS in the US (3 year average):

  16

- Average prevalence of HGPS in the US:
  16 in 346 million is about

  1 in 20 million people



*estimates routinely fall between 1 in 16 - 1 in 20 million people.

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Prevalence and World Population of Progeria

Given the world population on March 31, 2025

There are between **410** and **483** children living with Progeria worldwide

PRF strives to find every child with Progeria because in order to help every child, we must find every child

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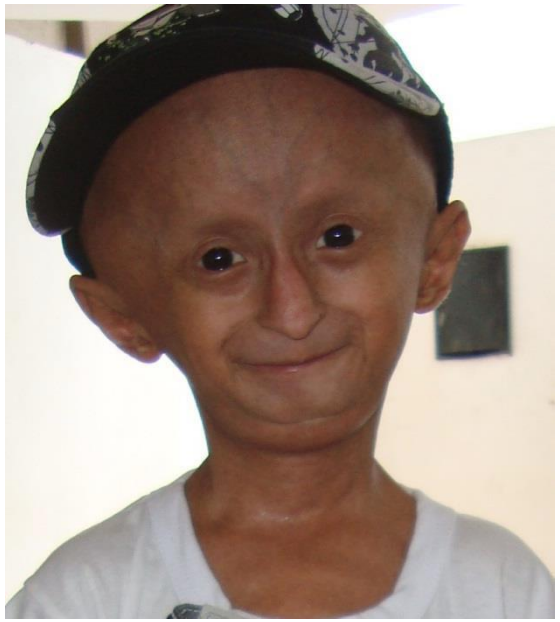
Using Prevalence To Find Children

We can now use the total population estimates for any given country, in order to understand whether we have found most or all children in a particular country.

- For example, as of March 31, 2025, 2024:



Brazil's population was estimated as

212,608,511 people

Using Prevalence, the number of children living with Progeria in Brazil is 212,608,511/20,000,000 = **11**

PRF has identified 9 of these 11 children, and is searching for the 2 others

* Data based on the latest *Worldometers* estimates

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International Progeria Registry*

Program Goals:

- Patient identification
- Outreach to patient families and their physicians
- A springboard for program enrollment

Registry forms available at
https://www.progeriaresearch.org/international-registry-2/

*PRF International Registry includes those with genetically confirmed or clinically suspected Progeria, as well as those with ZMPSTE24 and other possible progeroid syndromes

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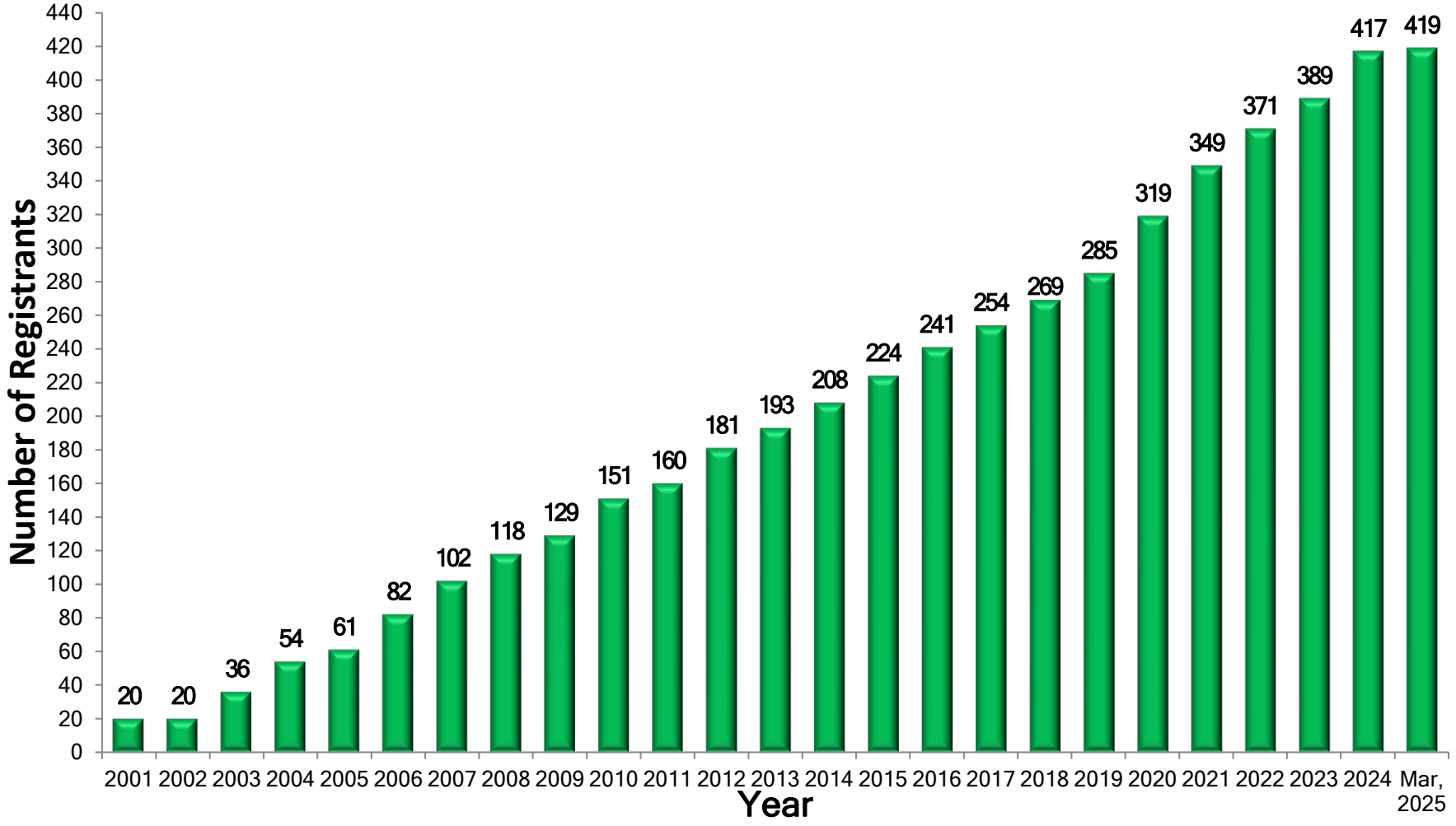
419 Children and Adults Have Been Registered With PRF



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From 73 Countries and 1 Territory

Algeria, Argentina
Australia,
Bangladesh
Belgium, Bolivia
Brazil, Bulgaria
Canada, Chile
China, Colombia
Czech Republic
Denmark
Dominican Republic
Ecuador, Egypt
England, Ethiopia
Finland, France
Germany, Guatemala
Guyana, Honduras
Hong Kong, India
Indonesia, Iran, Iraq
Ireland, Israel
Italy, Japan
Kazakhstan
Kyrgyzstan, Libya
Luxembourg, Malaysia
Mexico, Morocco

Nepal, Netherlands
New Zealand
Oman, Pakistan
Palestine
Papua New Guinea
Panama
Peru, Philippines
Poland, Portugal
Puerto Rico
Romania, Russia
Saudi Arabia
Serbia,
South Africa
South Korea
Spain, Sri Lanka
Suriname, Sweden
Switzerland, Tanzania
Thailand, Togo
Turkey, Ukraine
USA, Uzbekistan,
Venezuela
Vietnam

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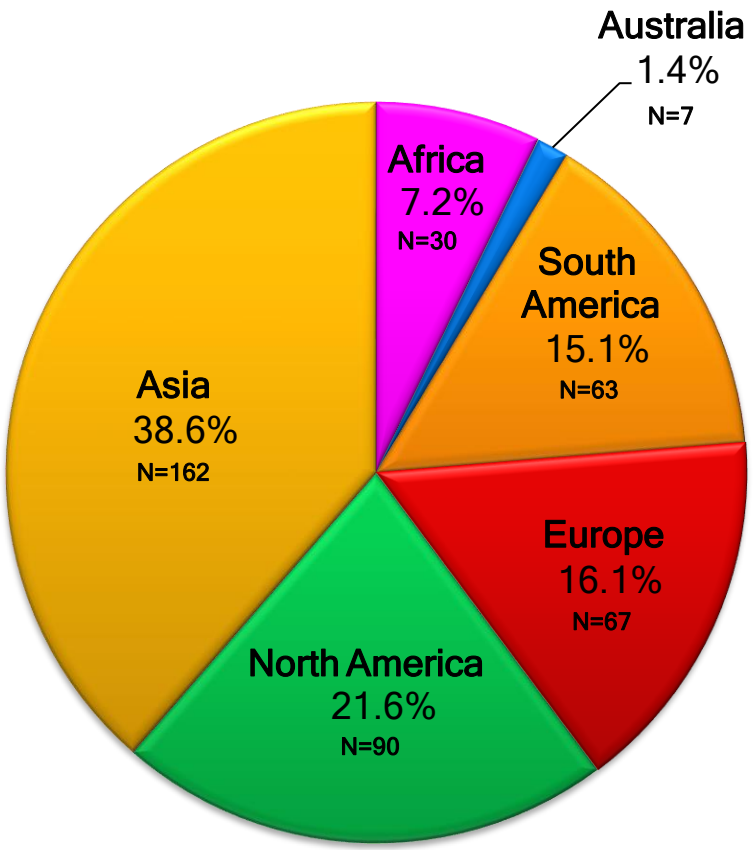
...And All Continents

Participation (%) By Continent



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PRF Diagnostics Program

Program Goal:

- Genetic Sequence Testing for Progeria-causing mutations

Pre-requisites for Testing:

- Registration with PRF International Registry
- One or more of the following
  - Family history – proband, prenatal
  - Phenotypic presentation – proband, postnatal
  - Relative of positive proband

Testing information available at:

https://www.progeriaresearch.org/the-prf-diagnostic-testing-program/

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Diagnostics Testing Summary

March 31, 2025

Total Number of Proband Tests Performed: 171

Exon 11 (HGPS) Mutations: 118

Other Progeroid Laminopathies (Exons 1 – 12): 13

ZMPSTE24 Mutations : 2

Average Number of Patients Tested Per Year : 6

All tests are performed in a Clinical Laboratory Improvement Amendments (CLIA) certified facility.

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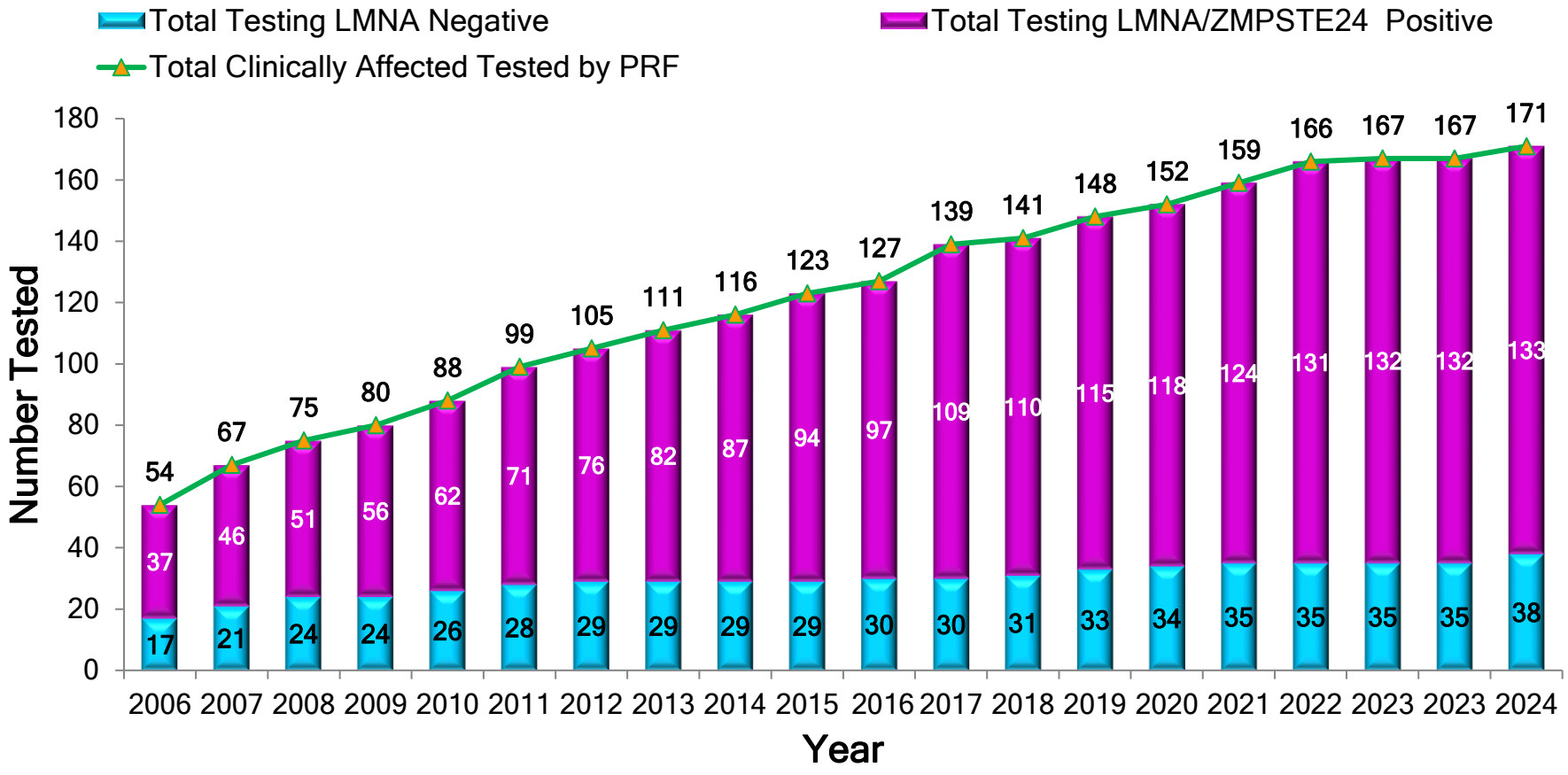
Mutations Identified Through PRF Diagnostics Program

DNA Mutation	Amino Acid Effect	Zygosity	Progerin Producing?	Number Diagnosed
Classic HGPS - LMNA Mutation				
1824 C>T, exon 11	G608G	heterozygous	Yes	104
Non Classic HGPS- LMNA Mutation				
1822 G>A, exon 11	G608S	heterozygous	Yes	4
1821 G>A, exon 11	V607V	heterozygous	Yes	2
1868 C>G, exon 11	T623S	heterozygous	Yes	1
1968+5 G>C, intron 11	None	heterozygous	Yes	2
1968+1 G>C, intron 11	None	heterozygous	Yes	3
1968+2 T>A, intron 11	None	heterozygous	Yes	1
1968+1 G>A, intron 11	None	heterozygous	Yes	1
Progeroid Laminopathy- LMNA Mutation				
1579 C>T, exon 9	R527C	heterozygous	No	1
1579 C>T, exon 9	R527C	homozygous	No	6
1580G>T, exon9	R527L	Homozygous	No	2
1619 T>C, exon 10	M540T	homozygous	No	3
331 G>A, exon 1	E111K	heterozygous	No	1
Progeroid Laminopathy- ZMPSTE24 Mutation				
1274T>C, exon 10	L425P	homozygous	No	2

Longitudinal Testing Data for PRF Diagnostics Program

Number of Affected Children/Adults Tested and the Number Testing Positive for *LMNA* Gene Mutation*



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PRF Cell & Tissue Bank

Program Goals:

- Provide a resource for researchers worldwide
- Ensure the sufficient availability of genetic and biological materials essential for research aimed at understanding the pathophysiology of disease and the links between Progeria, aging and heart disease
- Obtain long-term clinical data

Resource information available at: https://www.progeriaresearch.org/cell-and-tissue-bank/

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PRF Cell and Tissue Bank Holdings

As of March 31, 2025

Total Number of Participants: **404***

71 Dermal Fibroblast Lines from **47** affected and **24** parents

6 Immortalized Fibroblast Cell Lines from **1** affected and **5** parents

125 Lymphoblast Lines from **71** affected, **46** parents and **8** siblings

9 Induced Pluripotent Stem Cell Lines from **5** affected and **4** parents

* Participants may have donated multiple times
* Additional sample types are available for special projects upon request

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Mutations Available in PRF Cell & Tissue Bank

DNA Mutation	Amino Acid Effect	Zygosity	Progerin Producing?	Cell Type DFN=Dermal Fibroblast LBV= Lymphoblast
Classic HGPS - LMNA Mutation				
c.1824 C>T, exon 11	p.G608G	heterozygous	Yes	DFN, LBV, iPSC
Non Classic HGPS- LMNA Mutation				
c.1822 G>A, exon 11	p.G608S	heterozygous	Yes	DFN, LBV
c.1821 G>A, exon 11	p.V607V	heterozygous	Yes	LBV
c.1824 C>T, exon 11 & SMC3 c.562 A>G	p.G608G & p.K188E	heterozygous	Yes	DFN
c.1868 C>G, exon 11	p.T623S	heterozygous	Yes	LBV
c.1968+5 G>C, intron 11	---------	heterozygous	Yes	DFN
c.1968+5 G>A, intron 11	---------	heterozygous	Yes	DFN
c.1968+1 G>A, intron 11	---------	heterozygous	Yes	DFN, LBV
c.1968+2 T>C, exon 11	---------	heterozygous	Yes	DFN
c.1968+2 T>C, exon 11 & c.1968+2 T>A, exon 11	---------	heterozygous	Yes	DFN
Progeroid Laminopathy- LMNA Mutation				
c.1579 C>T, exon 9	p.R527C	heterozygous	No	LBV
c.1579 C>T, exon 9	p.R527C	homozygous	No	LBV
c.1580 G>T, exon 9	p.R527L	homozygous	No	LBV
c.1619 T>C, exon 10	p.M540T	homozygous	No	DFN
c.1762 T>C, exon 11	p.C588R	heterozygous	No	DFN
c.1930 C>T, exon 11	p.R644C	heterozygous	No	DFN
c.331 G>A, exon 1 & c.1158-44 C>T, intron 6	p.E111K	heterozygous	No	DFN, LBV
c.412 G>A	p.E138K	heterozygous	No	DFN
c.973 G>A, exon 6	p.D325N	heterozygous	No	DFN
Progeroid Laminopathy- ZMPSTE24 Mutation				
c.1274 T>C, exon 10	p.L425P	homozygous	No	DFN, LBV
c.743 C>T, exon 6 & c.1349 G>A, exon 10	p.P248L & p.W450Stop	heterozygous	No	DFN

PRF Cell & Tissue Bank Distribution

As of March 14, 2025:

253 Research Teams From **29** Countries Have Received

1665 Cell Lines

204 DNA Samples

467 Tissue, plasma, serum and other biological samples

36 Lonafarnib Samples

Senescent Progeria Fibroblasts in Culture

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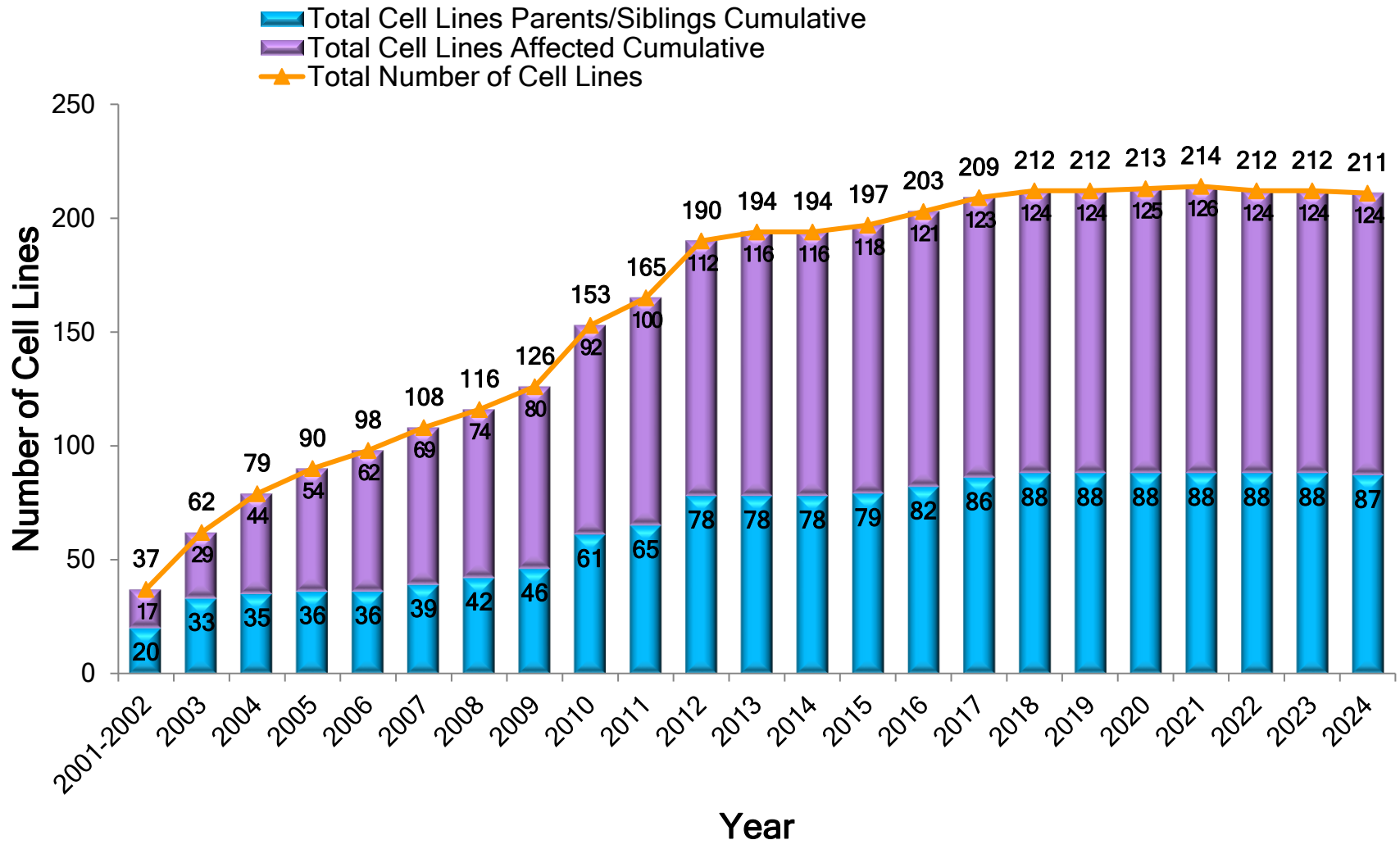
Number Of Cell Lines By Year



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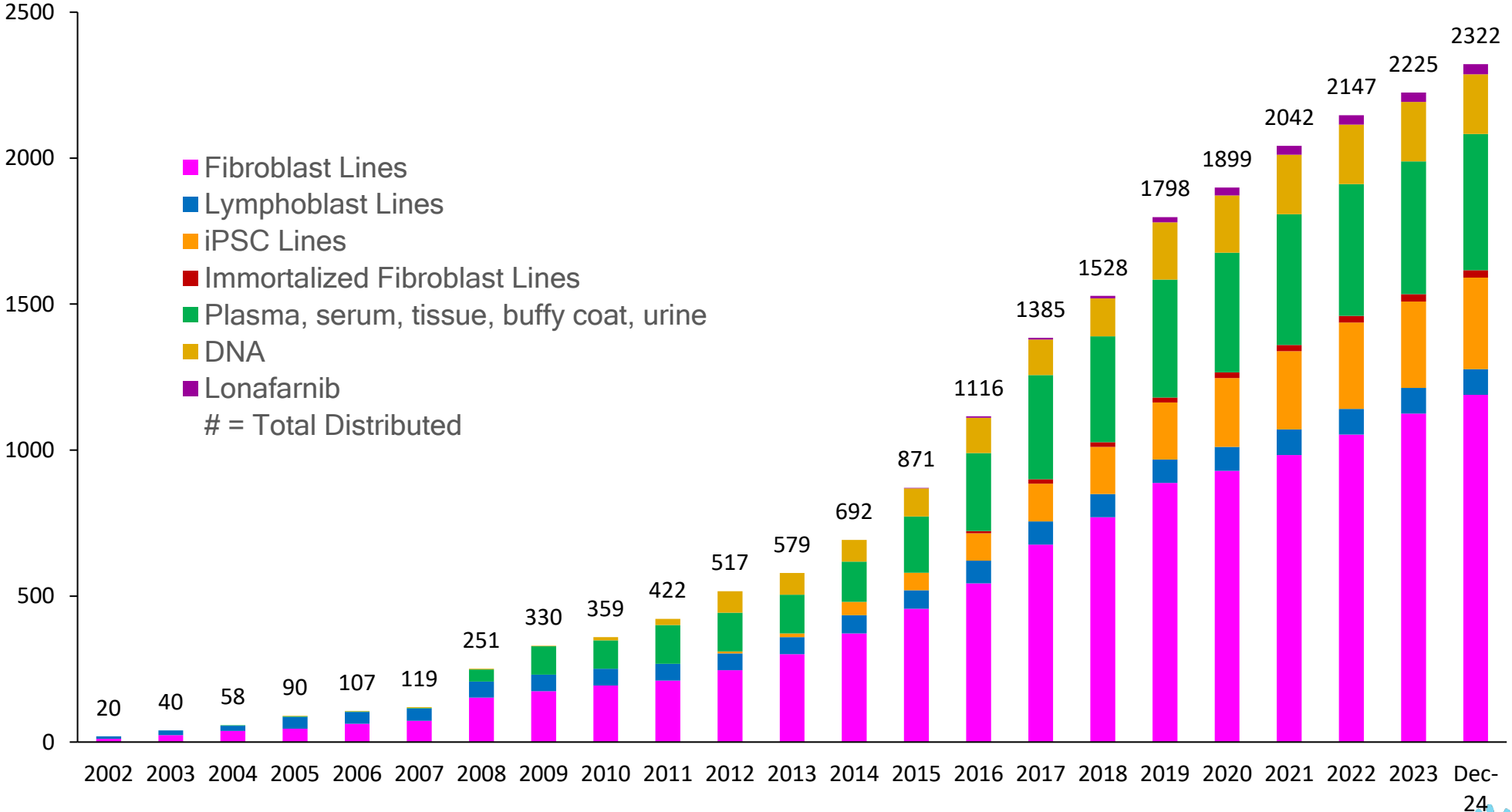
Cumulative Number of Biological Samples Distributed



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Cell and Tissue Bank Recipients

Cells and biological material have been distributed to
243 laboratories in **29** countries
Complete list of researchers available at: https://www.progeriaresearch.org/cell-and-tissue-bank-recipients

PRF Medical & Research Database

Program Goals:

- Collect the patient health records for living and deceased children with Progeria
- Obtain long-term clinical data
- Abstract data for longitudinal and cross-sectional analyses
- Better understand the clinical disease process in Progeria and aging related diseases
- Develop treatment strategies and recommendations for health care professionals and families

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How The PRF Medical & Research Database Works

- Project staff obtain the patient's medical records and film studies from birth throughout the participant's lifespan.
- Medical records include visits to: primary care physicians, specialty physicians, hospital emergency rooms, hospital admissions, dentists, physical therapy, occupational therapy and school health records.
- Retrospective data abstraction protocol allows for specifically targeted or broad spectrum of data.

Enrollment information available at: https://www.progeriaresearch.org/medical-database/

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Medical & Research Database Participation

223 Participants are enrolled from 57 countries and 1 US territory

Algeria
Argentina
Australia
Bangladesh
Belgium Brazil
Canada, Chile
China, Columbia
Denmark
Dominica Republic
Egypt, England,
Ethiopia
France, Germany
Guatemala,
Guyana
Honduras, India
Indonesia, Ireland
Israel, Italy
Japan, Kazakhstan

Libya, Mexico
Morocco, Nepal
Netherlands
Oman, Pakistan
Papua New Guinea
Peru, Philippines
Poland, Portugal
Puerto Rico
Romania, Russia
Senegal, Serbia
South Africa
South Korea
Spain, Sri Lanka
Suriname, Sweden
Tanzania, Togo
Turkey, Ukraine
USA, Venezuela
Vietnam

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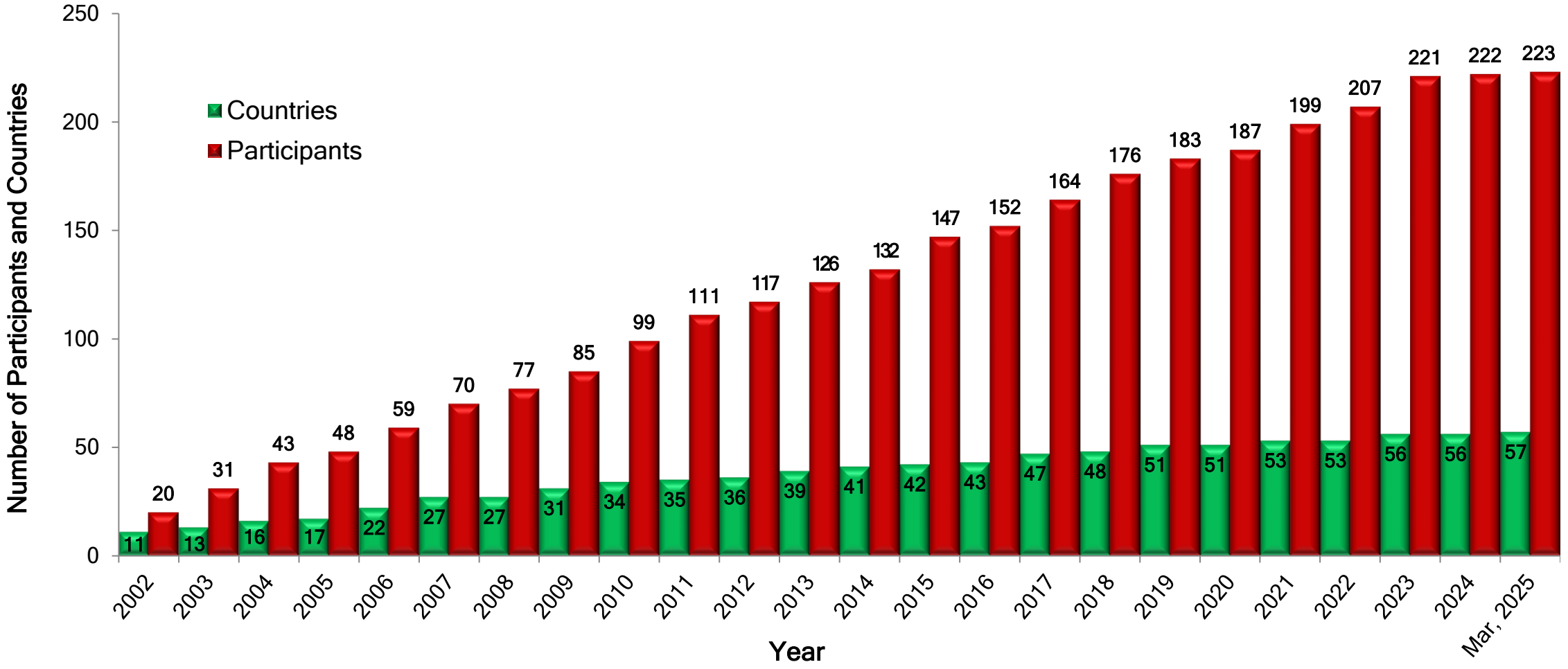
Medical & Research Database Longitudinal Enrollment



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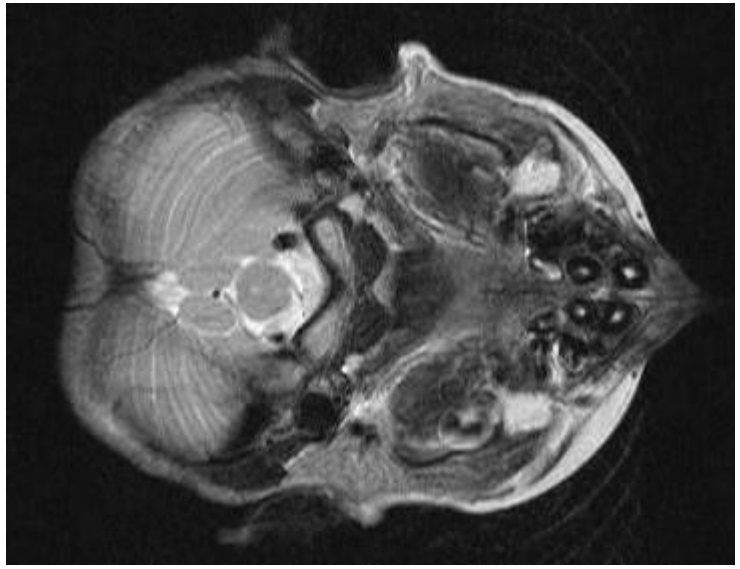
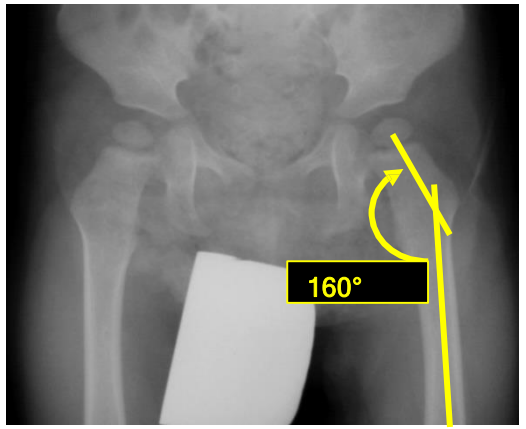
Types Of Data Collected

- Participants with Medical Records Reports: **166**
- Participants with Radiology Studies: **65**





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PRF Weighing-In Program

- A sub-program of The PRF Medical & Research Database
- Collects weight-for-age data prospectively:
  - Home scale provided by PRF
  - Parents weigh child weekly or monthly
  - Report weights electronically

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Weighing-In Program Participation

122 Participants are enrolled from 42 countries and 1 US territory

Argentina, Australia
Bangladesh
Belgium, Brazil
Canada, China
Colombia, Denmark
Dominican Republic
England, Germany
Guatemala
Honduras, India
Indonesia, Ireland
Israel, Italy, Japan
Mexico, Morocco

Nepal, Pakistan
Peru, Philippines
Poland, Portugal
Puerto Rico
Romania, Russia
Senegal
South Africa
South Korea
Spain, Sri Lanka
Togo, Tanzania
Turkey, Ukraine
USA, Venezuela
Vietnam

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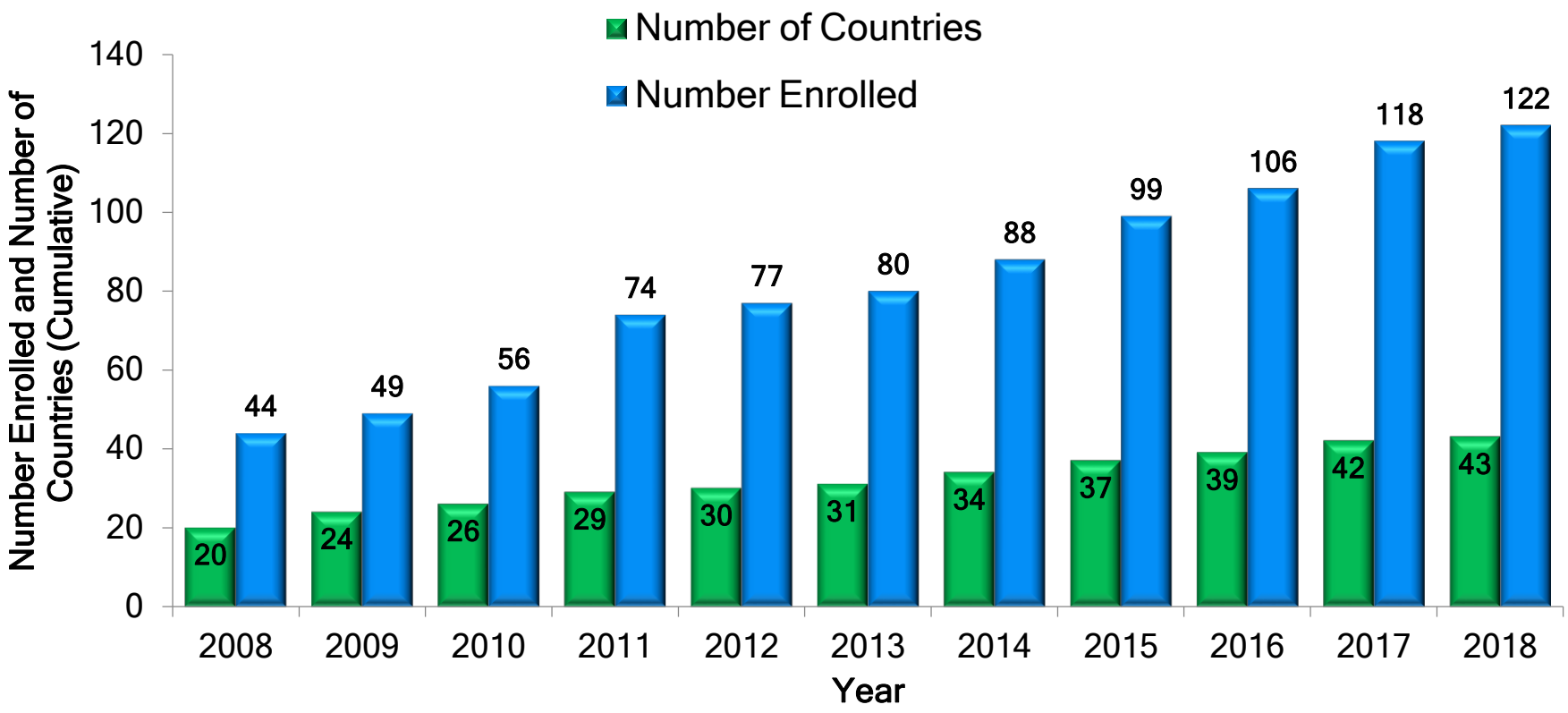
Participants Enrolled In The PRF Weighing-In Program and Countries of Residence



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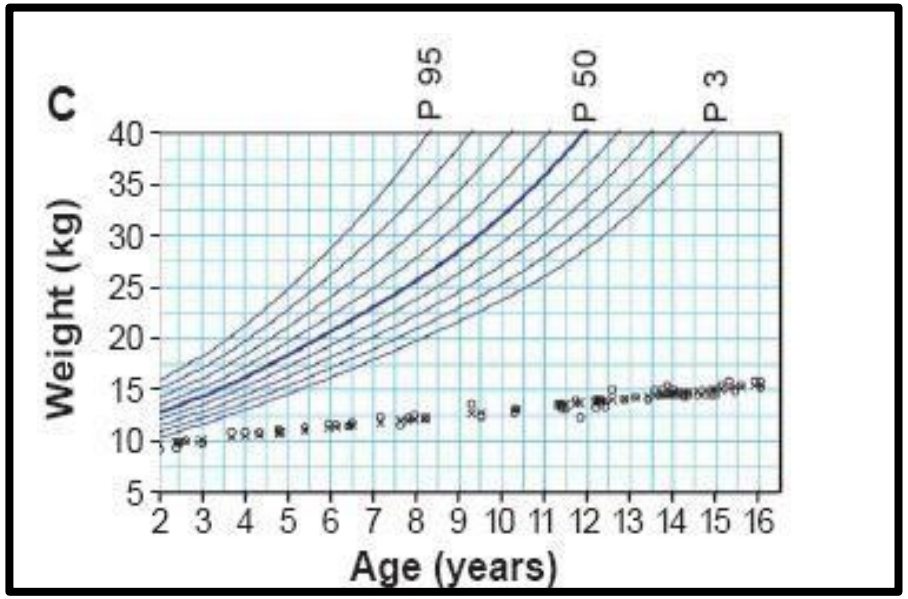
Clinical Trials And The Weighing-In Program

- Data from this program were key in the development of primary outcome measure for the first drug treatment trial for Progeria.

- As of December 1, 2018, 90 children from The PRF Weighing-In Program have entered clinical treatment trials using this data.



Failure to Thrive Starts Towards End of Year One

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PRF-Funded Clinical Treatment Trials

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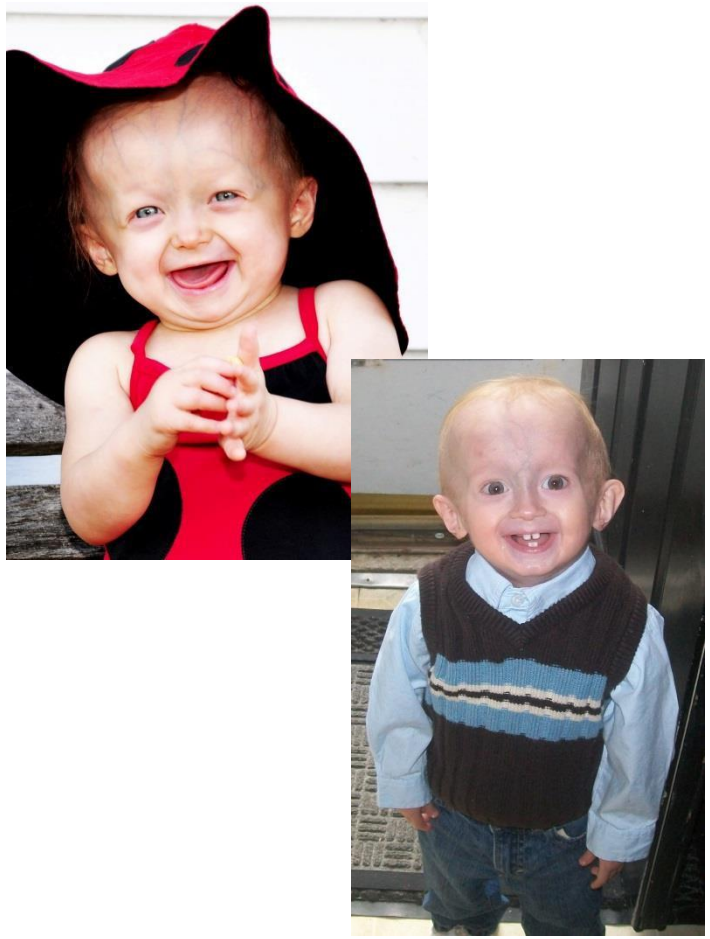
Clinical Drug Treatment Trials

Goals:

- To define the natural history of HGPS in quantifiable terms that will expand our ability to measure treatment outcome
- To assess the safety of new treatments for HGPS
- To measure effects of treatments for children with HGPS on disease status, changes in health, and survival



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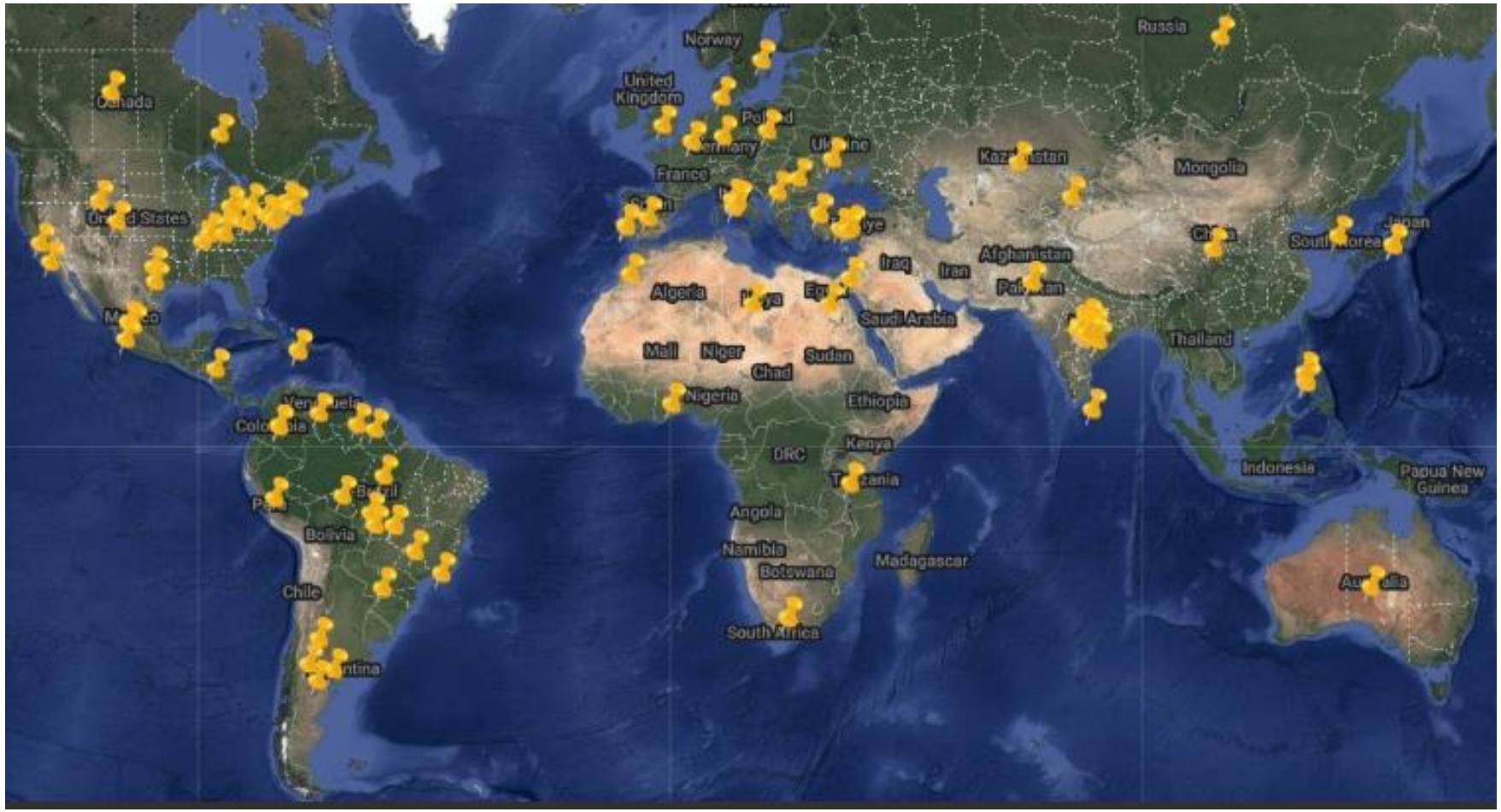
Participation in PRF Clinical Trials

109 Children have participated in PRF Clinical Trials from **42** countries

Argentina
Australia
Belgium, Brazil
Canada, China
Colombia
Denmark
Dominican Republic
Egypt
England
Germany
Guyana
Honduras
India, Israel
Italy, Japan
Kazakhstan
Libya
Mexico



Morocco, Pakistan
Peru, Philippines
Poland, Portugal
Romania
Russia, Serbia
South Africa
South Korea
Spain, Sri Lanka
Suriname
Sweden
Tanzania
Togo
Turkey
Ukraine
USA
Venezuela

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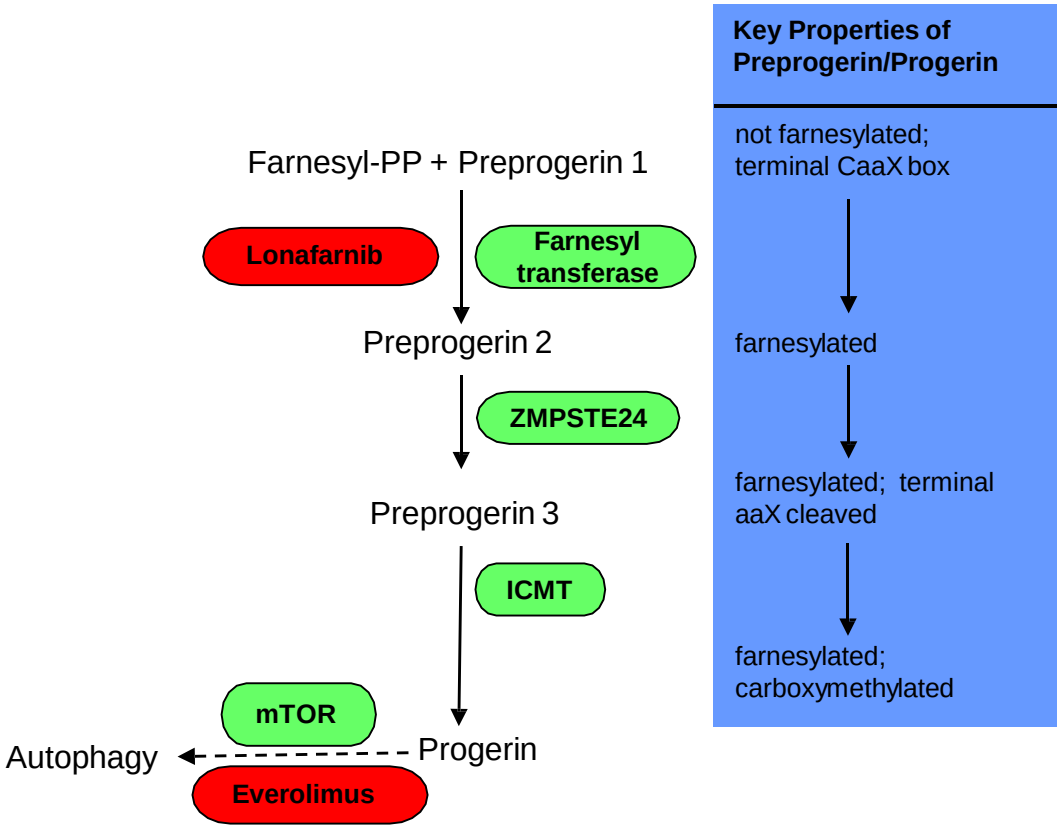
Current Therapeutic Intervention Strategies



Post-translational processing and medications currently under investigation in clinical treatment trials for Progeria. Items in green = enzymes. Items in red = clinical trial medications that inhibit corresponding enzymes. Lonafarnib is a farnesyltransferase inhibitor. Everolimus is a rapamycin analogue that inhibits mTOR and promotes cellular autophagy. FT=farnesyltransferase.

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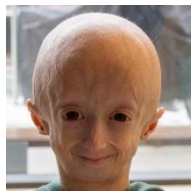
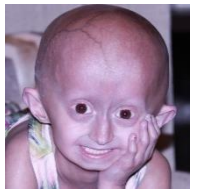
PRF-Funded Clinical Treatment Trials

Children & young adults have flown from all over the world to participate in clinical treatment trials 1-5 at the Boston Children's Hospital



Trial #	Year	Drug(s)	Phase	# Enrolled	Countries Represented
1	2007-2010	Lonafarnib	2	29	16
2	2009	Lonafarnib, Pravastatin, Zoledronate	Feasibility	5	2
3	2009-2013	Lonafarnib, Pravastatin, Zoledronate	2	45	24
	2014-2021	Lonafarnib	2 (Extension)	71	32
4	2016-2023	Lonafarnib, Everolimus	1/2	60	27
	2018-Present	Lonafarnib	2 (Extension)	63 *	30 *
5	2025-Present	Progerinin, Lonafarnib	2	10 *	7 *



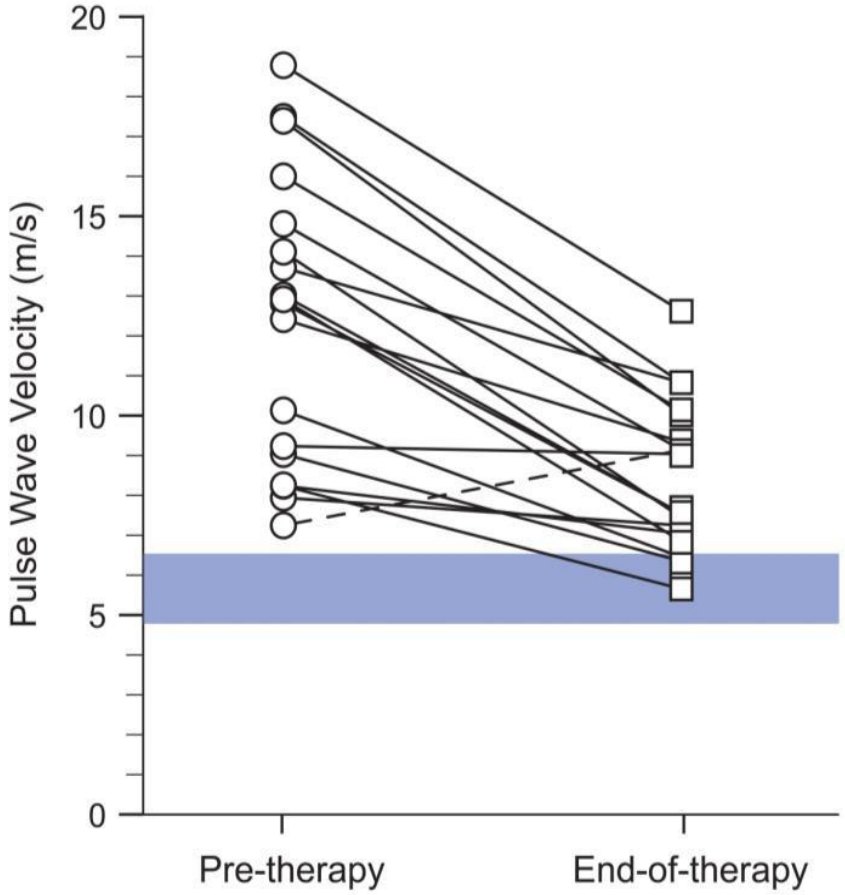
* As of March 31, 2025

Clinical Treatment Trial Efficacy Results

Lonafarnib, a type of farnesyltransferase inhibitor (FTI) is our first treatment for Progeria

- Results showed improvement in:
  - Rate of weight gain
  - Increased vascular distensibility
  - Improved bone structure
  - Better neurosensory hearing
  - Increased Lifespan

Gordon et al, PNAS, 2011



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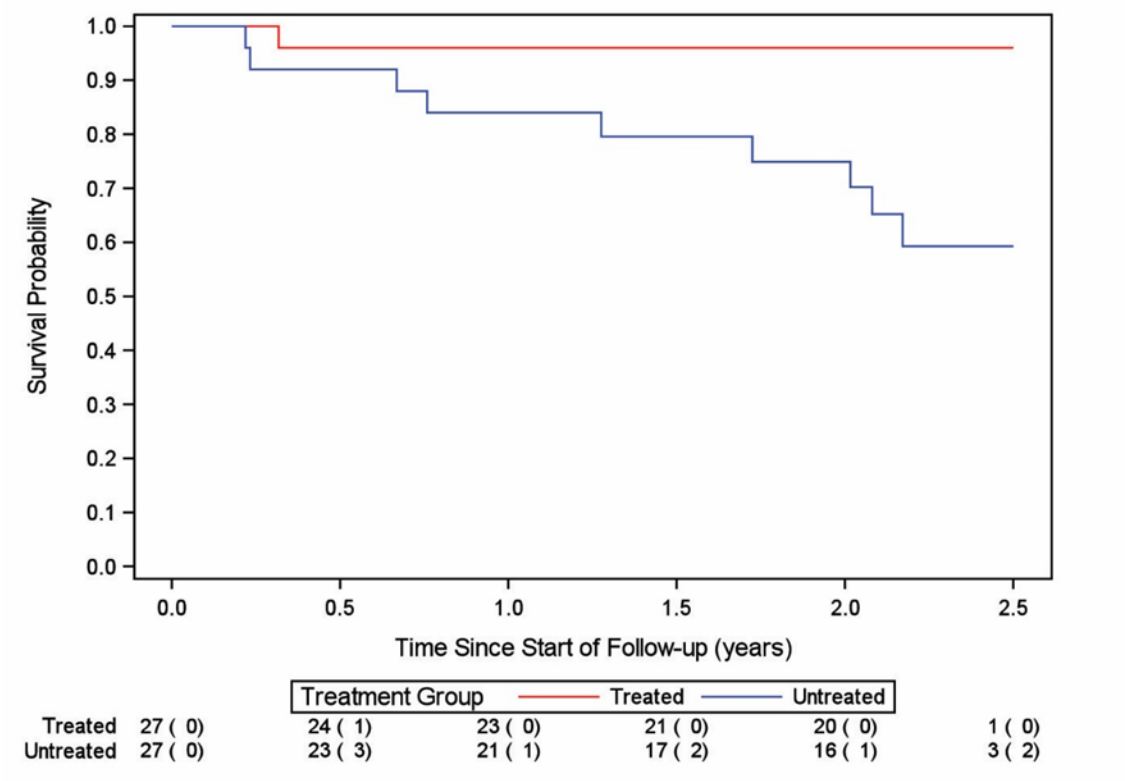
Positive Effects of Lonafarnib (Zokinvy) on Progeria: Results of PRF's Clinical Treatment Trials

- Average increased lifespan of 4.3 years
- Increased vascular distensibility
- Improved bone structure
- Better neurosensory hearing
- Modest increase in rate of weight gain



Gordon et al., PNAS, 2011 and
Gordon et al., JAMA, 2018
Gordon et al., Circulation 2023

JAMA | Preliminary Communication

Association of Lonafarnib Treatment vs No Treatment With Mortality Rate in Patients With Hutchinson-Gilford Progeria Syndrome

Leslie B. Gordon, MD, PhD; Heather Shappell, PhD; Joe Massaro, PhD; Ralph B. D'Agostino Sr, PhD; Joan Brazier, MS; Susan E. Campbell, MA; Monica E. Kleinman, MD; Mark W. Kieran, MD, PhD

3 Ways to Access Lonafarnib (Zokinvy)

Zokinvy (lonafarnib) is an FDA approved drug in the US. It is the current standard of care for those with Progeria. It is available through

1. Prescription in the US and in select non-US countries
2. PRF's clinical treatment trials
3. The manufacturer's (Sentynl) Managed Access Program in select non-US countries

We are far from finished!
We must forge ahead with increased intensity and collaborative efforts to find additional treatments, and the cure!

Please contact PRF at info@progeriaresearch.org for more information on how to access Zokinvy (lonafarnib) for your child or patient with Progeria

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Treatment Trial Collaborations For Success

- **The children are seen by physicians from:**
  - Boston Children's Hospital
  - Dana-Farber Cancer Institute
  - Brigham and Women's Hospital
- **Data were also generated by scientists from:**
  - Alpert Medical School at Brown University
  - Brown University School of Public Health
  - University of California Los Angeles
  - National Human Genome Research Institute
  - Schering-Plough Research Institute
- **Lonafarnib generously provided by Sentynl**
- **Everolimus generously provided by Novartis**

Clinical Trial Publications

Drug Effect:

Plasma Progerin in Patients With Hutchinson-Gilford Progeria Syndrome: Immunoassay Development and Clinical Evaluation. Gordon et al., *Circulation*, 2023;147(23):1734-1744

FDA approval summary for lonafarnib (Zokinvy) for the treatment of Hutchinson-Gilford progeria syndrome and processing-deficient progeroid laminopathies. Suzuki et al., *Genetics in medicine*, 2023;25(2):100335

Association of Lonafarnib Treatment vs No Treatment With Mortality Rate in Patients With Hutchinson-Gilford Progeria Syndrome. Gordon et al., *JAMA*, 2018, 319(16):1687-1695.

Survey of Plasma Proteins in Children with Progeria Pre-therapy and On-Therapy with Lonafarnib. Gordon et al., *Pediatric Research*, 2018;83(5):982-992

Clinical Trial of the Protein Farnesylation Inhibitors Lonafarnib, Pravastatin, and Zoledronic Acid in Children With Hutchinson-Gilford Progeria Syndrome. Gordon et al., *Circulation*, 2016 Jul 12;134(2):114-25.

Seeking a Cure for One of the Rarest Diseases: Progeria. Collins, *Circulation,* 2016 Jul 12;134(2):126-9.

Impact of Farnesylation Inhibitors on Survival in Hutchinson-Gilford Progeria Syndrome. Gordon et al., *Circulation*, 2014 Jul 1;130(1):27-34.

Moving from Gene Discovery to Clinical Trials in Hutchinson-Gilford Progeria Syndrome. King et al., *Neurology*, 2013 Jul 30;81(5):408-9.

Neurologic Features of Hutchinson-Gilford Progeria Syndrome after Lonafarnib Treatment. Ullrich et al., *Neurology*, 2013, 81:427-430.

Clinical Trial of a Farnesyltransferase Inhibitor in Children with Hutchinson-Gilford Progeria Syndrome. Gordon et al., *Proceedings of the National Academy of Sciences*, 2012 Sep 24.

General:

Clonal hematopoiesis is not prevalent in Hutchinson-Gilford progeria syndrome. Díez-Díez, et al., *GeroScience*. 2023;45(2):1231-1236

Pubertal Progression in Adolescent Females with Progeria. Greer et al., *Journal of Pediatric and Adolescent Gynecology*, 2018;31(3):238-241

Phenotype and Course of Hutchinson-Gilford Progeria Syndrome. Meredith et al., *New England Journal of Medicine*, 2008, 358(6): 592- 604.

Dermatology:

Initial Cutaneous Manifestations of Hutchinson-Gilford Progeria Syndrome. Rork et al., *Pediatric Dermatology*, 2014,1-7.

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Clinical Trial Publications Continued

Dental:

Microbiome at Sites of Gingival Recession in Children with Hutchinson-Gilford Progeria Syndrome. Bassir et al., *Journal of Periodontology*. 2018, 89(6): 635-644.

Hutchinson-Gilford Progeria Syndrome: Oral and Craniofacial Phenotypes. Domingo et al., *Oral Diseases*, 2009, 15(3): 187-195.

Cerebrovascular:

Imaging Characteristics of Cerebrovascular Arteriopathy and Stroke in Hutchinson-Gilford Progeria Syndrome. Silvera et al., *American Journal of Neuroradiology*, 2013 May;34(5):1091-7.

Cardiology:

Abnormal Myocardial Deformation Despite Normal Ejection Fraction in Hutchinson-Gilford Progeria Syndrome. Olsen, et al. *J Am Heart Assoc*. 2024;13(3)

Progression of Cardiac Abnormalities in Hutchinson-Gilford Progeria Syndrome: A Prospective Longitudinal Study. Olsen FJ, et al. *Circulation*. 2023;147(23):1782-1784.

Cardiac Abnormalities in Patients With Hutchinson-Gilford Progeria Syndrome. Prakask, et al., *JAMA Cardiology*, 2018, Apr 17;115(16):4206-4211.

Mechanisms of Premature Vascular Aging in Children with Hutchinson-Gilford Progeria Syndrome. Gerhard-Herman M, et al., *Hypertension*. 2012; 59(1):92-97.

Skeletal:

Baseline Range of Motion, Strength, Motor Function, and Participation in Youth with Hutchinson-Gilford Progeria Syndrome. Malloy et al., *Phys Occup Ther Pediatr*. 2023 Jan 10:1-20.

Skeletal maturation and long-bone growth patterns of patients with Progeria: a retrospective study. Tsai et al., *The Lancet. Child and Adolescent Health*. 2020 Apr;4(4):281-289.

Extraskeletal Calcifications in Hutchinson-Gilford Progeria Syndrome. Gordon et al., *Bone.* 2019 Aug;125:103-111.

Craniofacial Abnormalities in Hutchinson-Gilford Progeria Syndrome. Ullrich et al., *American Journal of Neuroradiology*. 2012 Sep;33(8):1512-8.

A Prospective Study of Radiographic Manifestations in Hutchinson-Gilford Progeria Syndrome. Cleveland et al., *Pediatric Radiology,* 2012 Sep;42(9):1089- 98. Epub 2012 Jul 1.

Hutchinson-Gilford progeria is a skeletal dysplasia. Gordon, et al., *Journal of Bone and Mineral Research*. 2011 Jul;26(7):1670-9.

Ophthalmology:

Ophthalmologic Features of Progeria. Mantagos et al., *American Journal of Ophthalmology,* 2017 Oct;182:126-132.

Audiology:

Otologic and Audiologic Manifestations of Hutchinson-Gilford Progeria Syndrome. Guardiani et al., *The Laryngscope*, 2011, 121(10): 2250-2255.

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Progerin as a Biomarker for Progeria

- Progerin is the toxic protein produced by cells with progeria in place of the normal lamin A protein
- Normal lamin A plays a role in cell division, but the toxic progerin gets stuck to the nuclear membrane of cells, and its accumulation causes progeria
- A biomarker is “a biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease” (National Cancer Institute)
- Treatments for progeria aim to decrease the amount of progerin produced by the body.

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Publication of the Progerin Biomarker

research-article

Circulation

ORIGINAL RESEARCH ARTICLE

Plasma Progerin in Patients With Hutchinson-Gilford Progeria Syndrome: Immunoassay Development and Clinical Evaluation

Leslie B. Gordon, MD, PhD; Wendy Norris, MS; Sarah Hamren, BS; Robert Goodson, BS; Jessica LeClair, PhD; Joseph Massaro, PhD; Asya Lyass, PhD; Ralph B. D'AgostinoSr, PhD; Kelsey Tuminelli, MS; Mark W. Kieran, MD, PhD; Monica E. Kleinman, MD

Dr. Gordon *et al.* 2023 developed an assay to measure progerin in blood plasma

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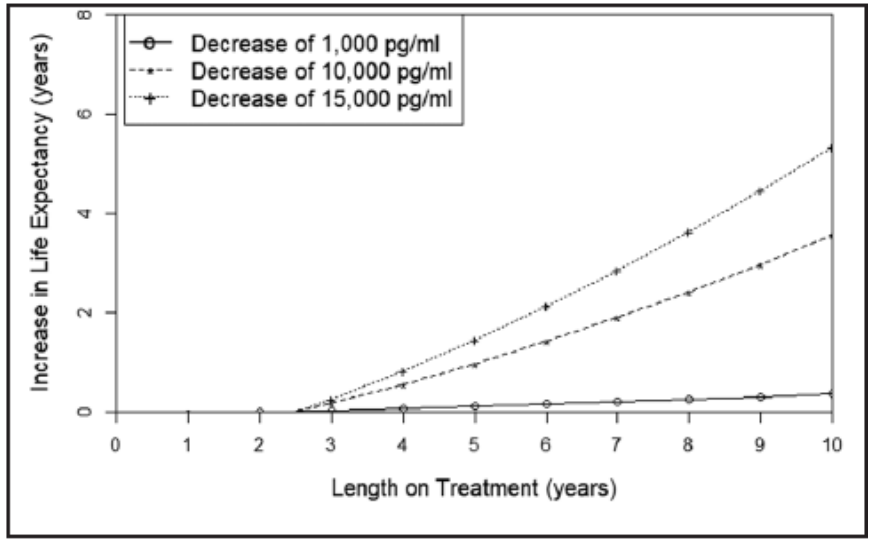
Further Findings of the Progerin Biomarker Study

- Plasma progerin levels were 95x higher in those with progeria than in the average healthy human
- Treatment with lonafarnib decreased progerin levels by 35-62% on average
- Lifespan increase was shown to be linked to decreased progerin levels and longer time on treatment
- Long-term treatment with lonafarnib (10+ years) resulted in a lifespan increase of about 35%



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PRF Grant Funding

As of March 31 , 2025:

- Since inception 281 grant application received and 85 funded
- PRF has funded 69 principal investigators from 55 institutions in 14 countries

- Lamina A, progerin, Lamin B in HGPS and aging
- Genetics and nuclear function
- Preclinical Drug Therapy
- Molecular Abnormalities and Therapies
- Vascular Pathology
- Mouse Models
- Stem Cell Investigations and Therapy
- Clinical Trials

* Submissions include Letters of Intent and Full Grants

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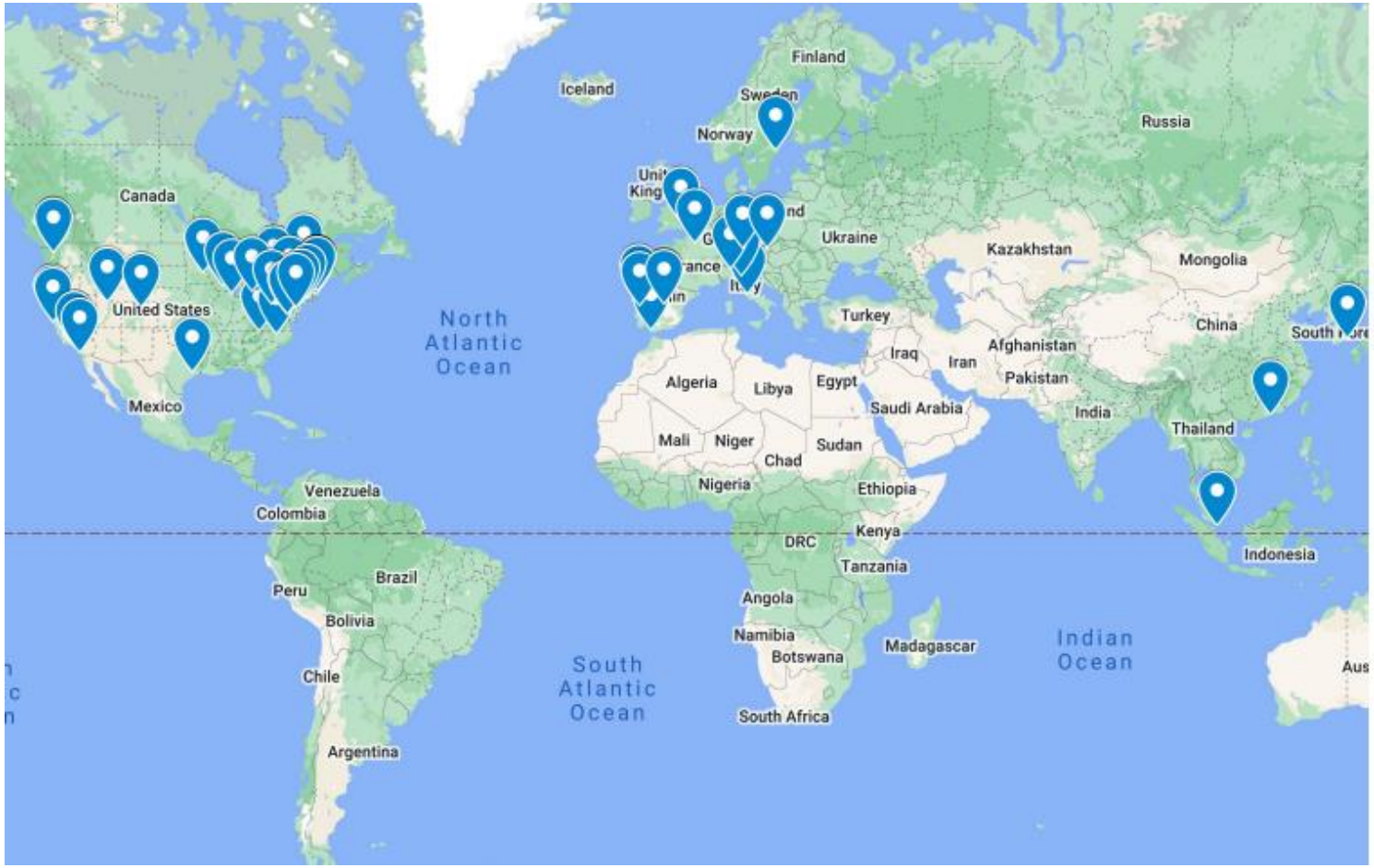
PRF Grantees

PRF has funded **69** principal investigators from **55** institutions in **14** countries

Complete list of Grantees available at: https://www.progeriaresearch.org/grants-funded/



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PRF Scientific Meetings

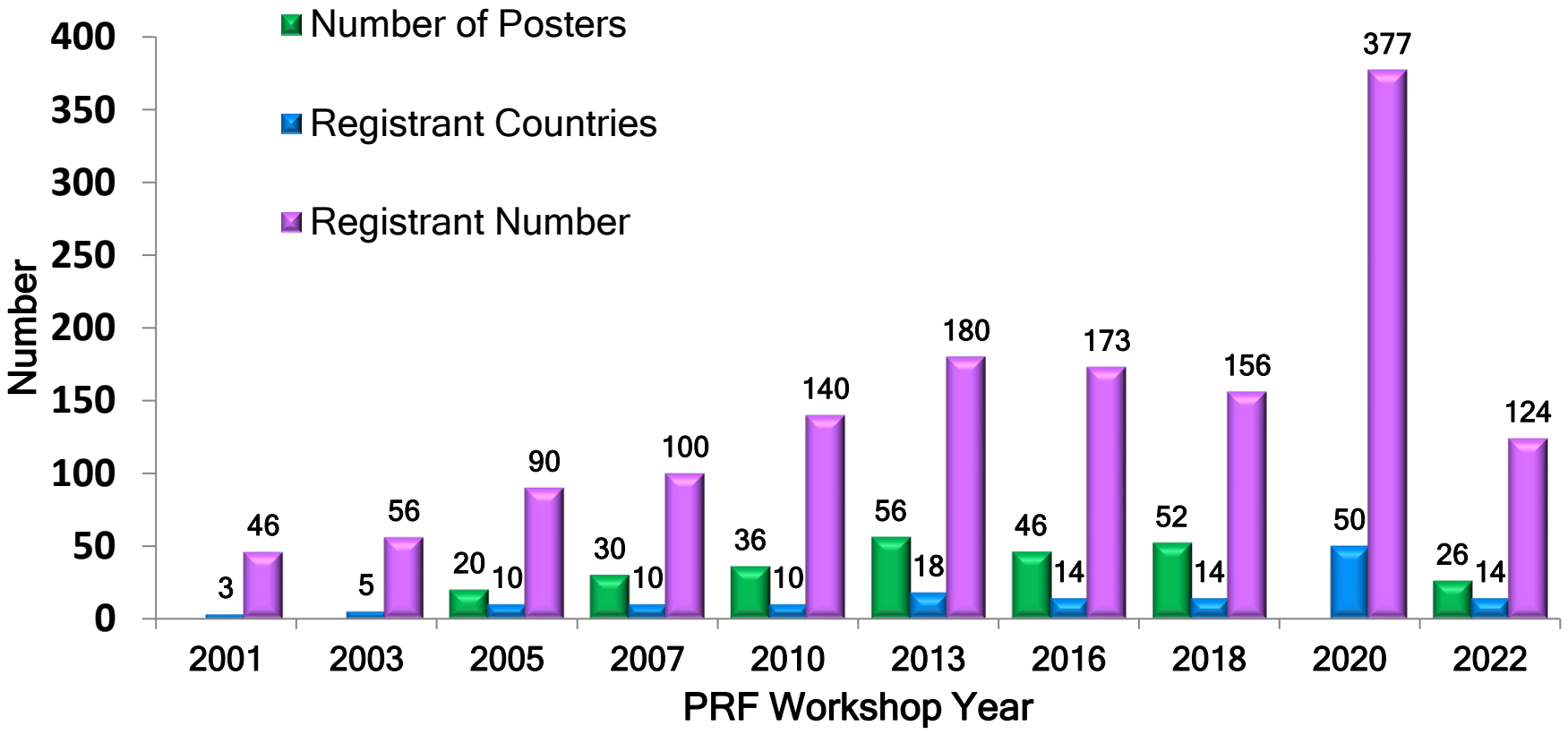
Meeting Goals:

- To promote collaboration between basic and clinical scientists toward progress in Progeria, cardiovascular, and aging research PRF has held international scientific meetings.

International Workshops Promoting Global Interest In Progeria, Cardiovascular Disease And Aging

- These are large multi-day workshops open to all scientists. Clinical and basic researchers spend intense days sharing data and planning new collaborations for progress towards treatments and cure.
- Various NIH Institutes have funded all international workshops through R13 and other granting mechanisms
- Other organizations have also generously sponsored workshops

Growth of Global Interest In PRF Workshops



* 2020 was a webinar. Posters N/A

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Subspecialty Scientific Meetings

Small, focused meetings designed to promote and support work in areas of high interest for Progeria

First Genetics Consortium Meeting – "Searching for the Progeria Gene", August 23, 2002, Brown University, Providence, RI

Second Genetics Consortium Meeting – "Post- gene Discovery", July 30, 2003, Bethesda, MD

Bone Marrow Transplant Meeting – "Forging Ahead by Exploring Potential Treatments", April 25-26, 2004, National Institutes of Health, Bethesda, MD

New Frontiers in Progeria Research (2012), Boston, MA

The first "Progeria Aortic Stenosis Intervention Summit", May 2, 2023, Virtual by Zoom

NIH National Heart, Lung, and Blood Institute

NIH National Human Genome Research Institute

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Scientific Publications

As of March 14, 2025:

193 Scientific articles have been published citing The Progeria Research Foundation Grants Funding Program

141 Scientific articles have been published citing PRF Cell & Tissue Bank resources:

- Publication list at https://www.progeriaresearch.org/prf-cell-and-tissue-bank-publications/

35 Scientific articles have been published citing The PRF Medical & Research Database:

- Publication list at www.progeriaresearch.org/medical-database/

30 Scientific articles have been published from clinical trial data

- See slide #54 and #55

4 Scientific articles have been published concerning PRF Scientific Workshops

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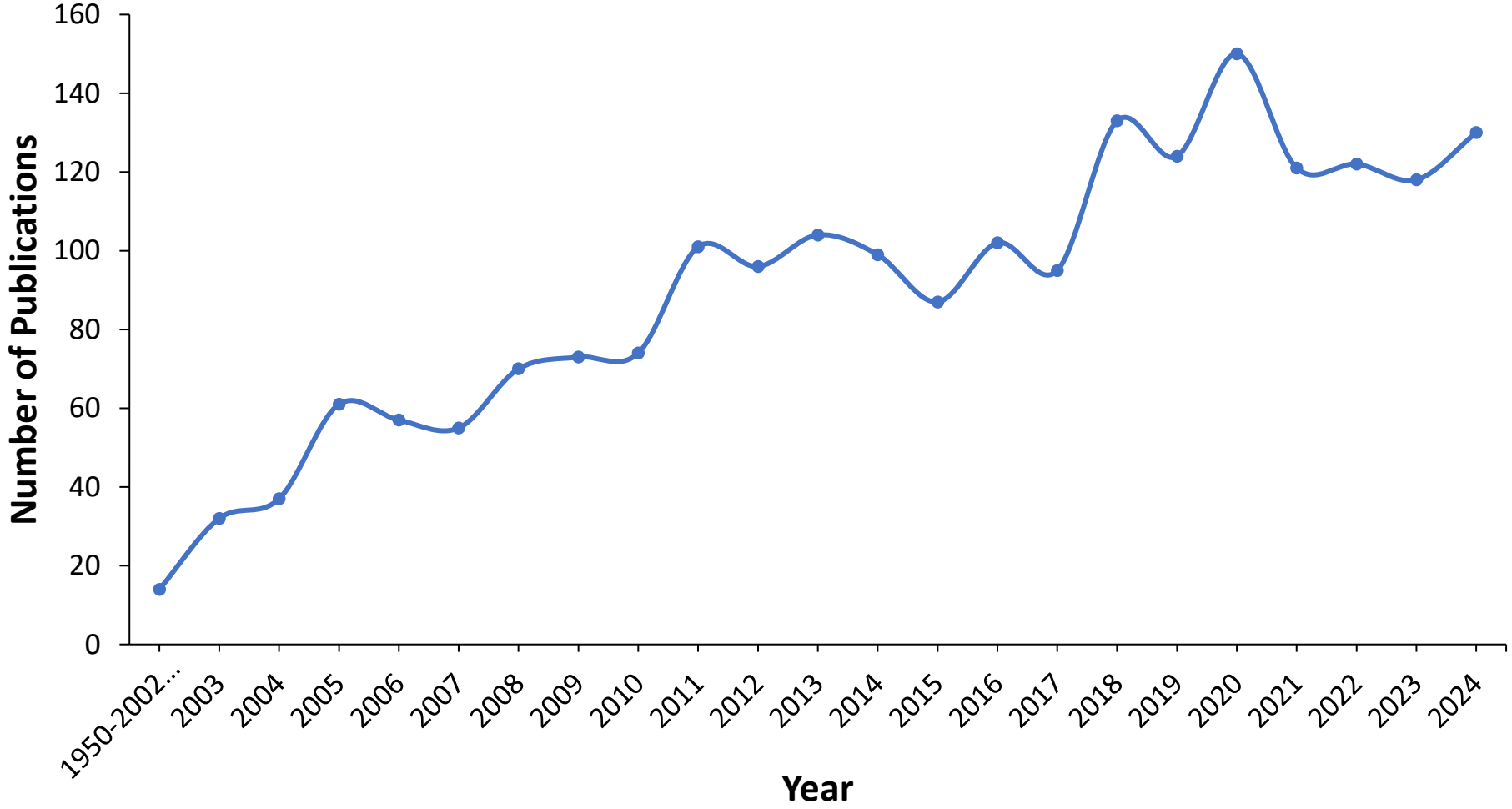
Progeria Related Publications

Today over 100 publications on Progeria per year are published in well known and peer-reviewed scientific journals read by researchers worldwide.



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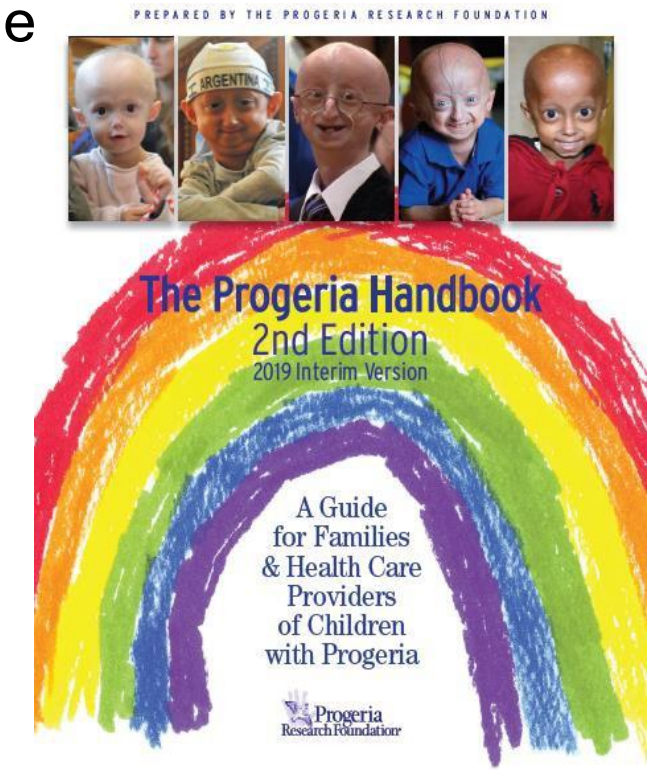
Progeria Clinical Care Handbook

The Progeria Handbook 2nd Edition. A Guide for Families & Health Care Providers of Children with Progeria. *The Progeria Research Foundation.* Leslie B. Gordon MD, PhD; Medical Director (editor) 2019.



- Provided in Chinese, English, Italian, Japanese, Portuguese and Spanish
- Expert contributors from Boston Children's Hospital
- Number of Progeria Care Handbooks distributed to families of those with Progeria and their care givers: **943**

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The Progeria Research Foundation

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Diagnosing…
Studying…
Treating…
CURING

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