PRF By The Numbers

Progeria Research Foundation

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

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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 Research Foundation

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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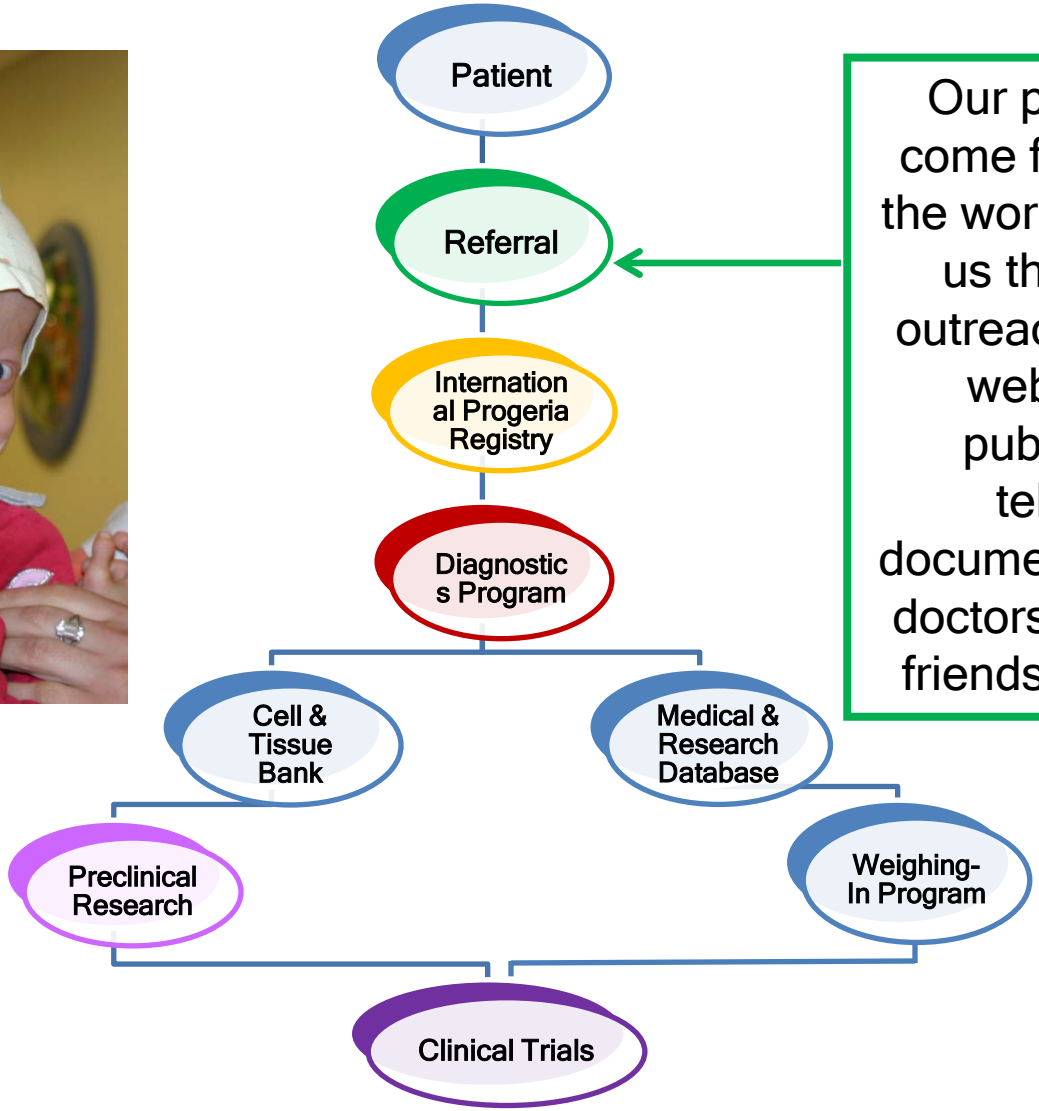
PRF Programs: It All Starts With The Children



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.

Progeria Research Foundation

Program Collaborations For Success

PRF Cell & Tissue Bank Core Laboratory

PRF Medical & Research Database
PRF Cell & Tissue Bank
PRF Diagnostics Program

PRF Cell & Tissue Bank : Lymphoblast Cell Line Generation

PRF Diagnostics Program Sequencing Laboratory

PRF Clinical Trials

PRF Cell Bank Submission: Immortalized Fibroblast Cell Lines

Non-HGPS Progeroid Patient Diagnosis

PRF Cell & Tissue Bank : iPS Cell Line Generation

Our Program Collaborators

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

- Brown University
  - Location of The PRF Medical & Research Database
  - Program IRB approval

BROWN
Alpert Medical School

BROWN
School of Public Health

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

Hasbro Children's Hospital
The Pediatric Division of Rhode Island Hospital
A Lifespan Partner

- PreventionGenetics
  - CLIA*-approved genetic sequence testing

PREVENTION GENETICS
DISEASE PREVENTION THROUGH GENETIC TESTING

- Rutgers University Cell and DNA Repository
  - CLIA*-approved lymphoblast generation and distribution

RUTGERS

- University of Ottawa
  - Induced Pluripotent Stem Cell (iPSC)
  - CLIA*-approved generation and distribution

uOttawa

*http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/IVDRegulatoryAssistance/ucm124105.html

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™

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

DANA-FARBER CANCER INSTITUTE

- NIH – funded Clinical and Translational Study Unit at Boston Children's Hospital

NIH National Institutes of Health
Turning Discovery Into Health

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Number of Living PRF-Identified Cases

As of January 1, 2017:

Total Number of Children with Progeria Worldwide: 144

HGPS* worldwide: 111

HGPS* in the United States: 16

Progeroid Laminopathies** worldwide: 33

Progeroid Laminopathies** in the United States: 9

*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

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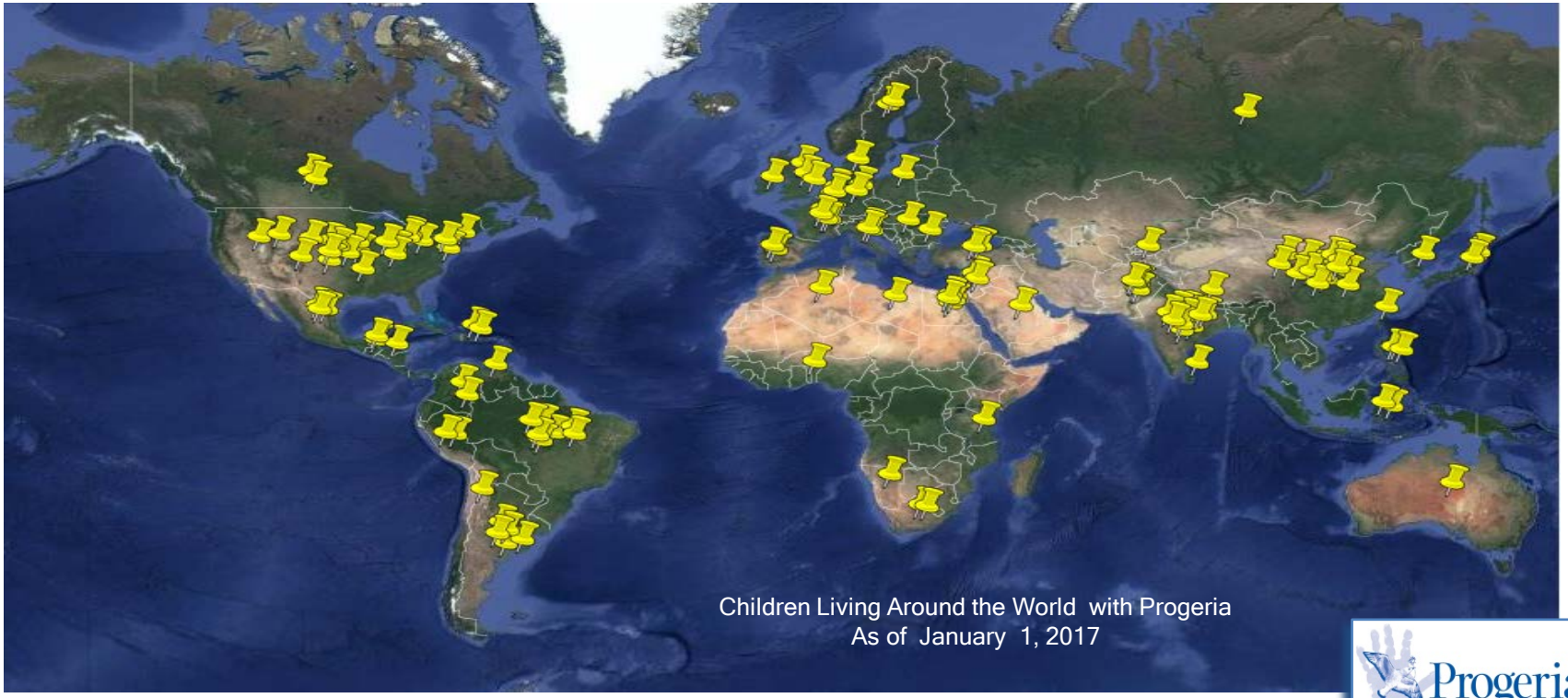
PRF-Identified Cases Reside In 46 Countries

Algeria	Canada	Dominican Republic	Guatemala	Israel	Namibia	Poland	South Africa	Taiwan
Argentina	Chile	Egypt	Honduras	Italy	Nepal	Portugal	South Korea	Tanzania
Australia	China	England	India	Japan	Pakistan	Russia	Sri Lanka	Togo
Belgium	Colombia	France	Indonesia	Libya	Peru	Saudi Arabia	Sweden	Turkey
Brazil	Denmark	Germany	Ireland	Mexico	Philippines	Serbia	Tajikistan	USA
								Venezuela



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…and Speak 30 Languages

Arabic	French	Italian	Pashto	Spanish	Tamil
Chinese	German	Japanese	Polish	Swahili	Telugu
Danish	Hebrew	Kannada	Portuguese	Swedish	Turkish
Dutch	Hindi	Korean	Russian	Tagalog	Urdu
English	Indonesian	Marathi	Serbian	Tajik	Uzbek

прогерии исследовательский фонд

مؤسسة أبحاث الشياخ

조로증 연구 재단

早衰症研究基金會

Progeria Araştırma Vakfı

Progeria रिसरच फाउंडेशन

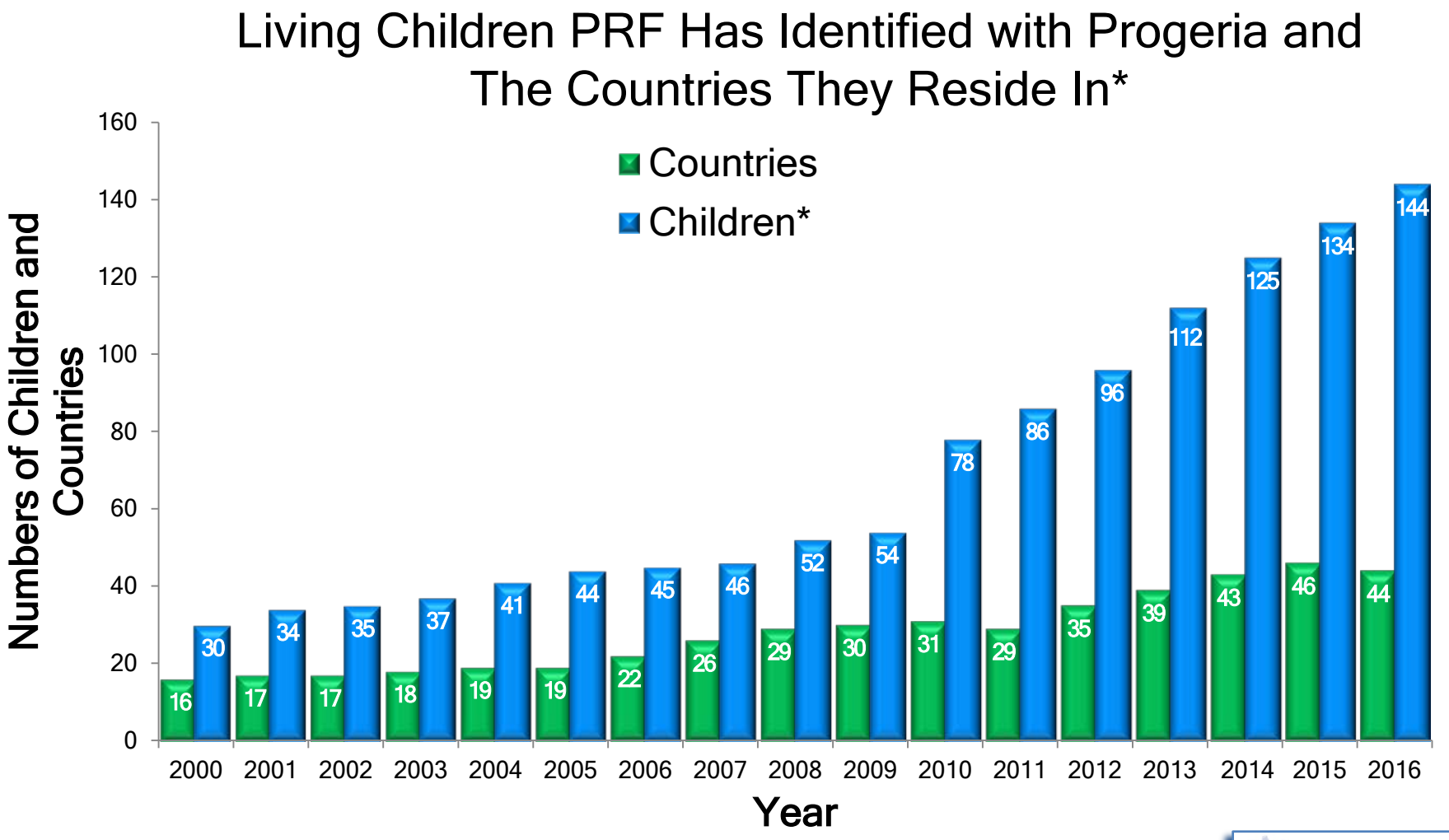
早老症研究財団

బాలుడ బాలిక వయస్సు ముదురుకండానే వృద్ధాప్యరూపంలోనికి వచ్చుట రీసెర్చ్ ఫౌండేషన్

As of January 1, 2017

Progeria Research Foundation

Every Year Our Numbers Grow



*When a child passes away, numbers are decreased.
Numbers include those with HGPS and genetically confirmed Progeroid Laminopathies

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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 estimates prevalence for years when the official US census provides a reliable population number.

Progeria Research Foundation

USA Prevalence of Progeria

January 2016 population statistics:

- The US population was:

  322,761,807 people

- Number of PRF-identified children with Progeria in the US:

  16

- Prevalence of HGPS in the US:
  16 in 323 million is about

  1 in 20 million people

Source: 2016 US population: http://www.census.gov/#

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Prevalence and World Population of Progeria

Given the world population as of January 2016

there are between **350** and **400** 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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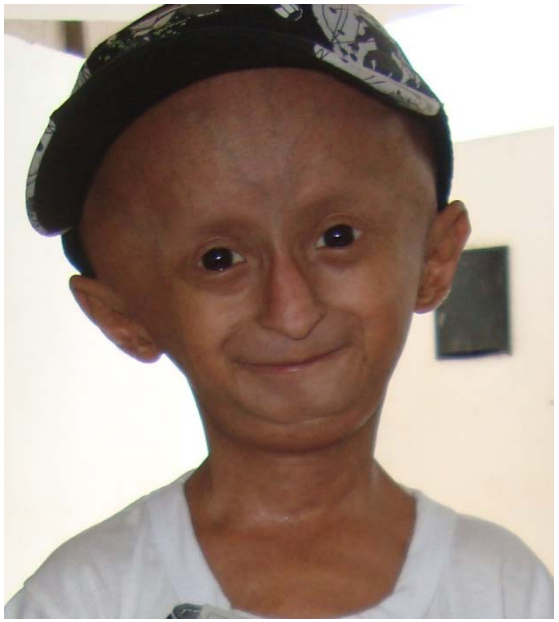
Using Prevalence To Find Children In A Certain Country

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 January 2016:



Brazil's population was estimated as

205,809,000 people

Number of children living with Progeria in Brazil is

205,809,000/20,000,000 = **10**

Source Brazil population: http://en.wikipedia.org/wiki/List_of_countries_by_population

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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 www.progeriaresearch.org/patient_registry

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

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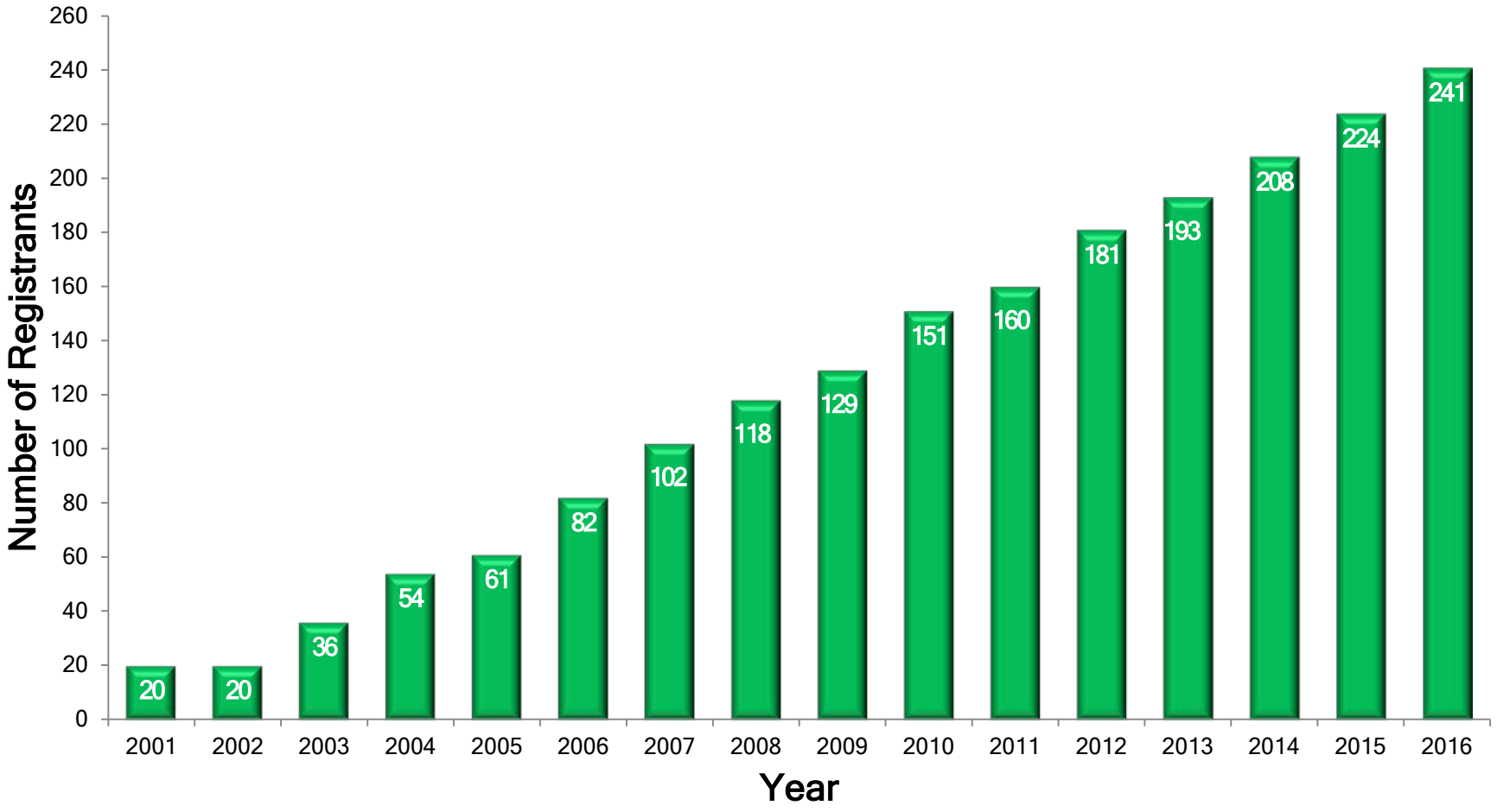
241 Children Have Registered With PRF



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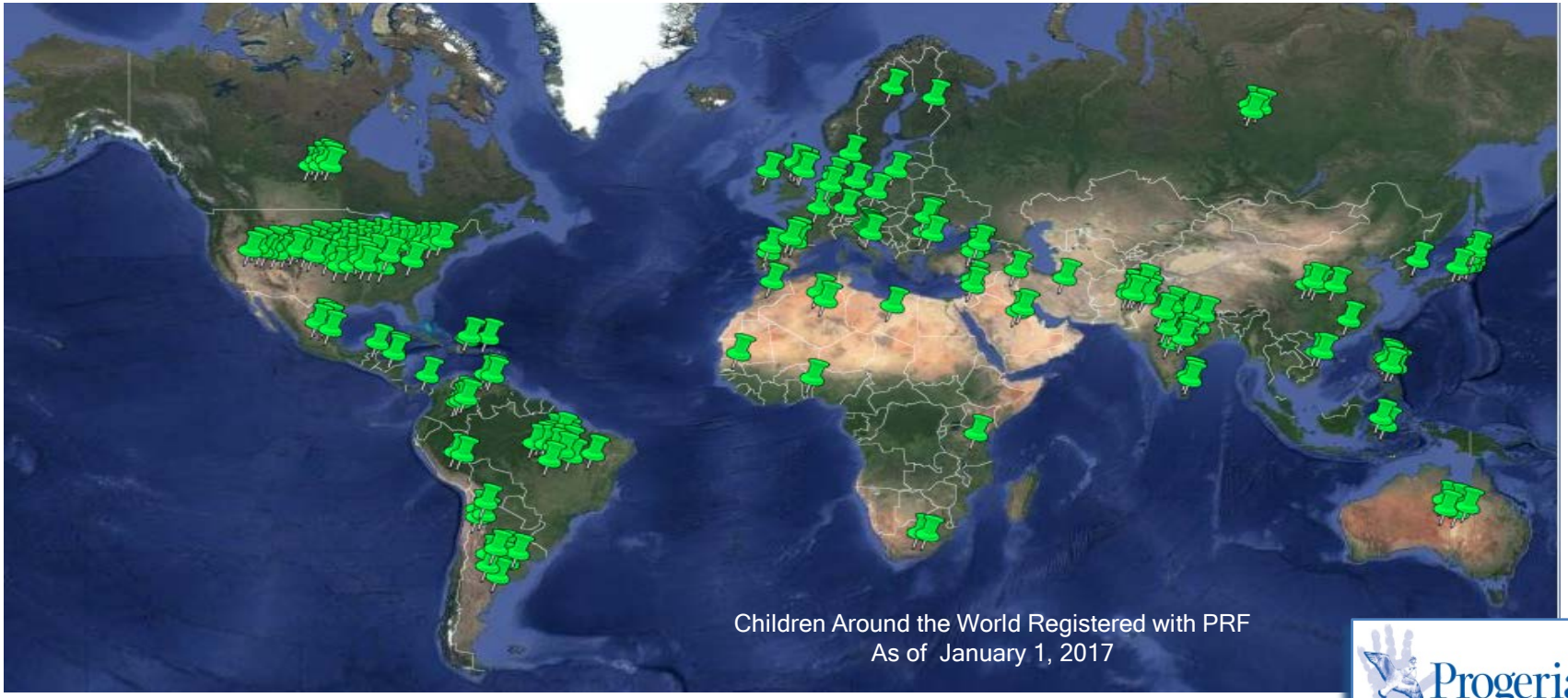
…From 55 Countries

Algeria	Canada	Dominican Republic	Honduras	Ireland	Morocco	Poland	Senegal	Switzerland
Argentina	Chile	England	Hong Kong	Israel	Netherlands	Portugal	South Africa	Tanzania
Australia	China	Finland	India	Italy	Pakistan	Puerto Rico	South Korea	Togo
Belgium	Colombia	France	Indonesia	Japan	Panama	Romania	Spain	Turkey
Brazil	Czech Republic	Germany	Iran	Libya	Peru	Russia	Sri Lanka	USA
Bulgaria	Denmark	Guatemala	Iraq	Mexico	Philippines	Saudi Arabia	Sweden	Venezuela
								Vietnam



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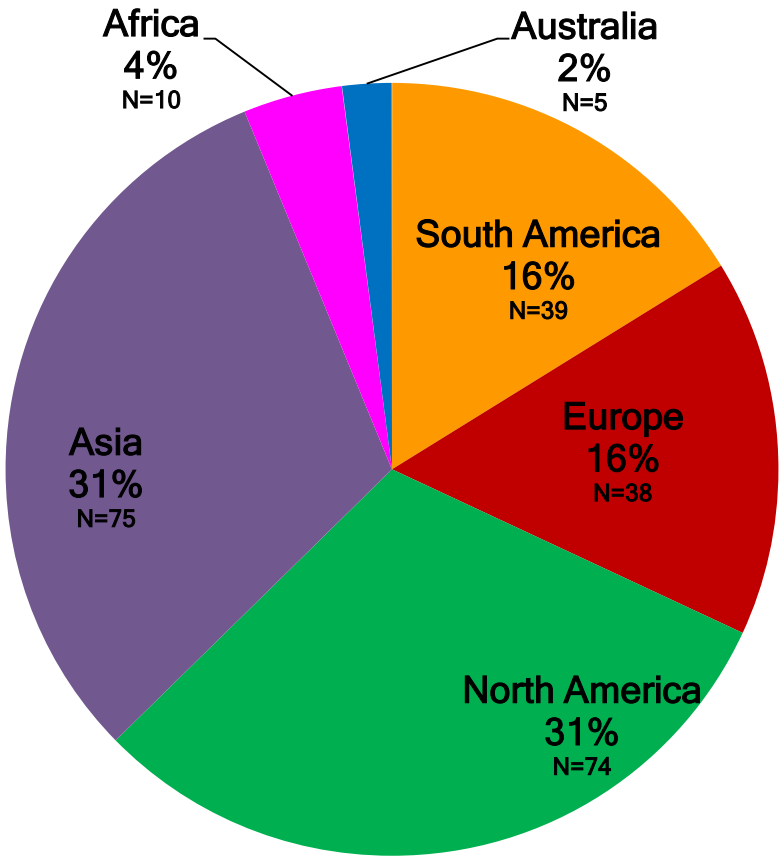
...And All Continents

Participation (%) By Continent



As of January 1, 2017

Progeria Research Foundation

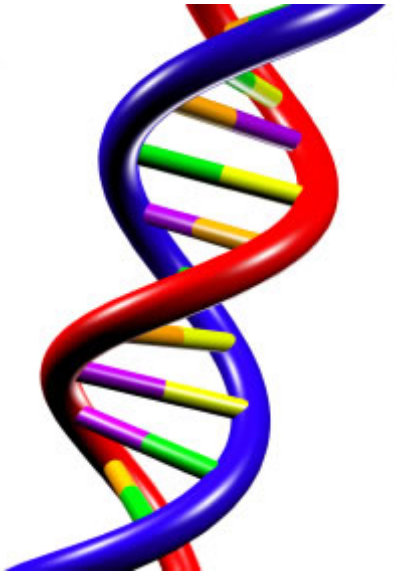
PRF Diagnostics Program

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

www.progeriaresearch.org/diagnostic_testing

Progeria Research Foundation

Diagnostics Testing Summary

As of January 1, 2017:

Total Number of Proband Tests Performed: 127

Exon 11 (HGPS) Mutations: 87

Other Progeroid Laminopathies (Exons 1 – 12): 10

Zmpste24 Mutations : 2

Average Number of Patients Tested Per Year : 10

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	74
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	---------	heterozygous	Yes	2
1968+1 G>C, intron 11	---------	heterozygous	Yes	2
1968+2 T>A, intron 11		heterozygous	Yes	1
1968+1 G>A, intron 11		heterozygous	Yes	1
Progeroid Laminopathy- LMNA Mutation				
1579 C>T, exon 9	A527C	heterozygous	No	1
1579 C>T, exon 9	A527C	homozygous	No	6
1580G>T, exon9	A527L	Homozygous	No	1
1619 T>C, exon 10	M540T	homozygous	No	1
331 G>A, exon 1	G111L	heterozygous	No	1
Progeroid Laminopathy- Zmpste24 Mutation				
1274T>C, exon 10	L425P	homozygous	No	2

As of January 1, 2017

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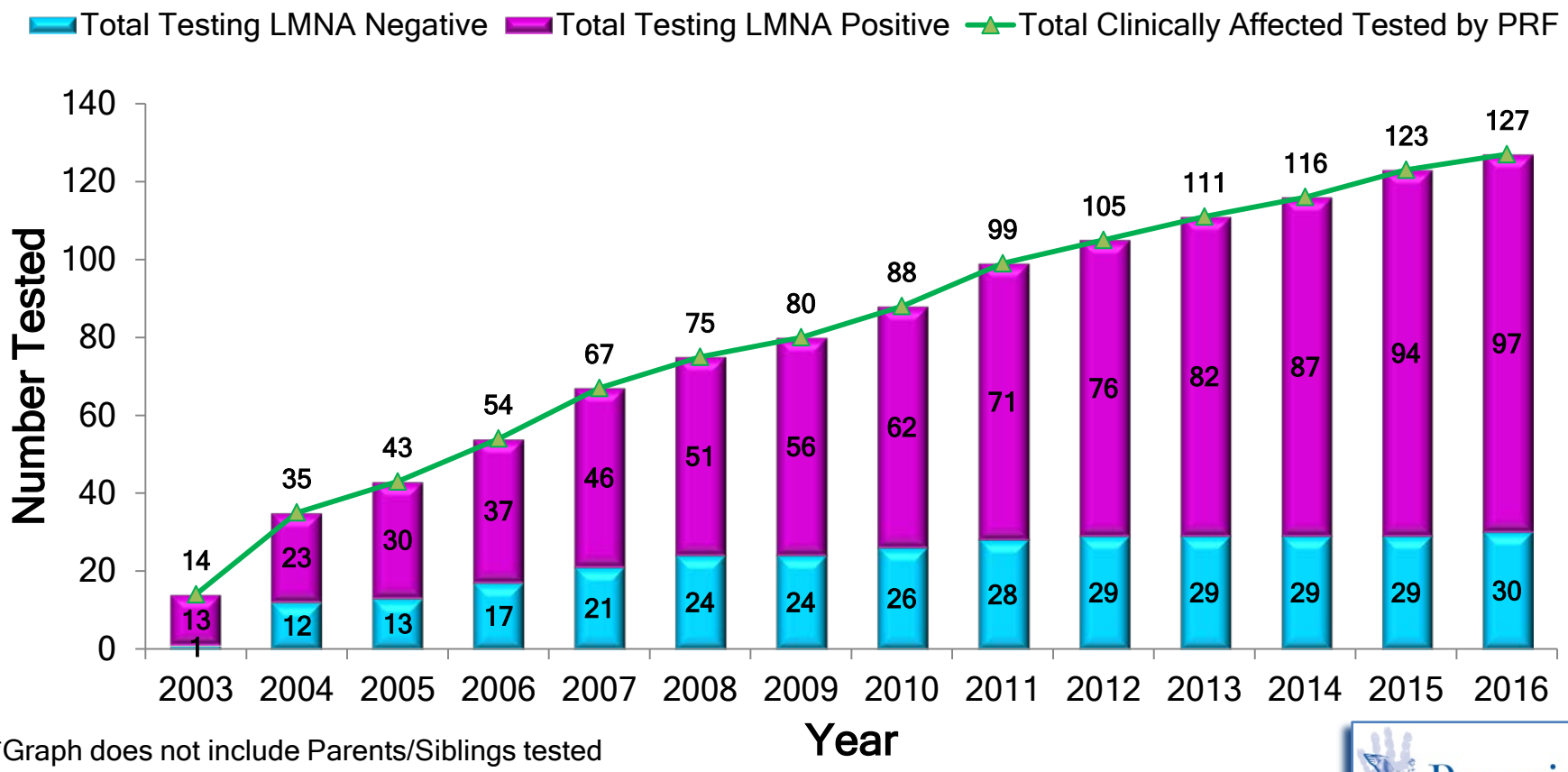
Longitudinal Testing Data for PRF Diagnostics Program

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



*Graph does not include Parents/Siblings tested

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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: www.progeriaresearch.org/cell_tissue_bank

Progeria Research Foundation

PRF Cell & Tissue Bank Holdings

As of January 1, 2017:

Total Number of Cell Lines: **205** From **219** Donors

- **65** Dermal Fibroblast Lines from **44** affected, **21** parents and **0** siblings
- **6** Immortalized Fibroblast Cell Lines from **2** affected and **5** parents
- **124** Lymphoblast Lines from **71** affected, **45** parents and **8** siblings
- **10** Induced Pluripotent Stem Cell Lines from **2** affected and **2** parents

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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	DFN
c.1868 C>G, exon 11	p.T623S	heterozygous	Yes	LBV
c.1762 T>C, exon 11	p.C588R	heterozygous	No	DFN
c.1968+5 G>C, intron 11	---------	heterozygous	Yes	DFN
c.1968+1 G>A, intron 11	---------	heterozygous	Yes	LBV
c.1968+2 T>C	---------	heterozygous	Yes	DFN
c.973 G>A, exon 6	p.A325A	heterozygous	No	DFN
Progeroid Laminopathy- LMNA Mutation				
c.1579 C>T, exon 9	p.A527C	heterozygous	No	LBV
c.1579 C>T, exon 9	p.A527C	homozygous	No	LBV
c.1580 C>T, exon 9	p.A527L	Homozygous	No	LBV
c.1619 T>C, exon 10	p.M540T	homozygous	No	DFN
c.331 G>A, exon 1	p.G111L	heterozygous	No	DFN, LBV
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.T450S	heterozygous	No	DFN

As of January 1, 2017

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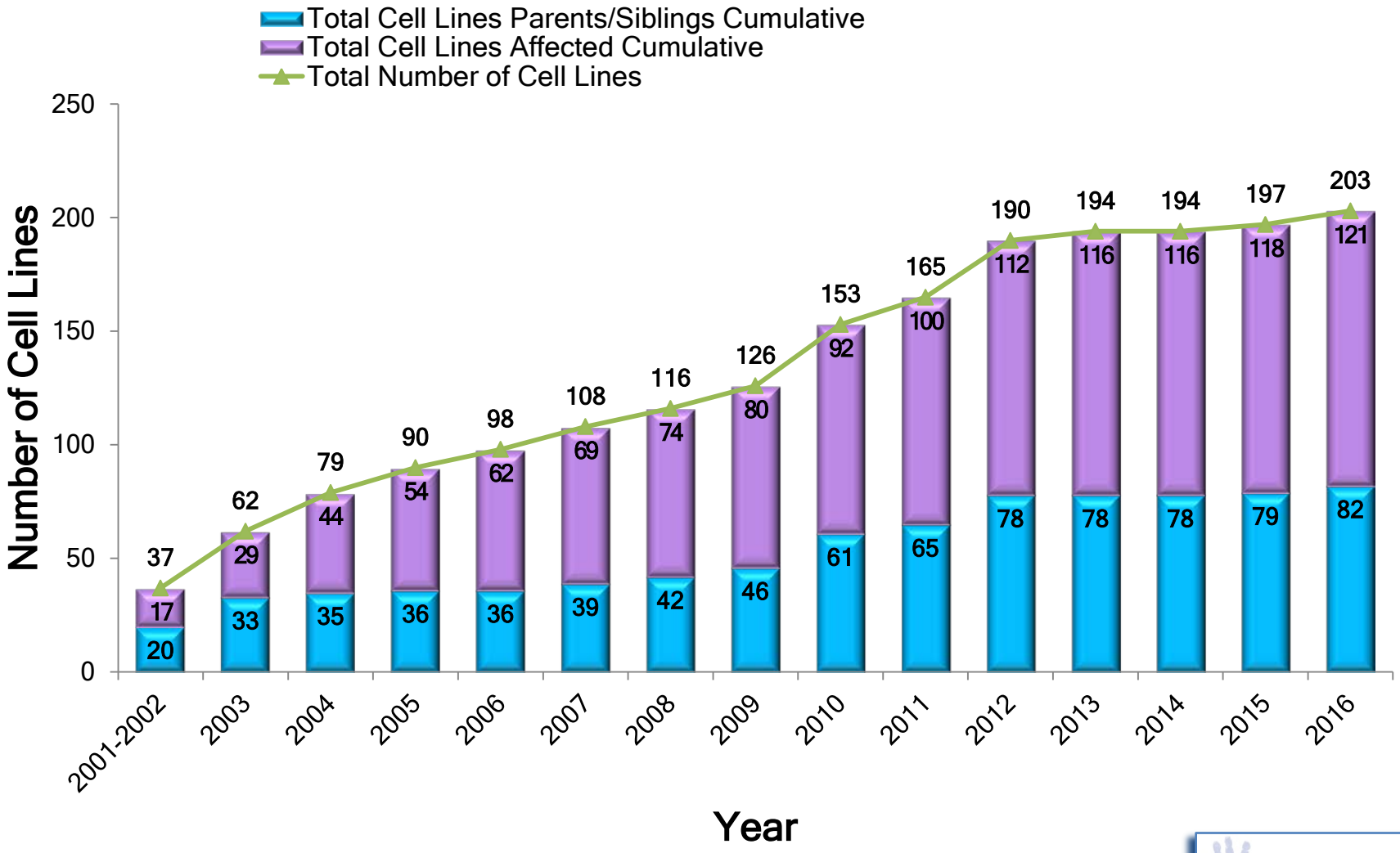
Number Of Cell Lines By Year



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PRF Cell & Tissue Bank Distribution

As of January 1, 2017:

124 Research Teams From **20** Countries Have Received

723 Cell Lines

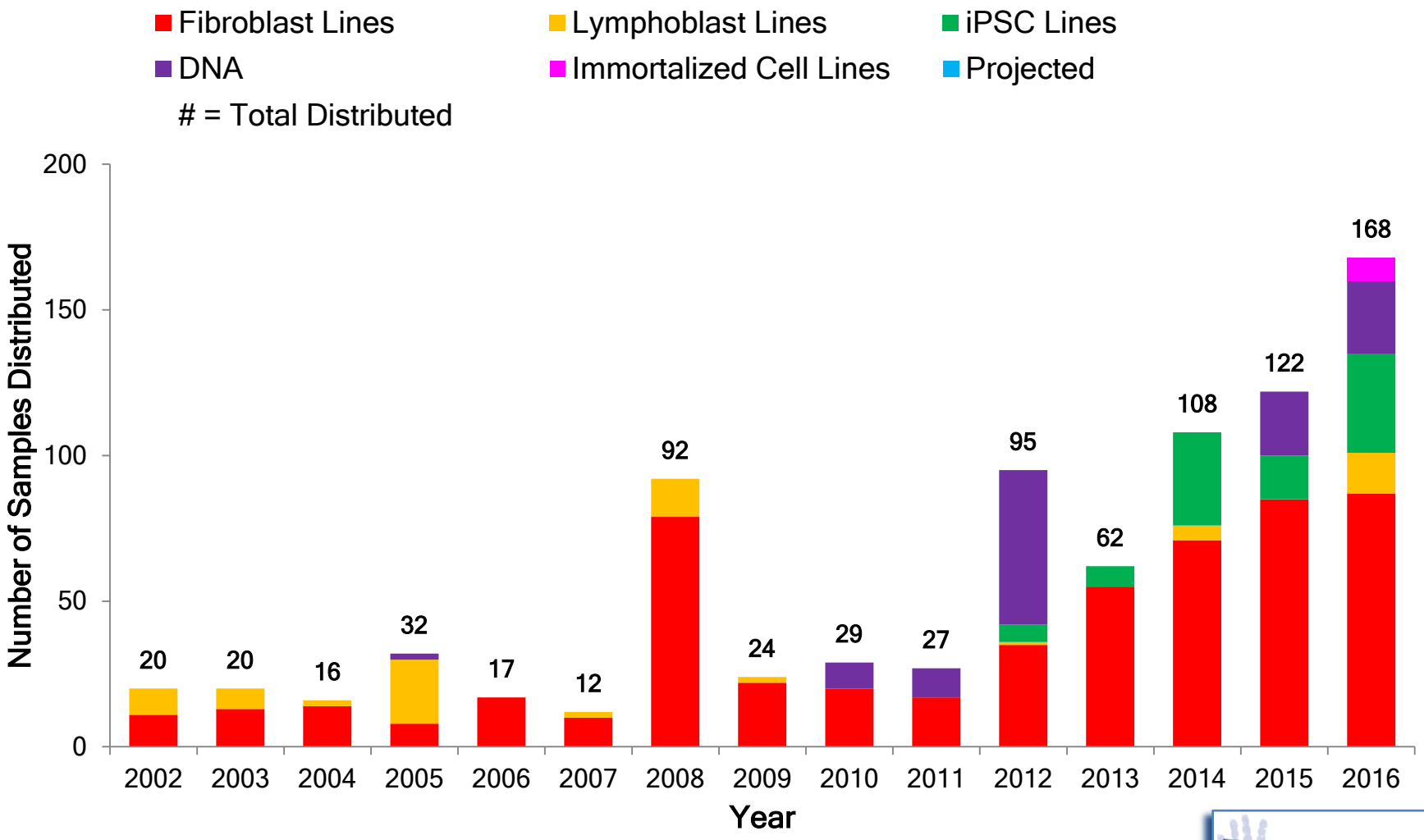
121 DNA Samples

269 Tissue, plasma, serum and other biological samples

Senescent Progeria Fibroblasts in Culture

Progeria Research Foundation

Biological Sample Distribution Over Time



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USA Cell & Tissue Bank Recipients

Recipient	Institution
Angelika Amon	Massachusetts Institute of Technology
Stelios Andreadis	U. of Buffalo
Shelley Berger	U of Pennsylvania
Bruce Blazer	U. of Minnesota
Ted Brown	Institute for Basic Research (IBR)
Judy Campisi	Buck Institute
Kan Cao	U. of Maryland
Francis Collins	National Genome Research Institute
Lucio Comai	U. of Southern California
John Cooke	Houston Methodist Research Institute
Mauro Costa-Mattioli	Baylor College of Medicine
Adrienne Cox	U. of North Carolina at Chapel Hill
Greg Crawford	Duke University Medical Center
Antonei Csoka	Howard University
Kris Dahl	Carnegie Mellon University
George Daley	Boston Children's Hospital
Channing Der	U. of North Carolina at Chapel Hill
Mohanish Deshmukh	U. of North Carolina at Chapel Hill
Dennis Discher	U. of Pennsylvania
Martin Dorf	Harvard Medical School

Recipient	Institution
Stephen Doxsey	U. of Massachusetts Medical School
Jack Elias	Brown University School of Medicine
Mike Erdos	National Institutes of Health
Jed Fahey	Johns Hopkins University
Toren Finkel	NIH
Shridar Ganesan	Cancer Institute of New Jersey
Abhimanyu Garg	U. of Texas Southwestern Medical Center
Glenn Gerhard	Temple University
Thomas Glover	U.of Michigan Medical School
David Gilbert	Florida State University
Robert Goldman	Northwestern University
Susana Gonzalo	St. Louis School of Medicine
Lilian Grigorian	Cedars Sinai Medical Center
Curtis Harris	National Institutes of Health
Martin Hetzer	Salk Institute
Steve Horvath	UCLA
Vishwanath Iyer	U. of Texas Austin
Jose Jalife	University of Michigan
David Kaplan	Tufts University

As of January 1, 2017

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USA Cell & Tissue Bank Recipients

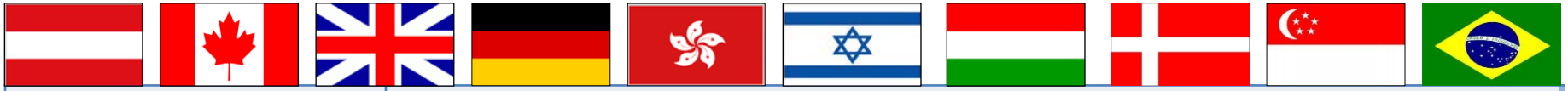
Recipient	Institution
Karen Katula	UNC - Greensboro
Timothy Kowalik	U. of Massachusetts Medical School
Dmitri Krainc	Massachusetts General Hospital
Jan Lammerding	Harvard University
Dudley Lamming	U of Wisconsin-Madison
Jeanne Lawrence	U. of Massachusetts Medical School
Joan Lemire	Tufts University School of Medicine
Kam Leong	Columbia University
Jason Lieb	U. of North Carolina at Chapel Hill
Shigemi Matsuyama	Case Western Reserve University
Andrew Mendelsohn	Regenerative Sciences Institute
Jeffrey Miner	Washington University
Tom Misteli	National Cancer Institute
Marsha Moses	Boston Children's Hospital
Elizabeth Nabel	National Heart, Lung & Blood Institute
Timothy Osborne	Sanford Burnham Medical Research Institute
Junko Oshima	U. of Washington
Bryce Paschal	U. of Virginia
Hamel Patel	U. Of California, San Diego

Recipient	Institution
Mary Patti	Joslin Diabetes Center
Taihao Quan	University of Michigan
Joseph Rabinowitz	Temple University
Ana Robles	National Cancer Institute
David Sabatini	Whitehead Institute
John Sedivy	Brown University
Christian Sell	Drexel University College of Medicine
Andrew Sonis	Boston Children's Hospital
Earl Stadtman	National Heart, Lung & Blood Institute
Dylan Taatjes	U. of Colorado
Marc Tatar	Brown University
George Truskey	Duke University
Alan Waldman	University of South Carolina
Steve Warren	Emory University School of Medicine
Howard Worman	Columbia University
Tom Wight	Hope Heart Institute
Joseph Wu	Stanford University
Yue Zou	East Tennessee State University

As of January 1, 2017

Progeria Research Foundation

International Cell & Tissue Bank Recipients



Recipient	Institution
Andrea Ablasser	Global Health Institute, Switzerland
Vicente Andrés Garcia	Centro Nacional de Investigaciones Cardiovasculares, Spain
Michael Blank	Bar Ilan University, Israel
Antonio Campos de Carvalho	Federal University of Rio de Janeiro, Brazil
Ana Carrera	Centro Nacional de Biotecnologia, Spain
Gordon Chan	University of Alberta, Canada
Lynne Cox	University of Oxford, England
Thomas Dechat	Medical University of Vienna, Austria
Annachiara DeSandre-Giovannoli	Laboratoire de Génétique Moléculaire, France
Karima Djabali	TU-Munich, Germany
Ma Dongrui	Singapore General Hospital. Singapore
J. El Molto	Molecular World, Inc, Canada
Maria Eriksson	Medicinsk Naringslara, Sweden
Gerardo Ferbeyre	Université de Montréal, Canada
Lino Ferreira	Center for Neuroscience and Cell Biology (CNC), Portugal
Marco Foiani	Instituto FIRC di Oncologia Molecolare , Italy
Alain Garnier	Université Laval, Canada
Yosef Gruenbaum	The Hebrew University of Jerusalem, Israel
Robert Hegele	University of Western Ontario, Canada
Anthony Hyman	Max-Planck-Institute of Molecular Cell Biology and Genetics, Germany
Christian Kubisch	Institute of Human Genetics, Germany
Kirsztian Kvell	University of Pecs, Hungary
Chiara Lanzuolo	CNR Institute of Cellular Biology & Neurobiology, Italy
Caterina La Porta	University of Milan, Italy

As of January 1, 2017

Progeria Research Foundation

International Cell & Tissue Bank Recipients

Recipient	Institution
Delphine Larrieu	University of Cambridge, England
Lucia Latella	National Research Council (CNR), Italy
Giovanna Lattanzi	ITOI-CNR Unit of Bologna , Italy
Jean-Marc Lemaitre	Institute of Functional Genomics, France
Nicolas Levy	Génétique Médicale et Développement, France
Frank Lyko	German Cancer Research Institute, Germany
Thorston Marquart	University of Münster, Germany
Scott Maynard	Danish Cancer Society Research Institute, Denmark
Ohad Medalia	University of Zurich, Switzerland
Denis Mottet	University of Liege, Belgium
Luis Pereira de Almeida	Center for Neuroscience and Cell Biology (CNC), Portugal
Neale Ridgway	University of Halifax, Canada
Kanda Sangthongpitag	Experimental therapeutics Centre, Singapore
Ok Sarah Shin	Korea University Guro Hospital, Korea
Michael Speicher	Medical University of Graz, Austria
William Stanford	University of Toronto, Canada
Michael Walter	University of Münster, Germany
Herbert Waldman	Max Planck Institute, Germany
Miguel Weil	Tel Aviv university, Israel
Jesús Vazquez Cobos	Centro Nacional de Investigaciones Cardiovasculares, Spain
Alex Zhavoronkov	Federal Clinical Research Centre, Russia
Zhongjun Zhou	University of Hong Kong, China

As of January 1, 2017

Progeria Research Foundation

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

Progeria Research Foundation

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.

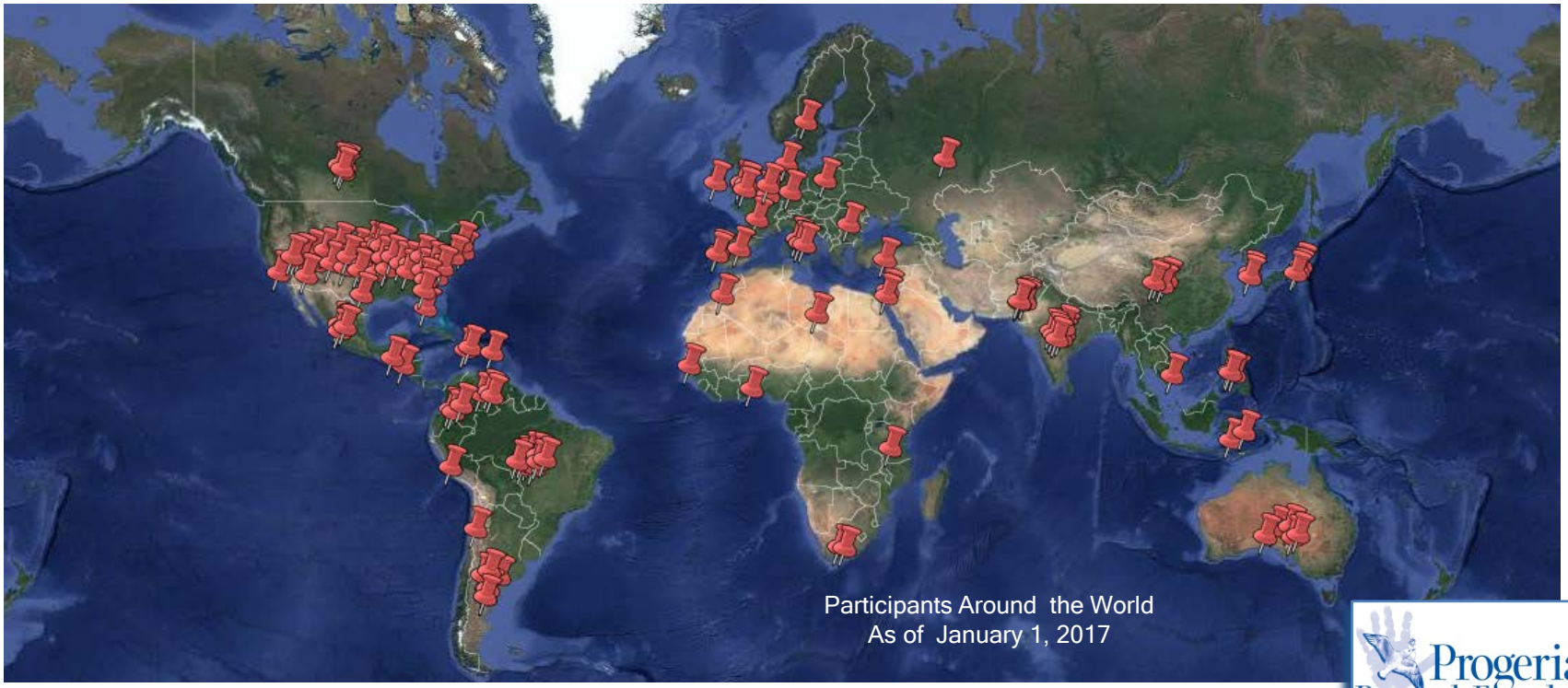
Enrollment information available at: www.progeriaresearch.org/medical_database

Progeria Research Foundation

Medical & Research Database Participation

152 Participants are enrolled from **42** countries and **1** US territory

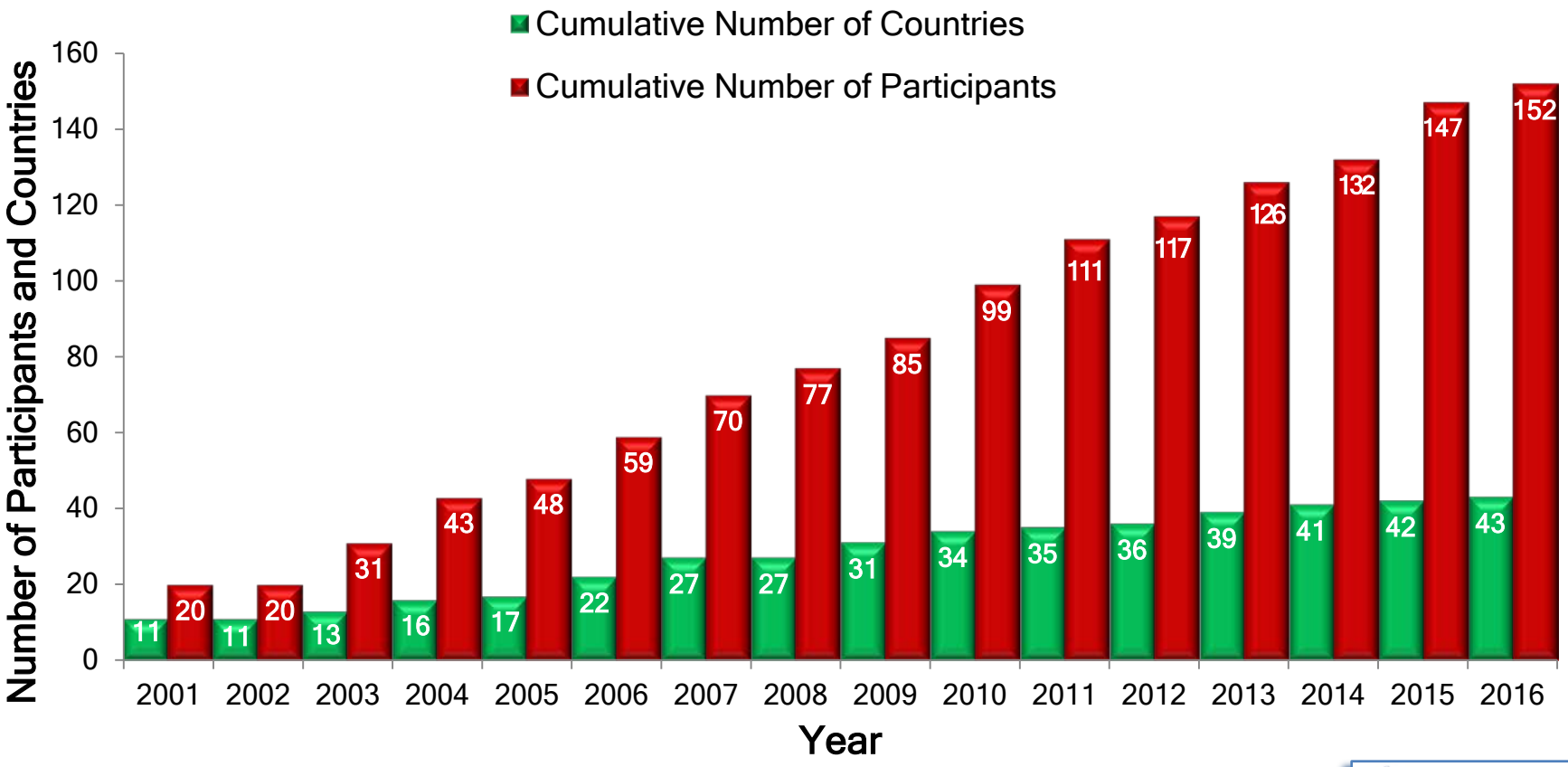
Argentina	Chile	England	India	Japan	Peru	Russia	Tanzania
Australia	China	France	Indonesia	Libya	Philippines	Senegal	Togo
Belgium	Colombia	Guatemala	Ireland	Mexico	Poland	South Africa	Turkey
Brazil	Denmark	Germany	Israel	Morocco	Portugal	South Korea	USA
Canada	Dominican Republic	Honduras	Italy	Netherlands Pakistan	Puerto Rico Romania	Spain Sweden	Venezuela Vietnam



Progeria Research Foundation

Database Longitudinal Enrollment

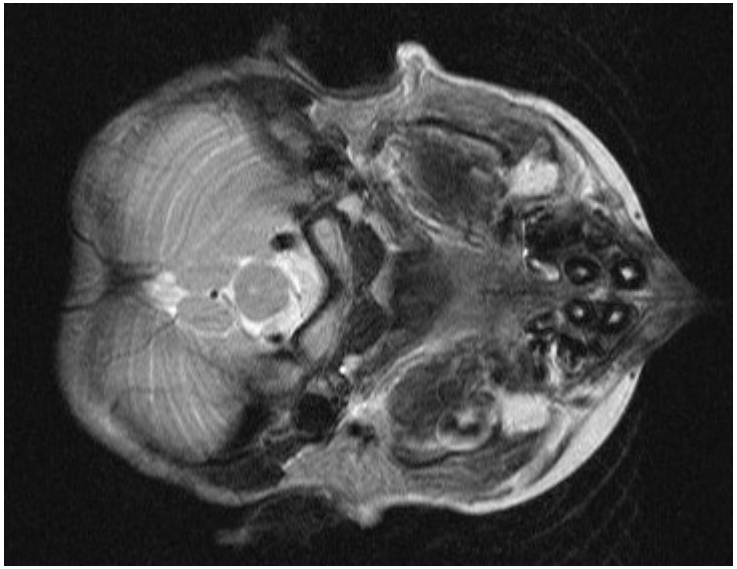
Children Enrolled in The PRF Medical & Research Database and the Countries of Residence

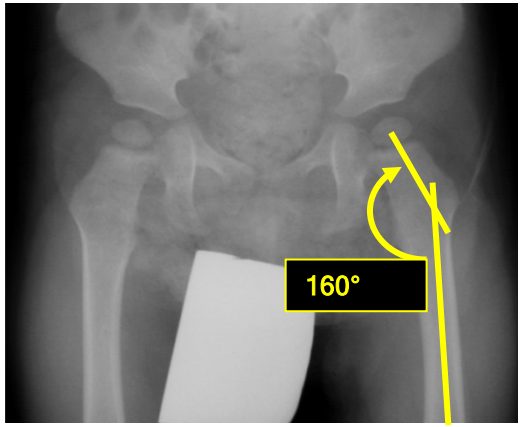


Progeria Research Foundation

Types Of Data Collected

- Participants with Medical Records Reports: 121
- Participants with Radiology Studies: 59





As of January 1, 2017

Progeria Research Foundation

PRF Weighing-In Program

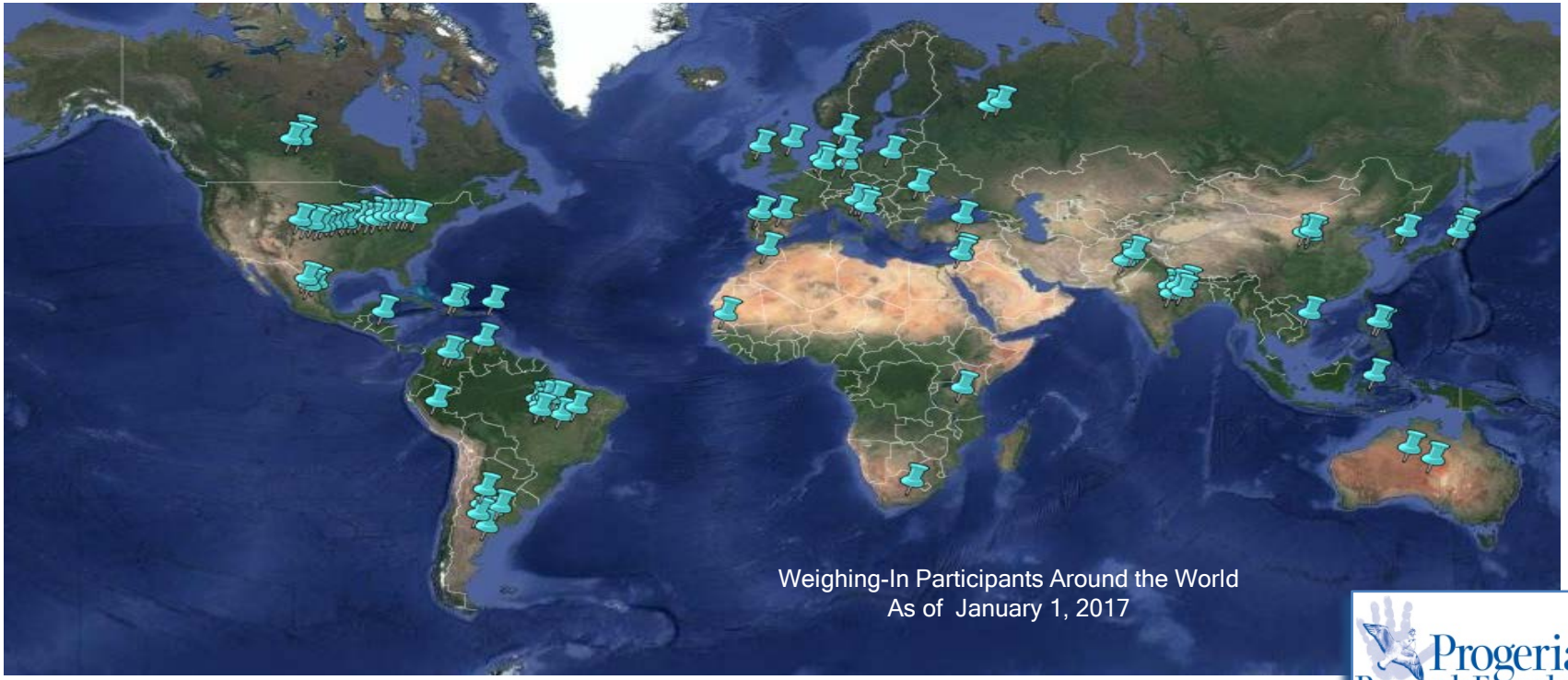
- A sub-program of The PRF Medical & Research Database
- Collects weight-for-age data prospectively:
  - Home scale provided by PRF
  - Parents weigh child weekly or monthly
  - Report weights electronically

Progeria Research Foundation

Weighing-In Program Participation

106 Participants are enrolled from **38** countries and **1** US territory

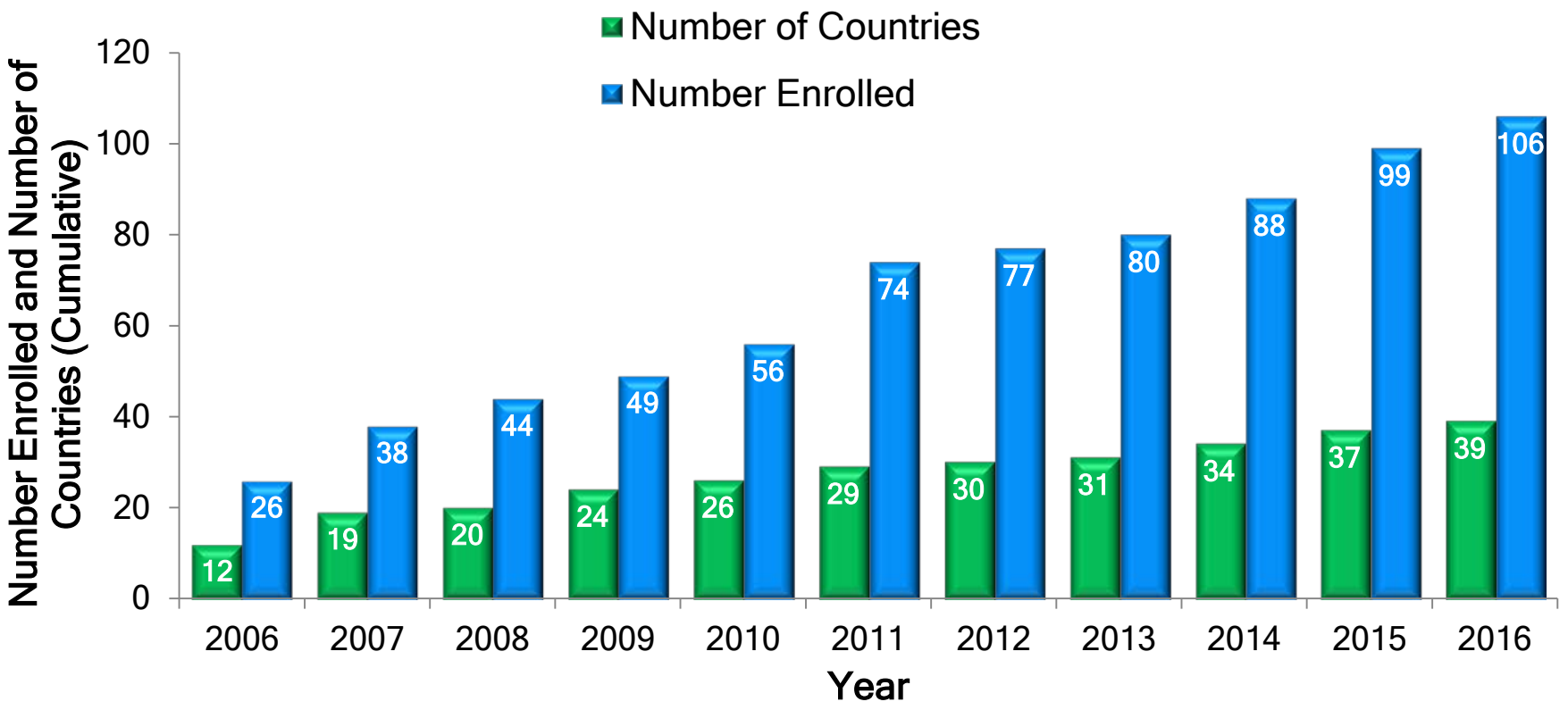
Argentina	China	England	Ireland	Morocco	Portugal	South Africa	Turkey
Australia	Colombia	Germany	Israel	Pakistan	Puerto Rico	South Korea	USA
Belgium	Denmark	Honduras	Italy	Peru	Romania	Spain	Venezuela
Brazil	Dominion Republic	India	Japan	Philippines	Russia	Tanzania	Vietnam
Canada		Indonesia	Mexico	Poland	Senegal	Togo	



Weighing-In Participants Around the World
As of January 1, 2017

Progeria Research Foundation

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



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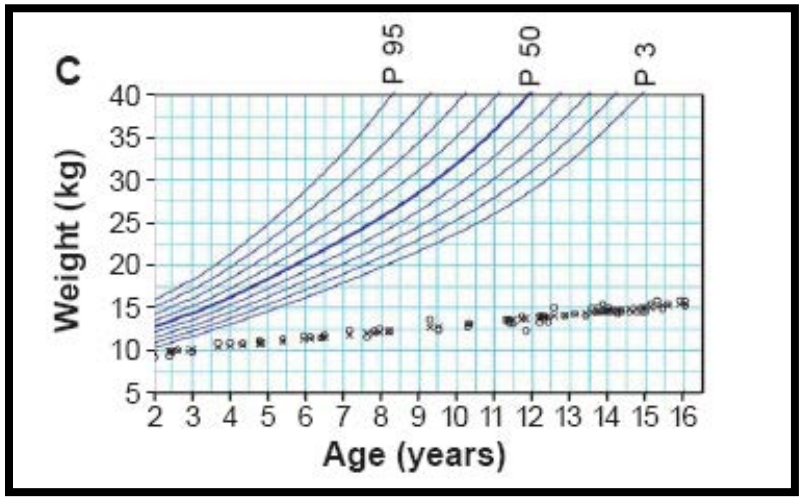
Clinical Trials And The Weighing-In Program

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

- As of January 1, 2017, **78** children from The PRF Weighing-In Program have entered clinical treatment trials using this data.



Failure to Thrive Starts Towards End of Year One

Progeria Research Foundation

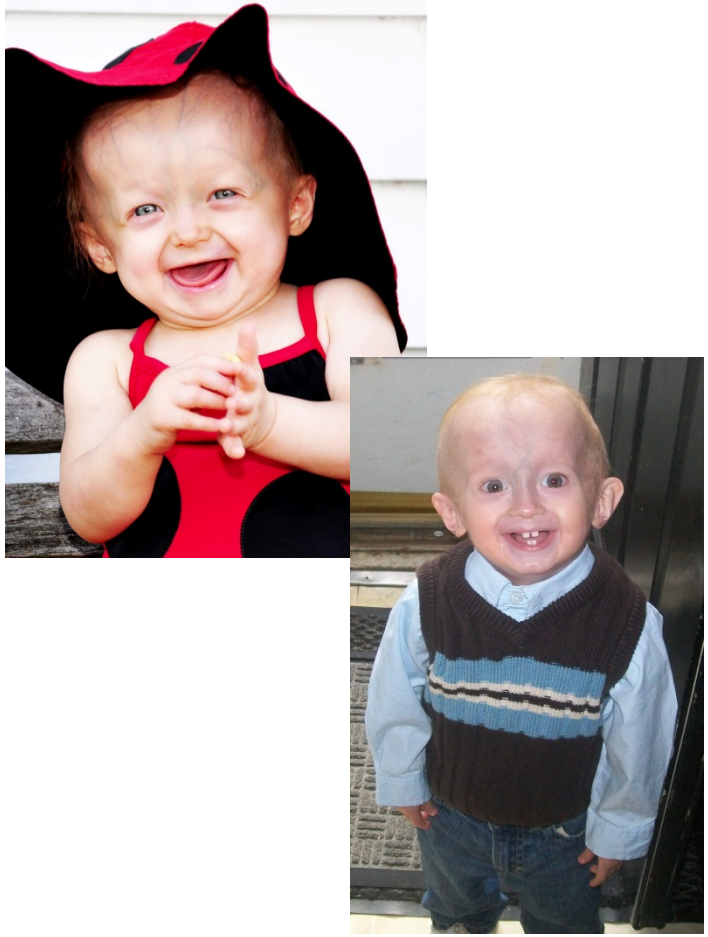
PRF-Funded Clinical Treatment Trials

Progeria Research Foundation

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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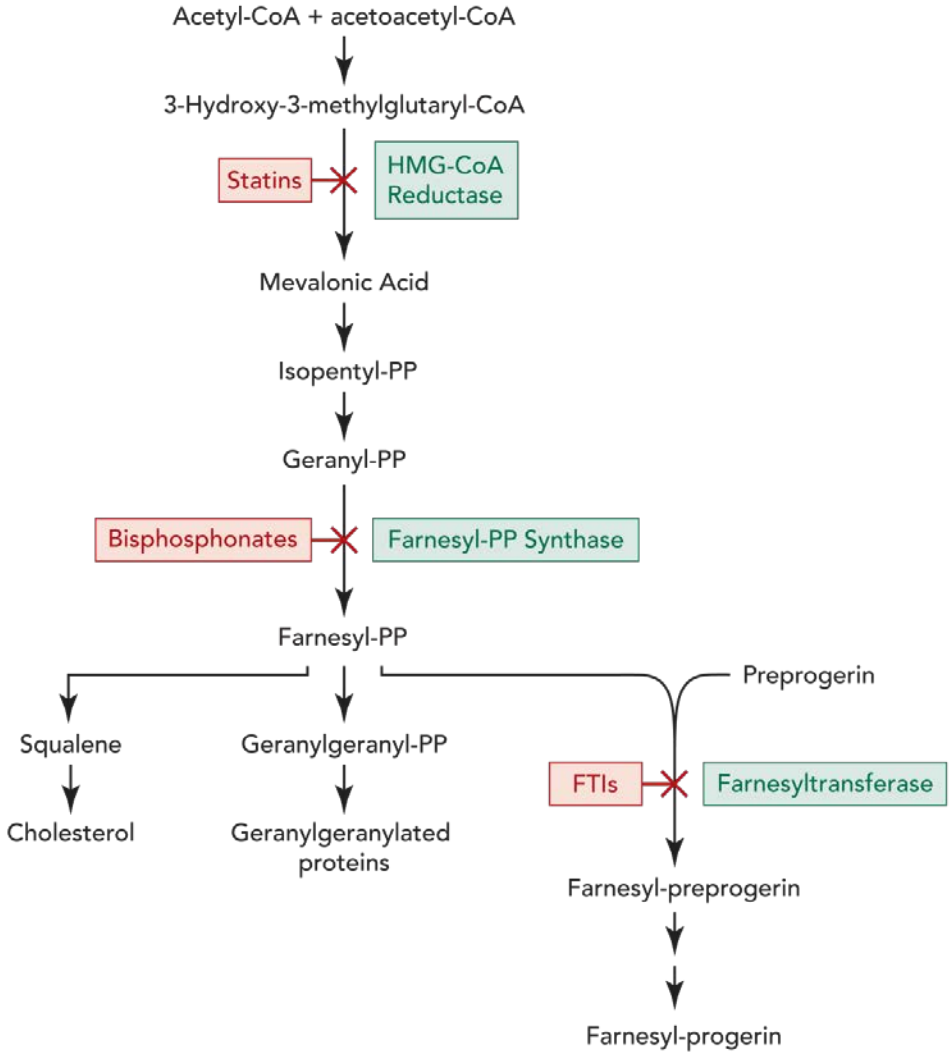
Current Therapeutic Intervention Strategies

Medications That Inhibit Farnesylation of Progerin



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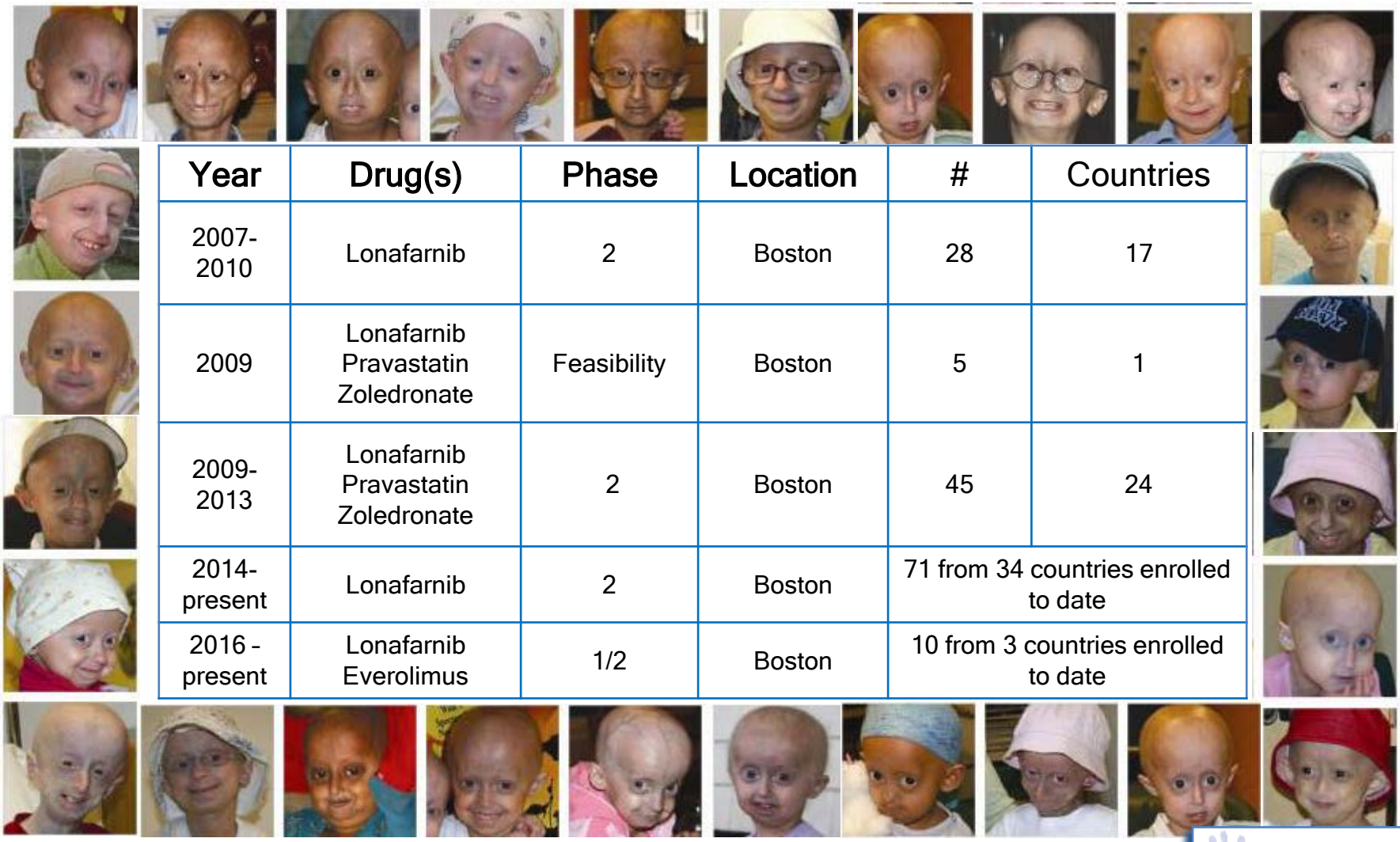
PRF Funds Clinical Treatment Trials



Year	Drug(s)	Phase	Location	#	Countries
2007-2010	Lonafarnib	2	Boston	28	17
2009	Lonafarnib Pravastatin Zoledronate	Feasibility	Boston	5	1
2009-2013	Lonafarnib Pravastatin Zoledronate	2	Boston	45	24
2014-present	Lonafarnib	2	Boston	71 from 34 countries enrolled to date	
2016 – present	Lonafarnib Everolimus	1/2	Boston	10 from 3 countries enrolled to date	

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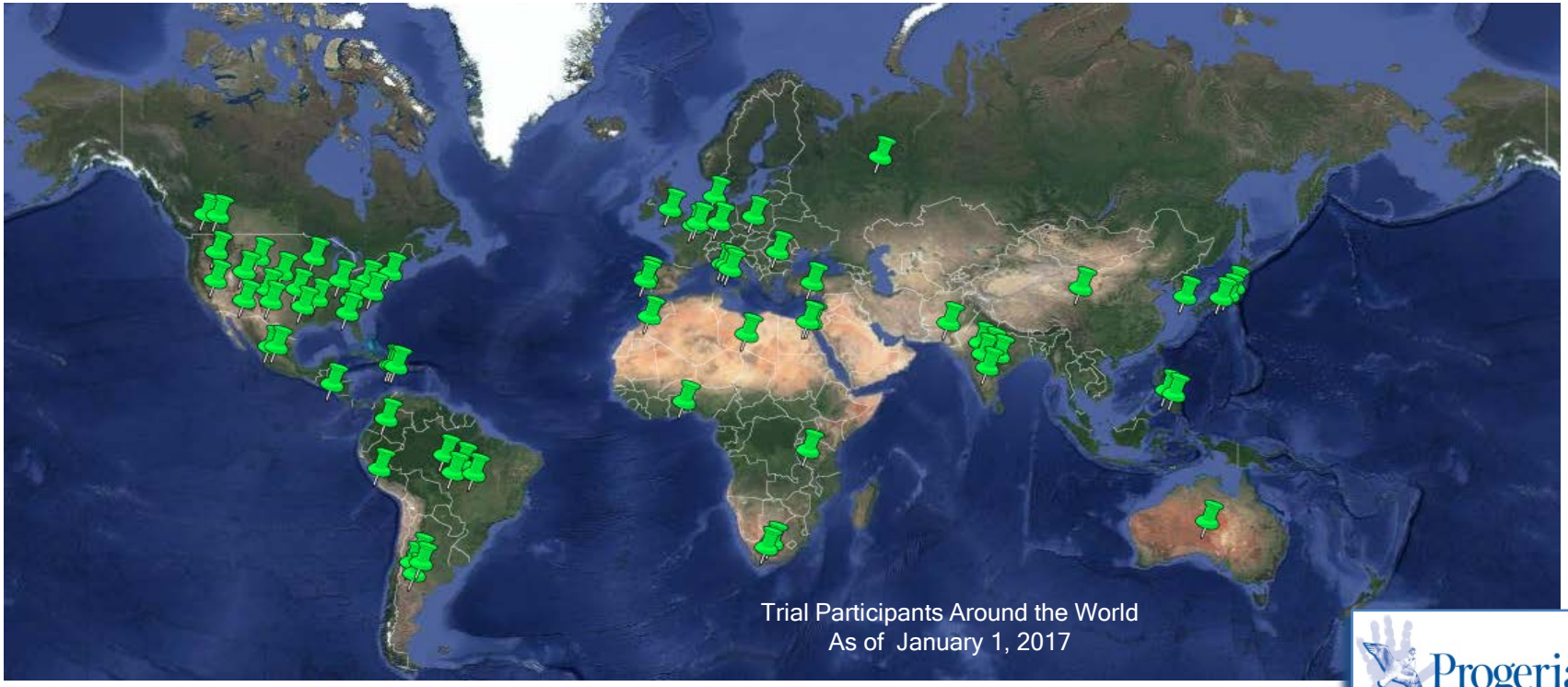
Participation in PRF Clinical Trials

83 Children have participated in PRF Clinical Trials from **34** countries:

Argentina	Canada	Dominican Republic	India	Libya	Peru	Romania	Sweden	USA
Australia	China	England	Israel	Mexico	Philippines	Russia	Tanzania	Venezuela
Belgium	Colombia	Germany	Italy	Morocco	Poland	South Africa	Togo	
Brazil	Denmark	Honduras	Japan	Pakistan	Portugal	South Korea	Turkey	



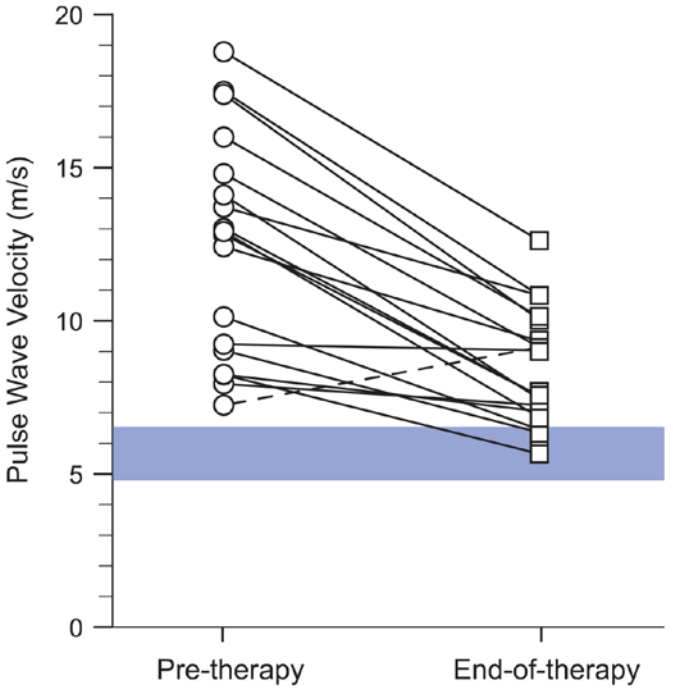
Treatment Trial Collaborations For Success

- **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 Eiger**
- **Everolimus generously provided by Novartis**

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



Gordon et al, PNAS, 2011

Progeria Research Foundation

Clinical Treatment Trial Publications

Drug Effect:

- Temsirolimus Partially Rescues the Hutchinson=Gilford Progeria Cellular Phenotype, Gabriel et al, Plos One, 2016, 11(12):1-25.
- 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 FS. *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.
- 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.
- Neurologic Features of Hutchinson-Gilford Progeria Syndrome after Lonafarnib Treatment. *Neurology*, 2013, 81:427-430.

Dermatology:

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

Imaging:

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

Cardiology:

- Mechanisms of Premature Vascular Aging in Children with Hutchinson-Gilford Progeria Syndrome. Gerhard-Herman M, et al., *Hypertension*. 2012 Jan;59(1):92-97; Epub 2011 Nov 14.

Skeleton:

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

As of January 1, 2017

Progeria Research Foundation

PRF Grants Program

Program Goals:

- Attract high level researchers to the field of Progeria
- Foster high quality publications
- Stimulate novel research that will lead to larger grants from other resources such as NIH, Ellison Foundation, and others
- Provide ability for researcher to thrive in the field
- Foster researchers of interest to PRF's mission

Grants program information available at
www.progeriaresearch.org/research_funding_opportunities

Progeria Research Foundation

PRF Medical Research Committee

Volunteer MRC Reviews Grant Applications Semi-annually

Back Row (L to R): Tom Glover PhD, Vicente Andrés Garcia PhD, Tom Mistelli PhD, Maria Eriksson PhD, W Ted Brown MD, PhD, Frank Rothman PhD (emeritus), Bryan Toole PhD(chair)

Front Row (L to R): Monica Kleinman MD, Christine Harling-Berg PhD, Judy Campisi PhD, Leslie Gordon MD, PhD, Marsha Moses PhD

Progeria Research Foundation

PRF Granting Structure

- Innovator Awards:
  - 2 years, up to $75,000 per year
  - Allows an investigator to embark on new areas and produce enough preliminary data to compete for longer-term funding by NIH and/or other agencies.
- Established Investigator Awards:
  - Up to 3 years, up to $100,000 per year.
  - For senior investigators established either in the field of Progeria or a field that can be directly applied to Progeria
- Specialty Awards:
  - Funding amounts and lengths flexible
  - For smaller, technology-driven projects, e.g., sequencing, drug screening, obtaining cell lines, antibody preparation, animal models, other

Progeria Research Foundation

Grant Funding Rates And Topics

As of September 1, 2016, The PRF funding rate is **33%**

- Since inception, **193** grant applications received and **64** funded
- PRF has funded **56** principal investigators from **45** institutions in **13** 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

Progeria Research Foundation

USA PRF Grantees

GRANTEE NAME	INSTITUTION
Jemima Barrowman	Johns Hopkins University
Juan Carlos Belmonte	Salk Institute for Biological Studies
Ted Brown	The Institute for Basic Research in Developmental Disabilities
Kan Cao	National Institutes of Health; University of Maryland
Christopher Carroll	Yale University
Francis Collins	National Institute of Health
Lucio Comai	University of Southern California
John P. Cooke	Houston Methodist Research Institute
Kris Dahl	Carnegie Mellon University
Jed W. Fahey	Johns Hopkins School of Medicine
Loren Fong	UCLA
Michael Gimbrone	Brigham & Women's Hospital
Thomas W. Glover	University of Michigan
Robert Goldman	Northwestern University
Leslie B. Gordon	Tufts University School of Medicine; Brown University
John Graziotto	Massachusetts General Hospital
Brian Kennedy	Buck Institute for Research on Aging
Jan Lammerding	Cornell University
Dudley Lamming	University of Wisconsin Madison

As of September 1, 2016

Progeria Research Foundation

USA PRF Grantees

GRANTEE NAME	INSTITUTION
Joan Lemire	Tufts University of Medicine
Jason Lieb	University of North Carolina
Monica Mallampalli	The Johns Hopkins School of Medicine
Susan Michaelis	The Johns Hopkins School of Medicine
Thomas Misteli	National Cancer Institute
Marsha Moses	Harvard Medical School; Boston Children's Hospital
Junko Oshima	University of Washington
Bryce Paschal	University of Virginia
Joseph Rabinowitz	Temple Medical School
John M. Sedivy	Brown University
Dale Shumaker	Northwestern University
Michael Sinensky	East Tennessee State University
Brian Snyder	Beth Israel Hospital
Dylan Taatjes	University of Colorado
Jakub Tolar	University of Minnesota
Katherine Ullman	University of Utah
Thomas Wight	Benaroya Research Institute
Katherine Wilson	Johns Hopkins University
Stephen Young	UCLA
Yue Zou	EastTennessee State University

As of September 1, 2016

Progeria Research Foundation

International PRF Grantees








GRANTEE NAME	INSTITUTION
Vicente Andrés Garcia	Centro Nacional de Investigaciones Cardiovasculares, Spain
Samuel Benchimol	York University, Toronto, Canada
Bum-Joon Park	Pusan National University, Korea
Claudia Cavadas	University of Coimbra, Portugal
Jesús Vazquez Cobos	Centro Nacional de Investigaciones Cardiovasculares, Spain
Thomas Dechat	Medical University of Vienna, Austria
Karima Djabali	Technical University of Munich, Germany
Maria Eriksson	Karolinska Institute, Sweden
Gerardo Ferbeyre	Université de Montreal, Canada
Célia Ferrera de Oliveira Aveleira	University of Coimbra, Portugal
Roland Foisner	Medical University of Vienna, Austria
Evgeny Makarov	Brunel University, England
Silvia Ortega-Gutiérrez	Universidad Complutense de Madrid, Spain
Charlotte Sorenson	Aarhus University, Denmark
William Stanford	University of Toronto, Canada
Colin Stewart	Institute of Medical Biology, Singapore
Anthony Weiss	University of Sydney, Australia
Zhongjun Zhou	University of Hong Kong, China




As of September 1, 2015

Progeria Research Foundation

PRF Scientific Meetings

Meeting Goals:

- To promote collaboration between basic and clinical scientists toward progress in Progeria, cardiovascular, and aging research

PRF has held **11** international scientific meetings

2016 PRF Workshop

Progeria Research Foundation

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

NIH National Institute on Aging

NIH National Institutes of Health
Turning Discovery Into Health

NIH National Human Genome Research Institute

NIH National Center for Advancing Translational Sciences

ORDR Office of Rare Diseases Research

NIH National Heart, Lung, and Blood Institute

NIH NATIONAL CANCER INSTITUTE

The Ellison Medical Foundation

The Max and Victoria Dreyfus Foundation, Inc.

afar american federation for aging research

carly cares

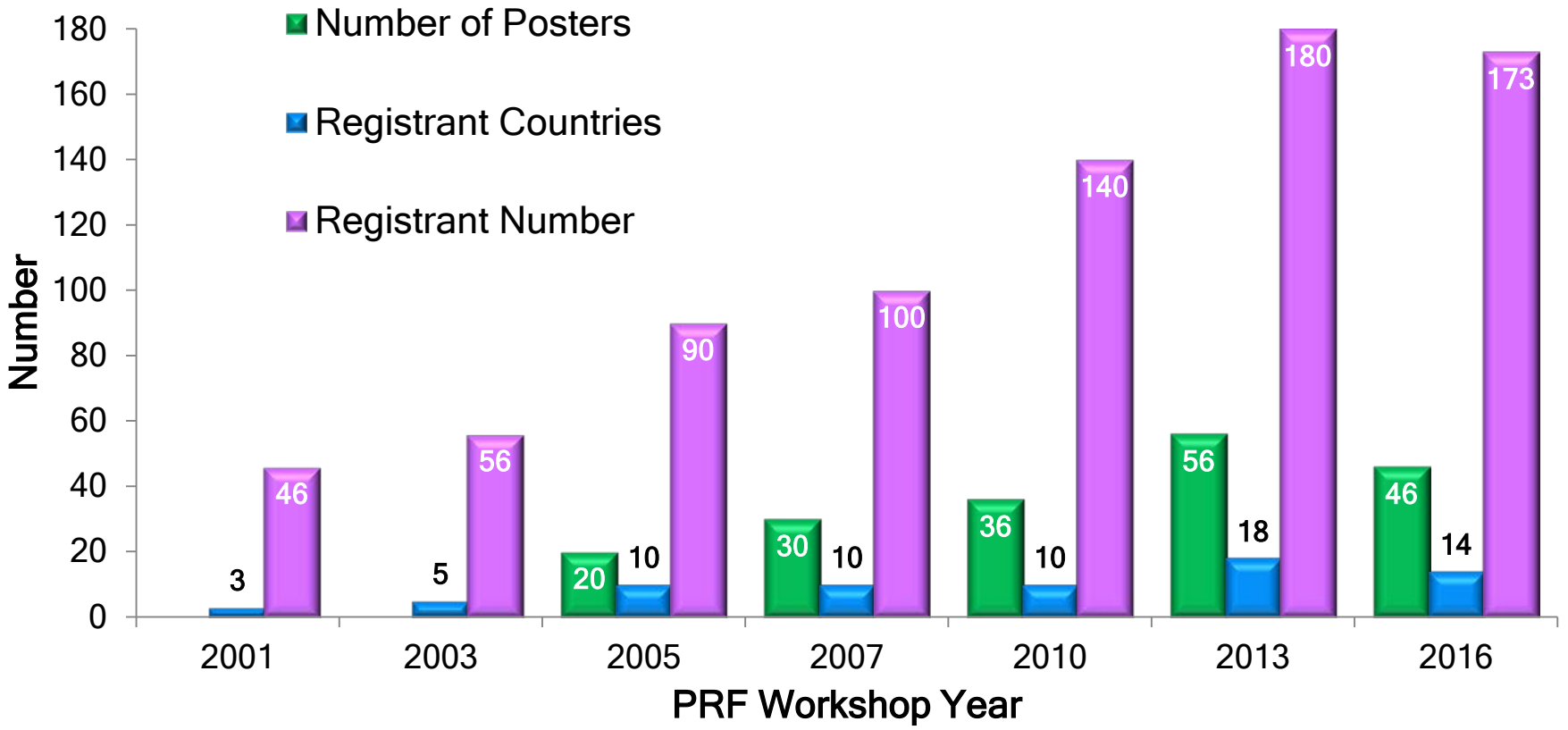
HOLOGIC The Science of Sure

DSF Charitable Foundation

Celgene *Committed to improving the lives of patients worldwide®*

Progeria Research Foundation

Growth of Global Interest In PRF Workshops



Progeria Research Foundation

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

Progeria Research Foundation

NIH National Heart, Lung, and Blood Institute

NIH National Human Genome Research Institute

Scientific Publications

As of January 1, 2017:

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

- Publication list at www.progeriaresearch.org/cell_tissue_bank

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

- Publication list at www.progeriaresearch.org/medical_database

6 Scientific articles have been published from clinical trial data

- See slide #54

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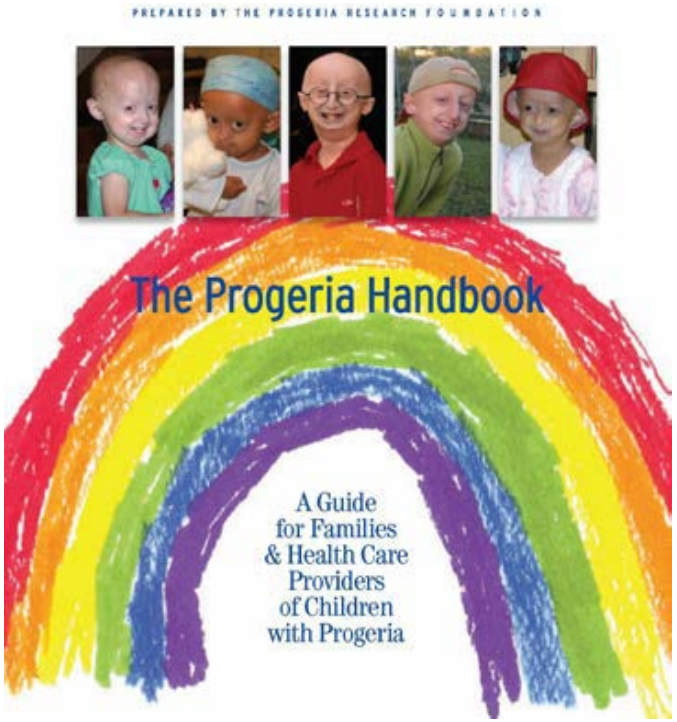
Progeria Clinical Care Handbook

The Progeria Handbook. A Guide for Families & Health Care Providers of Children with Progeria. *The Progeria Research Foundation.* Leslie B. Gordon (editor) 2010.



- Provided in English, Spanish and Portuguese
- Expert contributors from Boston Children's Hospital
- Number of Progeria Care Handbooks distributed to families of those with Progeria and their care givers: **501**

As of January 1, 2017

Progeria Research Foundation

NIH Natural History Study

- From 2005-2006, PRF participated in an NIH/NHGRI sponsored natural history study that included **15** children with Progeria conducted at the NIH Clinical Research Center.

Goal: to understand the disease processes that drive Progeria.

The NEW ENGLAND JOURNAL of MEDICINE

Phenotype and Course of Hutchinson-Gilford Progeria Syndrome
Merideth et al, NEJM, 2008, vol 358, 592-604

NIH Clinical Center
NATIONAL INSTITUTES OF HEALTH

NIH National Human Genome Research Institute

Progeria Research Foundation

The Progeria Research Foundation

Finding…
Diagnosing…
Studying…
Treating…
CURING

Progeria Research Foundation

Together We *WILL* Find The Cure!

www.progeriaresearch.org