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

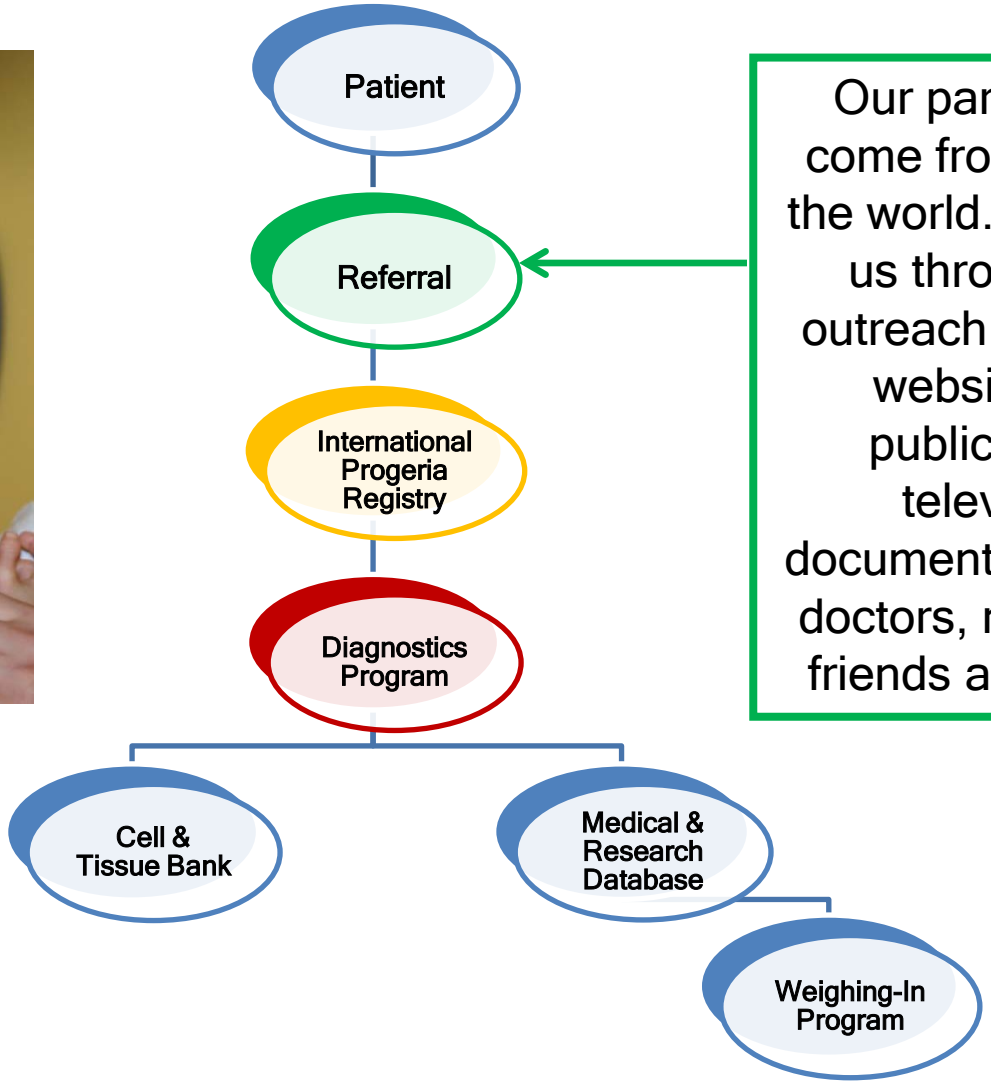
Our Target Audience

- 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

Progeria Research Foundation

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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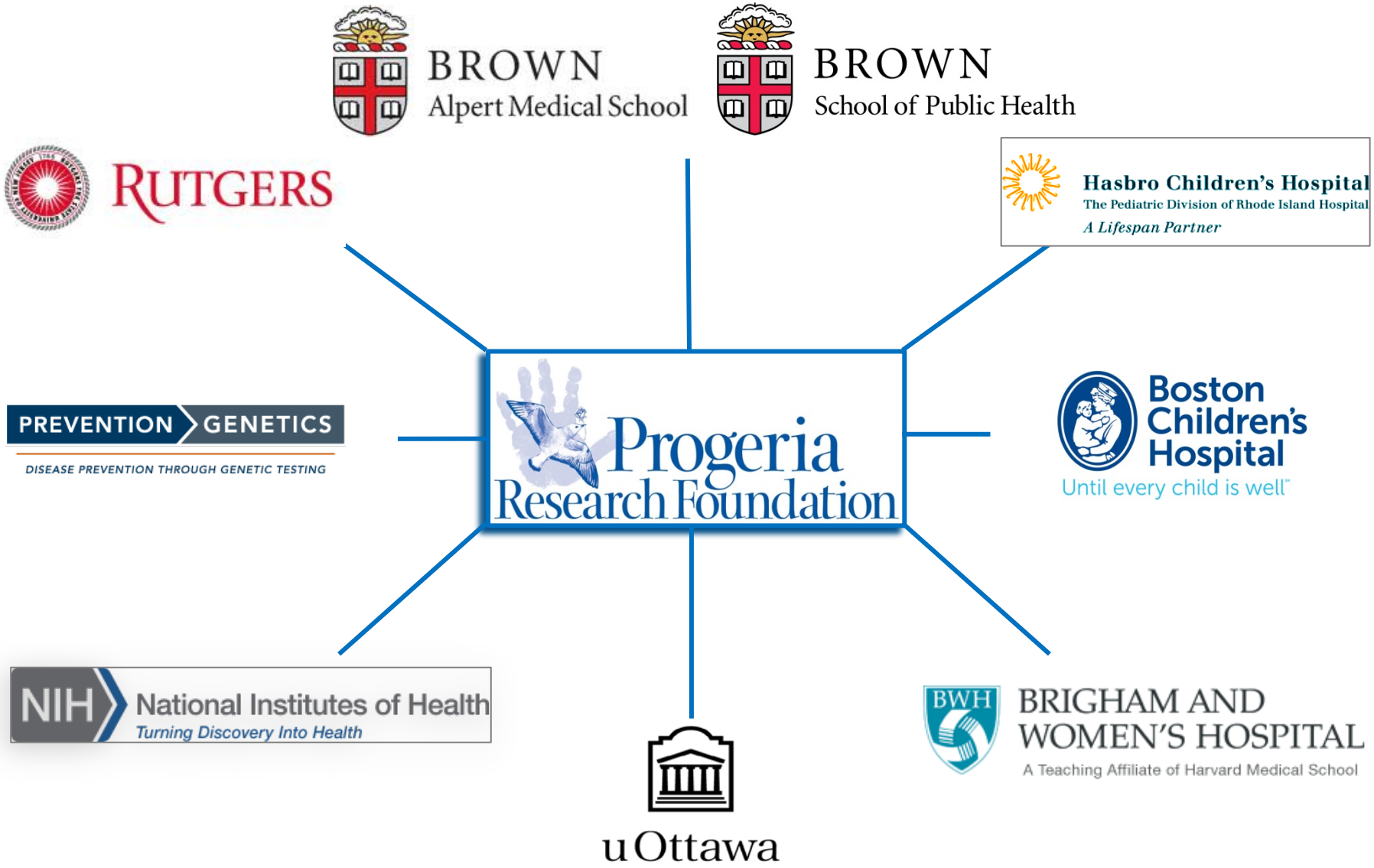
Collaborations For Success



Our Program Collaborators

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

- 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 October 1, 2014:

Total Number of Children with Progeria Worldwide: 123

HGPS* worldwide: 99

HGPS* in the United States: 15

Progeroid Laminopathies** worldwide: 24

Progeroid Laminopathies** in the United States: 6

*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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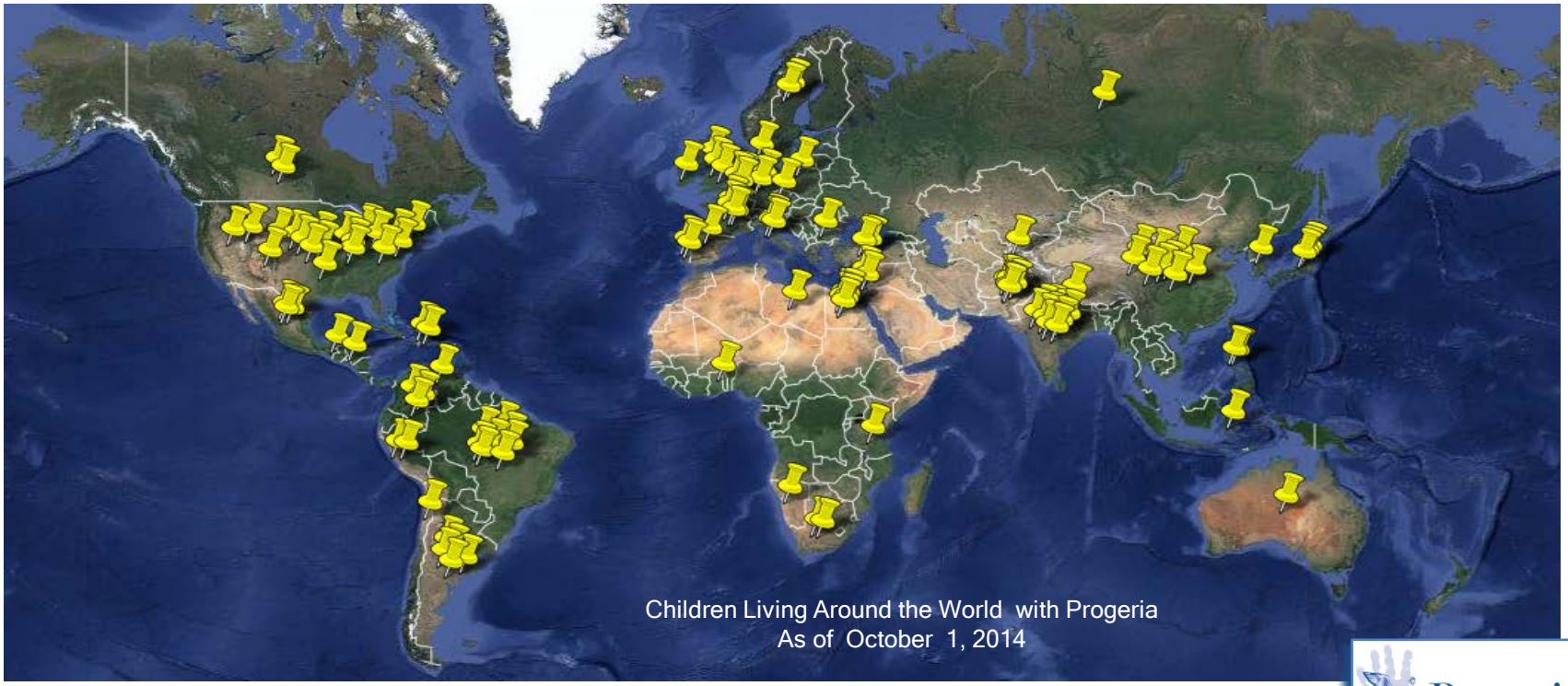
PRF-Identified Cases Reside In 43 Countries

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



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…and Speak 28 Languages

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

прогерии исследовательский фонд

مؤسسة أبحاث الشياخ

早衰症研究基金會

Progeria रिसरच फाउंडेशन

조로증 연구 재단

Progeria Araştırma Vakfı

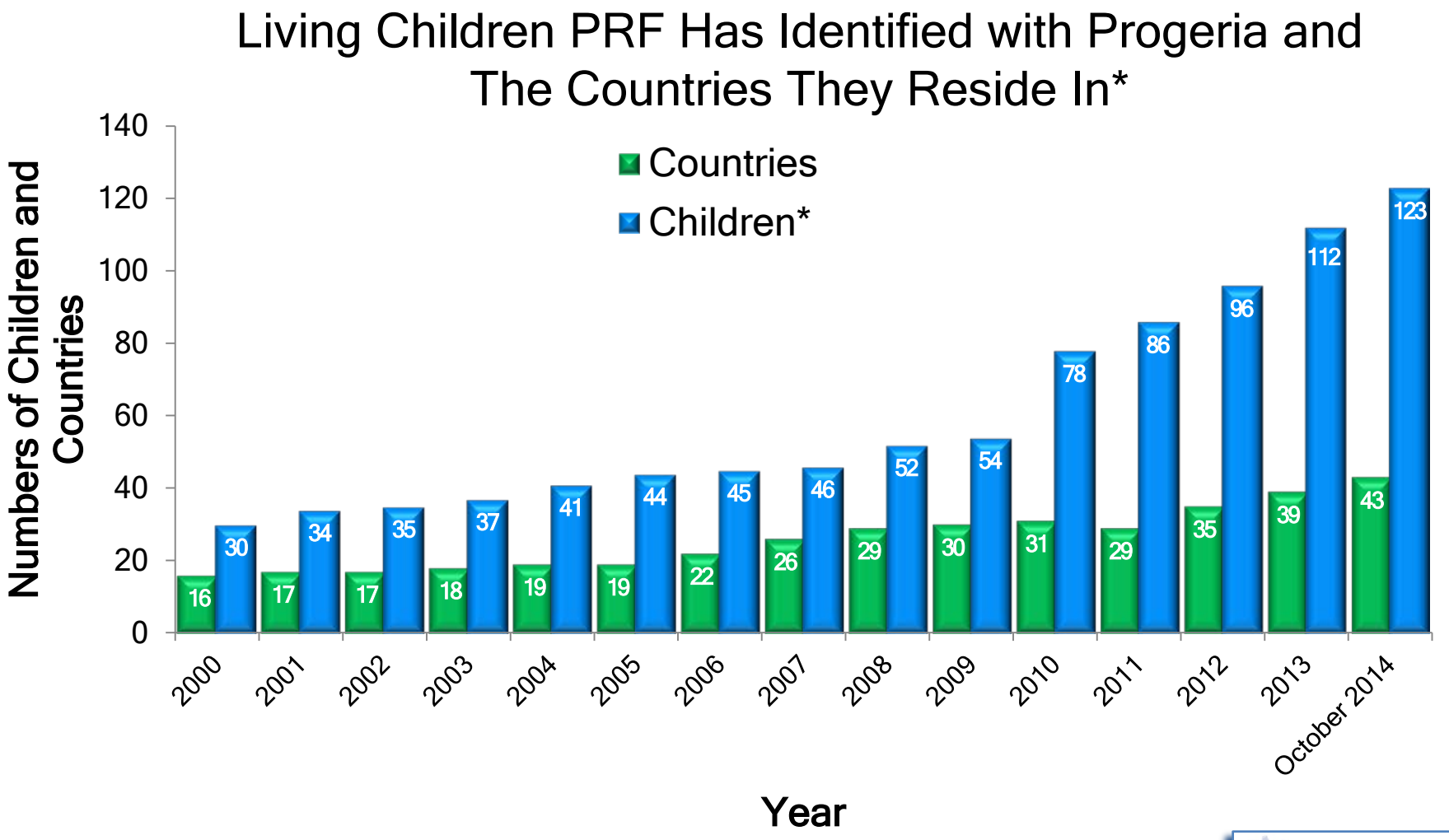
早老症研究財団

బాలుడ బాలిక వయస్సు ముదురుకండానే వృద్ధాప్యరూపంలోనికి వచ్చుట రీసెర్చ్ ఫౌండేషన్

As of October 1, 2014

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.

USA Prevalence of Progeria

July 1, 2013 population statistics:

- The US population was:

  316,128,839 people

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

  17

- Prevalence of HGPS in the US:
  17 in 316 million is about

  1 in 18 million people

Source: 2013 US population: http://www.census.gov/#

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Prevalence and World Population of Progeria

Given the current world population, as of July 2013

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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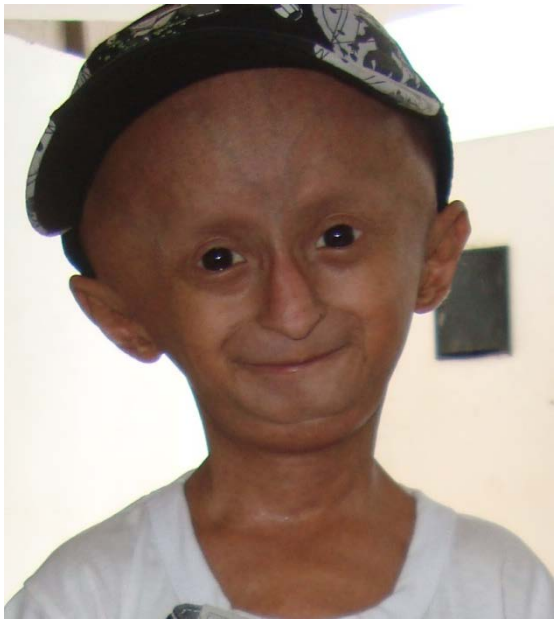
Using Prevalence To Find Children In A Certain Country

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 July 1, 2013:



- Brazil's population was **201,032,714** people
- Number of children living with Progeria in Brazil is

201,032,714/18,000,000 = **11**

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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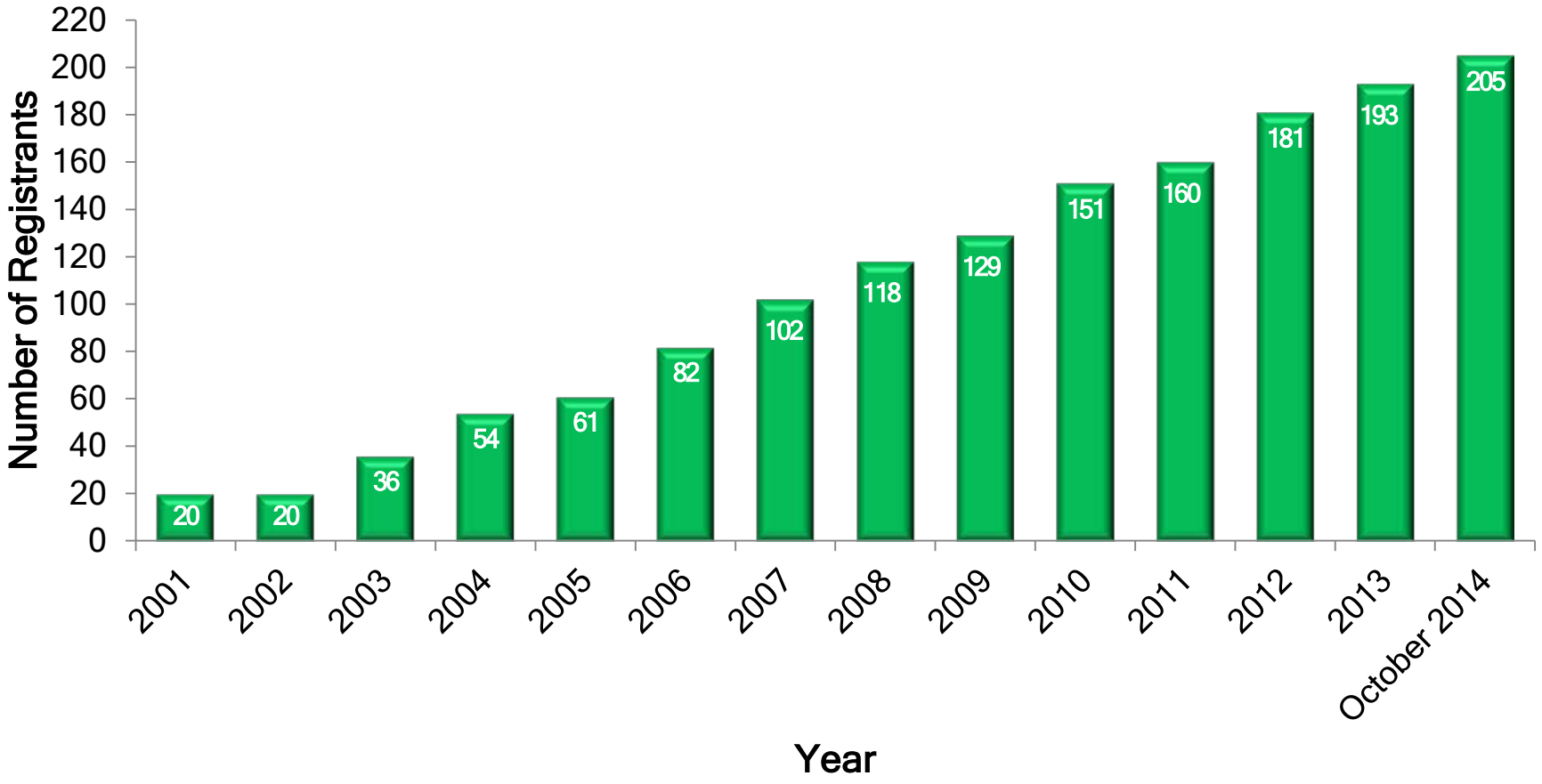
205 Children Have Registered With PRF



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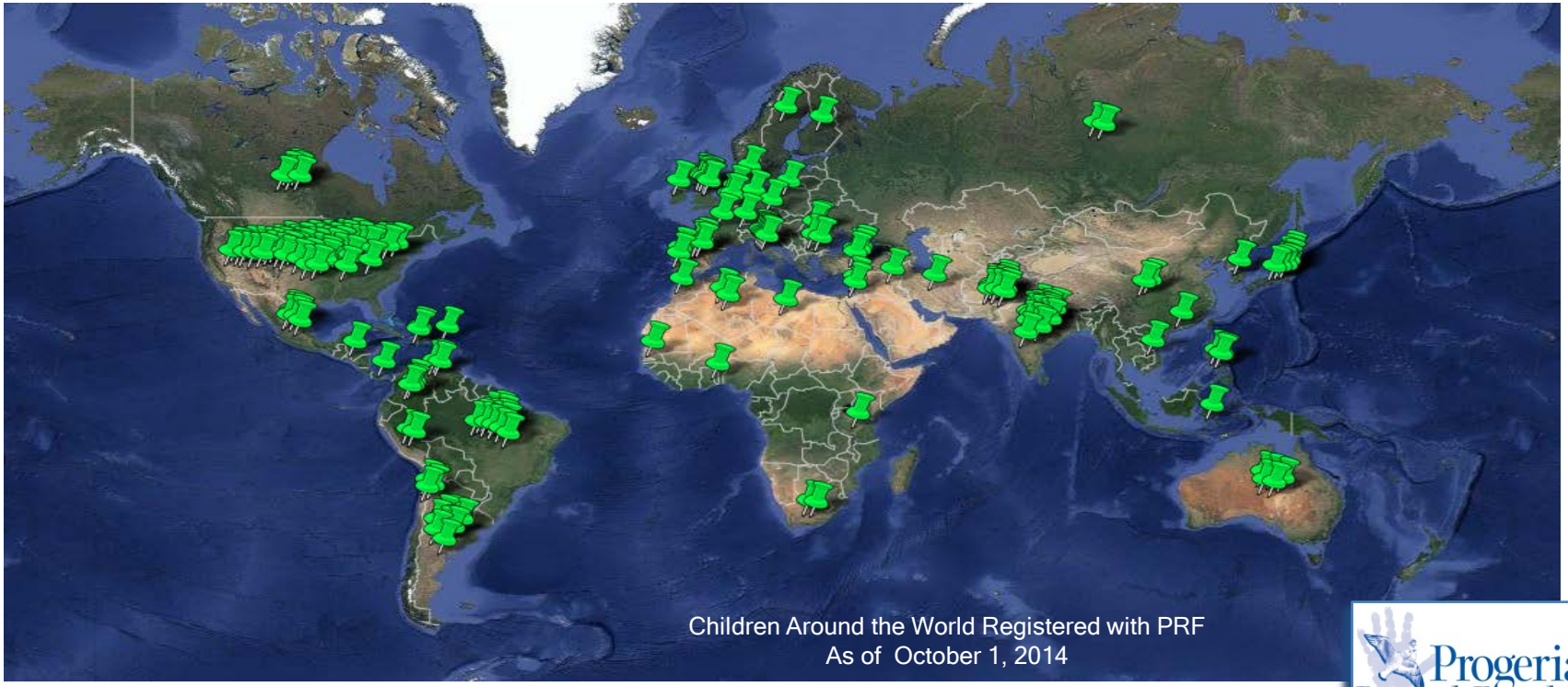
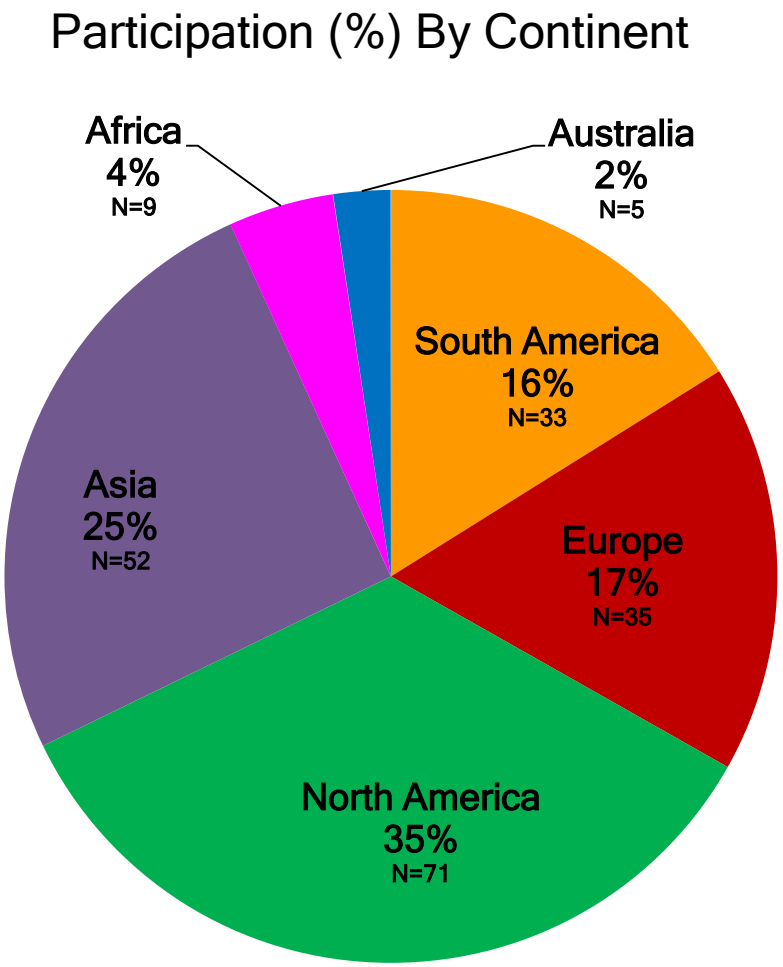
…From 52 Countries

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



...And All Continents



As of October 1, 2014

Progeria Research Foundation

PRF Diagnostics Program

Program Goal:

- Genetic Sequence Testing for Progeria-causing mutations

Pre-requisites for Testing:

- Registration with PRF International Registry
- Possible indications for genetic testing
  - Proband, prenatal – family history
  - Proband, postnatal - clinical presentation
  - Relative of positive proband

Testing information available at

www.progeriaresearch.org/diagnostic_testing

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Diagnostics Testing Summary

As of October 1, 2014:

Total Number of Proband Tests Performed* : 115

HGPS Mutations: 77

Zmpste24 Mutations: 2

Non-HGPS LMNA Mutations: 9

Average Number of Patients Tested Per Year : 10

All tests are performed in a Clinical Laboratory Improvement Amendments (CLIA) certified facility.
*An individual may have undergone multiple tests

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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	65
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+1 G>A		heterozygous	Yes	1
Progeroid Laminopathy- LMNA Mutation				
1579 C>T, exon 9	A527C	heterozygous	No	1
1579 C>T, exon 9	A527C	homozygous	No	5
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 October 1, 2014

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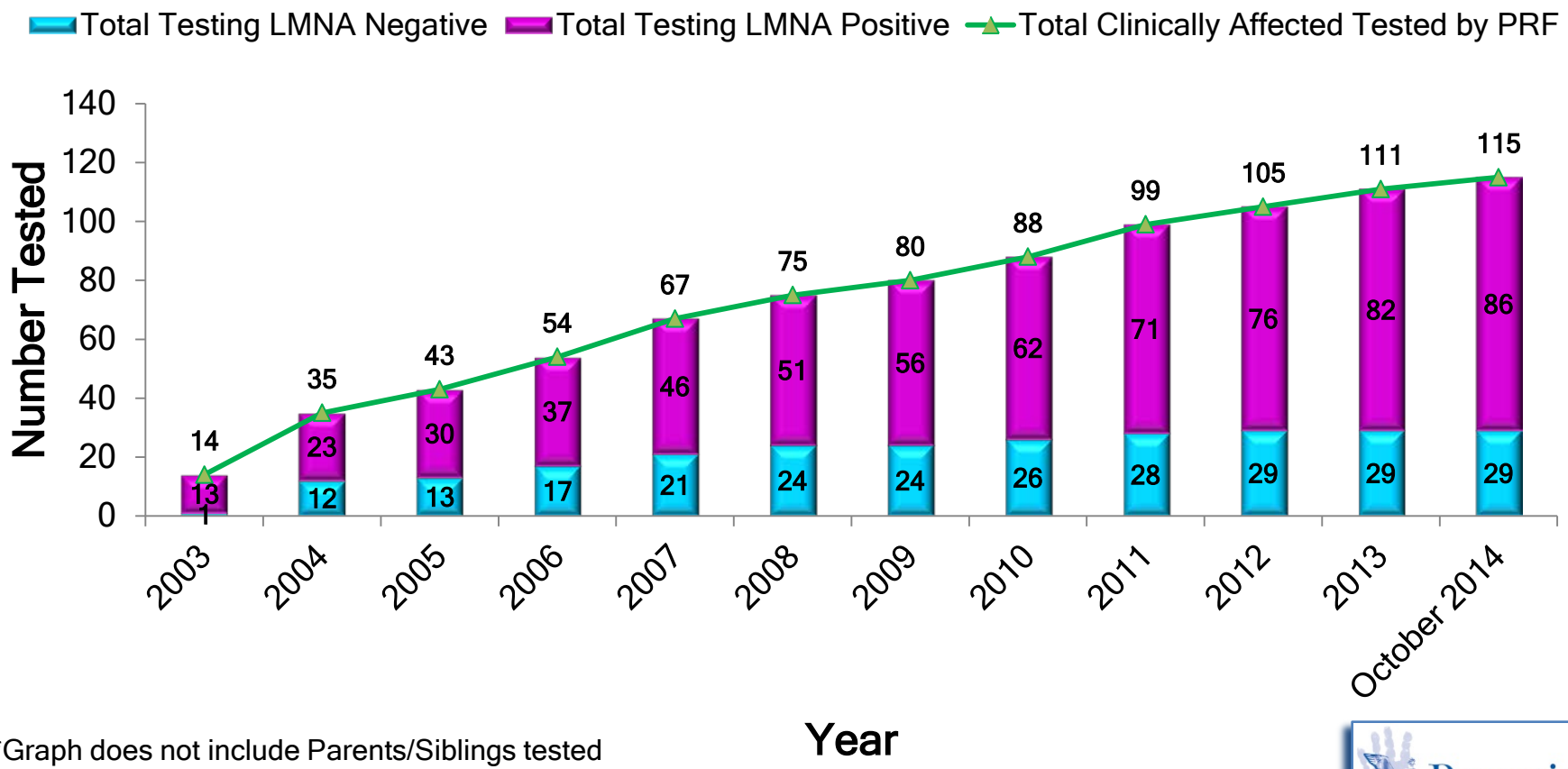
Longitudinal Testing Data for PRF Diagnostics Program

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

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PRF Cell & Tissue Bank Holdings

As of October 1, 2014:

Total Number of Cell Lines: **194** From **193** Donors

65 Dermal Fibroblast Lines from **44** affected, **21** parents and **0** siblings

120 Lymphoblast Lines from **67** affected, **45** parents and **8** siblings

9 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>A	---------	heterozygous	Yes	DFN
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 October 1, 2014

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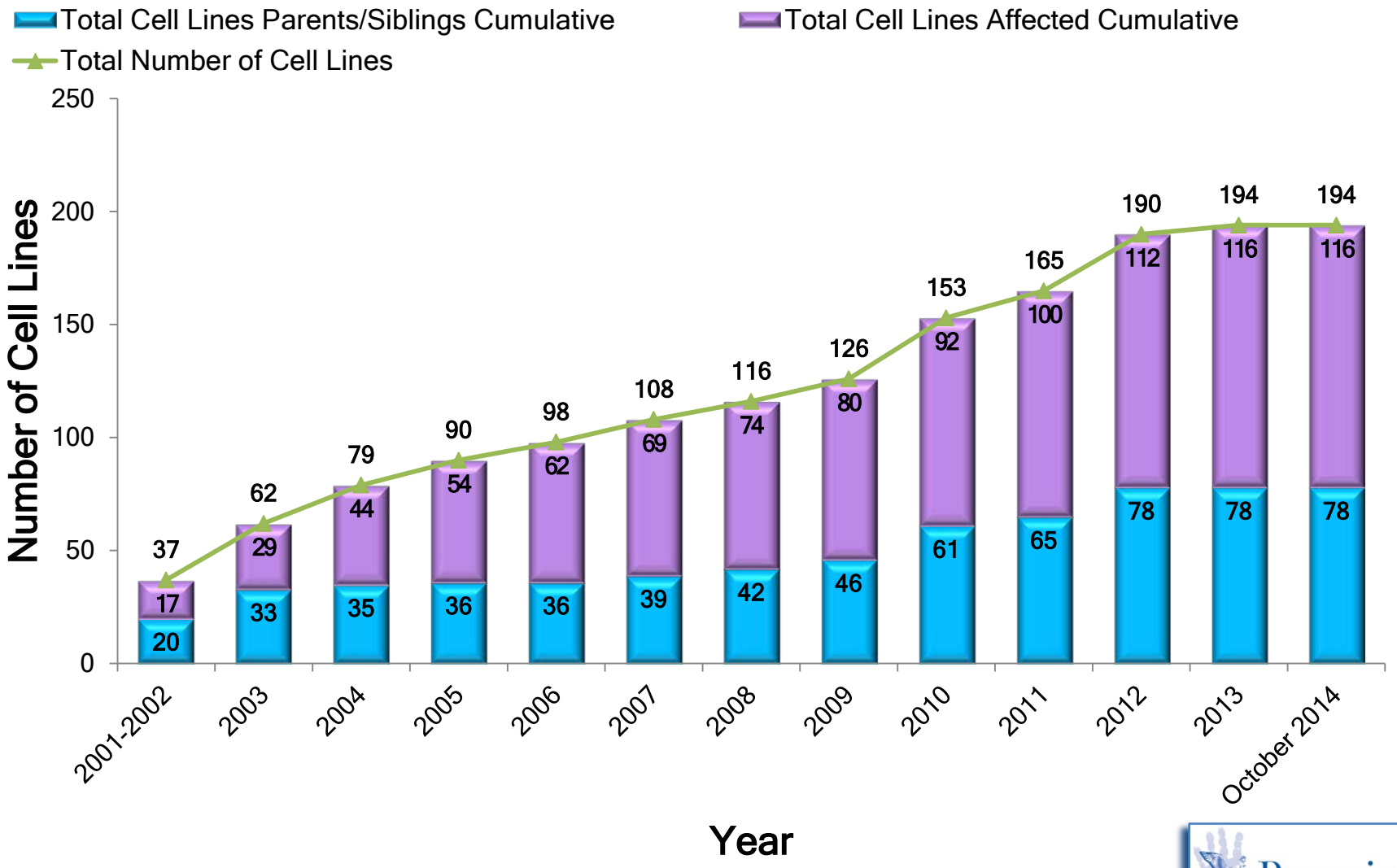
Number Of Cell Lines By Year



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PRF Cell & Tissue Bank Distribution

As of October 1, 2014:

71 Research Teams From **15** Countries Have Received

407 Cell Lines

61 DNA Samples

34 Types of Tissues

Senescent Progeria
Fibroblasts in Culture

Progeria Research Foundation

USA Cell & Tissue Bank Recipients

Recipient	Institution	Recipient	Institution
Bruce Blazar	University of Minnesota	Kris Dahl	Carnegie Mellon University
Ted Brown	NYS Institute for Basic Research in Developmental Disabilities	George Daley Harith Rajagopalan Andrew Sonis	Boston Children's Hospital
Kan Cao	University of Maryland	Junko Oshima	University of Washington
Judy Campisi	Buck Institute	Stephen Doxsey Timothy Kowalik Jeanne Lawrence	University of Massachusetts Medical School
Francis Collins	National Human Genome Research Institute	David Kaplan	Tufts University
Lucio Comai	University of South California	Mary Patti C. Ronald Kahn	Joslin Diabetes Center
Adrienne Cox Channing Der Kohta Ikegami Jason Lieb Mohanish Dekmukh	University of North Carolina at Chapel Hill	Michele Olive Betsy Nabel Earl Stadtman Gabriela Viteri	National Heart, Lung and Blood Institute
Greg Crawford	Duke University Medical Center	Abhimanyu Garg	University of Texas Southwestern Medical Center
John Sedivy Marc Tatar	Brown University	Tom Misteli Christin Hanigan Ana Robles	National Cancer Institute

As of October 1, 2014

Progeria Research Foundation

USA Cell & Tissue Bank Recipients

Recipient	Institution	Recipient	Institution
Dennis Discher	University of Pennsylvania	Shridar Ganesan V Ginjala	University of Medicine & Dentistry of NJ
Thomas Glover	University of Michigan Medical School	Bryce Paschal	University of Virginia
Robert Goldman	Northwestern University	Christian Sell	Drexel University College of Medicine
Susana Gonzalo	St. Louis School of Medicine	Dylan Taatjes	University of Colorado
John Graziotto Dmitri Krainc	Massachusetts General Hospital	Bryan Toole Joan Lemire	Tufts University School of Medicine
Tom Wight Ingrid Harten	Hope Heart Institute	Alan Waldman	University of South Carolina
Vishwanath R. Iyer	University of Texas at Austin	Steve Warren	Emory University School of Medicine
Jan Lammerding	Harvard University	Yue Zou	East Tennessee State University
Jeffrey Miner	Washington University	Antonei Csoka	Howard University

As of October 1, 2014

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International Cell & Tissue Bank Recipients

Recipient	Institution
Thomas Dechat	Medical University of Vienna
Michael Speicher	Medical University of Graz
Neale Ridgway	University of Halifax
William Stanford	University of Toronto
J. El Molto	Molecular World, Inc
Gerardo Ferbeyre	Université de Montréal
Robert Hegele	University of Western Ontario
Alain Garnier	Université Laval
Lynne Cox	University of Oxford
Michael Walter	University of Münster
Karima Djabali	TU-Munich
Herbert Waldman	Max Planck Institute
Zhongjun Zhou	University of Hong Kong
Yosef Gruenbaum	The Hebrew University of Jerusalem
Kirsztian Kvell	University of Pecs
Alex Zhavoronkov	Federal Clinical Research Centre for Pediatric Hematology, Oncology and Immunology

As of October 1, 2014

Progeria Research Foundation

International Cell & Tissue Bank Recipients

Recipient	Institution
Chiara Lanzuolo	CNR Institute of Cellular Biology & Neurobiology
Giovanna Lattanzi	ITOI-CNR Unit of Bologna
Marco Foiani Amit Kumar	Istituto FIRC di Oncologia Molecolare
Lucia Latella	National Research Council (CNR) Rome
Maria Eriksson	Medicinsk Naringslara
Vicente Andres Garcia	Centro Nacional de Investigaciones Cardiovasculares
Lino Ferreira	Center for Neuroscience and Cell Biology (CNC)
Ohad Medalia	University of Zurich
Nicolas Levy	Génétique Médicale et Développement, Faculté de Médecine de la Timone
Annachiara DeSandre-Giovannoli	Laboratoire de Génétique Moléculaire, Hôpital d'Enfants La Timone
Jean-Marc Lemaitre	Institute of Functional Genomics, Montpellier, France
Ok Sarah Shin	Korea University Guro Hospital

As of October 1, 2014

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.

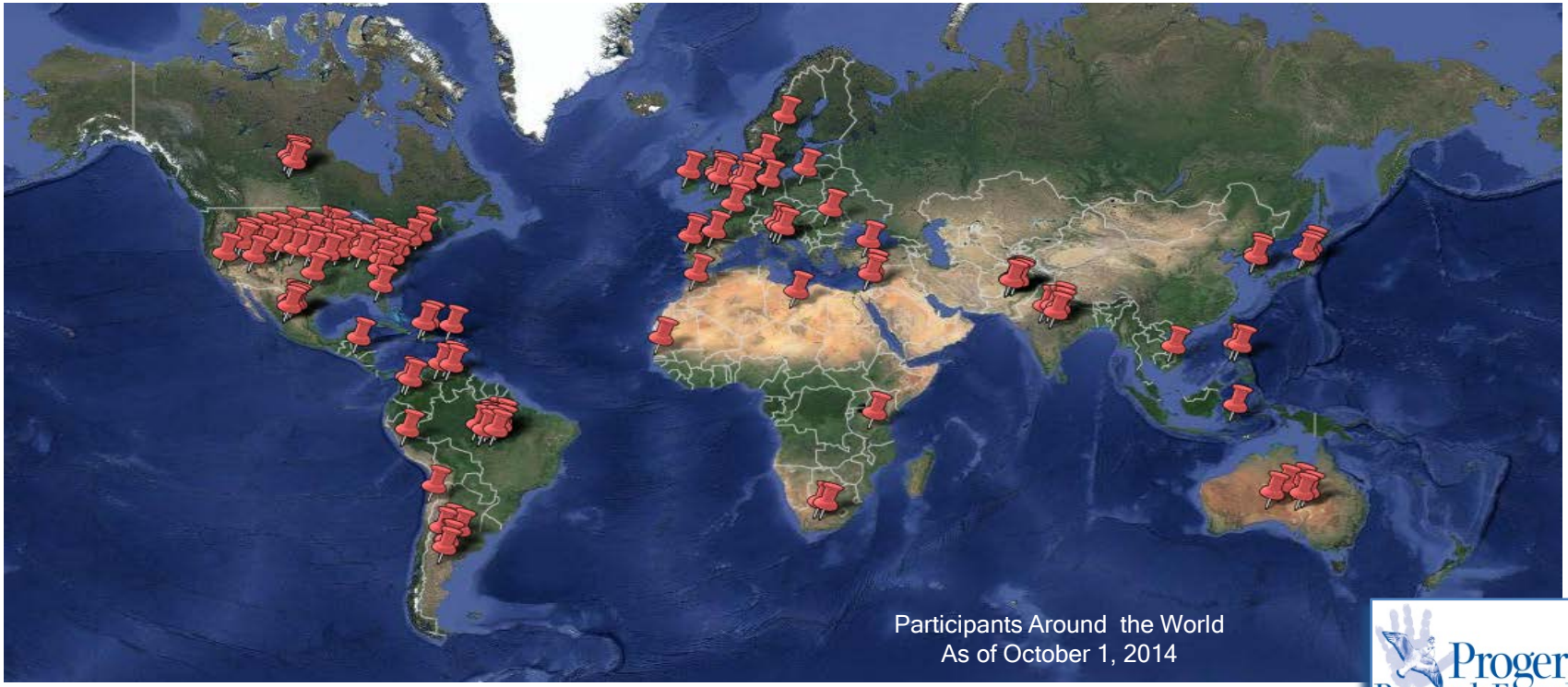
Enrollment information available at: www.progeriaresearch.org/medical_database

Progeria Research Foundation

Medical & Research Database Participation

129 Participants are enrolled from **39** countries and **1** US territory

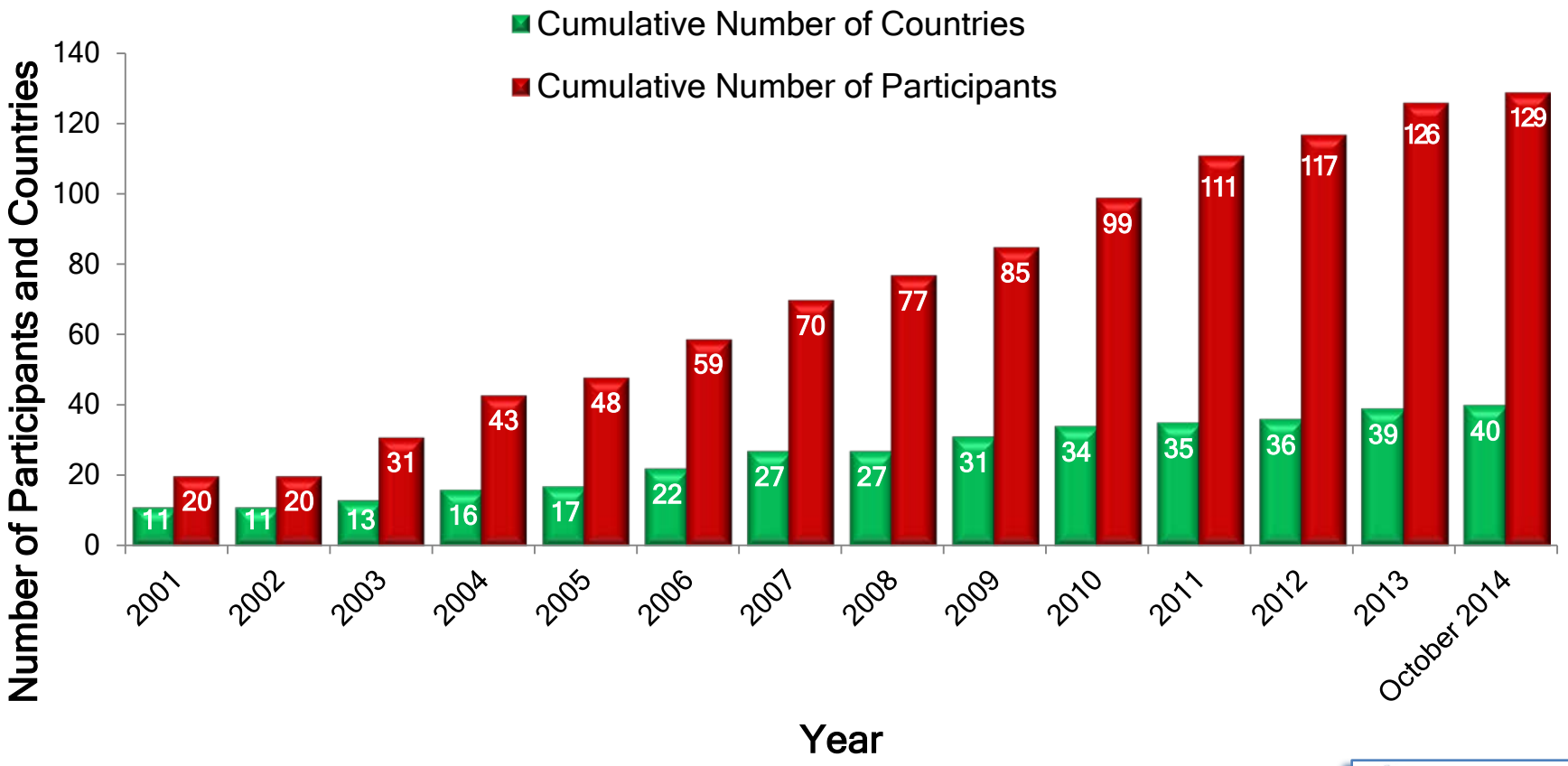
Argentina	Chile	France	Ireland	Mexico	Philippines	Senegal	Tanzania
Australia	Colombia	Germany	Israel	Morocco	Poland	South Africa	Turkey
Belgium	Denmark	Honduras	Italy	Netherlands	Portugal	South Korea	USA
Brazil	Dominican Republic	India	Japan	Pakistan	Puerto Rico	Spain	Venezuela
Canada	England	Indonesia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



Participants Around the World
As of October 1, 2014

Database Longitudinal Enrollment

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



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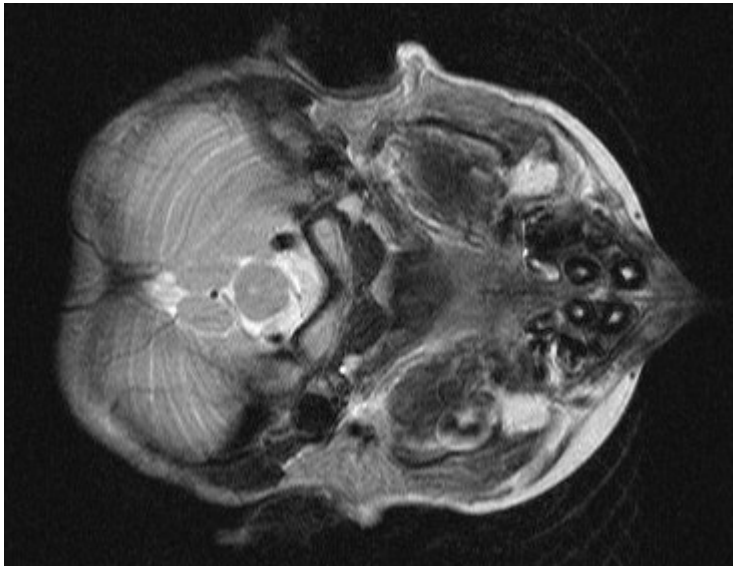
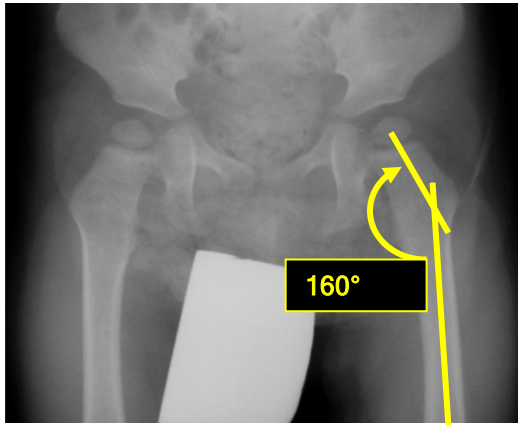
Types Of Data Collected

- Participants with Medical Records Reports: 101
- Participants with Radiology Studies: 56





As of October 1, 2014

Progeria Research Foundation

PRF Weighing-In Program

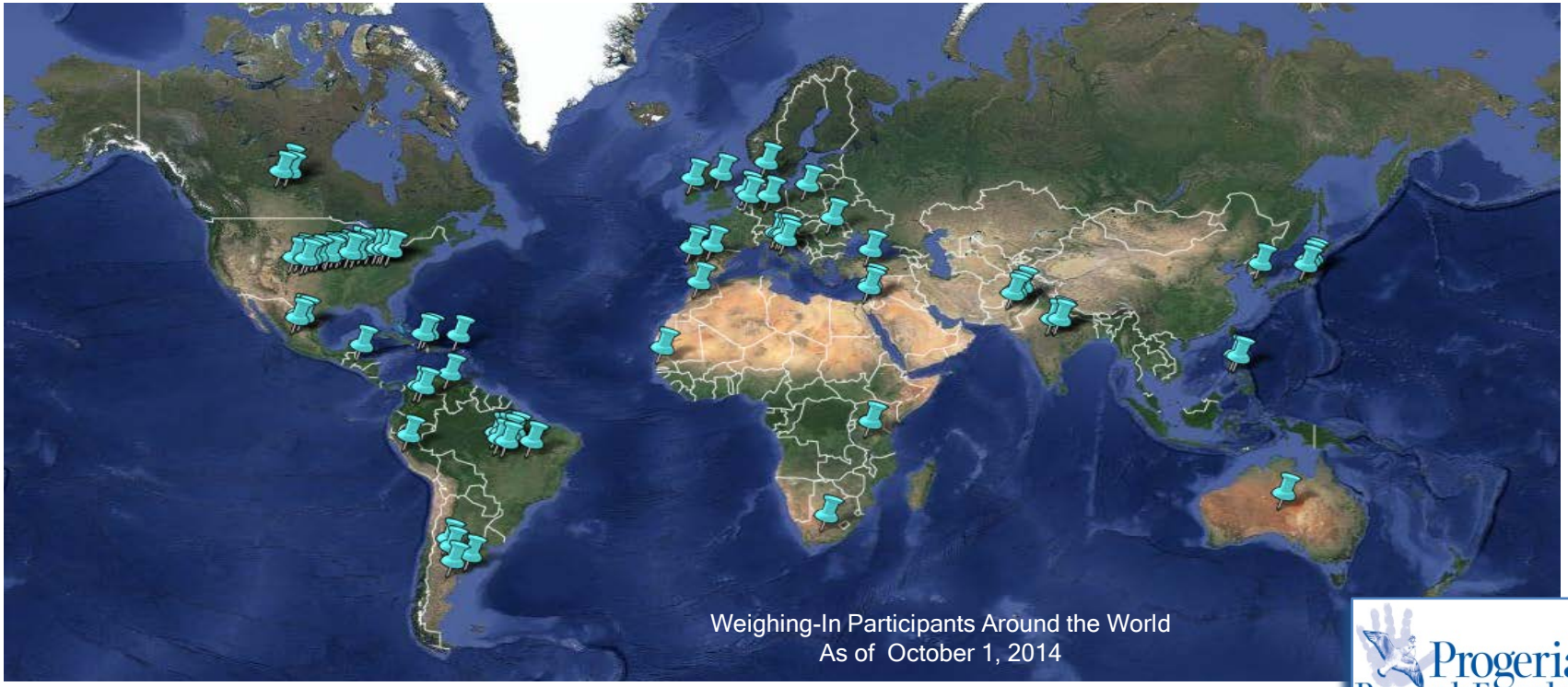
- A sub-program of The PRF Medical & Research Database
- Collects weight-for-age data prospectively:
  - Home scale provided by PRF
  - Parents weigh child weekly or monthly
  - Report weights electronically

Progeria Research Foundation

Weighing-In Program Participation

85 Participants are enrolled from **32** countries and **1** US territory

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



Weighing-In Participants Around the World
As of October 1, 2014

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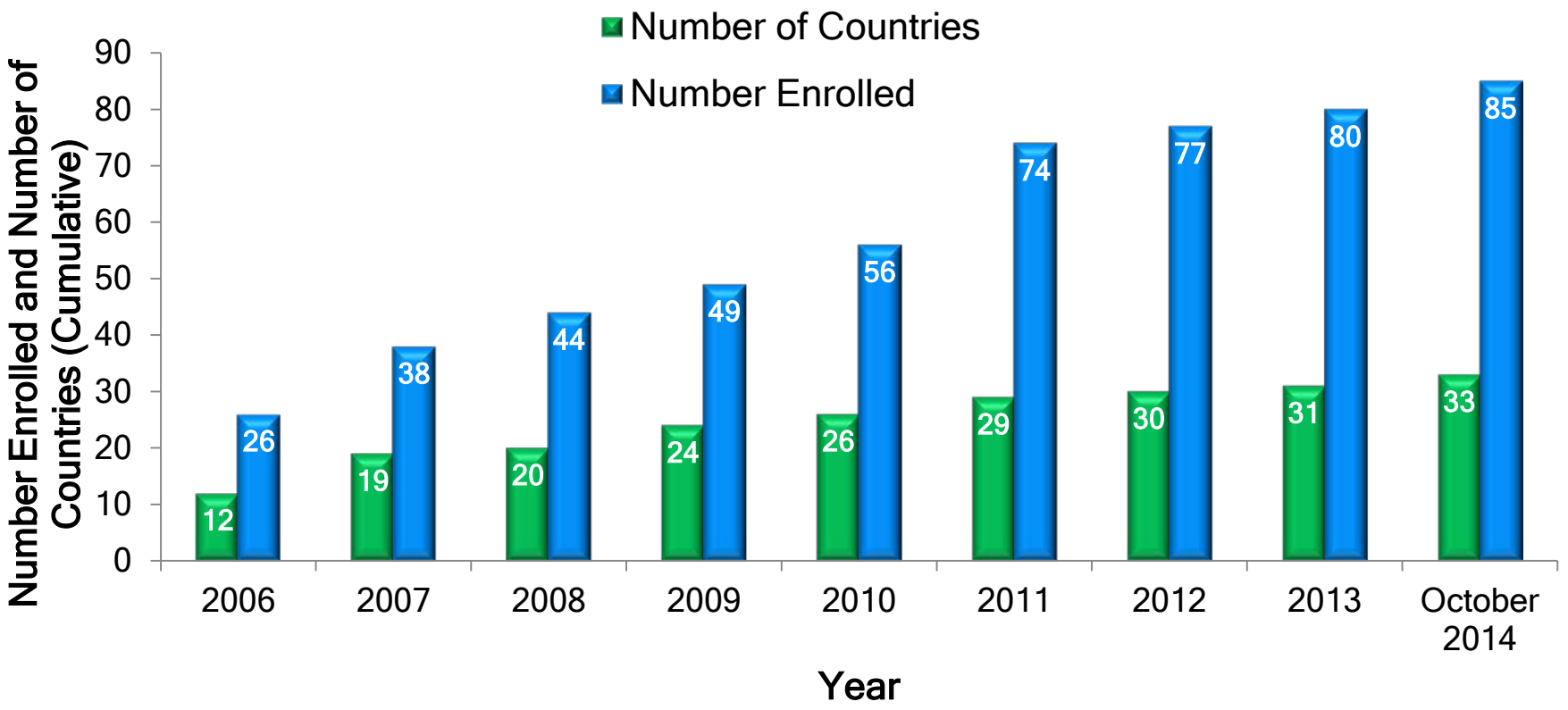
Participants Enrolled In The PRF Weighing-In Program and Countries of Residence



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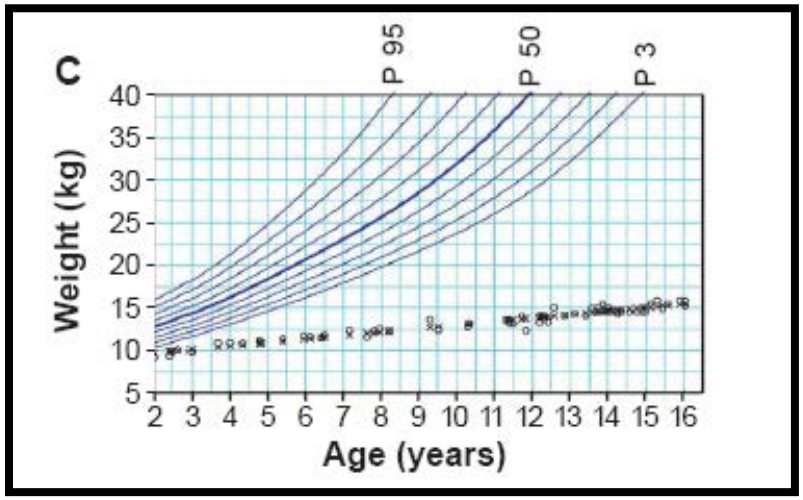
Clinical Trials And The Weighing-In Program

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

- As of October 1, 2014, **53** 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 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

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PRF Medical Research Committee

Volunteer MRC Reviews Grant Applications Semi-annually

Back Row (L to R): Tom Misteli, PhD; Judy Campisi, PhD; Christine Harling-Berg, PhD; Leslie Gordon, PhD, MD; Ted Brown, MD, PhD
Front Row (L to R): Frank Rothman, PhD; Tom Glover, PhD; Bryan Toole, PhD (chair)
Not Pictured : Monica Kleinman, MD

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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

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Grant Funding Rates And Topics

As of July 1, 2014, The PRF funding rate is **39.6%**

- Since inception, **139** grant applications received and **55** funded
- PRF has funded **51** researchers from **35** labs in **10** 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

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USA PRF Grantees

GRANTEE NAME	INSTITUTION	GRANTEE NAME	INSTITUTION
Jemima Barrowman Katherine Wilson	Johns Hopkins University	Joan Lemire	Tufts University School of Medicine
Ted Brown	The Institute for Basic Research in Developmental Disabilities	Jason Lieb	University of North Carolina
Kan Cao	National Institutes of Health University of Maryland	Monica Mallampalli Susan Michaelis	The Johns Hopkins School of Medicine
Christopher Carroll	Yale University	Thomas Misteli	National Cancer Institute
Lucio Comai	University of Southern California	Junko Oshima	University of Washington
Kris Dahl	Carnegia Mellon University	Bryce Paschal	University of Virginia
Karima Djabali	Columbia University	John M. Sedivy	Brown University
Loren Fong	UCLA	Michael Sinensky	East Tennessee State University
Michael Gimbrone	Brigham & Women's Hospital	Brian Snyder	Beth Israel Hospital
Thomas W. Glover	University of Michigan	Dylan Taatjes	University of Colorado
Robert Goldman Dale Shumaker	Northwestern University	Jakub Tolar	University of Minnesota
Leslie B. Gordon	Tufts University School of Medicine Brown University	Katherine Ullman	University of Utah
John Graziotto	Massachusetts General Hospital	Thomas Wight	Benaroya Research Institute
Brian Kennedy	Buck Institute for Research on Aging	Stephen Young	UCLA
Jan Lammerding	Cornell University	Yue Zou	East Tennessee State University

As of July 1, 2014

International PRF Grantees

GRANTEE NAME	INSTITUTION	
Vincente Andres Garcia	Centro Nacional de Investigaciones Cardiovasculares	
Thomas Dechat	Medical University of Vienna	
Maria Eriksson	Karolinska Institute	
Evgeny Makarov	Brunel University	
Gerardo Ferbeyre	Université de Montreal	
William Stanford	University of Toronto	
Samuel Benchimol	York University, Toronto	
Zhongjun Zhou	University of Hong Kong	
Anthony Weiss	University of Sydney	
Colin Stewart Vandana Ramachandran	Institute of Medical Biology	

As of July 1, 2014

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

2010 PRF Workshop

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7 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 **7** workshops through R13 and other granting mechanisms

Other organizations have also generously sponsored workshops

NIH National Institutes of Health
Turning Discovery Into Health

The Ellison Medical Foundation

afar american federation for aging research

NIH National Center for Advancing Translational Sciences

ORDR Office of Rare Diseases Research

NATIONAL INSTITUTE ON AGING
National Institutes of Health

NATIONAL CANCER INSTITUTE

NIH National Heart, Lung, and Blood Institute

Celgene

genome.gov
National Human Genome Research Institute
National Institutes of Health

THE MAX AND VICTORIA DREYFUS FOUNDATION

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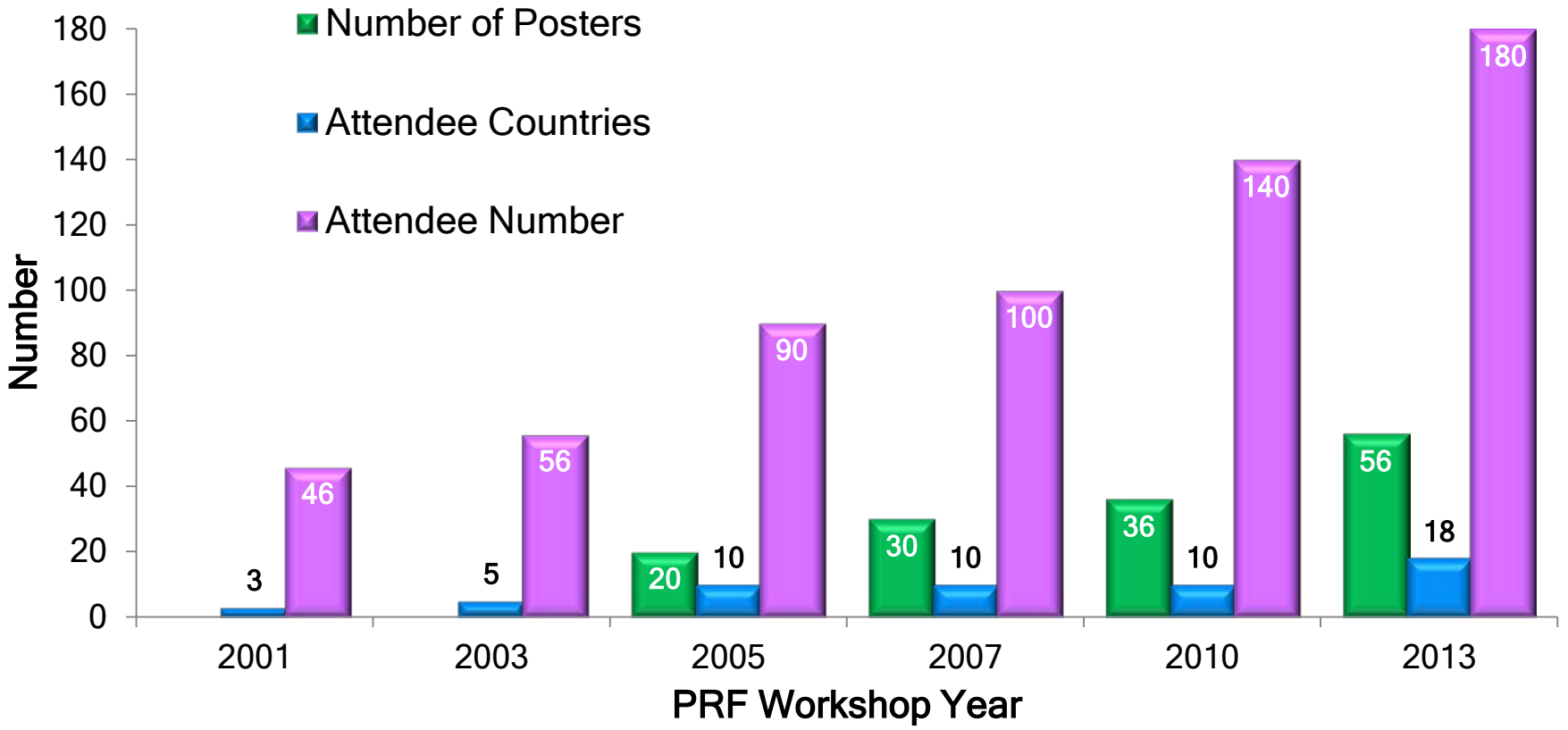
Growth of Global Interest In PRF Workshops



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4 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 (2011), Boston, MA

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NIH National Heart, Lung, and Blood Institute

genome.gov National Human Genome Research Institute National Institutes of Health

Scientific Publications

As of October 1, 2014:

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

- Publication list at www.progeriaresearch.org/cell_tissue_bank

24 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 #64

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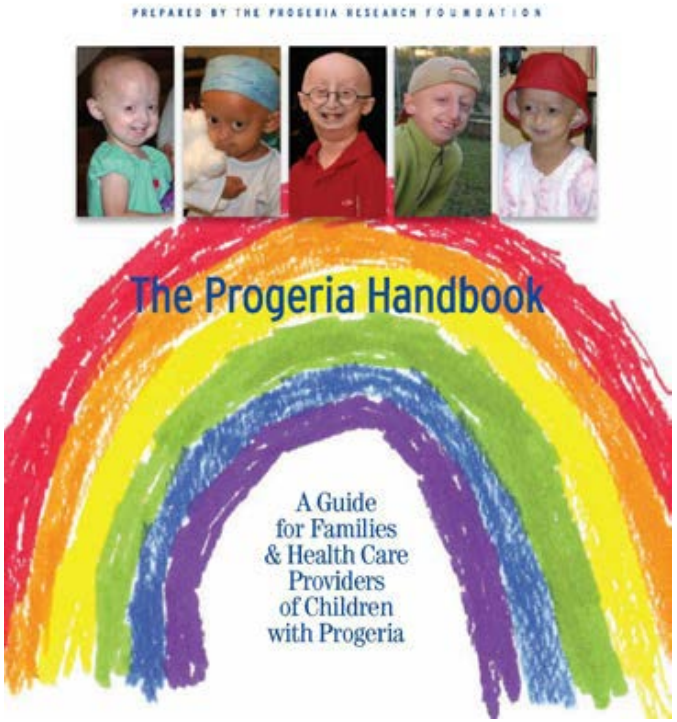
Progeria Clinical Care Handbook

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: **460**

As of October 1, 2014

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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

genome.gov
National Human Genome Research Institute
National Institutes of Health

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NIH Natural History Study Publications

As of October 1, 2014:

- Phenotype and course of Hutchinson-Gilford progeria syndrome. Gordon LB, Clauss S., Sachdev V, Smith AC, Perry MB, Brewer C, Zalewski C, Kim J., Soloman B, Brooks BP, Gerber LH, Turner ML, Domingo DL, Hart TC, Graf J, Reynolds JC, Gropman A, Yanovski JA, Gerhard-Herman M, Collins FS, Nabel EG, Cannon RO 3rd, Gahl WA, Introne WJ. *New England J. Med.*, 2008 Feb 7;358(6):592-604.

- Hutchinson-Gilford progeria syndrome: oral and craniofacial phenotypes. Domingo DL, Trujillo MI, Council SE, Merideth MA, Gordon LB, Wu T, Introne WJ, Gahl WA, Hart TC. *Oral Dis.* 2009 Apr;15(3):187-195. Epub 2009 Feb 19.

- Otologic and Audiologic Manifestations of Hutchinson-Gilford Progeria Syndrome. Guardiani E, Zalewsi C, Brewer C, Merideth M, Introne W, Smith AC, Gordon L, Gahl W, Kim HJ. *Laryngoscope.* 2011 Oct; 212(10):2250-2255.

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PRF-Funded Clinical Treatment Trials

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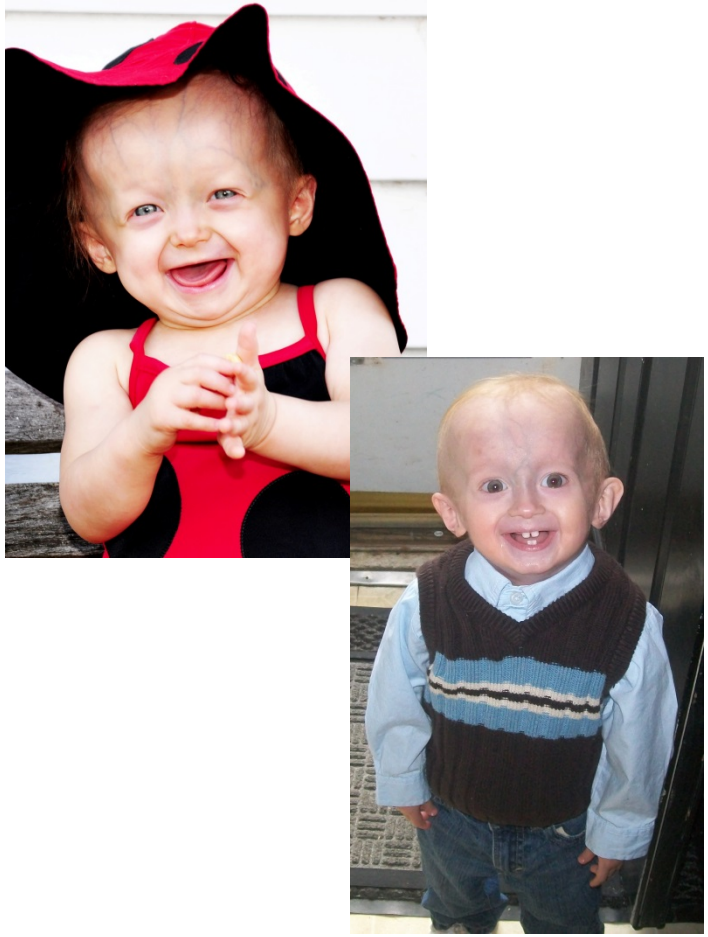
Clinical Drug Treatment Trials

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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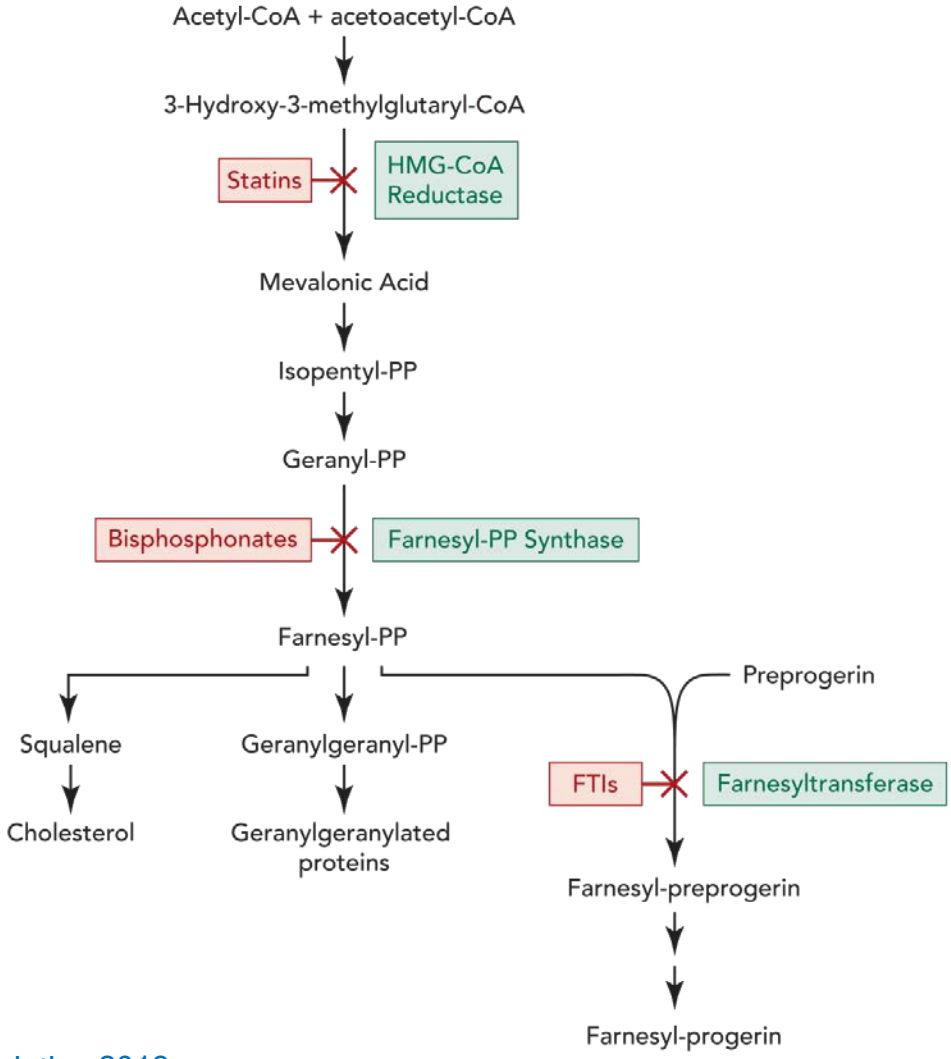
Current Therapeutic Intervention Strategies

Medications That Inhibit Farnesylation of Progerin



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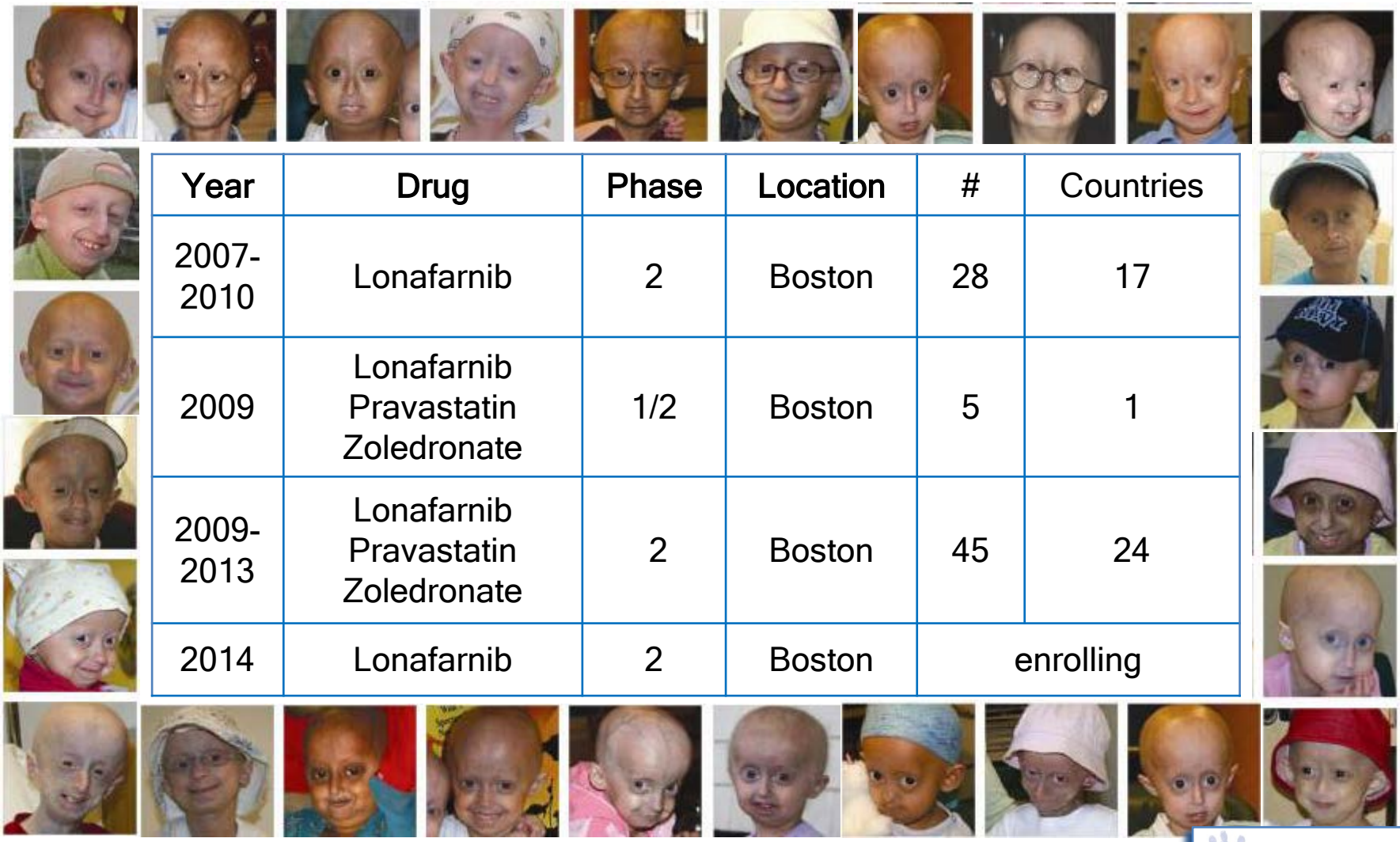
PRF Funds On-Going Clinical Treatment Trials



Year	Drug	Phase	Location	#	Countries
2007-2010	Lonafarnib	2	Boston	28	17
2009	Lonafarnib Pravastatin Zoledronate	1/2	Boston	5	1
2009-2013	Lonafarnib Pravastatin Zoledronate	2	Boston	45	24
2014	Lonafarnib	2	Boston	enrolling	

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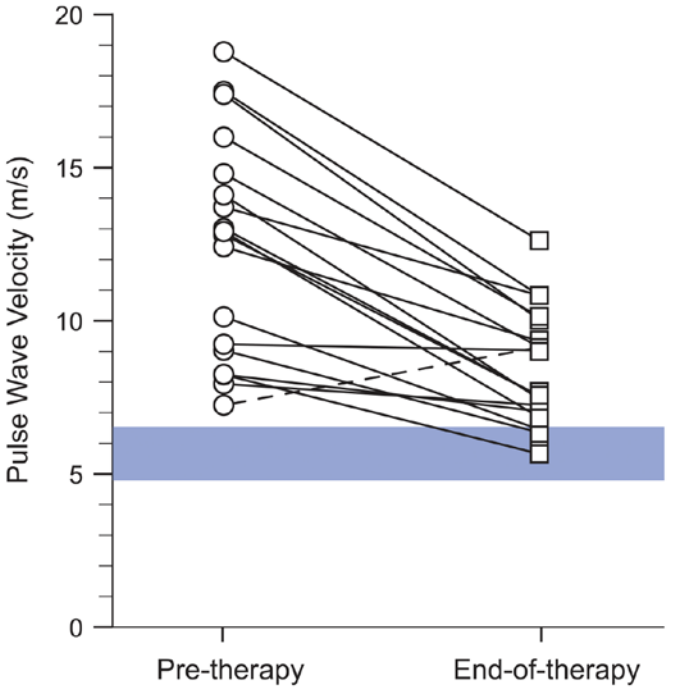
Treatment Trial Collaborations For Success

- **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 Merck**

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

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Clinical Treatment Trial Publications

As of October 1, 2014:

- **Dermatology:** Initial Cutaneous Manifestations of Hutchinson-Gilford Progeria Syndrome – *Pediatric Dermatology*, 2014,1-7.
- **Drug Effect:** Neurologic Features of Hutchinson-Gilford Progeria Syndrome after Lonafarnib Treatment – *Neurology*, 2013, 81:427-430.
- **Drug Effect:**, 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.
- **X-ray:** 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.
- **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., *J Bone Miner Res*. 2011 Jul;26(7):1670-9.

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Finding…
Diagnosing…
Studying…
Treating…
CURING

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Together We *WILL* Find The Cure!

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