



The Progeria Research Foundation

www.progeriaresearch.org

February, 2008

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BACK COVER

2007 Was an Amazing Year for PRF!

It has been an exciting year of intense progress toward our ultimate goal of developing treatments and a cure for children with Progeria. Thank you all for your steadfast support – **Together, we can accomplish anything!**

Progeria Clinical Drug Trial Fully Enrolled, Well Underway

In October 2007, the first-ever Progeria Clinical Drug Trial became fully enrolled - an exciting milestone in this historic trial! Twenty-eight children from sixteen countries are participating, ages 3 to 15.

And thanks to your support, PRF has now raised \$1.6 of the \$2 million needed to fund the trial. Let's make 2008 the year this campaign reaches its goal! [See pages 8-9 for more details.](#)

Niccolo from Italy and Julieta from Argentina are all smiles as they play in the hallway at Children's Hospital Boston's General Clinical Research Center.



PRF's 5th Scientific Workshop a Resounding Success

It was another dynamic, stimulating meeting of nearly 100 scientists and clinicians whose work continues to drive this fast-growing field of study. Attendees from 11 countries and 16 states – an all-time high! – gathered to share recent data, talk about new research directions, and set the stage for the next round of progress towards treatments and a cure for Progeria. [More on pages 4-5.](#)

Runners Race for PRF at the 112th Boston Marathon

Another first! PRF will be officially represented at this year's race. See page 12 for details and learn how you can sponsor these committed women.



Paula Kelly and Wendy Webber Nelson will have Sam cheering them on at the finish line.

PRF's Mission:

To discover the cure and effective treatments for Progeria and its aging-related disorders.

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You can be the first to hear
the latest PRF news!

Send us your email address
to learn of research
breakthroughs and other
events as the news happens.

info@progeriaresearch.org

Message from the President & Executive Director

Hello everyone,

When I write our newsletters, I am always delightfully amazed at the sheer volume of news to report on. This issue is certainly no exception! The number of new publications and grants, the success of the 5th scientific workshop, the record-breaking number of events and the amounts they raised, and the additional millions of people that we have reached all add up to a remarkably successful 2007, bringing us ever closer to our goal of finding a cure for Progeria.

More exciting changes include PRF's newest board members:

Karen N. Ballack, Esq. is a partner in the Silicon Valley office of Weil, Gotshal & Manges, LLP. She has extensive experience as an intellectual property transactional attorney, with emphasis on representing technology companies, particularly in the computer, internet, semiconductor, biotechnology, pharmaceutical and medical device industries. She also serves on the firm's Pro Bono Committee, Diversity Committee and Women@Weil Leadership Committee.

Chuck Bresnahan is the former defensive coordinator for the Cincinnati Bengals professional football team. He has been an NFL coach since 1994, previously with Cleveland, Indianapolis and the Oakland Raiders. He graduated from the US Naval Academy in 1982 and has enjoyed a long, successful career as a coach and sportsman.

Kim Paratore has been involved as a PRF volunteer since its inception, having chaired the first three Night of Wonder galas, as well as numerous other PRF fundraising events. Kim has also been involved in dozens of fundraising efforts for other charities. She currently serves on The Wenham Village Improvement Society.

PRF is proud to have these three dynamic people on its Board of Directors. With their diverse experience and expertise, they are sure to play an important role on PRF's governing body.

Thank you all for making the content in this newsletter possible. You are truly what drives our progress toward the cure!

I wish you all a happy, healthy and peaceful 2008.



They are gone
from our sight,
but never our memories

In Loving Memory...

Gone from our touch,
but never our hearts.



Wiradianty

Wiradianty “Ranti”, 11 years old, from Indonesia



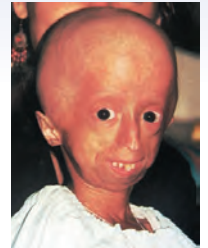
Zoe

Zoe, 13 years old, from Puerto Rico



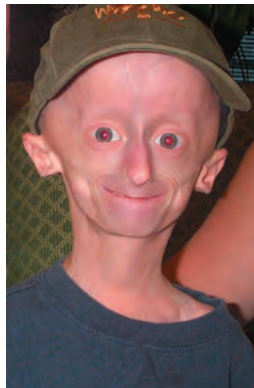
Ory

Ory, 10 years old, from the United States



Menecksche

Seth, 13 1/2 years old, from the United States



Seth

Burcu, 20 years old, from Turkey



Burcu

Maria, 9 years old, from Mexico



Maria

Menecksche, 13 years old, from Germany



2007 Progeria Research Foundation Workshop Reaches New Heights of Collaboration and Advancement of Progeria Research

Since 2001, PRF has organized five scientific conferences, all of which have had a profound impact on the course of Progeria research. These meetings have helped elevate Progeria research from a position of minimal scientific recognition to a vibrant field which includes new avenues for studying the mechanisms of aging and cardiovascular disease.

In November 2007, PRF held its 5th conference, a 3-day meeting in Boston, MA. Speakers included leading scientists in the fields of heart disease, aging, genetics, and laminopathies.

Workshop Organizing Committee:

Drs. Leslie Gordon, Christine Harling-Berg, and Frank Rothman

Workshop Advisory Panel:

Drs. Robert Goldman, George Martin, Susan Michaelis, Tom Misteli, and Huber Warner.

Major Session Topics:

- **Cardiovascular Disease:** Talks by Drs. Marie Gerhard-Herman (Harvard, Boston), Elizabeth Nabel and Francis Collins (NIH, Bethesda) centered on characterizing heart disease in children with Progeria and in mouse models of Progeria. Presentations compared Progeria with cardiovascular disease in the general aging population. Dr. Nabel presented data from ongoing analysis of the NIH natural history study. Dr. Collins showed exciting new data on the effects of FTI drug treatment in Progeria mice.



Dr. Elizabeth Nabel, Director of the National Heart, Lung and Blood Institute, talks about cardiovascular disease in Progeria.

- **Aging:** Dr. Karima Djabali (Columbia U., New York) explored evidence that the Progeria protein called "progerin" is present not only in children with Progeria, but also in human cells and tissue of the non-Progeria, aging population. Dr. Yue Zou, (E. Tennessee State U.) focused on how cell signaling and cell cycling in aging and Progeria cells compare. Both presentations highlighted that we can understand cellular aging better by studying Progeria.

- **Laminopathies:** The gene responsible for Progeria is called LMNA ("lamin-A"), and diseases found on the gene are called laminopathies.



Dr. Joanna Bridger (Brunel U., England) and Dr. Jan Lammerding (Harvard, Boston) demonstrated how studying each laminopathy yields valuable information on all of these diseases by comparing studies of Progeria and laminopathy cell abnormalities with normal cell properties.

• Lamin Biology and Nuclear Membrane Proteins:

Presentations by Dr. Robert Goldman (Northwestern U., Chicago), Dr. Lucio Comai (UCLA, Los Angeles), Dr. Michael Sinensky (East Tennessee State U.) and Dr. Bryce Paschal (U. Virginia Med. School) focused on various aspects of the biochemistry of normal and abnormal protein processing in nondiseased states and in Progeria. Studies reveal that there are several points along the processing pathways that may lead to treatments or a cure for Progeria. Studying both normal and abnormal pathways are essential to these goals.

• Bone, endocrine, extracellular matrix and dermatological studies of Progeria:

Dr. Catherine Gordon (Children's, Boston) compared Progeria with diseases such as osteoporosis, insulin resistance, and scleroderma. Data was derived from baseline findings from studies conducted at Children's Hospital Boston, and clinical chart analysis from PRF's Medical & Research Database. In addition, Dr. Stephen Young (UCLA, Los Angeles) presented studies of fat loss in Progeria.



Progeria clinical drug trial Principal Investigator Dr. Mark Kieran talks about FTI use in the trial, and results from other cancer trials using FTIs. The ongoing Progeria clinical trial was clearly a main topic of interest.

• Treatment Strategies:

Dr. Mark Kieran, (Children's, Boston) presented the design and rationale of the ongoing clinical trial using the drug lonafarnib (an FTI) for Progeria and other diseases. Studies on improvement of disease after FTI treatment of Progeria mouse models was presented by Dr. Francis Collins.

Dr. Irina Conboy (U. California, Berkeley) presented results from studies on the effects of stem cell replacement to overcome increased rates of cell death in Progeria.

PRF has brought together scientists and clinicians from all over the world, to share their cutting edge scientific data and foster collaboration in the fight against this lethal disease. Many of the workshop attendees have said the workshops and other programs that PRF offers are essential to conducting Progeria-related work.



Dr. Carlos Lopez-Otin on "Exploring Progeria therapies: lessons from mouse models"

Other potential strategies for future treatment of Progeria were presented by Dr. Carlos Lopez Otin (U. Oviedo, Spain) who has conducted exciting new drug treatments in a mouse model of Progeria, and by Dr. Tom Misteli (NIH) who is searching for novel drug treatments in Progeria using a newly developed small molecule drug screen.

"People are watching what is going on with Progeria and how this progresses. I know some, especially the rare disease communities, are keeping a close eye on what we are doing here. It's very exciting to be part of it."

– Tom Misteli from the National Cancer Institute.



Dr. Tom Misteli



Sammy and his mom, from Italy, were part of a unique panel of families that shared their experiences of living with Progeria..



Dr. Susan Michaelis (Johns Hopkins, Baltimore, MD), a member of the workshop advisory committee, chairing the closing session.



Dr. Frank Rothman, workshop organizer and member of PRF's Medical Research Committee, chairs a panel discussion on 2007 workshop lessons and future research directions, with Drs. Tom Glover, Francis Collins, Yosef Gruenbaum and Ted Brown.

"I know of no other rare genetic disease that has gone from gene discovery to clinical trial in under four years – a phenomenal testament to the hard work of The Progeria Research Foundation."

- Francis Collins, MD, PhD,
Director of the National Human Genome Research Institute that mapped the human genome, workshop speaker and co-discoverer of the Progeria gene.

ATTENDEE FEEDBACK RAVES ABOUT PRF!

Here is what some of the participants had to say on their workshop evaluations:

"An excellent mixture of basic science with clinical research..."

"A great meeting. You are really making a difference! I wish all disorders had such a well-organized foundation to support and encourage research and progress..."

"The best part was connecting with others doing Progeria research to gain knowledge and insight from experts. I now know lots of people I can contact to help with my aspect of Progeria research..."

"Everyone should be very proud of the accomplishments made and I look forward to what the future holds for Progeria discovery..."

Many thanks to our scientific advisory panel, our session chairs, and our workshop sponsors:



PRF Research Grants Surpass \$1.5 Million Mark!

Four more grants funded in 2007

Since its inception 8 years ago, PRF has awarded **23 grants** to researchers throughout the world to help advance the field of Progeria research, reaching a landmark total investment of just **over \$1.5 million!** The high-quality work produced by these scientists has resulted in important findings published in well-respected journals, which in turn creates even wider interest in what many deem one of the fastest-growing areas of science.

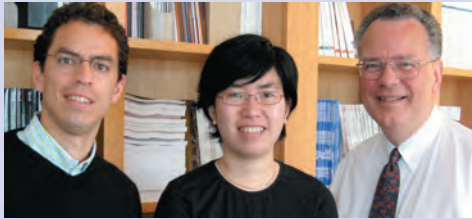
Here are the latest researchers to join in our efforts:

Michael A. Gimbrone, Jr., MD,

Brigham and Women's Hospital (BWH), Boston, MA

Endothelial Dysfunction and the Pathobiology of Accelerated Atherosclerosis in Hutchinson-Gilford Progeria Syndrome (HGPS)

Progeria affects multiple organ systems in various ways, but perhaps its most serious manifestations are in the cardiovascular system, where it results in an unusually severe and accelerated form of atherosclerosis,



Gimbrone (far right), with project collaborators Drs. Guillermo Garcia-Cardena and Belinda Yap

leading to fatal heart attacks or strokes at an early age. The heart and blood vessels are lined by a transparent, single-cell-thick membrane, consisting of vascular endothelial cells (ECs), which nor-

normally forms nature's container for blood. Pathologic changes in this vital lining, collectively termed "endothelial dysfunction", are now recognized as critical to the development of vascular diseases, such as atherosclerosis. The purpose of this study is to determine how the mutant protein progerin influences the structure and function of ECs, potentially leading to endothelial dysfunction. This study promises to provide mechanistic insights into the vascular pathologies of HGPS, and hopefully will lead to novel strategies for its effective treatment.

Dr. Gimbrone is a Professor of Pathology at Harvard Medical School and Chairman of Pathology at BWH, and Director of the BWH Center for Excellence in Vascular Biology.

Bryce M. Paschal, PhD,

University of Virginia School of Medicine, Charlottesville, VA

Nuclear Transport in Hutchinson-Gilford Progeria Syndrome

Progeria is caused in part by abnormalities in the wall of the nucleus. The nucleus is at the center of each cell, and contains our DNA. Nuclear pores allow the movement of molecules back and forth across the nuclear wall, so that they can communicate with the rest of the cell. Chromatin is the complex of DNA and protein



that makes up chromosomes. As a principle component of the nuclear wall, lamin A (which is mutated in Progeria) contributes structural plasticity to the nuclear wall, provides attachment sites for chromatin, and organizes nuclear pore complexes in the membrane. Dr. Paschal is exploring how defects in the nuclear lamina observed in HGPS affect the structure and function of the nuclear pore complex.

Dr. Paschal is Associate Professor of Biochemistry and Molecular Genetics at the University of Virginia School of Medicine, where he is a member of the Center for Cell Signaling and the UVA Cancer Center.

Thomas N. Wight, PhD,

The Hope Heart Program, Benaroya Research Institute at Virginia Mason, Seattle, WA

The use of a mouse model of HGPS to define the influence of Lamin AD50 expression on vascular extracellular matrix production and the development of vascular disease.



The extracellular matrix (ECM), or connective tissue, is comprised of molecules that surround cells and act as both structural support and a means for a cell to communicate with its neighbors. During the development of atherosclerosis, these molecules change and drive the development of the plaque - a process that takes

decades in most humans. In Progeria, this process is drastically accelerated and the specific changes in ECM are not fully understood. Using a mouse model of Progeria, Dr. Wight and his doctoral student, **Ingrid Harten, M.S.**, will study the effect that the Progeria gene has on changes in a group of connective tissue molecules, called proteoglycans, which are known to play a significant role in atherosclerotic plaque development.

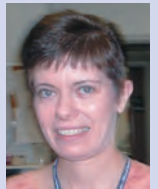
Dr. Wight is a Research Member at the Benaroya Research Institute and an Affiliate Professor of Pathology at the University of Washington. He is a past awardee of an American Heart Established Investigatorship, has served on NIH and AHA study sections, and currently is on the editorial board of four scientific journals.

Jemima Barrowman, PhD,

Johns Hopkins School of Medicine (JHSM), Baltimore, MD

Fundamental Mechanism of Lamin A Processing: Relevance to the Aging Disorder HGPS

HGPS is caused by a mutation in the gene encoding lamin A. Normally, lamin A undergoes a transient series of biochemical modifications to its C-terminus, including the addition of a lipid (farnesyl) and a carboxyl methyl group. In this study, Dr. Barrowman will investigate the possibility that the permanent retention of the carboxyl methyl group may contribute to progerin's toxic cellular effects. If so, drugs that inhibit carboxyl methylation could also be considered as a potential therapeutic option for progeria. He will also investigate the possibility that progerin may mimic lamin B, a permanently farnesylated relative of lamin A.



Dr. Barrowman is a Postdoctoral Researcher in the Department of Cell Biology at JHSM, working in the laboratory of PRF research grantee Dr. Susan Michaelis, whose lab has made important contributions in documenting the potential benefits of using farnesyl transferase inhibitors (FTIs) to treat Progeria.

Scientific Publications Show Progeria Research is Thriving

PRF grantees lead the charge...

Every year, more scientific discoveries are published that advance our understanding of Progeria. These publications are read by millions of scientists and physicians, and stimulate research throughout the world. Researchers rely on PRF grant funding, the PRF Cell & Tissue Bank and the PRF Medical & Research Database for their discoveries. Here are highlights of PRF-supported scientific publications:

In October 2007, two articles were published in the esteemed medical journal *Pediatrics*, a journal of the American Academy of Pediatrics, and the most-cited journal in its field. These articles discussed the essential contribution of PRF Medical & Research Database information in designing the Progeria clinical drug trial.



Dr. Mark W. Kieran

“New Approaches to Progeria” is written by Progeria clinical drug trial Principal Investigator **Dr. Mark W. Kieran** of Dana-Farber Cancer Institute and Children’s Hospital Boston, and **Drs. Leslie Gordon and Monica Kleinman**, Drs. Gordon and Kleinman are the Progeria drug trial co-chairs, and Dr. Kleinman is a member of

PRF’s Board of Directors. This article highlights the progress made in this field, and introduces the scientific community to the Progeria clinical drug trial. The article states, “In the span of less than a decade this disease has progressed from an interesting phenotype to



Dr. Monica Kleinman with Sam

one in which the gene defect has been identified, animal models have been created and tested with drugs that target the primary disease pathway, and significant clinical baseline data for the support of a clinical trial have been obtained.” *Pediatrics* Oct;120(4):834-41.



Dr. Leslie Gordon

“Disease Progression in Hutchinson-Gilford Progeria Syndrome: Impact on Growth and Development”, by PRF’s Founder and Medical Director **Leslie B. Gordon, MD, PhD, Kathleen M. McCarten, MD, Anita Giobbie-Hurder, MS, Jason T. Machan, PhD, Susan E. Campbell, MA, Scott D. Berns, MD, MPH, and Mark W. Kieran, MD, PhD**. This article sets forth the scientific basis for using weight as the primary parameter in the current Progeria clinical drug trial. The weight data was obtained entirely from the PRF Medical & Research Database. This article also describes new findings in the growth and development of bone disease in Progeria, using X-rays collected and analyzed from the Database. *Pediatrics*.120 (4):824-33.



Dr. Stephen G. Young

“Increased Progerin Expression Associated With Unusual LMNA Mutations Causes Severe Progeroid Syndromes”, by **Casey L. Moulson, Loren G. Fong, Jennifer M. Gardner, Emily A. Farber, Gloriosa Go, Annalisa Passariello, Dorothy K. Grange, Stephen G. Young, and Jeffrey H. Miner** is a study of two patients with extraordinarily severe forms of Progeria. Cells from these patients improved when treated with an FTI.

Thus, FTIs may prove to be useful even when progerin expression levels are unusually high. *Human Mutation* 0, 1-8, April 2007

Eliminating the synthesis of mature lamin a reduces disease phenotypes in mice carrying a hutchinson-gilford progeria syndrome allele, by **Yang SH, Qiao X, Farber E, Chang SY, Fong LG, Young SG**. These studies suggest that compositional changes in the nuclear lamina can influence both the steady-state levels of progerin and the severity of progeria-like disease phenotypes. *J Biol Chem*. 2008 Jan 4

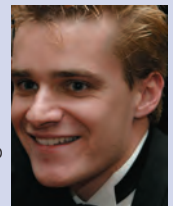
Treatment with a farnesyltransferase inhibitor improves survival in mice with a Hutchinson-Gilford progeria syndrome mutation, by **Yang SH, Qiao X, Fong LG, Young SG**. This study found that the FTI significantly improved the survival of Progeria mice, and also improved body weight curves and reduced the number of spontaneous rib fractures. This study provides further evidence for a beneficial effect of an FTI in Progeria. *Biochim Biophys Acta*. 2007 Nov 26

The Mutant Form of Lamin A that Causes Hutchinson-Gilford Progeria Is a Biomarker of Cellular Aging in Human Skin, by **McClintock D, Ratner D, Lokuge M, Owens DM, Gordon LB, Collins FS, Djabali K**. Findings demonstrate that progerin expression is a biomarker of normal cellular aging and may potentially be linked to terminal differentiation and senescence in elderly individuals. *PLoS ONE*. 2007 Dec 5

Accelerated telomere shortening and replicative senescence in human fibroblasts overexpressing mutant and wild-type lamin A, by **Huang S, Risques RA, Martin GM, Rabinovitch PS, Oshima J**. This study demonstrates that changes in lamina organization may cause accelerated telomere attrition, which leads to rapid replicative senescence and progeroid phenotypes. *Exp Cell Res*. 2008 Jan 1;314(1):82-91.

Involvement of xeroderma pigmentosum group A (XPA) in progeria arising from defective maturation of prelamin A, by **Liu Y, Wang Y, Rusinol AE, Sinensky MS, Liu J, Shell SM, Zou Y**. This study proposes that the uncharacteristic localization of xeroderma pigmentosum group A (XPA) contributes to the premature aging phenotypes observed in progeria. *FASEB J*. 2007 Sep 11

Mechanisms of cardiovascular disease in accelerated aging syndrome, by **Capell BC, Collins FS, Nabel EG**. This review highlights recent advances in the biology of premature aging uncovered in progeria and other accelerated aging syndromes, advances that provide insight into the mechanisms of cardiovascular diseases ranging from atherosclerosis to arrhythmias. *Circ Res*. 2007 Jul 6;101(1):13-26.



Brian C. Capell

Mouse models of the laminopathies by **Stewart CL, Kozlov S, Fong LG, Young SG**. This team has created mouse lines carrying some of the same mutations that result in progeria, mice lacking lamin B1, and mice expressing only one of the A type lamins. These mouse lines are providing insights into how changes to the lamina affect the mechanical integrity of the nucleus and signaling pathways that may contribute to disease. *Exp Cell Res*. 2007 Jun 10;313(10):2144-56.

Cell nuclei spin in the absence of lamin b1, by **Ji JY, Lee RT, Vergnes L, Fong LG, Stewart CL, Reue K, Young SG, Zhang Q, Shanahan CM, Lammerding J**. Mutations of the nuclear lamins cause a wide range of human diseases, including HGPS. A-type lamins are frequently studied in Progeria, but few data exist on the biological role of B-type lamins. These findings demonstrate that lamin B1 serves a fundamental role within the nuclear envelope: anchoring the nucleus to the cytoskeleton. *J Biol Chem*. 2007 Jul 6;282(27):20015-26.

continued on page 8

A lamin A protein isoform overexpressed in Hutchinson-Gilford progeria syndrome interferes with mitosis in progeria and normal cells, by Cao K, Capell BC, Erdos MR, Djabali K, Collins FS. Demonstrating that small amounts of progerin exist in normal fibroblasts, and a significant percentage of these progerin-expressing normal cells are binucleated, implicating progerin as causing similar mitotic defects in the normal aging process, these findings present evidence of mitotic abnormality in HGPS and may shed light on the general phenomenon of aging. *Proc Natl Acad Sci USA* 2007 Mar 20; 104(12):4949-54.



Dr. Robert D. Goldman

Alterations in mitosis and cell cycle progression caused by a mutant lamin A known to accelerate human aging, by Dechat T, Shimi T, Adam SA, Rusinol AE, Andres DA, Spielmann HP, Sinensky MS, Goldman RD. Study results provide insights into cell cycle abnormalities and the mechanisms responsible for premature aging and also shed light on the role of lamins in the normal process of human aging. *Proc Natl Acad Sci USA* 2007 Mar 20; 104(12):4955-60.

For a more comprehensive scientific publications in Progeria, you can do a PubMed search at www.ncbi.nlm.nih.gov, typing in "Hutchinson Gilford Progeria"

Worldwide Awareness Continues in Many Other Ways...

How else does information about Progeria reach millions of people – including researchers, clinicians, families and the general public – worldwide? Here are just some of the ways PRF has helped bring Progeria to the forefront of scientific research efforts:

Books and Magazines:

Dr. Leslie Gordon wrote a chapter on Progeria for the *World Book Online Reference Center* www.worldbookonline.com/wb/Article?id=ar447180 and the print edition of the *2008 World Book Encyclopedia* (In Press)

Dr. Gordon's feature article *Progeria: Growing Old Too Fast* appeared in *Your World*, a publication of the Biotechnology Institute. Online at www.biotechinstitute.org/yourworld.html, print edition Fall 2007, Vol. 16 (2).

Dr. Gordon, W. Ted Brown and Frank Rothman wrote a chapter entitled *LMNA and the Hutchinson-Gilford Progeria Syndrome and Associated Laminopathies* for the book *Inborn Errors of Development: The molecular basis of clinical disorders of morphogenesis* (2007, 2nd ed.) 139: 1219-1229. (In Press)

Dr. Gordon and PRF's Executive Director Audrey Gordon, Esq. have also contributed to National Geographic's book entitled *Medical Mysteries* (In Press).

Presentations:

In May 2007, PRF's Medical Director Dr. Leslie Gordon had the honor of presenting *The Charles O. Cooke, MD Distinguished Visiting Lecture* at Brown University's Commencement in Providence, Rhode Island. Her talk was entitled, "Taking Progeria from Obscurity to the Cutting Edge: A Parent-Scientist's Perspective on Saving Children with a Premature Aging Disease". The person chosen for this distinction is one who works "... in any branch of medicine which can hold promise of significant and lasting benefit to medical education at Brown or to the community in the delivery of health care services."

Progeria Clinical Drug Trial in Full Swing!

The trial officially began on May 7th, 2007, with two children arriving in Boston for their first of seven research visits over a two-year period. An average of two families have been flying to Boston each week since then, and in October 2007, the trial became fully enrolled.

The children are returning to Children's Hospital Boston every four months, for testing and to receive a new supply of the drug, called lonafamilib (or FTI). They stay in Boston for 3-8 days each visit, and when at home, the Boston team works with their local doctors on periodic health reports and oversight of the child's condition.

"Ambassadors" Continue to Play a Major Role

PRF's Volunteer Ambassadors are keeping very busy! These volunteers pick up families from the airport (accompanied by a translator if necessary) and provide important information such as their hospital schedule, as well as water, snacks and small gifts for the children. They then bring them to their place of lodging and help get them settled in. The Ambassador Program has proven very effective in helping the families adjust to the trial's logistical demands, particularly for those who do not speak English.



Ambassador Audrey Lampert (2nd from left) at Logan airport with Claudia and her mom, who flew in from Portugal in January. With them are Priscila and friend, Simmons College students who translated for the group.

PRF has amassed a team of volunteer translators speaking thirteen languages to help bridge the language gap for the non-English speaking families involved in the trial. Please contact us at translators@progeria-research.org if you are fluent in any of the following languages – we can

always use more translators on our team! Spanish, Italian, Hebrew, Arabic, Polish, Romanian, Urdu, Danish, Dutch, Telugu, Japanese, Portuguese, and Korean.



Milagros, 7, from Argentina, plays in the game room in between testing appointments.



Sumaira, 7 years old, from Pakistan was the 28th child to enroll in the clinical drug trial.



Vasile, 8, from Romania, and "friends" spend the day at Children's Hospital Boston.



Jesper, 10 years old, from Denmark



Michiel, 8, from Belgium with Hayley, 9, from England in June 2007 at Children's Hospital Boston. The children have now been together for three visits to Boston



We're in the Final Stretch...

Thanks to your support, PRF has raised \$1.6 of the \$2 million needed to fund this drug trial. This money pays for the clinical testing, in-hospital medically trained translators, flights, food, staff, and medical care. Let's make 2008 the year we reach our trial campaign goal!

To donate on line, please visit:
http://www.progeriaresearch.org/ways_to_donate.html

All the Comforts of Home

Almost all of the families are being housed at either The Family Inn of Brookline or Children's Hospital Boston's Devon Nicole House (DNH). Both have generously donated the lodging, and are exceptionally accommodating. The families (and PRF), in turn, are very appreciative of the amenities and hospitality provided.

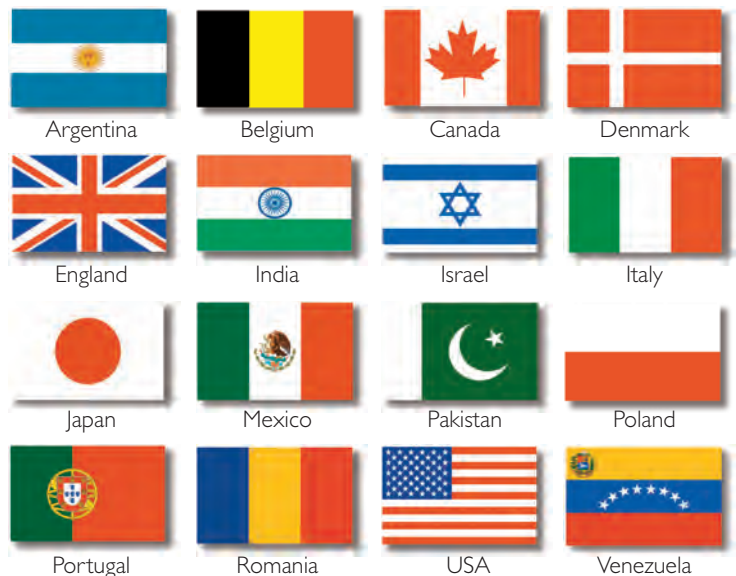
News of PRF and the Trial Reaches Millions

In January 2007, The Progeria Research Foundation and the drug trial were featured in a front-page feature article in the Wall Street Journal.

In October 2007, PRF and the trial gained additional exposure, mainly to a science/research audience, when two articles on the clinical trial parameters were published in Pediatrics (see page 7).

And in November 2007, baseline clinical studies of the children enrolled in the trial were presented at PRF's International Scientific Workshop on Progeria (see pages 4-5). These cutting-edge discoveries regarding the pathological basis of disease in Progeria are helping us to understand more about the disease process and how best to treat the children.

Children come to Boston from the following countries:



Hundreds Rev it Up for Night of Wonder 2007!



Raising an astonishing, record-breaking \$340,000, this year's event will surely Drive the Cure!

A sold-out crowd gathered on November 10th at The Royal Sonesta Hotel in Cambridge, Massachusetts for an incredible evening of excitement, as the live auction reached new heights and bidders went wild for sports tickets, luxury trips and lots more.

This year's theme put people in the driver's seat to find a cure for Progeria, as the gala is PRF's major fundraiser.

Guests were entertained by auctioneer Paul Zekos and wowed by the race theme décor, as they bid on over 200 auction items, dined on gourmet food and drink – including our signature "time trial-tinis" – and danced to music by The New Life Band.

Thank you to everyone who helped make this event a phenomenal success!



To get everyone "geared up" for the evening, a Race Car and Pro All Stars Series driver Joey Porciello were on hand. Pictured by the car are Sarah, Dan and Ryan Berns.



PRF Executive Director Audrey Gordon looks on as Sam Berns wows the crowd just before the live auction, crying out, "Ladies and Gentlemen, Start Your Engines!"



Gala co-chairs Debbie Ponn and Vickie Robbin, with car designer and Overhaulin' star Chip Foose, the honorary chair.

THANK YOU TO OUR SPONSORS - Your generosity is WONDERful!





Sponsors Elliott and Marjorie Hillback at the VIP reception.



Ivy and Peter Dorflinger enjoy the evening's festivities.



Bob and Linda Mendelson are all smiles for the night's success.



Congratulations to Julie Pritchard (l), who was awarded this year's Amy Award by PRF Medical Director Leslie Gordon. The Amy Award is given to PRF volunteers with exceptional qualities of optimism and dedication to PRF's mission.



These guests are all smiles during the dinner/dancing part of the evening.



Sponsors Cheryl and Richard Durgan won tickets to the Superbowl!



Ladies from sponsor Karen Martin Fund have a blast at their third Night of Wonder.



Everyone gets ready to bid at the live auction, which was the highlight of the evening!

Anonymous
Linda and Bob Mendelson
Elaine and Skip Wohlner
Leslie Gordon and Scott Berns
David Elovitz
Tricia and Bob Flynn

Burt & Barbara Gordon
Hayden Wood Insurance Agency
Robyn & Tom Milbury
Norseland, Inc.
Persian Acceptance Corp.
Elliott & Marjorie Hillback
Foundation

Karen A. Martin Memorial Fund
Therese and Kurt Melden
Kim & Joe Paratore
Debbie & David Ponn
Vickie & Stu Robbin

We continue to be amazed by - and grateful to - the ever-growing number of families who help raise money in their own communities around the globe. Most never ran an event before, but with the help of their friends, family and PRF staff, they succeed. We salute these courageous parents, grandparents, aunts, uncles and their supporters, because it is only **Together** that **we WILL find the cure!**

Middleboro, Massachusetts: 2nd Annual Walk to Honor Kristian McGuinness

Classmates, teachers, friends and family of Kristian came together at his former school on a warm, sunny Sunday in September – what would have been Kristian’s 5th birthday – for a 2-mile walk in his memory. Thank you to all who participated, and for honoring Kristian in this way.



Volunteers in front of the bright blue balloons that were let go at the start of the race.

Markesan, Wisconsin: 3rd Annual Megan Nighbor Benefit

Hundreds turned out last April for a full day of activities as they raised money for the First-Ever Progeria Clinical Trial. Everyone enjoyed food, raffles, a bake sale like you’ve never seen, a fantastic live auction and pledge bowling. The event raised nearly half the amount needed to pay for one child to participate in the trial!



Megan and her miniature pony Star, a surprise gift at the 2nd annual event.

South Africa: Golf for Beandri

The friends and family of Beandri, who just turned two, organized a golf day and dinner at Irene Country Club near Pretoria, SA’s capital. Although Beandri slept most of the day, everyone else enjoyed a terrific day on the course. Many thanks to sponsor Struben Street Motors – and to Beandri’s family, who plans to make this an annual event!



Evansville, Indiana: 3rd Annual Sarah Kennedy Golf Tournament

It was another amazing year, thanks to Sarah’s grandfather Chris Kempf, who now organizes this event every spring for nearly 150 golfers at Eagle Valley Golf Course. How wonderful!

Italy: “Italian Association For Progeria - Sammy Basso” Holds More Events

This group of family and friends of Sammy continues to raise money and awareness for Progeria research through a variety of events and media opportunities. Sammy has appeared on popular talk shows, and is now well-known around the country!



The Association’s logo, featuring Sammy’s favorite reptile, the salamander.

Chapter News

Pennsylvania: Grandparents organize PRF’s 5th chapter

PRF welcomes Carolyn and Jim Schoonover, grandparents of 1-year-old Cameron and directors of PRF’s newest chapter, to our team! They have already raised thousands of dollars selling their “Purses for Progeria”, hand-knit creations made with love by dozens of volunteer knitters. Order yours today by emailing purses4progeria@comcast.net



Cameron enjoys a Thanksgiving treat.

California: Foose Family Drives Events with Car Community

YearOne’s Braselton Bash Shatters Fundraising Record. It was a stunning “upset”: the 2007 Braselton Bash in Georgia raised over \$125,000 for Progeria research – UNBELIEVABLE! It started with a VIP Texas Hold ‘em Poker Tournament and live auction. Then thousands turned out the next day for the car show, autographs with Chip, and a silent auction. The staff and event volunteers worked in the blazing heat without a single complaint – in fact, when thanked, they just said they were happy to help such a great cause.



The check presentation: Vickie, Debbie, Audrey, Chip, YearOne President Kevin King, Marci, Mike and Pat

3rd Time's a Charm for Santa Barbara "Wheels and Waves" Show

For the 3rd Year in a row, PRF's CA chapter has teamed up with this fun car show. Chip and his family (especially mom Terry!) were hard at work selling tickets and t-shirts, auctioning off Foose items, and signing autographs for fans. Each year they have increased the amount raised!

Ohio: Halko Family Inspires Community to Hold Events

2nd Annual Kaylee's Course 5k: Running at Full Steam!

It was another successful run, with hundreds participating to support Kaylee and her family. This year brought in even more sponsors, walkers and runners – TERRIFIC!



Kaylee and friends race to the finish line

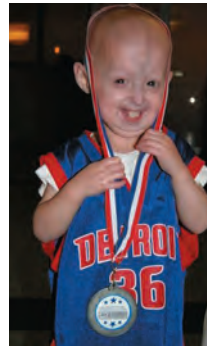
Getting into the Holiday Spirit

For the last 2 years, Whitehouse Christmas Tree Farm donated \$5 for every tree sold in December. Hundreds came out to the farm to support PRF's Ohio chapter.

Kaylee and farm owner Duke Wheeler are all smiles for the holidays!



Michigan: Lindsay Makes Miracles Happen



2nd annual Miles for Miracles

Fun Run/Walk. Hundreds came out for this fun family event, a 3 mile run/2 mile walk at Fountain Park in Flat Rock, MI. Thanks to the generous sponsors, auction item donors and others, they raised a record-breaking amount – AMAZING!

Lindsay is all smiles at a Detroit Pistons game as she and her parents receive the Michigan Heroes Award for their efforts to fight Progeria.

England: "Hayley's Hope- Progeria Research in the UK" is Music to our Ears

Hayley's family and friends continue to raise funds for PRF by promoting the CD Voices of Tomorrow through benefit concerts and autograph signings by Hayley, and they have held other events as well. The family has also appeared in several TV, radio and newspaper pieces locally and nationally to promote awareness of Progeria research – REMARKABLE!

Hayley is starstruck as American Idol's Simon Cowell checks out the *Voices of Tomorrow* CD

You can buy the CD and other items at http://www.progeriaresearch.org/shop_in_our_store.html



Don't Miss These Upcoming Events!

Please Sponsor Boston Marathon Runners Running for Children with Progeria

April 21, 2008 in Boston, MA: Come cheer on Paula Kelly, Wendy Webber Nelson and Meg Gannon as they run in the 112th Boston Marathon, one of the world's most well-known and prestigious road racing events, on behalf of PRF.

Please sponsor Paula and Wendy by donating at www.firstgiving.com/PRF

Meg will be running her 4th Boston marathon – whew! – wearing a t-shirt with all the kids' names that are participating in the trial. **On April 28, 2008,** Meg and co-organizer Tom Spataro will hold a **"Drive for Dreams" Golf Tournament** at the Pinehills Golf Club in Plymouth, MA to help benefit PRF. Go to www.progeriaresearch.org/drivefordreams for more information on how you can be a part of this event, which features dinner and an auction after a fun day on the course.

Thank you, Meg, Paula and Wendy, for taking on such a monumental challenge to help raise awareness and funds for children with Progeria.

Miracle Makers in 2007

We are continually amazed – and grateful – to the many students, companies and others who learn of PRF's important work and join in to help.

Please visit www.progeriaresearch.org/get_involved for lots of ideas on how you can be part of making the miracle of a cure happen.

ROCK ON!

The 4th graders at St. Joan of Arc in Ohio raised almost \$6,100 at a Rock-A-Thon they held in February 2007, where they danced for hours to raise money for PRF, in honor of Kaylee



Halko. The parents were so pleased and proud of their children that they had an All School Assembly to announce the amount raised and show a slide show presentation of the event. Thank you, 4th graders, you did an amazing job! "The children had so much fun that night," said teacher/organizer Sandy McKinnon.

Piano Practice-a-thon is Music to PRF's Ears!



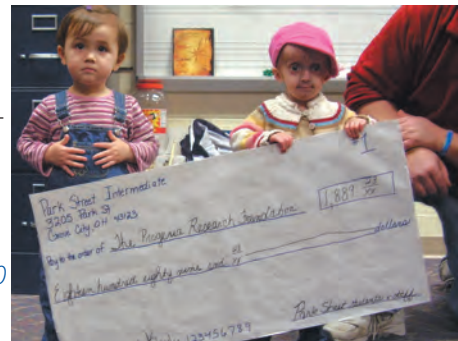
Pianist and piano instructor Shuai Wang-Bertalan of Cleveland, Ohio and her students got sponsors to support each minute they practiced during the month of February. This talented group raised \$500. Thank you for "Playing for Progeria"!

Long Time Supporter Donates Art Sales \$ to PRF

Mort Halper has not only supported PRF since its inception, but he is also a lifelong recreational artist. In July 2007, his family surprised him for his birthday by holding his first solo show, where dozens of his beautiful pottery creations were displayed. Mort then donated the sales from this show to PRF. (Mort was also a finalist in the 2007 Texas Hold 'em Poker Tournament, and donated his winnings from that event to PRF as well.) Mort and Brenda, his wife of 47 years, continue to help make the world a more beautiful place, through both art and their charitable giving.

Park Street Intermediate School Spreads PRF Message

During February 2007, Mrs. Lee's 5th grade class at Park Street Intermediate School in Grove City, OH, raised awareness and held events for the school's 800 students. A variety of events were held, including a bake sale, coin boxes and a pajama day. The event was such a success that Columbus TV stations and newspapers showed up to get the scoop. Amazing job, kids!



Kaylee, right, and her cousin Julia accept a "check" for nearly \$2,000

Family Vacation Leaves Lasting Impression

After meeting Sam, a boy with Progeria, while on vacation in Hawaii, Andrew, of Sammamish, WA organized a school bake sale to benefit PRF, enlisting the help of some friends. The bake sale was a huge success, with many students donating their allowances to the cause.

Andrew also created a storyboard on Progeria for the school's science fair, and made a presentation to his entire class. Thanks, Andrew!



Andrew and his friends helped raise over \$500.

Splish Splash for a PRF Car Bath!

With hose and sponge in hand, Valerie of sunny Magalia, California helped raise funds and awareness for PRF. Thanks to Valerie's hard work, some suds and some sun, she raised nearly \$150 with a carwash she held in April 2007. Now that's good, clean fun!

High School Student Goes the Extra Mile.

Theresa, a student at Romulus High School in Michigan, decided to hold a Walk-a-thon as part of her "Senior Project". Theresa went all out, designing her own brochures and pledge sheets, and setting up donation cans across town. The event raised over \$1,300! "Thank you for helping me through this project", said Theresa,



"It was an amazing experience." We thank YOU, Theresa, and hope other students will follow your example for their school projects.

Walkers get ready for the start of the Romulus Walk-A-Thon

Let's Do Lunch! After meeting Megan Nighbor, a member of PRF's Ambassador Family, Elizabeth Aiken from Greenville, South Carolina knew she had to do something to help raise awareness and funds for PRF. In June 2007, she organized a luncheon and silent auction, and over a hundred women showed up! They enjoyed catered food and wine, bid on auction items, browsed the wares of three vendors (who donated a part of their sales), and viewed a fashion show. Elizabeth continues to be involved, bringing in several hundred dollars every few months through the Coins to Cure Progeria® cans, which she has placed in stores across Greenville. "It is amazing how much energy you have when working for something important", she says. Thank you, Elizabeth, we agree!

Ladies enjoy good food and good company, for a good cause. The event raised over \$1,100!



Hats Off to Lial Elementary School!

After Kaylee and her mother visited Lial Elementary School in Whitehouse, OH to spread awareness about Progeria, students at the school decided to hold a "Hats-On Day" to raise money for PRF. Each student got sponsors, and wore those sponsor names on their hats. The event raised nearly \$700 for PRF. Please join us in saying "Hats Off" to Lial Elementary School!

Let's Hear it for the Band!

The Phatt Daddies jazz band of Massachusetts' North Shore also continues to support PRF through their artistic talents. This group has been playing together for years, just for fun, at clubs in the area. And when they are asked to play privately at an event like a birthday or retirement party, they agree as long as a donation is made to PRF. Now THAT'S music to our ears!

Lemonade Cools the Walkers, Warms PRF's Heart



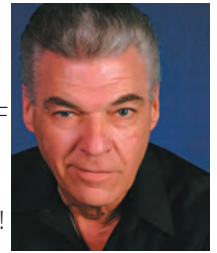
Caroline, a student at Smith Elementary School in Danvers, Massachusetts, raised nearly \$200 for PRF by selling lemonade to thirsty walkers at the school's walk-a-thon. She also gave informational speeches during morning school announcements, educating her fellow students about Progeria and asking them to stop by her stand to help fund Progeria research. "You should be proud of your efforts both for what these funds can do in the battle against Progeria, and for raising awareness at Smith School", says school treasurer Mrs. Crum. Way to go, Caroline!

Counting on Every Penny

After doing research on Progeria with two fellow students for chemistry class, Sarah from Baltimore, Maryland, decided to turn the school project into a fundraiser. Sarah created a poster about Progeria, and set up a Coins to Cure Progeria® can in her classroom. Students from her class and beyond donated for 4 months. We love it when kids help kids with Progeria!

Actor "Jason" Makes a Not-So-Scary Gesture

Steve Dash, the actor who portrayed "Jason" in Friday the 13th Part 2, was very generous when approached by PRF supporter Al Baca. Steve sent signed bookplates for use in Al's PRF eBay auctions, several autographed photos and even a cash donation! Thanks Steve, we're glad you're on our side when you take off the mask!



Rhode Island Boys Continue to Celebrate Birthdays for PRF

For the 2nd year in a row, brothers Dylan, 11, and Orion, 9, celebrated their birthdays with one very special wish – instead of gifts, they asked friends and family to donate to PRF. They must have been good all year, because they raised an amazing \$750. Thank you, boys, for selflessly turning your birthday into a celebration for children with Progeria!

Peabody Student Continues to Collect for PRF

When 14 year old Eric from Peabody, Massachusetts wasn't able to participate in PRF's 6th International Race for Research, he found another way to help: Eric took up a collection and raised \$100. This isn't the first – or the last - time Eric has supported PRF. In 2006 he donated a portion of his Bar Mitzvah money, and he continues to help. Thanks for sticking with us, Eric, PRF needs more steadfast supporters like you!

Big Heart in the Outback

Daniel, a 10 year old boy from just outside Queensland Australia, saw a television program on Progeria, and knew right away what he wanted to do: Every year Daniel saves up money to donate to charity, so he sent PRF \$60 for the clinical drug trial. "I saw the photos of the kids on your web site. There are some my age and I'm sure they like doing the same



things I do like playing football, swimming and skateboarding." YES! Kids with Progeria like the same activities other kids their age enjoy. We hope other boys and girls follow your example, Daniel, and we'll reach our \$2 million goal in no time!

Daniel with some of his swimming medals and trophies.

Company Jeans Days Benefit PRF

FirstSource Laboratory Solutions in Carmel, Indiana holds "Jeans Day" every Friday, with employees paying \$1 to participate. FirstSource chose PRF as the charity to whom they donate their monthly proceeds; since November 2006, they have raised \$1,730. Thank you, FirstSource employees – your comfort on Fridays brings us comfort as well!

And many thanks to Gail Hochberg and everyone at Katten, Muchin, Rosenman LLP for recently holding a Jean's Day at their company. Many other companies have chosen PRF to benefit from their Casual Fridays – how about getting yours to do the same?!

There are dozens of others whose extraordinary and generous acts have made them Miracle Makers – too many to list here! Please go to www.progeriaresearch.org/miracle_makers.html to enjoy reading all about them.

PRF On the Move:

So many Wonderful Ways we Continue to Grow and Spread the Word!

PRF on Front Page of Wall Street Journal

For 8 months, Pulitzer prize-winning health reporter Amy Dockser Marcus followed PRF's Medical Director, Dr. Leslie Gordon, and her colleagues through the process of preparing for the clinical drug trial for children with Progeria. PRF was then featured in Marcus' front page article in the January 29, 2007 issue. The piece highlights PRF's efforts to drive Progeria research towards treatment and a cure. With an audience of 2.1 million, the trial and PRF's tremendous progress received worldwide exposure.

Old at Age 3 Book Published

A compelling and courageous tribute to author Keith Moore's son Zachary, who died of Progeria at the young age of 3, is now available. The book offers a rare and vivid window into a world that chronicles family life and the many joys and challenges the Moore's experienced in caring for their brave and joyous son. 25% of the proceeds from book sales are generously being donated to PRF. To learn more, visit www.oldatage3.com



It was another banner year for PRF's 6th Annual International Race for Research in PRF's home town of Peabody, Massachusetts. With over 230 people running, walking, and pushing infants in strollers on a sunny day, we raised \$20,000. Here, the winners of the 5K enjoy the awards ceremony.

PRF Billboard is Seen by Thousands

In June 2007, PRF got a huge boost in raising awareness with a billboard on busy route 1 in Foxboro, MA. Many thanks to Carroll Advertising and Rodman Ford for underwriting the entire project!



Thank you to our major sponsor, and the numerous others who generously supported this event.



The Progeria Research Foundation

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- Mother of recently-diagnosed Zach,
11 months old

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