

NEW TYPES AND NEW APPROACHES TO OI

On behalf of the Osteogenesis Imperfecta Foundation, Children's Brittle Bone Foundation and the Buchbinder Family, welcome to the *2008 New Types and Approaches to Osteogenesis Imperfecta* scientific meeting.

This meeting provides the first opportunity to synthesize our understanding of recessively inherited forms of OI, to examine the range of clinical presentation, to understand the roles of the enzymatic systems involved and to examine how insights gained from both animal and human studies might lead to more effective treatments of recessive forms of OI and of the more common dominantly inherited forms.

We are proud to bring together, over the next several days, outstanding researchers and clinicians who will each bring their expertise to the discussions and presentations. This meeting, as in years past, will help us improve communication, build networks and consult on issues, questions and difficult cases. We look forward to a dynamic exchange of information and ideas.

Thank you for making time to attend this year's meeting and for bringing your expertise, existing knowledge and ideas to each of the upcoming discussions. We are fortunate to have the continued support of the Buchbinder Family this year, making it possible to bring together the best minds working on OI and bone research today. This meeting was also made possible in part by a grant from NIAMS, which is partially funded by NICHD and the Office of the Director, NIH.

Thank you again and have a wonderful meeting.

Osteogenesis Imperfecta Foundation

Children's Brittle Bone Foundation

The Buchbinder Family

**A special thank you is extended to this year's meeting co-chairs Dr. Peter Byers and Dr. Matthew Warman.*

WELCOME

We have organized this meeting to take advantage of the recent high interest in the newly recognized recessively inherited forms of OI in the hope that clues to the pathogenesis of these disorders may help to design better therapies across the board for people with OI. The two new genes in humans, *CRTAP* and *LEPRE1*, produce proteins that interact, but the relationships between these proteins, type I collagen and the product of the *SMPD3* gene, sphingomyelin phosphodiesterase 3, remain incompletely mapped. Yet, it is the common elements that will probably help us to understand the treatable elements of OI and guide our search for effective elements.

We hope that this meeting, which will bring together some of the most experienced clinicians, clinical investigators, and basic investigators, will provide the synergy that we have seen at previous meetings about OI to reach the new insights that will drive forward our understanding and generate new directions for basic and clinical investigations. We hope that you will take this opportunity to throw off any reluctance that you may have and join in a vigorous and synthetic discussion to open these new pathways forward.

Peter Byers

Matt Warman

Co-Chairs, 2008 Scientific Meeting, New Types and New Approaches to OI

AGENDA

All functions will be held in the Chicago Room, unless otherwise noted.

Sunday, April 27, 2008

6-8 pm **Welcome Reception**
 Rosemont II Room

Monday, April 28, 2008

7:30-8:30 am **Breakfast**

8:30am **Introduction and Welcome**

SESSION I: CRTAP AND OI

Moderator: Brendan Lee, Baylor College of Medicine

8:45am **Identification of CRTAP, mouse model, and humans with mutations**
Roy Morello, Baylor College of Medicine

9:10am **OI type VII, a unique recessive OI phenotype among Canadian Native families**
Francis Glorieux, Shriners Hospital, Montreal

9:35am **Lethal type VII OI-CRTAP mutations, clinical and biochemical consequences**
Joan Marini, NICHD/NIH

10:10-10:30am **Discussion and Break**

SESSION II: LEPRE1/P3H1 AND OI

Moderator: Joan Marini, NICHD/NIH

10:30am **Type VIII OI: LEPRE1/P3H1 mutations and founder effects**
Joan Marini, NICHD/NIH

10:50am **Clinical effects, populations specific mutations and OI**
Dustin Baldrige, Baylor College of Medicine

11:10am **Prolyl 3-hydroxylation in collagens-enzymes, functions and consequences**
Janice Vranka, Shriners Hospital, Portland

11:30am **LEPRE-a polymorphic, polyfunctional protein**
Kevin McCarthy, Louisiana State University

11:50am **Structural consequences of lack of prolyl 3-hydroxylation in type I collagen**
Hans Peter Bächinger, Shriners Hospital, Portland

12:10pm **Reciprocal effects of null mutations in CRTAP and LEPRE1**
Shawna Pyott, University of Washington

12:30-1:45pm **Break, Discussion and Lunch**
Atrium

SESSION III: ANIMAL MODELS OF RECESSIVE OI

Moderator: Matthew Warman, Boston Children's Hospital & Harvard University Medical Center

1:45pm **The *fro/fro* mouse, a model of *Spmc3* deficiency and OI**
Christophe Poirier, University of Chicago

2:05pm **The *oim/oim* mouse, a defect of $\text{proc}\alpha 2(\text{I})$ chain stability-genotype and phenotypes**
Charlotte Phillips, University of Missouri

2:25pm **Homozygosity for a COL1A1 point mutation in mice**
Antonella Forlino, University of Pavia, Italy

2:50-3:20pm **Discussion and Break**

SESSION IV: RECESSIVE COLLAGEN MUTATIONS IN HUMANS

Moderator: Dan Cohn, Cedars-Sinai Medical Center

- 3:20pm **Recessive OI due to mutations in type I collagen genes**
Anne de Paepe, Ghent University, Belgium
- 3:40pm **Osteoporosis psuedoglioma syndrome**
Matthew Warman, Boston Children's Hospital & Harvard University Medical Center
- 4pm **29 year follow up of a child with deficiency of α 2(I) chains and OI**
F. Michael Pope, Cardiff University, London, Edinburgh & Glasgow
- 4:30pm **Discussion**
- 7-9pm **Dinner**
Gateway Room

Tuesday, April 29, 2008

- 7:30-8:30 am **Breakfast**
Chicago Room
- 8:30am **Keynote address: The Brain -Bone Connection, Something to Keep in Mind**
Gerard Karsenty, Columbia University Medical Center

SESSION V: RECESSIVE FORM OF OI, INSIGHTS INTO MECHANISMS AND IMPLICATIONS FOR TREATMENT

Moderator: Michael Whyte, Washington University

- 9:30am **Distinctive histological and radiological features of CRTAP and LEPRE1 mutations**
Deborah Krakow, Cedars-Sinai Medical Center
- 9:50am **Treatment of children with CRTAP mutations with bisphosphonates-outcomes and effects**
Frank Rauch, Shriners Hospital, Montreal
- 10:10am **Non-lethal type VIII OI: clinical, radiographic and histological findings**
Joan Marini, NICHD/NIH
- 10:30-11am **Discussion and Break**
- 11am **Surgical treatment of children with recessive OI-challenges and successes**
Francis Glorieux, Shriners Hospital, Montreal
- 11:25am **Unexpected recurrent OI-parental mosaicism or recessive inheritance?**
Peter Byers, University of Washington
- 11:40am **Discussion**
- 12-1:15pm **Lunch**
Atrium

Continued on page 4.

SESSION VI: THERAPEUTIC CHALLENGES IN TREATMENT OF RECESSIVE OI

Moderator: Peter Byers, University of Washington

- 1:15pm **ER stress-associated apoptosis in aga2 mouse model with COL1A1 C-propeptide mutation**
Thomas Lisse, National Institutes of Health
- 1:35pm **Stem cells and other therapeutic adventures in mice with OI**
Christopher Niyibizi, Pennsylvania State University
- 1:55pm **Stem cell intervention with humans with OI**
Edwin Horwitz, Children's Hospital of Pennsylvania
- 2:15pm **To be tried-is there a new generation of medical therapies for recessive OI?**
Michael Whyte, Washington University
- 2:35pm **Discussion, Summary and Wrap-up**
Peter Byers and Matthew Warman
- 3:30pm **Meeting Adjourned**

SPEAKERS AND MODERATORS

Hans Peter Bächinger, Ph.D., is a Senior Investigator in the Research Department of Shriners Hospital for Children in Portland, OR and Professor in the Department of Biochemistry and Molecular Biology at the Oregon Health & Science University. Dr. Bächinger received his Ph.D. in Biophysics in 1979 at the Biocenter of the University of Basel, Switzerland, under the guidance of Professor Jürgen Engel. In 1980 he joined Professor John Fessler's laboratory at UCLA as a postdoctoral fellow. He was appointed Assistant Professor of Medicine and Biochemistry at the Medical University of South Carolina in Charleston, SC, in 1982. In 1984 he moved to Shriners Hospital for Children in Portland. During his Ph.D. thesis, Dr. Bächinger studied the directional folding of collagen triple helices and he has maintained his interest in the stability and folding of this unique structure. His current interests are the biosynthesis of collagens, especially posttranslational modifications and the physico-chemical characterization of extracellular matrix proteins.

Dustin Baldrige is pursuing a combined MD/PhD degree at the Medical Scientist Training Program of Baylor College of Medicine in Houston, Texas. He is currently studying in the laboratory of Dr. Brendan Lee, MD, PhD in the Molecular and Human Genetics Department, where he is investigating the molecular pathogenesis of recessive Osteogenesis Imperfecta caused by mutations in the genes *LEPRE1* or *CRTAP*. His future plans include running a genetics laboratory as a research physician at a major academic medical center.

Peter Byers, M.D., is Professor of Pathology and Medicine (Medical Genetics) at the University of Washington, where he is a medical geneticist who specializes in seeing individuals with forms of genetic connective tissue disorders, including OI. He serves as director of the University's Medical Genetics Clinic and of the Collagen Diagnostic Laboratory. He has published widely on osteogenesis imperfecta as well as other disorders of collagen synthesis, including forms of Ehlers–Danlos, and on the Marfan syndrome. He was editor of the *American Journal of Human Genetics* from 1993-1999 and recently completed a term as President of the American Society of Human Genetics. He earned his M.D. at Case Western Reserve University, completed his residency in internal medicine at the University of California Hospitals in San Francisco and fellowship training in Medical Genetics at the University of Washington after spending three years at the NIH, and joined the faculty at the University of Washington in 1977. He serves on the Osteogenesis Imperfecta Foundation's Medical Advisory Council, which he has chaired, and has also served as a board member of the American Society for Human Genetics, and as a member and president of the American Board of Medical Genetics. He is a speaker at the biennial National Conference on OI. He served on the planning committee for the 1999 New Research Strategies in OI Workshop, and was co-chair of the 2006 Scientific Meeting Planning Committee and co-chair of the Type I Scientific Meeting.

Daniel H. Cohn, M.D., Ph.D., is a research scientist and Co-Director of the International Skeletal Dysplasia Registry at Cedars-Sinai Medical Center. He is also Professor of Human Genetics and Pediatrics in the Geffen School of Medicine at University of California, Los Angeles (UCLA). Dr. Cohn has conducted research on the molecular basis of a diverse group of skeletal dysplasias, including osteogenesis imperfecta, the type II collagenopathies, pseudoachondroplasia, multiple epiphyseal dysplasia, disorders of the sulfation pathway and Dyggve-Melchior-Clausen dysplasia. Dr. Cohn earned his bachelor's degree from University of California, Santa Barbara. He earned his doctorate degree from Scripps Institution of Oceanography at University of California, San Diego, and carried out postdoctoral research in the Department of Pathology at University of Washington, Seattle.

Anne de Paepe, M.D., is director of the Centre for Medical Genetics at the Ghent University Hospital and full professor of medical genetics at the Ghent University, Ghent, Belgium. Her research interests involve clinical and molecular research in the field of heritable connective tissue disorders such as Marfan Syndrome, Osteogenesis Imperfecta, Ehlers-Danlos Syndrome and others. She is an active member in different genetic societies and medical advisory boards within her own University as well as at the national and international level. She has authored more than 250 peer-reviewed publications.

Antonella Forlino, Ph.D., is currently an Associate Professor at the Department of Biochemistry “A. Castellani”, Section of Medicine and Pharmacy at the University of Pavia, Italy. Dr. Forlino received her Degree in Biology in 1991, her PhD in Biochemistry in 1995 and the Specialty Degree in Genetics in 1997 at the University of Pavia, Italy. She began her biochemical studies on collagen in Osteogenesis Imperfecta patients during her degree under the direction of Prof. Cetta at the Center for the Study of Connective Tissue Disorders at the Department of Biochemistry and she continued her research in the same field during both PhD and Specialty School. From 1995 to 1999 Dr. Forlino obtained a postdoctoral fellowship at NICHD, NIH in Bethesda under the supervision of Dr. Joan C Marini. During this fellowship she generated and characterized the first knock in murine model for Osteogenesis Imperfecta. In 2000 Dr. Forlino moved back to the department of Biochemistry of the University of Pavia where she obtained an Associate Professor position at the Department of Biochemistry. She continued her studies on Osteogenesis Imperfecta using her murine model and focusing her attention on the study of OI phenotypic variability using transcriptomic and proteomic approaches. She maintained and still has a constructive collaboration with her former mentor Dr. Marini. Recently her major interest is focused in the characterization of OI mutant stem cells and in the application of stem cell therapies for Osteogenesis Imperfecta. Dr. Forlino’s research also includes other connective tissue disorders, in particular she is interested in the study and characterization of cellular and murine models for Diastrophic Dysplasia and Prolidase Deficiency.

Francis Glorieux, O.C., M.D, Ph.D., is the director of research and the founder of the Genetics Unit at the Shriners Hospital for Children in Montreal, Canada. He is also a professor of surgery, pediatrics and human genetics at McGill University. Dr. Glorieux has studied many facets of bone and mineral metabolism and genetic bone disease, including osteogenesis imperfecta. He helped establish a program of molecular diagnosis of collagen defects, and another program to study bones in growing children, helping to define the characteristics of the various forms of OI and defining new types of OI. Since 1992, Dr. Glorieux has been conducting clinical trials to study the effectiveness of pamidronate and alendronate in children with severe OI. Results of these studies have been published in several journals including the New England Journal of Medicine. He chaired the organizing committee for the 7th International Research Conference on OI, held in Montreal in 1999. In 2003, he was the recipient of the Elsevier Award of the International Bone and Mineral Society, and the Jonas Salk Award of the Ontario March of Dimes. Dr Glorieux was recently made an Officer of the Order of Canada, the country’s highest honor for lifetime achievement. Dr. Glorieux is a member of the OI Foundation’s Medical Advisory Council, and speaker at the biennial National Conference on OI.

Edwin M. Horwitz, M.D., Ph.D., is an Associate Professor of Pediatrics in the Division of Oncology / Blood and Marrow Transplantation at The Children’s Hospital of Philadelphia and The University of Pennsylvania School of Medicine. Dr. Horwitz graduated from the Medical Scientist Program at the Indiana University School of Medicine, receiving his Ph.D. in Biological Chemistry in 1985 and his M.D. in 1988. He then went to Washington University School of Medicine in St. Louis, Missouri where he completed his training in pediatrics and pediatric hematology/oncology and developed an interest in stem cell biology and stem cell transplantation. After serving as an Instructor in Pediatrics at Washington University, he was recruited to St. Jude Children’s Research Hospital where he began his translational research program focused on mesenchymal stromal cells and the development of bone marrow stem cell therapies for genetic disorders. In 1999, Dr. Horwitz reported the first clinical trial demonstrating that bone marrow stem cells can be successfully transplanted into children with osteogenesis imperfecta and generate clinical benefits. This was the first prospective trial of bone marrow transplantation focused on a nonhematopoietic tissue and the first proof of nonhematopoietic donor marrow cell engraftment with clinical benefit in patients. Subsequently, Dr. Horwitz reported the first clinical trial of isolated, allogeneic mesenchymal stromal cell therapy. He utilized gene-marking in this trial to demonstrate unambiguous engraftment of the ex vivo expanded cells and clinical benefit explicitly attributed to the mesenchymal cells in children with osteogenesis imperfecta. Dr. Horwitz continues to investigate cell therapy strategies in his laboratory and rapidly translate his findings to clinical trials, including his current work focused on nonadherent marrow cell strategies. He was recently recruited to The Children’s Hospital of Philadelphia where he serves as a physician investigator and the Director of Cell Therapy. He has been honored for his early work by being named the Outstanding Young Investigator in Hematology by the American Society for Pediatric Hematology/Oncology and subsequently has received a Doris Duke Foundation Clinical Scientist Award, the Outstanding Achievement Award from the International Symposium of Molecular Medicine and has been elected a member of the American Society of Clinical Investigation.

Gerard Karsenty, M.D., Ph.D., is currently the Paul A. Marks M.D. Professor and Chairman of the Department of Genetics and Development at Columbia University College of Physicians and Surgeons in New York City. Dr. Karsenty received his M.D. and Ph.D. degrees from the University of Paris where he began to develop his interest in endocrinology and skeleton biology. He was then a Postdoctoral Fellow in the laboratory of Dr. Benoit de Crombrughe from 1986 to 1990. Prior to moving to Columbia University in 2006, Dr. Karsenty was a faculty member at the M.D. Anderson Cancer Center and at Baylor College of Medicine in Houston, Texas. Dr. Karsenty's research interests include the transcriptional control of osteoblast differentiation and the genetic bases of the different functions exerted by the skeleton

Deborah Krakow, M.D., is currently an Associate Professor of Obstetrics and Gynecology and Human Genetics at Cedars-Sinai Medical Center and the David Geffen School of Medicine at UCLA, Los Angeles, CA. Dr. Krakow received her Bachelor of Science at Arizona State University and her M.D. at the Chicago Medical School. She completed fellowships in Maternal-Fetal Medicine and Medical Genetics. She began her studies in the area of osteogenesis imperfecta under the mentorship of Daniel H. Cohn, PhD. Dr. Krakow is interested in the prenatal ultrasound and radiographic findings in osteogenesis imperfecta. She is a member of the OI Foundation's Medical Advisory Council and a speaker at the Foundation's biennial National Conference on OI.

Thomas Lisse, Ph.D., is a post doctoral fellow within the Bone and Extracellular Matrix Branch at the National Institute of Child Health and Human Development (NICHD). He received his B.S. from Purdue University, and earned both his M.S. and Ph.D. from the Institute of Cell Biology and Immunology at the Technical University of Stuttgart, Germany. He conducted his doctoral research at the The Helmholtz Zentrum München (formerly The German National Research Center) within the Institute of Experimental Genetics and the German Mouse Clinic phenotyping center. He was the recipient of the GIF (German Israeli Science Foundation) and ANABONOS EU grant rewards for his doctoral research. He is currently studying the effects of hammerhead ribozyme and pharmacological treatments for OI within the Brl mouse. He is also investigating the collagen defect in the Aga OI mouse model.

Joan Marini, M.D., Ph.D., is Chief of the Bone and Extracellular Matrix Branch, National Institute of Child Health and Human Development (NICHD). She has led the long-term NIH OI program, in which clinical and bench research are fully integrated. Her lab generated the Brl mouse model for type IV OI and has recently been among the leading labs studying recessive forms of OI. Other research topics of her group include mosaic parents, the cell biology of OI osteoblasts, hammerhead ribozymes for gene therapy and using the Brl mouse to test pharmacological treatments for OI. She has served as a principal or associate investigator for numerous clinical protocols studying OI, including protocols studying the use of growth hormone or bisphosphate therapy, and is currently completing a pamidronate dose trial. She received her M.D. from the Johns Hopkins University School of Medicine, completed her pediatric internship at Johns Hopkins Hospital, and served as a pediatric resident at Georgetown University Hospital. She completed Genetics specialty training at the NICHD, NIH. Marini also earned a Ph.D. in physiological chemistry from the Johns Hopkins University. She has been on the program committees for several International OI Meetings, on the planning committee for the 1999 New Research Strategies in OI Workshop and chaired the 2001 workshop. She is a long standing member of the OI Foundation's Medical Advisory Council and served a term as MAC chair during which she established the tradition of OI Foundation Research Workshops.

Kevin McCarthy, Ph.D., received his Ph.D. in 1987 from the Department of Anatomy at Albany Medical College, Albany, New York. Prior to formal graduation, he moved in 1986 to the Department of Cell Biology at the University of Alabama at Birmingham (UAB) to join the laboratory of John Couchman, Ph.D. as a postdoctoral fellow to develop an expertise in proteoglycans and extracellular matrix biology. After being promoted in 1990 to Assistant Professor in the Department of Cell Biology at UAB, Dr. McCarthy continued his research direction in the area of chondroitin sulfate proteoglycans and their role in the progression of diabetic nephropathy. In 1997 he moved his laboratory to LSU Health Sciences Center to join the Department of Pathology as an Associate Professor in the Division of Research, with a joint appointment in the Department of Cell Biology and Anatomy. Since then, Dr. McCarthy has been promoted to Full Professor in both departments and currently holds the position of Director for the Division of Research in the Department of Pathology. His research interest still focuses on the cell and molecular biology of proteoglycans in the context of renal function and the progression of renal disease.

Roy Morello, Ph.D., graduated from the University of Brescia in Italy and then completed his post-doctoral studies in Dr. Brendan Lee laboratory at Baylor College of Medicine, Houston, TX . Dr. Morello has since transitioned to an Assistant Professor position in the Department of Molecular and Human Genetics. His research interests consist in genetic aspects and pathogenesis of human disease, with a focus on skeletal dysplasias and kidney glomerulopathies, and in the biology and function of collagens and of matrix molecules more in general.

Christopher Niyibizi, Ph.D., is currently an Associate Professor of Orthopaedics and Rehabilitation and Biochemistry and Molecular Biology at Penn State College of Medicine, Hershey PA. Dr. Niyibizi received his MSc. Degree in Biochemistry from Rutgers University before moving to McGill University in Montreal Canada. While at Rutgers University, Dr. Niyibizi began his studies on collagen biochemistry under the direction of Dr. Peter Fietzek of the department of Biochemistry then headed by Dr. Darwin Prockop. Dr. Niyibizi then moved to Montreal Canada and attended McGill University where he received a Ph.D. in Biochemistry in the Division of experimental Medicine in 1985. After completing his Ph.D. studies, Dr. Niyibizi pursued postdoctoral fellowships at Harvard Medical School and University of Washington in Seattle where he continued his studies in Collagen Biochemistry and the pathologies that result from them. Dr. Niyibizi moved to the University of Pittsburgh and continued his studies on connective tissue biochemistry with major interest on the application of stem cells and gene therapies for Osteogenesis Imperfecta. Dr. Niyibizi's research continues to focus on stem cells and bone regeneration with emphasis on OI at his present institution.

Charlotte L. Phillips, Ph.D., is an Associate Professor of Biochemistry and Child Health at the University of Missouri School of Medicine, Columbia Missouri. Dr. Phillips is also board certified in Clinical Medical Genetics (American Board of Medical Genetics) and has been at the University of Missouri since December 1994. Prior to joining the University of Missouri faculty Dr. Phillips was a post-doctoral Fellow at Duke University Medical Center in the Department of Medicine and the Division of Dermatology where she began her work with inherited connective tissue disorders in 1987. Dr. Phillips received her PhD in Biochemistry from North Carolina State University, where she worked on reproductive hormone regulation. Dr. Phillips began her career in osteogenesis imperfecta at Duke University as a Michael Geisman Research Fellow in 1991 under the mentorships of Dr. Sheldon Pinnell and Dr. Richard Wenstrup. She has worked continuously in basic and applied research related to collagen and osteogenesis imperfecta ever since and her research has been supported by both private and federal granting agencies.

Christophe Poirier, Ph.D., is a mouse geneticist. He received his PhD from the University Pierre et Marie Curie, Paris, France in 1997. Dr. Poirier performed two post-doctoral trainings at the RIKEN institute, Tsukuba, Japan (1997-2001) and at Baylor College of Medicine, Houston, TX. He is now working at the Medical College of Georgia, Augusta, GA. Their main interest is to study the molecular mechanisms that regulate bone strength in order to develop new strategies to diagnose and treat human skeletal dysplasia such as osteogenesis imperfecta. The strategy is to identify genes that cause mouse disorders similar to osteogenesis imperfecta.

Francis Michael Pope, M.D., F.R.C.P., is a full-time NHS Dermatologist at the West Middlesex University Hospital, Isleworth Middlesex UK. He also runs, in his spare time a National UK Clinical Service for Inherited Defects of Connective Tissue, from the Chelsea & Westminster Hospital London. He qualified in Medicine (M.B BCh), in Cardiff in 1963, at the Welsh National School of Medicine. Subsequently, after house jobs in Surgery, Medicine, Obstetrics and Paediatrics, he trained in Dermatology, Cutaneous Genetics and Internal Medicine, in Cardiff, London and Liverpool in the late 1960's. Whilst in London, he carried out a complete ascertainment of PXE patients in England & Wales, on which he wrote an MD Thesis. Later, in the early 1970's he concentrated upon Collagen Mutations in the Ehlers Danlos Syndrome at Johns Hopkins (Professor McKusick) and the NIH (George Martin & Karl Piez). Later from 1976 to 1995, he ran the MRC Dermatology Research Group at the Clinical Research Centre, Northwick Park Hospital, where he was a tenured MRC Clinical Scientist and worked on Ehlers Danlos Syndrome, Osteogenesis Imperfecta, Cutis Laxa and PXE. After the MRC shut Northwick Park in 1995, the group briefly transferred to Cambridge (1995 -1997) and partly to Cardiff (1997-2000), before funding ceased. Since then his Connective Tissue activities have been predominantly clinical, although he still runs a small research lab at Northwick Park in the Institute of Clinical Research, mainly funded by the UK Ehlers Danlos Support Group.

Shawna Pyott received her Bachelor's of Science degree from the University of Washington in 1996. Following her undergraduate education she spent five years in a research laboratory studying the progression of ulcerative colitis to colon cancer under the guidance of Dr. Teresa Brentnall at the University of Washington. At the end of 2001 Ms. Pyott entered the field of clinical cytogenetics where she stayed until beginning her graduate education in the Department of Pathology at the University of Washington where she is currently a second year graduate student under the guidance of Dr. Peter Byers.

Frank Rauch, M.D., is Assistant Director of Clinical Research at the Shriners Hospital for Children and Assistant Professor of Pediatrics at McGill University in Montreal, Canada. Dr. Rauch is a graduate of the Technical University of Munich, Germany, and did his pediatric training at the Children's Hospital of the University of Cologne, Germany. He has performed research projects on pediatric bone diseases for the past 15 years. In 2001, he started working with Dr. Glorieux at the Shriners Hospital in Montreal. Since then, his research has focused on osteogenesis imperfecta, investigating in particular the effect of bisphosphonate treatment.

Janice Vranka, Ph.D., is currently a Postdoctoral Research Associate in the laboratory of Hans Peter Bächinger at the Shriners Hospitals for Children in Portland, Oregon. Dr. Vranka received her Ph.D. at Oregon Health and Science University in the Department of Biochemistry and Molecular Biology in 1997. After completing her Ph.D. studies in the field of MMPs and TIMPs involved in eye-related diseases, Dr. Vranka has pursued postdoctoral studies in the laboratory of Hans Peter Bächinger. There she has worked in the field of collagen biophysical chemistry, as well as in the study of key enzymes involved in collagen biosynthesis. She has been involved in the characterization of the family of prolyl 3-hydroxylase enzymes and the identification of the complex of proteins consisting of prolyl 3-hydroxylase 1 (P3H1) and cartilage-associated protein (CRTAP) in which mutations have only recently been shown to cause osteogenesis imperfecta. Additionally, Dr. Vranka has been involved in the recent development of prolyl 3-hydroxylase 1 deficient mice in the Bächinger lab as a model system to study the underlying mechanism of a newly identified, recessive form of osteogenesis imperfecta. Dr. Vranka's research is focused on understanding how mutations in P3H1 or CRTAP in humans lead to a severe OI-like bone disorder involving the collagen architecture where there are no primary defects in collagen genes.

Matthew Warman, M.D., went to college at Brown University and to medical school at Cornell University. After medical school he trained in Pediatrics at the Children's Hospital in Washington, D.C., in Genetics at the Children's Hospital in Boston, and he performed post-doctoral research with Professor Bjorn R. Olsen at Harvard Medical School. Dr. Warman's clinical and scientific interests focus on heritable diseases, particularly those that affect the skeletal system. In 1994 Dr. Warman established an independent laboratory and clinical program in the Department of Genetics and Center for Human Genetics at Case Western Reserve University and University Hospitals of Cleveland. He and the members of his laboratory are committed to identifying genetic causes of skeletal disease, to understanding how these genes participate in the biology of the skeletal system, and to using this knowledge to improve the skeletal health of the human population. In 2006, Dr. Warman returned to Boston, where he is continuing his research and clinical work as the Director of the Orthopaedic Research Laboratories at Boston Children's Hospital, Professor of Genetics and Orthopaedics at Harvard Medical School, and Investigator with the Howard Hughes Medical Institute. Dr. Warman is a member of the OI Foundation's Medical Advisory Council and a speaker at the biennial National Conference on OI.

Michael P. Whyte, M.D., developed and is Medical-Scientific Director of the Center for Metabolic Bone Disease and Molecular Research at Shriners Hospitals for Children in St. Louis. He is also Professor of Medicine, Pediatrics, and Genetics at Washington University School of Medicine, St. Louis and is on staff at Barnes -Jewish Hospital and Children's Hospital, St. Louis. The Research Center serves as a national resource for diagnosis, treatment, and investigation of disorders of bone and mineral metabolism and skeletal dysplasias in children. Whyte and his colleagues currently follow about 150 children with OI. He has authored or coauthored more than 200 scientific papers or book chapters concerning metabolic bone disease. He earned his M.D. at the State University of New York, Brooklyn, and completed his residency in internal medicine at Bellevue Hospital in New York before spending two years as a Clinical Associate at the NIH followed by a fellowship in endocrinology and then joining the faculty of the Washington University School of Medicine, St. Louis. He is a former chair and current member of the OI Foundation's Medical Advisory Council and he served on the planning committee for the 1999 New Research Strategies in OI Workshop. He co-chaired the 2004 Type I Scientific Meeting and the 2006 Scientific Meeting. Dr. Whyte is a speaker at the biennial National Conference on OI.

