

A GOAL FOR LIFE

For Friends and Supporters of the Ara Parseghian Medical Research Foundation



Dear Friends,

It has been an extremely busy summer and we have much to be grateful for.

Through the tireless efforts of many, the research continues to move forward and we are excited about the development of several promising therapies. As you read through this newsletter you will see from the highlights some of the incredible research progress being made, the many events that took place across the country and the prevailing attitude of perseverance and hope.

We wish to extend our sincere thanks to all of our loyal supporters who continue to contribute on so many levels, allowing the Foundation to move forward with the funding of critical research. Your ongoing support provides the encouragement to

“Never, never, never give up.”

– Winston Churchill

With deep gratitude,

Cindy and Mike Parseghian

NP-C Scientific Conference Highlights

by Dr. Holly Goodson and
Dr. Richard Taylor

Some 75 researchers and family members from around the world attended the Michael, Marcia, and Christa Parseghian Scientific Conference for Niemann-Pick Type C on June 13-15. The event included 3 days of scientific presentations, posters sessions, events for families, and shared receptions and meals.

Researchers came from universities and institutes around the United States and across the globe, including Chile, Switzerland, Sweden, the United Kingdom, Canada, France, and Brazil. Many of the presenters represented teams of researchers from several institutions. The conference fosters innovative collaborations. In the words of Cindy Parseghian, “I hope you have found this to be a real fertile ground for collaborations. It has been the collaborations that have really moved the research forward. I hope you continue to reach out to one another throughout the year and form those collaborations.”

(cont'd. on page 2)

NP-C Scientific Conference Highlights (cont'd. from page 1)

The opening day's session was dedicated to research related to the fundamental cellular biology and biochemistry underlying the disease:

Suzanne Pfeffer of **Stanford University** presented "NPC1: Mediated cholesterol export from lysosomes."

William E. Balch of the **Scripps Research Institute** presented "Global analysis of NPC1 Proteostasis Biology in Niemann-Pick Type C Disease."

Nicholas L. Cianciola of **Case Western University** presented "Adenovirus RID uncovers a novel pathway requiring ORPIL for lipid droplet formation independent of NPC1."

Olaf Wiest of the **University of Notre Dame** presented "Computational studies of the cholesterol transport between NPC2 and the N-terminal domain of NPC1."

Dorothy I. Mundy of the **University of Texas Southwestern Medical Center** presented "Role of Caveolin-1 in cholesterol efflux from lysosomes: Involvement in Niemann-Pick Type C Disease."

Michael A. Castello of **Loma Linda University** presented "Unveiling pathogenic mechanisms in Niemann-Pick Type C Disease."

After Thursday's dinner at Warren Golf Course, **Karen Quandt**, chair of the board of the National Niemann-Pick Disease Foundation, told the story of her 16-year-old son Ty, who was diagnosed eight years ago and has visited the research mice at Notre Dame. "Niemann-Pick has not stopped his personality," she said. "We know that you're all working hard to find a treatment for this disease, and we're forever grateful for your work." In addition, **Jacqueline Imrie**, a clinical

nurse specialist from Manchester, England, described the launch in April of an International Niemann-Pick Disease Registry with 11 partners in seven European Union countries and 17 international collaborators. The registry aims among other things to provide information that could support research and help identify and recruit patients for clinical trials.

The second day's morning session was dedicated to discovery and preclinical stage chemotherapeutic development including HDAC inhibitors and cyclodextrin-based agents:

Paul Helquist of the **University of Notre Dame** presented "Development of Small Molecule Tools for the Study of NPC Disease."

Frederick R. Maxfield of **Weill Cornell Medical College** presented "Testing Histone Deacetylase Inhibitors as NPC Therapeutics."

Maria Praggastis of **Washington University School of Medicine** presented "The NPC1I1061T knock-in mouse as a model of NPC1 disease and novel tool for drug discovery."

Jorge L. Rodriguez-Gil of the **National Institutes of Health** presented "Somatic cell defect predicts onset of neurological symptoms in lysosomal storage disease."

Frank W. Pfrieger of the **University of Strasbourg, France**, presented "Reactions of a CNS neuron to impaired intracellular cholesterol transport."

Daniel S. Ory of **Washington University School of Medicine** presented "Biomarkers for Monitoring Response to Cyclodextrin Therapy in NPC1 Disease."



*Olaf Wiest, Ph.D.,
University of Notre Dame*



*Suzanne Pfeffer, Ph.D.,
Stanford University*



*Dr. Frederick R. Maxfield, Ph.D.,
Weill Medical College Cornell*

NP-C Scientific Conference Highlights (cont'd. from page 2)

Stephen L. Sturley of **Columbia University Medical Center** presented "Exacerbate-Reverse", a genetic strategy to identify therapeutic targets for treatment of human Niemann-Pick Type C disease."

Forbes D. Porter of the **National Institutes of Health** presented "Therapeutic trials for Niemann-Pick Disease, Type C1: Biomarker Development and Initiation of 2-Hydroxypropyl- β -Cyclodextrin Clinical Trial."

E. Mitchell Seymour of the **University of Michigan Medical School** and the **Michigan Institute for Clinical and Health Research** presented "Opportunities and challenges in repurposing FDA-approved drugs or biologics to treat rare disease."

A Friday afternoon reception included a poster session where:

Jarred Pickering of the **University of Notre Dame** presented "Regulation of Cholesterol Homeostasis with GEX1A, A Potential Lead for Niemann-Pick Type C Disease."

Cristin D. Davidson of **Albert Einstein School of Medicine** presented "Efficacy of alpha-, beta-, and gamma-cyclodextrins in the treatment of a murine model of Niemann-Pick type C disease."

Rayk Hubner of **Medical University of Rostock, Germany**, presented "Modeling of Niemann-Pick type C1 disease using patient-specific induced pluripotent stem cells."

Hiroko Nagase of **Tufts University** presented "Correction of NPC phenotype by TFEB activation."

Katherine M. Byrd of the **University of Notre Dame** presented "Synthesis of Small Molecule Tools for the Study of NPC Disease."

Silvana Zanlungo of **Pontificia Universidad Católica de Chile** presented "c-Abl modulation of HDAC2 levels is a key mechanism in Niemann-Pick C pathology."

Fabrizio Vacca of **University of Geneva, Switzerland**, presented "HPCD induces exocytosis of endocytic organelles: A possible mechanism for cholesterol storage reversal in NPC cells."

Kanagaraj Subramanian of the **Scripps Research Institute** presented "Global analysis of NPC1 Proteostasis Biology in Niemann-Pick Type C Disease."

Luis A. Milla of **Stanford University** and **Howard Hughes Medical Institute** presented "Genetic analysis in a Drosophila model of NPC disease."

After an exciting full day of research presentation and interaction, a reception and dinner for all conference attendees and guests was held in the press box overlooking Notre Dame stadium.

On Saturday, the final sessions included continued presentations on cyclodextrin research, the neurological effects of the disease, and the identification of biomarkers critical for following disease progression and the evaluation of therapeutic efficacy:

- **Leslie McCauliff** of **Rutgers University** presented "Cholesterol transport in NPC: Site-directed mutagenesis of NPC2 reveals sterol transport domains, and the therapeutic use of cyclodextrin polymers in NPC-deficient cells."

- **David H. Thompson** of **Purdue University** presented "Evaluation of 2-Hydroxypropyl- β -Cyclodextrin Polymer Derivatives in NPC2-/- Fibroblasts and as Potential MRI Contrast Agents."

- **Charina M. Ramirez** of the **University of Texas Southwestern Medical Center** presented "Late-Start Administration of 2-Hydroxypropyl- β -Cyclodextrin Ameliorates Liver Disease and Extends Lifespan in Niemann-Pick Type C1 Mice."

- **Steven U. Walkley** of **Albert Einstein College of Medicine** presented "Intrathecal 2-hydroxypropyl- β -cyclodextrin therapy in aged cats."

- **Lawrence S. B. Goldstein** of the **University of California San Diego** presented "Implications of disrupted autophagy on cholesterol trafficking, neuronal survival and strategies for drug development in NPC1."

- **Andrew P. Lieberman** of **University of Michigan Medical School** presented "Npc1 Acting in Neurons and Glia is Essential for the Formation and Maintenance of CNS Myelin."

- **Md. Suhail Alam** of the **University of Notre Dame** presented "Plasma Biomarkers and Disease Therapies in Murine Models of Niemann-Pick Type C Disease."

The next conference will be held on June 12-14, 2014 at the University of Notre Dame. We look forward to another year of great advances in NP-C research. ■

Recently Approved Grants as of July 2013

Lawrence S. B. Goldstein, Ph.D. – Distinguished Professor of Cellular & Molecular Medicine and Neurosciences, University of California, San Diego
TITLE: “Identifying Drugs for NP-C Disease using Neurons from Induced Pluripotent Stem Cells.”

Paul Helquist, Ph.D. – Professor & Associate Chair for Research, The University of Notre Dame, Richard Taylor, Ph.D., Professor & Associate Dean for Research, The University of Notre Dame
TITLE: “Design and Synthesis of Small Molecule Agents for Studies and Treatment of NP-C Disease.”

Laura Liscum, Ph.D. – Professor, Tufts University
TITLE: “Correction of the NP-C Disease Phenotype by TFEB Activation.”

Frederick R. Maxfield, Ph.D. – Professor and Chairman, Biochemistry, Weill Medical College of Cornell University
TITLE: “In Vitro and Vivo Tests of the Efficacy of Histone Deacetylase Inhibitors for NP-C Disease.”

Daniel S. Ory, M.D. – Professor of Medicine, Cell Biology and Physiology, Internal Medicine, Washington University
TITLE: “Histone Deacetylase Inhibitors for Treatment for NPC1 Disease.”

Suzanne Pfeffer, Ph.D. – Professor and Chairman of Biochemistry, Stanford University School of Medicine
TITLE: “NPC1-Mediated Export of Cholesterol from Lysosomes.”

Forbes D. Porter, Ph.D. – Senior Investigator, National Institute of Child Health & Human Development
TITLE: “PET Imaging of HP-B-CD in Niemann-Pick Disease, Type C-1.”

Sarah Spiegel, Ph.D. – Professor & Chair, Virginia Commonwealth University
TITLE: “FTY720 – A Novel Approach for Treatment of Human Niemann-Pick Type C Disease.”

Judith Storch Ph.D. – Professor, Rutgers University and David H. Thompson Ph.D., Professor, – Purdue University
TITLE: “Cholesterol Transport by NPC Proteins and Novel Cyclodextrins.”

Stephen L. Sturley, Ph.D. – Associate Professor, Columbia University Medical Center
TITLE: “Modifying NP-C Disease.”

Kanagaraj Subramanian, Ph.D. – Research Associate, The Scripps Research Institute
TITLE: “Impact of Proteostasis Regulators on Global NPC1 Proteome and Interactome in Niemann-Pick Type C Disease.”

David H. Thompson, Ph.D. – Professor, Purdue University
TITLE: “Development of Multivalent β -Cyclodextrin Polymer Constructs as Potential Delivery Vehicles for Niemann-Pick Type C Therapy”

Charles H. Vite, D.V.M., Ph.D. – Associate Professor of Veterinary Neurology and Neurosurgery, University of Pennsylvania
TITLE: “The Treatment of Niemann Pick Type C Cats with Histone Deacetylase Inhibitors”.



*“Each life, no matter how brief,
forever changes the world.”*

From all of us at the Parseghian Foundation we extend our deepest sympathies to the Marella family. Dana Jesse Marella, age 19, lost her courageous battle with NP-C disease on July 12th. We send our love and prayers to the Marella family and friends.

Dana’s Angels Research Trust, founded by Dana’s parents, Phil and Andrea Marella, partnered often with APMRF in funding research projects.

Heartfelt Thanks

Walk for Ashton

Melinda Johnson, a Kindergarten teacher at Washington Elementary School in Mechanicsville, Virginia, holds a very special place in her heart for 11 year-old Ashton Friedl, a student she had in her class in 2008.

Every year since then, Melinda has organized a school-wide event, The Walk for Ashton. This year's walk took place on May 10th and again the community rallied around this event to help their classmate.

Many, many thanks to Melinda and this very caring community.



Ashton Friedl in pink!



"Pink Nic"

The second annual It Comes In Pink, "Pink Nic", honoring Ashton Friedl, was held on May 4th at the Richmond International Raceway.

The Richmond, VA community has graciously supported the Friedl family and this wonderful, family oriented event was an afternoon of great fun, great music and great people, raising awareness and funds for NP-C research.

Ashton's outlook on life is cheerfully positive as evidenced by her ever-present smile....a reminder to all to appreciate the little things in life.

Thank you to family, friends and the Richmond community for their ongoing generosity which means so much to the Friedl family and to NP-C families everywhere.

Irish Legends Golf Dinner & Auction

This incredible event held on June 12th at the Lost Dunes Golf Club in Bridgman, MI celebrated its 7th year! Coach Parseghian, Coach Holtz and Coach Kelly were all in attendance for this event that benefits the foundations of all 3 coaches.

Always a good turnout with a field of 125 golfers and the support of several other legendary sports greats – Joe Kernan, Reggie Brooks, Gerry Faust, Max Scodro and Mark May, the day was full of food, drink and lively conversation.



Coaches Parseghian, Kelly and Holtz enjoying the Irish Legends event

The evening included an interview of the three coaches by Mark May covering their careers and their perspectives on the current state of college football.

Coach Holtz brought the famed leprechaun suit worn by Mark May when Notre Dame completed its exciting undefeated regular season. The suit was auctioned off with much fanfare and a good time was had by all. Thanks, once again, to Skip Strzelecki, Angela Monger, Jim Moriarity, and Mike Dolan for this great event.

(cont'd. on page 6)

Heartfelt Thanks (cont'd. from page 5)

Parseghian Classic

Surrounded by the splendid beauty of Pebble Beach, this three day event held on June 21st-24th, was spectacular! Participants enjoyed rounds of golf on The Pebble Beach Golf Links and The Links at Spanish Bay, the camaraderie of old friends, new acquaintances, delicious cuisine, and a Sunday evening to remember. The evening's special guests included Amanda Bane and her family. Amanda, age 21, was diagnosed with NP-C two years ago.

To complete the evening and weekend, singer/songwriter Amy Grant, a devoted friend of the Parseghian family and Foundation, lent her "helping hand" to the weekend's magic. Emily Lord, a Notre Dame Alum and talented singer, also performed with great style and grace.



Splendor on the links at Pebble Beach



Dean Crawford with Cindy Parseghian, Amanda Bane and mom, Amy Bianchi

We thank Cristi Ganyard, Jean Gorman and the wonderful committee at UND whose tireless efforts make this event successful and meaningful. A big thank you to all of the participants whose support we greatly appreciate.

Mark your calendar with next year's dates – June 6–8, 2014.

Road to Discovery...4 years...11,266 miles

On June 27th, the Notre Dame Dean of Science, Greg Crawford embarked on his fourth cross country bike ride, continuing his quest to raise awareness and funds to support NP-C research.

Riding 3500 miles from Los Angeles, CA, to Baltimore MD, Greg met with NP-C families and Notre Dame Alumni and took every opportunity to further his ultimate goal – saving lives by finding an effective treatment or cure for NP-C as soon as possible.

This year's ride ended in Baltimore where Greg attended the 21st Annual National Niemann Pick Disease Foundation Family Support and Medical Conference on August 1st where he received an enthusiastic welcome.

Dean Crawford's efforts raised \$500,000 during this summer's journey which will be used to fund a new clinical trial that holds great promise in treating NP-C disease.

We applaud Greg for his unwavering dedication, his boundless energy, and his vision of a world without NP-C disease.

We would also like to extend our gratitude to the Notre Dame Federal Credit Union for their generous sponsorship.



Dean Crawford with Jessica Leoni and friends

In Memory of Our Dear Friend Dave Sitton

A familiar and charismatic presence at many Foundation events, Dave was the ultimate champion for charitable causes, passionate about Tucson and Southern Arizona, the arts, and University of Arizona Rugby. Dave died on August 12th at the age of 58.

This past spring, Dave had an inspiration to bring together his U of A Rugby team with the UND Rugby team to begin an annual tradition and fundraiser benefitting the Parseghian Foundation. His goal was achieved and the first Ara Parseghian Cup Match was held on March 10th. It was a beautiful day, Coach Sitton's competitive instincts were in full force, U of A Rugby prevailed...but the huge, soft heart of Dave Sitton came shining through. Everyone felt the passion he had for this cause which extended far beyond the Rugby field. It is hard to believe that Dave will not be on the sidelines at the Notre Dame match scheduled for next April. We hope this event continues for many seasons to come as a reminder to all to "show up, with your game face on, ready to play."

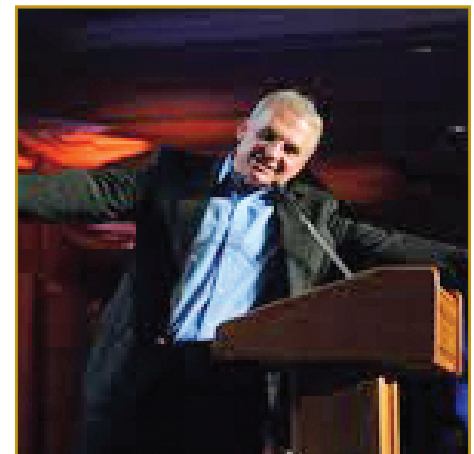
Dave leaves a legacy of giving to others that will live on.



Dave Sitton



Coach Sitton and Coach O'Leary at the First Annual Parseghian Cup Rugby Match



Dave Sitton, a frequent MC at many Parseghian Foundation Events

PLEASE NOTE OUR NEW MAILING ADDRESS:

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Amy Grant Lives Her Lyrics

“Everybody needs a helping hand,
Take a look at your fellow man
And tell me what can I do today
Everybody needs a helping out
If that ain't what it's all about
Tell me what
What can I do
What can I do today”

In 1997, Amy performed at the “One More Victory, Ara” gala in Tucson. Only two weeks after Michael Parseghian’s sudden death from complications from NP-C disease, emotions were raw. Amy embraced the Parseghian family with compassion and a heartfelt statement of “How can I help?” From that moment, Amy has never left the side of Cindy and Mike Parseghian.

Amy’s career, spanning over 35 years, stretches from her roots in gospel music into an iconic pop star, songwriter, television personality, and philanthropist. Grant has sold more than 30 million albums and won six Grammys® in multiple categories, beginning with the platinum selling “Age to Age” in 1982. She also has six #1 hits, including “Baby, Baby,” and “Every Heartbeat” and is one of only two Christian artists to be awarded a star on the legendary Walk of Fame in Hollywood. Her recent album “How Mercy Looks From Here” continues her journey of faith and discovery.

Over the last 16 years, Amy has performed at numerous benefits for the APMRF, helping to raise millions of dollars for NP-C research.

Her support has not stopped at lending her musical talents. She has become a source of strength and support for the Parseghian family. She has also intimately experienced the struggles of NP-C children and their families whom she has met at numerous APMRF events around the country. As a mother of a blended family of 5 children with Vince Gill, Amy has welcomed NP-C children into her life and anguished over many of their deaths.

Amy recently performed at the Parseghian Classic at Pebble Beach in June, where she shared the path of her music, artistry and faith with a deep, vulnerable honesty. The NP-C community has been blessed with Amy’s compassion, support and continued generosity. In addition to her work with the Foundation, she also supports the American Red Cross, Challenge Aspen, Compassion International and numerous other charities.

Thank you, Amy, for touching our lives and for always being there to lend a helping hand...



Amy Grant with Marcia and Christa Parseghian, Tucson 1998