WINTER 2011

A GOAL FOR LIFE

For Friends and Supporters of the Ara Parseghian Medical Research Foundation

"Gratitude makes sense of our past,
Brings peace for today, and Creates a vision for tomorrow."

Dear Friends,

In this season of Thanksgiving, we are reminded of the incredible support that has been showered on the Ara Parseghian Medical Research Foundation and on our family over the last seventeen years. We never anticipated the outpouring of prayers, support and generosity from the thousands of individuals who stepped forward to help us when our children Michael, Marcia and Christa were diagnosed with Niemann Pick Type C disease.

The Foundation has been blessed by an army of volunteers. It is the volunteers that make the work of the Foundation possible. The volunteers are the back bone of the organization; running hundreds of fundraising events, making sure every donation is counted and acknowledged, and overseeing the research efforts.

We continue to be in awe of the organizers of fundraising events who spend much time and energy raising funds to support the research efforts into NP-C. NP-C families are learning first-hand the generosity of their own communities of family and friends and how these efforts are making a difference in the understanding of NP-C. In this newsletter, you can read about fundraisers in Indiana, Michigan, Arizona and Virginia. In addition, the Foundation has received donations from every state in the USA and from countries all over the world.

We are fortunate to have a host of researchers committed to developing a therapy for NP-C children. The NP-C researchers are an incredible group of men and women committed to making a difference in the lives of those afflicted with NP-C. Our researchers collaborate on a level not commonly found in the research arena. Through hard work and determination, these research efforts are leading to therapies. In the next year, the TRND project at the National Institutes of Health, will begin a drug trial using cyclodextrin, a compound APMRF funded researchers have studied extensively. More discussion of this trial is contained in the newsletter.

As the quote above states, our gratitude comes from the years of experiencing the generosity of so many. We know all NP-C families are grateful for the volunteers, researchers, and donors who are helping to create a vision for tomorrow when NP-C children will have full lives unencumbered by the ravages of this disease.

From our family to yours we wish you the joy of family, the gift of friends and the presence of peace for the New Year.

Mike and Cindy Parseghian

Cindy & Mike Parseghian with their son Ara and his wife Cicely.

Therapeutics for Rare and Neglected Diseases

NP-C disease has been chosen as one of the diseases for the Therapeutics for Rare and Neglected Diseases (TRND) program at the National Institutes of Health (NIH). Dr. Forbes Porter, Dr. Chris Austin and Nicole Yanjanin, members of the TRND Team, have worked closely with APMRF and NP-C researchers for several years to pursue a therapy for NP-C. The following letter from the TRND researchers provides an update for the NP-C community on the current developments regarding cyclodextrin, a potential treatment for NP-C. The APMRF funded researchers have extensively investigated the potential of using cyclodextrin as a therapy for NP-C. These research efforts have resulted in the TRND project selecting cyclodextrin as a therapy candidate. The TRND Team and APMRF are committed to facilitating the effort to develop safe and effective therapies for NP-C disease.

The TRND Team

Dear families and friends of the NPC community,

There has been a large, collaborative effort to initiate a cyclodextrin clinical trial at the National Institutes of Health (NIH) to systematically evaluate the safety and efficacy of cyclodextrin therapy for the treatment of Niemann-Pick type C (NPC) disease. As many of you are aware, we met with the Food and Drug Administration (FDA) in November to discuss the development program for cyclodextrin.

The exceptional work that has been done in NPC animal models has guided the design of a human clinical trial. Together with the Therapeutics for Rare and Neglected Diseases (TRND) group at the NIH, as well as several NPC researchers, Johnson & Johnson, and consultants from RRD International, LLC, we are working to submit an Investigational New Drug (IND) application to FDA.

The first step in submitting the IND application to FDA (the perquisite to an initial clinical trial in patients) was to request a pre-IND meeting with FDA to receive the Agency's feedback on our development program before the IND application is officially submitted. We met with the FDA review division staff to discuss the proposed development plan for cyclodextrin and needs for the IND application package. The meeting was positive and the Agency provided helpful feedback focusing on the drug safety and toxicology data. We will have an additional meeting with FDA to focus on the clinical trial design, and FDA is working with us to get that meeting scheduled before the end of the year.

We view this as a very positive step toward pursuing cyclodextrin as a potential treatment for NPC disease. We are planning a scientifically rigorous trial that will allow us to test cyclodextrin in our patients safely and in a way that will provide as much information as possible. While specific details of the trial will not be available until we have agreement from FDA and approval from the NIH ethics review board, we will share information with the NPC community as it is available.

We continue to work toward our goal of starting the trial next year and feel that with the recent FDA feedback, we are on track to do so.

Thank you for your continued support and encouragement as we work together to find a treatment for NPC disease. This fight would not be possible without all of you.

Sincerely,

The TRND Team

Heartfelt Thanks...

Once again, fans of college football and the game of golf came together to help three great charities and meet University of Notre Dame coaching legends Ara Parseghian, Lou Holtz and current Fighting Irish football coach, Brian Kelly. The fifth annual *Irish Legends Charity Golf Classic* took place on June 26-27th. ESPN personalities Rece Davis and Mark May hosted the kick-off "Evening with Legends" and the golf tournament followed at Lost Dunes Golf Club in nearby Bridgman, MI. We wish to thank Skip Strzelecki, Angela Monger and friends, for their enthusiasm, time and commitment, making this event a huge success, year after year.

ND Coaches at Irish Legends event – Gerry Faust, Ara Parseghian, Lou Holtz and Brian Kelly.

The fourth annual *"BReaK Thru Golf Outing"*, hosted by the Smith family of Lafayette, IN, was a day of golf, friends and gratitude for the wonderful support that this community has shown the Smith Family in their fight against NP-C. Honoring three of their children, Braden, Keaton and Riley, this event was held at the Lafayette Elks Country Club on August 6th. The proceeds from this event continue to support NP-C research at Purdue University and the University of Texas Southwestern Medical Center.

Mike Lee celebrates his win and raises awareness and funds for NP-C.

Mike Lee, Notre Dame alumnus and boxing champion, held the first ever professional boxing event at Notre Dame's Purcell Pavilion on September 16th as he took on light heavyweight Jacob Stiers. *"The Fight Like A Champion"* event was supported by an enthusiastic crowd and Lee, decked out in his school's gold and blue, treated the fans to a unanimous decision in his favor bringing his record to 7-0. Mike Lee through the Mike Lee Foundation pledged that all profits from this unique event would be donated to the APMRF and the Robson Community Learning Center in South Bend. Thank you, Mike, for your passion in supporting the fight for NP-C disease.

"Stars on the Avenue" held at the Tucson Museum of Art on a beautiful evening in September provided a chance for guests to wine, dine and dance and to honor the 2011 Physicians of the Year. Presented by the Pima County Medical Society (PMCS), this event benefited the Parseghian Foundation and two other local Tucson charities. Thank you to our longtime friend, Dr. Alan Rogers, and PMCS, for their enduring support and for coordinating this fun evening.

On October 30th, family and friends of Ashton Friedl gathered again this year to enjoy the third annual, *"It Comes In Pink"* event. Held at the Children's Museum of Richmond, VA, guests were treated to delicious food offerings, a great auction and the lively tunes of King Edward & the BD's Band. Ashton, age 9 and her younger sister Emily, age 6 look forward to this event and according to their grandfather, Chuck Friedl, relive the fun and festivities all year long! We thank Kevin Currie for his continued enthusiasm and organizational skills and for all who support Ashton and the Friedl family.

Ashton Friedl enjoying the festivities at the "It Comes In Pink" event.

The best in bench-to-bedside research: honoring Cindy Parseghian

By Dr. Suzanne Pfeffer

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Imagine a scenario in which a group of scientists with a common goal agree to meet every year at a lovely location to share their results and to discuss the most important next steps needed to move that science forward. The group would work under the pre-sumption that all results, reagents and information would be shared openly and all members would collaborate wherever possible to help the group achieve its shared goal. The meetings would end with a panel discussion to help identify the most important next steps to be taken over the subsequent 12 months. Members would support each other during manuscript and grant reviews and cooperate wherever possible to move the science forward. Sound unusual? If only all research could be carried out this way.

Cindy Parseghian, president of the **Ara Parseghian Medical Research Foundation**, established precisely this type of framework to bring together researchers seeking a cure (or beneficial treatments) for Niemann-Pick Type C disease. Niemann-Pick Type C is a genetic disorder in which homozygous carriers of mutations in NPC1 or NPC2 proteins accumulate excess cholesterol and glycosphingolipids in their lysosomes. The disease causes progressive neurological deterioration leading to death, usually during childhood. Sadly, Cindy lost three of her four children to NPC disease. In 1994, together with her husband, Michael, and well-known, former Notre Dame football coach (and father-in-law) Ara Parseghian, Cindy created a foundation to support NPC research and bring together clinicians and researchers to try to find a cure. In 1997, with support from the APMRF, the gene for NPC1 was identified; in 2000, the gene responsible for NPC2 disease also was identified. Cindy has devoted countless hours over many years to fundraising for NPC research; the APMRF recently helped create the Center for Rare and Neglected Diseases at the University of Notre Dame to carry forward NPC disease research. This summer, Notre Dame's dean of sciences, Gregory Crawford, and his wife, Renate, rode their bicycles **more than 2,000 miles** to raise funds and awareness for NPC disease.

Suzanne Pfeffer and Cindy Parseghian, president of the Ara Parseghian Medical Research Foundation.

The APMRF continues to sponsor annual conferences to bring lab findings more quickly to the clinic. Topics presented range from the molecular roles of NPC1 and NPC2 proteins to the initial results of pilot trials of potential drug therapies in affected children. Some scientists report results from high-throughput drug screens designed to identify compounds that clear cholesterol from the lysosomes of cultured mutant cells; others report on studies of genetically modified mice generated to determine which parts of the cerebellum are most sensitive to loss of NPC function or which drugs may benefit mouse or cat models of the disease. Parents of children with NPC disease also attend these meetings and remind the scientists that time is not on their side. The stories told by parents leave every researcher wishing he or she could do more.

What is unique about these meetings is the gathering of basic researchers together with clinicians and families as well as the requirement that all discussions be carried out completely open. The expertise of everyone present is brought to bear on how best to do more for children with NPC disease. Could this model be applied to other diseases or important scientific questions? Because NPC disease affects only about one in 100,000 individuals, there is not a large number of patients or researchers working in this area. This is a serious disadvantage when

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The best in bench-to-bedside research: honoring Cindy Parseghian

By Dr. Suzanne Pfeffer

(cont'd. from page 4)

planning clinical trials, but it can be a significant advantage in terms of facilitating interactions among key researchers and encouraging open dialogue.

Mutations in NPC1 protein are responsible for 95 percent of disease cases. This protein spans the membrane 13 times and has three large lumenal domains, each containing numerous disulfide bonds. More than 250 different mutations have been described, located in every region of this large glycoprotein. American Society for Biochemistry and Molecular Biology members **Daniel Ory** (Washington University) and **William Balch** (the Scripps Research Institute) have shown that NPC mutant proteins are poorly exported from the endoplasmic reticulum after synthesis due to slow folding. Similar mutations have been found in the cystic fibrosis anion transporter (CFTR); thus, the same compounds that may help drive misfolded CFTR to the cell surface or increase CFTR expression might also be of value to NPC patients. Indeed, in cell culture models, ASBMB member **Frederick Maxfield** (Weill Cornell Medical College) and collaborators have found that histone deacetylase inhibitors may increase levels of functional NPC protein in lysosomes. Other therapeutic strategies currently being used involve cholesterol chelation by cyclodextrin or glycosphingolipid synthesis inhibition by miglustat (N-butyl-deoxynojirimycin or Zavesca).

These days, there is a lot of interest in translating lab discoveries into patient therapies. Yet there are few examples that I am aware of that demand and reward the kind of close, successful collaboration achieved by APMRF scientists and clinicians. The National Institutes of Health's Clinical and Translational Science Award consortium was established in 2008 with the goal of reducing the time it takes for laboratory discoveries to become treatments for patients and to engage communities in clinical research efforts. With a budget of $500 million per year and 60 medical school members, the CTSA program also seeks to address the critical need to train the next generation of clinical and translational researchers.

CTSA directors, take note: Cindy Parseghian knows how to foster the most productive interactions between NPC researchers. Her approach should serve as a guide to stimulate collaborative science to tackle any disease. Researchers take note: When we share a common goal, the entire community wins. When we share our results, we can only benefit from the feedback obtained. Cures will be found fastest if we work together. The paths to the cures will be straightest if we draw them together. Cindy Parseghian, we salute you.

Give the gift of life...

Looking for a gift for a loved one, friend or client?

In this season of giving please consider a tribute in their name to the Parseghian Foundation. When you make a donation (whether honor or memorial), a card advising of your gift will be sent to the person(s) you indicate. Call APMRF at (520) 577-5106, make a donation online at www.parseghian.org or use the enclosed envelope.

Mark Your Calendar

January 21, 2012 – Every January the local community of family, friends, benefactors, and businesses in Las Vegas, NV come together to honor and support 14 year old Ty Quandt through a benefit concert and silent auction called "A Touchdown for TY". Under the energetic direction of Verna Burrows, grandmother to Ty, this year marks the seventh year of this great event. For more information go to: www.touchdown4ty.com or call Verna Burrows at 702.363.5443.

Ara Parseghian Medical Research Foundation

3530 E. Campo Abierto
Suite 105
Tucson, AZ 85718
Phone: (520) 577-5106
Fax: (520) 577-5212
www.parseghian.org

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Parseghian Classic

Benefitting Niemann-Pick Type C Research

June 22-24, 2012

The package will include a three night stay at The Lodge at Pebble Beach, a welcome dinner and reception on June 22, a round of golf at The Links at Spanish Bay on June 23, a round of golf at Pebble Beach Golf Links on June 24, and a final reception and dinner on June 24. Check out is on June 25. Full golf and non-golf packages are available.

Please visit niemannpick.nd.edu for more information about this event and the research it will support. If you have questions please contact Cristi Ganyard at (574) 631-3070 or cganyard@nd.edu.