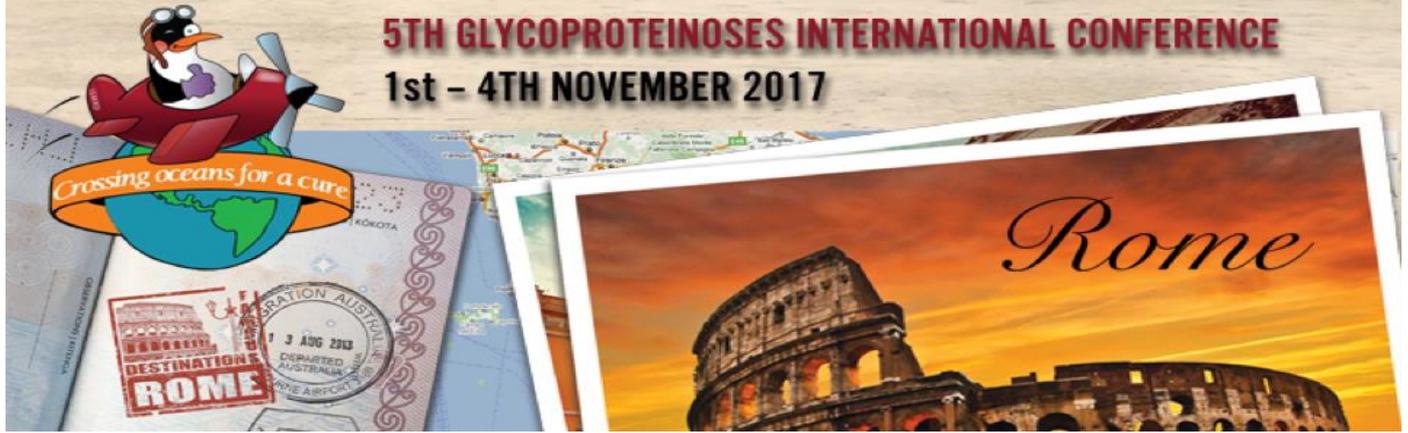


5TH GLYCOPROTEINOSES INTERNATIONAL CONFERENCE

1st – 4TH NOVEMBER 2017



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Our Mission and Vision

ISMRD is the leading advocate for families world-wide affected by Glycoprotein Storage Diseases.

Through partnerships built with medicine, science and industry we seek to detect and cure these diseases, and to provide a global network of support and information.

We seek a future in which children with Glycoprotein Storage Disease can be detected early, treated effectively and go on to live long, healthy and productive lives.

ISMRD supports the following disorders

Alpha Mannosidosis, Aspartylglucosaminuria, Beta Mannosidosis, Fucosidosis, Galactosialidosis, Mucopolidosis II alpha/beta (I-Cell Disease), Mucopolidosis III alpha/beta (Pseudo-Hurler Polydystrophy), Mucopolidosis III Gamma, Schindler Disease and Sialidosis



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Donations

ISMRD is a 501(c) charitable organisation based in the United States serving a global constituency. We provide our services, which include our newsletter, website, outreach activities and support of research, without requesting monthly dues or any other financial restrictions. We gratefully accept donations that will enable us to continue toward our goal of a future free of the tragic consequences of Glycoprotein Storage Diseases.

Donations can be made via our website using



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From the President's Desk

*By Jackie James
President, ISMRD*



It is with great pleasure that I can introduce two new ISMRD board members, as well as two new members of our Scientific Advisory Board! Welcome to Shirley Jamil, England and Dan Peach, New Zealand, who are joining our board of directors, and to Associate Professor Amelia Morrone and Associate Professor Enrico Moro who are joining our Scientific Advisory Board. We look forward to working with you!

We would like to extend our sincere thanks to retiring Scientific Advisory board members, John Hopwood, Mark Haskins and Barbara Burton. We very much appreciate the time and the work you have put in on behalf of ISMRD and its members.

Our conference in Rome this past November was a tremendous success. We had 18 countries represented: Algeria, Australia, Austria, Brazil, Denmark, France, Germany, Italy, Lithuania, New Zealand, Norway, Saudi Arabia, Slovenia, Spain, Sweden, the Netherlands, the UK and the US! Eight of our disorders were represented: Alpha Mannosidosis, Beta Mannosidosis, Aspartylglucosaminuria, Fucosidosis, Galactosialidosis, Sialidosis, Mucopolysaccharidosis Alpha/Beta and Mucopolysaccharidosis III Gamma.

It was amazing to see families connecting and to see the encouragement and support that sharing life experiences brought about. ISMRD is so much more than an organization, it is family. As you will read in the conference reports in this newsletter, many of the scientists attending the conference were very moved by the family stories and made lasting connections with our families.

Look for reports about the conference in this issue from family members, Dan Peach, Juanita Van Dam, Shirley Jamil and Ciska Posdijk and from our Scientific Advisory Board members, Alessandra D'Azzo and Richard Steet.

We also have some lovely photos of the awards dinner and of the children attending the children's program during the conference. I know these will provide wonderful memories for all those that attended.

Another exciting moment was when we received a letter from the Vatican, assuring us that the Pope was keeping us in his thoughts and prayers. You will see a copy of this letter in this newspaper. I had written to the Pope back in April, with the hopes that there might be a chance for the kids to meet him. Even though that did not happen, it was still so exciting to receive a letter from the Vatican to advise us that the Pope was thinking about and praying for us!

I would like to extend a very warm thank you to our donors that made this conference possible. Chiesi, Ultragenyx, Everylife Foundation, Sanofi Genzyme, Amicus Therapeutics and The Wagner Foundation. Without their support this conference would not have been possible. I would also like to thank our Rome-based event planner, Symposia, for all of their help in putting this conference together and their on the ground support during the meeting.

As many of you already know, we are planning our next conference in Atlanta, Georgia in 2019! We hope that this will be our biggest conference yet, and look forward to seeing old friends and meeting new ones. More details will be coming soon, but make a note on your calendars for summer 2019! We hope to see you there!

Finally I would like to take this opportunity to wish each of you a lovely holiday season and a very happy New Year.

Jackie James
ISMRD Board President
Mom to Anna, ML III



Letter of blessing from the Vatican

ISMRD was honoured and awed to receive a letter of blessing from the Vatican. In his letter below, Secretary of State, Cardinal Pietro Parolin, conveys Pope Francis's blessing of wisdom, strength and peace upon all present at the conference. Cardinal Parolin also emphasises a theme that runs through many of the conference reports that you will read in this newsletter: the strong role that solidarity plays in our journey to find treatments and cures for our diseases.



NUNZIATURA APOSTOLICA
IN ITALIA

Roma, 31 ottobre 2017

Prot. N. 4197/17

His Holiness Pope Francis sends cordial greetings to all those participating in the 5th International Conference for Glycoprotein Storage Diseases, and he assures them of his spiritual closeness. As families gather together with health care professionals and researchers, he hopes that the conference will not only provide further scientific insights, but also be an occasion of solidarity among all those affected by these diseases. Above all, His Holiness prays that this gathering will promote awareness of the need to show compassion and understanding to those suffering illnesses, and to their families and caregivers. For "it is fundamentally important that we promote greater empathy in society, and not remain indifferent to our neighbour's cry for help, including when he or she is suffering from a rare disease" (Address to Participants of the International Conference on the Progress of Regenerative Medicine and Its Cultural Impact, 29 April 2016). With these sentiments, Pope Francis invokes upon all present the divine blessings of wisdom, strength and peace.

Cardinal Pietro Parolin
Secretary of State



Ms. Jackie James
President of the International Advocate for
Glycoprotein Storage Diseases
Lifestyle Hotel
Roma



Family Conference Reports

Dan Peach



Dan Peach has recently joined the Board of the ISMRD. He is passionately committed to curing rare Lysosomal Storage Disorders through a tightknit community of researchers, clinicians, patients and families. Dan has seen and experienced first-hand the daily battle of Mucopolysaccharidosis I, also known as Sialidosis. Dan joins ISMRD with over 15 years experience in market research and analytics that enables him to stay at the cutting edge of new discoveries and how they may be applicable to Lysosomal conditions. Dan lives in New Zealand. He writes below about his experience of the conference in Rome.

After a long and somewhat uncomfortable journey, I touched down in Rome for the fifth Glycoproteinoses International Conference. Until now I had spent years searching for medical professionals who knew about any Lysosomal Disorder, let alone Mucopolysaccharidosis I (MLI). Finally, I had come to a place where I was surrounded by people connected by common adversaries in a country whose history was full of battles won and new territories gained. I was excited to meet the extended Lysosomal community and meet some of today's greatest researchers who were scheduled to present, share and network in ways that are simply not possible via a mobile phone.

Within a few hours of arriving in Rome with my sister, we were eating and drinking with new, yet strangely familiar, friends. They were relatable and shared much of the journey I thought was so unique to me.

On Wednesday, my sister and I paired up with some brilliant graduate researchers from St Jude Children's Research Hospital, Memphis, Tennessee. We had a world of fun getting lost in Rome, going shopping for Italian shoes and becoming great friends. It was an odd experience for me to become friends with researchers outside a meeting centred around MLI. Being a group of friends led to us sharing about ourselves as people first and as patients or researchers a very distant second. It was the perfect way to start the conference.

Wednesday night was when I got to meet my friends and pseudo family members over dinner. I met friends who had Lysosomal Disorders for the first-time face-to-face and a sense of community and hopefulness began to grow. I met my long-time friend Dr Alessandra d'Azzo and recently acquired friend Dr Camilo Toro who both radiate knowledge, which is like gold for someone like me seeking answers. I met many other researchers that night who would, over the coming days, become friends.

Throughout the conference, I joined the researchers' stream as it is a rare occasion to have access to the depth of knowledge which was held in that room; you couldn't pry me away. Every presentation built on from the library of research regularly available, and, it came directly from those who were

pursuing and developing the very ideas they spoke about. I was overloaded, but so happy to see how much progress was being made.

On Thursday I was invited to speak to the researchers about my personal journey and the things I had experienced through observation and things that I had experienced in my own body. I was able to share about the wider impacts Lysosomal Disorders have on siblings, spouses, children and parents. Which is why I believe community is so paramount when it comes to Lysosomal conditions. I was honoured to speak and will always cherish the opportunity I had to tell my story with its context and explain what inspires me to believe better days are always ahead.

Finally, and most importantly, on Saturday I co-chaired a family session on MLI with my sister and Dr Toro. Again having patients and medical professionals connecting is a special event which was a major theme to the conference. I think we can learn a lot from personal dedication but we can learn infinitely more as a dedicated collective.

Rome was a turning point for me. I am no longer searching for answers alone, but I am part of a community of fantastic people who are finding answers together. I left Rome enriched with friends, family and knowledge that I simply could not have achieved on my own. With that I say Arrivederci! to Rome – I hope we all meet again soon.

Shirley Jamil



Shirley is mother to Sam who has MLIII. Shirley and her husband Shamim have another child, Edward, who is unaffected.

Shirley runs her own business as an Holistic therapist offering treatments such as Acupuncture, Massage, Bowen Technique, Reflexology and Reiki, which she also uses to help ease Sam's pain and keep it under control.

Shirley works to promote awareness of Mucopolysaccharidosis, including through photographing wristbands in interesting locations and posting to social media and review sites. She also promotes to families, in particular in the UK and Europe, the support available to them within the ISMRD.

We travelled to Rome to meet families affected by Mucopolysaccharidosis and other rare diseases.

I was asked to do a presentation on our life as a family living with Mucopolysaccharidosis III. Sam is 15 now, and his health has deteriorated quickly over the past year. I tried to keep it positive, but sometimes it all just gets to you and brings you down. Sam still keeps smiling, singing and drumming. If he's happy, we're happy.

We thought it was important for us all to attend as a family this time. (Sam and I went alone to the last ISMRD conference in Missouri.) My husband Shamim could speak to other fathers and share thoughts, fears and dreams for the future of our kids. It's not just the mums who care and suffer.

It was important for younger brother Edward to get to meet other siblings who were also silent carers for their affected siblings. To be able to share possible feelings of confusion or resentment at being either a carer, or how it could have been if they too were affected.

Families travelled in from Australia, New Zealand, the USA, the Netherlands, France, Norway, Lithuania, Spain, Slovenia, Austria, Saudi Arabia, the UK and of course Italy to find out what if any progress was being made on links to finding cures or ways to improve the lives of those affected.

The scientific talks were way over our heads at times, but it showed how much research was being done in the background. Progress has been moving along at a quicker pace than previously. But never quick enough for the families I suppose.

The great news for us is that research has started on the Gene therapy for MLII which in turn will help those with MLIII.

The family breakout sessions were much more comfortable and intimate with geneticist, doctors and researchers answering our many questions on how, why and importantly- when?

We spoke with many other families about their experiences. When did they get the diagnosis, what were the symptoms, what surgeries, what helps?

Shamim and myself discussed how we were dipping in and out of people's lives, asking personal questions, supporting other families by just talking. People who in other ways had no common day-to-day similarities to ourselves, apart from having a child with a rare disease and feeling isolated.

Subconsciously, you were looking at the other children and possibly comparing and thinking, they're worse/better than ours, we recognize those symptoms, daring to dream when you see another and she/he doesn't look that badly affected and they're older.

The kids had a brilliant time getting to know each other at Gladiator School, Clown Class and the museum. Naturally, some kids were on phones a lot, but looking closer, they were translating their languages to talk to each other.

What shines out through the tears constantly welling, choked throats and biting of lips of parents trying to keep it together as they spoke about their children was the hope we all hold on to. The hope that a cure might be found soon.

We had smiling faces, heard sounds of laughter and tears, and shared hugs. Emotions that are the same across all continents, races, religion and gender.

Rare diseases don't discriminate. They can affect anyone. But together, we will help and support each other. You can never underestimate the power of unity when all you want to do is to stop your child from suffering.



Juanita Van Dam



Our family trip to Rome, Italy for the 5th Glycoproteinosis ISMRD Conference was an amazing experience. Being our first overseas holiday as a family as well as our first ISMRD Conference was mind blowing!

Meeting other children who have the exact same condition as Damian and Jesse-Rose was such a blessing. We have more family members now. Sam (MLIII) and Ziga (MLIII) as well as Sam's brother Ed became fast friends with Damian. Where English may have been a barrier it was transcended by Google translate and mobile phones haha.

Jesse-Rose became best friends with Ziga's sister Dasa and Pernille (ML3) who did not speak the same language, so their universal language was playing.

Listening to the specialists and scientists was sometimes difficult, sometimes emotional. They are giving hope to families where previously there was none. When we first received Damian and Jesse-Rose's diagnosis, we were told there was no known cure, little to no research and very little treatment other than surgeries. To hear the level of research now into Gene Therapy and Bone Disease was very heart-warming and exciting. I had many questions that I was able to ask and I especially loved the family program where my questions were answered as well as other parents had questions that I also



wanted to know the answer to. Hearing others' journey with these diseases helped us feel less isolated.

We definitely feel connected to a larger family now and loved the amazing opportunity to have met everyone including the professional community.

Sam , Ed, Damian, Jesse-Rose, Dasa and Ziga at the conference in Rome. These children hail from Australia, England and Slovenia.

Ciska Posdijk

My daughters Dorenda (18 years old) and Hannah (17 years old) both have Sialidosis Type 1. When they, their father Marinus-Jan and I, Ciska (their mother) left The Netherlands for the conference in Rome we didn't know what to expect. This was the first time we had attended a conference.

The girls both had a lot of questions for the investigators/specialists and they were especially very keen on meeting Dr d'Azzo to hear what is going on in her lab.



I can truly say that it was confronting and emotional to attend the conference, but it also brought us insight into how many people are working so very hard every day to make things better for children/adults with a glycoproteinoses storage disease. It was such an unique opportunity to meet specialists, investigators and families at one conference.

The first night was a special night. After we had a warm welcome from Jackie James and Jenny Noble we had dinner with the families, specialists and investigators.

We met Dr d'Azzo, and she introduced us to Dr Camilo Toro from the USA, who knows a lot about Sialidosis patients and what helps with the day-to-day care.



As parents we attended parts of the scientific program as well. In the meantime, our daughters could rest in the comfortable family room. Afterwards we had the chance to meet our own specialist Dr Gepke Visser, from the Netherlands and could have lunch with her while talking about the scientific parts.

She got in touch with Dr. Camilo Toro as well and they will keep in touch and he will get in touch with the girls' neurologist from the Netherlands.

On Friday night we also had the awards dinner with live music and we could relax and get to know the other families better.

Saturday morning was our family morning with the specialists and families affected by Sialidosis. We met a few other families, it was good but also hard and emotional to share our stories and we made the decision to stay in contact.

Thank You ISMRD for everything you organised and also thank you sponsors. We went home with more hope in our hearts and knowing we don't have to fight this battle alone.

We hope we will meet you all again.





Scientific Conference Reports

Alessandra d'Azzo



Alessandra D'Azzo is a Full Member and Endowed Chair in Genetics and Gene Therapy at St Jude's Children's Research Hospital, Memphis, Tennessee. She is Chair of ISMRD's Scientific Committee, and ISMRD's Scientific Chair for the conference in Rome.

Here she outlines the conference presentations, and relays her personal reactions to the conference.

Following the trend of past conferences, the 5th Glycoproteinoses Conference brought basic scientists and clinicians from around the world to Rome, Italy, to share with patients and their families the latest discoveries. This year's Conference was special in many ways. It was the first to be held in Europe, with the intent of strengthening connections among affected families around the globe, so that everyone will be more informed and supported. This goal was achieved successfully, also because for the first time the scientific program included presentations from patients and family members. This initiative turned out to be particularly inspiring for the scientists and clinicians, as well as for the patients and their families.

Each scientific session began with introductory lectures on other lysosomal storage diseases (LSDs) and then focused on a specific group of glycoproteinoses. Overall the Conference gave new insights into the current status of the research on glycoproteinoses and the translation of these studies to the clinic; it also emphasized the role of the lysosomal system in basic cellular processes that might parallel clinical conditions seen more frequently in adults.

Dr. Stuart Kornfeld opened the Conference with a beautiful keynote address that provided a historical perspective on glycoproteins and glycoprotein-storage diseases. Dr. Fran Platt then described the involvement of the cytoskeletal network in impaired phagocytosis of macrophages in Niemann-Pick type C disease, broadening our understanding of its pathogenesis. Day 1 continued with two sessions: one dedicated to α -Mannosidosis and another focused on Mucopolipidosis II and III (MLII and MLIII, respectively). Dr. Dag Malm delivered a comprehensive, historical overview of α -Mannosidosis. Dr. Sara Cathey then introduced a novel diagnostic method that labels and quantifies oligosaccharides in glycoproteinoses. Dr. Tommaso Beccari spoke about the lysosomal and plasmatic forms of α -Mannosidase and summarized results of enzyme-replacement therapy (ERT) in a mouse model of the disease. Dr. Line Borgwardt reported the current status of a clinical trial for Valmanase alfa, the human recombinant α -Mannosidase being tested as a potential Enzyme Replacement Therapy. Dr. Troy Lund gave an overview of hematopoietic cell transplantation in patients with glycoproteinoses, and the session closed with an interesting report by Dr. Balraj Doray, who described an engineered Glc-NAc-1 phosphotransferase that enhances the secretion of lysosomal enzymes.

Session II was opened by Dr. David Wenger, who presented encouraging results on treating Krabbe disease in the Twicher mouse with bone marrow transplantation and cerebral injection of an adeno-associated virus vector expressing the therapeutic enzyme. Dr. Thomas Braulke described impaired B-cell to plasma-cell differentiation and dysfunctional osteoblasts in an MLII-knockin mouse model.

These findings were complemented by Dr. Heather Flanagan-Steet's presentation on a zebrafish model of MLII, which presents with severe dysmorphic chondrocytes due to upregulation of TGF β . Dr. Richard Steet then described a novel approach to labeling sialylated plasma membrane proteins in GNPTAB-null cells that uncovered changes in numerous glycoproteins, including multiple receptor tyrosine kinases, suggesting that impaired lysosomal targeting can impact the activity of key growth factor receptors. Dr. Enrico Moro showed results in zebrafish models of Gaucher disease and iduronate sulfatase deficiency, which have enabled the identification of the cellular pathways affected by the enzyme deficiencies. Dr. Allison Bradbury described the well-established center for large animal models of human genetic diseases [at the University of Pennsylvania (Philadelphia, PA)]. She emphasized the importance of using large animal models to test gene therapy and its effectiveness in ameliorating disease progression. Finally, Dr. Lin Liu closed Session II by presenting the BioID method and describing the association of the COPD subunit of the coatamer with the N-terminal portion of GNPTAB, which is required for proper localization to the Golgi.

On Day 2, Session III focused on Sialidosis and Galactosialidosis. The presentations provided a breadth of information, from studies of disease pathogenesis and links to adult diseases, to the development of new therapies and diagnostic methods. Prof. Generoso Andria opened the Session by highlighting landmark studies that led to the discovery of protective protein/cathepsin A (PPCA) as the primary defect in Galactosialidosis. Dr. Alessandra d'Azzo provided an overview of the molecular pathophysiology of Sialidosis and its connection to aging. Dr. Noelia Escobedo described defects in lymphatic pathways in the mouse model of Sialidosis and their potential implications in neurodegeneration, and Dr. Ida Annunziata described mechanisms regulating lysosomal function. Dr. Vish Koppaka presented encouraging results from preclinical studies of recombinant PPCA therapy for Galactosialidosis. Dr. Laura Canafoglia explained the different forms of myoclonus in Sialidosis by using electroencephalographic approaches and differential therapy determined by diagnosis. Finally, Dr. Amelia Morrone presented the full array of diagnostic tests used to identify LSDs and their potential pitfalls.

The last day started with an introductory lecture by Prof. Renzo Guerrini who underlined the connection between lysosomal storage disorders and myoclonus epilepsy, a recurrent clinical complication in several glycoproteinoses. Session IV focused on Aspartylglucosaminuria, Fucosidosis and Schindler disease. Dr. Ritva Tikkanen conveyed a promising personalized therapy for AGA based on the use of betaine and an FDA-approved undisclosed substance. Dr. Xin Chen showed promising preclinical results using an adeno-associated virus approach that rescues behavioral phenotypes in a mouse model of AGA. Dr. Torben Lübke then detailed his development of the first mouse model of Fucosidosis that faithfully recapitulates the human disease and an attempt to perform ERT with the missing enzyme. Dr. Matthew Ellinwood described the effect of ganglioside synthesis in the context of a Galnac transferase/AGA double-knockout model and its profound impairments in neuronal and glial interactions. Dr. Ida Schwartz presented a complex case report of a patient with MLIII in Brazil. Finally, Dr. Cinzia Bellettato, on behalf of Dr. Maurizio Scarpa, discussed the establishment of MetabERN, a unified registry for the European Reference Network.



Although reports about recent basic, translational, and clinical discoveries were fascinating and full of promise, the most invigorating and moving talks were given by patients and their families. Dr. Malm, Jenny Noble, Paul Wagner, Daniel and Faith Peach, and Jean and Paul Leonard talked about living with these diseases, their daily struggles, their faith in the scientists, and their hope for future treatments. The Conference closed with the motto, "Embrace and Endure," and an arrivederci until we come together again in Atlanta, Georgia, for the 6th Glycoproteinosis Conference in 2019.

Richard Steet



Dr Steet is Associate Professor of Biochemistry and Molecular Biology at the Complex Carbohydrate Research Center at the University of Georgia, USA. He has agreed to be ISMRD's Scientific Chair for the next ISMRD conference to be held in Atlanta, Georgia in the northern summer of 2019.

Here he tells us about his experience of the conference in Rome.

It was my earnest pleasure to see old friends and new faces gather in Roma this past November for another ISMRD conference. The city warmly welcomed our group and I know many had the time to explore the historical (and culinary!) wonders Roma has to offer. On the scientific front, this conference was highlighted by significant increases in our understanding of the molecular pathogenesis of the glycoproteinoses as well as encouraging steps towards therapy.

We were updated in many key areas, including the application of gene therapy for ML and enzyme replacement therapy for galactosialidosis, as well as the development and characterization of new model systems.

The conference was also an opportunity to seed new collaborations among the researchers in attendance, and the level of cooperation and interaction within this group has never been more prevalent than now. We were able to honor two of the pioneers in the field of lysosomal biology, Dr. Stuart Kornfeld and Dr. Sandra d'Azzo, with lifetime achievement awards for their scientific and personal contributions to research on glycoproteinoses and to the ISMRD community.

What I took away most from this meeting was the strong sense of friendship that has developed between the families and the researchers. We are on this journey together – and the opportunity to share stories, ideas, hugs and laughter is invaluable. I am thankful to all the families for their willingness to engage and support the researchers in this field. You continue to be our motivation! I invite all of you to join us in Atlanta in 2019 as we gather once more to strengthen the connections we made in Roma, share our ideas and explore new ways to unravel the roadblocks in these disorders and improve the quality of life for your children.

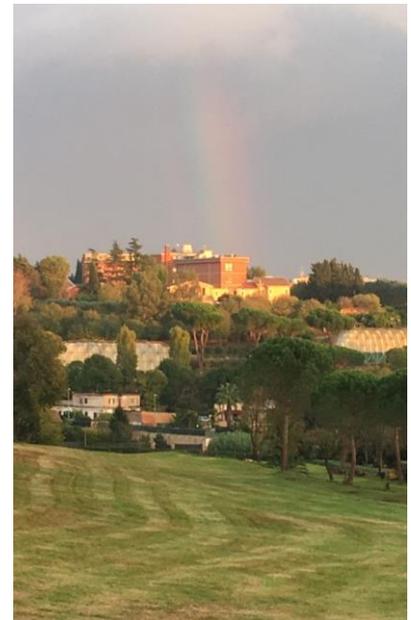


Photo of Rome taken by Dr Steet just outside the conference venue





Our Children







Awards Dinner

The awards dinner was a gala affair. The event was accompanied by The String Quartet playing well-known baroque, classic and opera music.

The lavish three course meal had a distinctive Italian flavour including beef carpaccio, Paccheri pasta with beef ragu and parmesan shavings, herb-crusted pork loin with caramelised apple and chocolate, vanilla and passionfruit profiteroles.

Awards were presented to Alessandra d'Azzo and Stuart Kornfeld for a life time of services to research and knowledge of Lysosomal Storage Diseases.

ISMRD Board member, John Forman, also received in absentia an award for his life time of advocacy and support of families and patients living with rare diseases and for helping in the development of ISMRD.







Donors

ISMRD would like to say a **very special thank you** to the following organisations and companies who have very generously given donations to support the 5th International Conference on Glycoproteinoses



THE WAGNER FOUNDATION



Next ISMRD Conference

6th Glycoproteinases International Conference

Atlanta, Georgia, USA

Summer 2019

ISMRD has established a location and timeframe for our next international conference. It will be held in Atlanta, Georgia during the northern summer of 2019.

It will be every bit as exciting, fun and rewarding as the Rome conference.

Put it in your diary and start fundraising and making your preparations now!

You do not want to miss this conference!

