



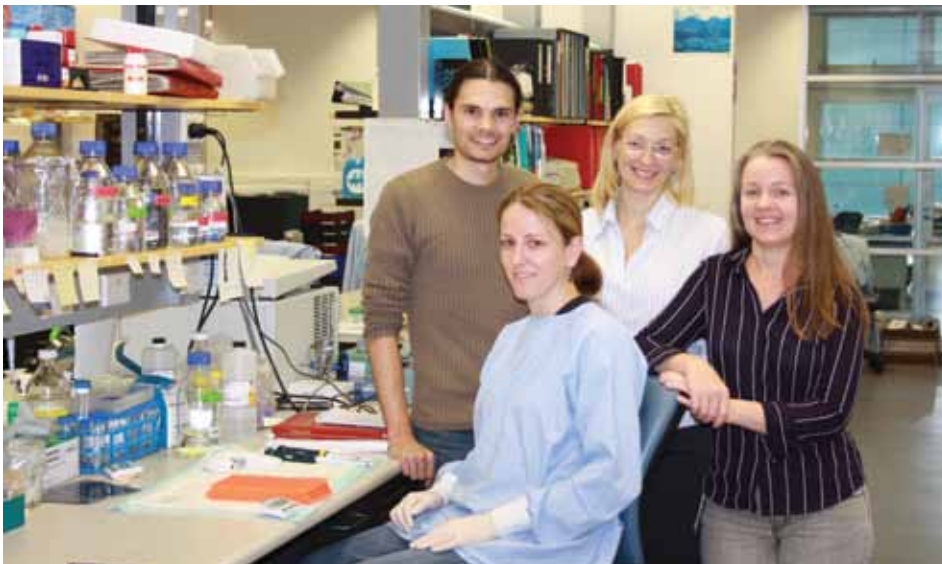
UPDATE

inmr
the childr^en's hospital at Westmead
The Institute for Neuroscience and Muscle Research

The newsletter of the Institute for Neuroscience and Muscle Research

December 2009

An exciting new era



Community support has helped the Institute for Neuroscience and Muscle Research (INMR) raise \$800,000 over the past year – a time of great change and outstanding achievements.

After taking over from Professor Robert Ouvrier as Head of the INMR, Professor Kathryn North has overseen the expansion of the Institute's research focus to include more neurological conditions that affect children, including multiple sclerosis,

brain tumours and hydrocephalus.

The INMR team has also cemented collaborations with leading clinical trials treatment centres based in the United States and Europe, ensuring patients now have access to treatments locally - as soon as they become available.

Professor North said an endorsement of how the Institute had grown, to become an internationally renowned centre for neuromuscular diseases, was reflected in the number of awards and

prizes consistently presented to INMR staff and the Institute's name change in June to better reflect its activities.

"Other examples of our success include increasing competitive grant funding, publications in high quality journals and our membership within international networks such as TREAT-NMD in Europe and the Cooperative International Neuromuscular Research Group (CINRG) in the US," Prof North said.

The changing of the guard at the INMR has included the appointment of Dr Russell Dale, originally from the Great Ormond Street Hospital in London, as Deputy Head. Prof Ouvrier still remains actively involved in the Institute as Foundation Head and Senior Advisor.

Professor North said thanks to the generosity of its supporters, the future for the INMR was very bright: "Our shared vision has had a direct and significant benefit on a large number of children and each day we answer more questions and provide improved diagnosis and care for our patients and their families."

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Teenagers perspective

Jacob's Story

My name is Jacob Lancaster. I am 16 years old and suffer from a cruel muscle wasting disease called Duchenne Muscular Dystrophy. Having Duchenne has not only affected me physically but also socially and emotionally.

On July 1st, 1998, ironically on my 5th birthday, I got diagnosed with this hideous disease. At that age I didn't understand the significance of the condition but my parents sure did. My family and I were living in Cook Islands due to my fathers business from 1995 to 1999. I would run around our backyard in Cook Islands climb and swim pretty much all of the time...

It was almost like I knew I wouldn't be able to walk forever. It was weird.

In the first painful year of the diagnosis of this condition I began falling over time and time again. Climbing up that same grassy hill that I had been climbing up for years was getting that little bit harder. At that stage I knew something wasn't right. My family and I packed up and headed back to Australia. It would be the start of many treatments, physio, check ups, tests and hospital visits that were going to be a crucial and time-consuming part of my life. My first manual wheelchair was ordered.

At the age of 7, I went on steroids in the hope of reversing some of the progression of this condition. There were plenty of pros and cons to this decision but after a 10-month trial I decided to quit the steroids due to an extravagant amount of weight gain and a dramatic change of behaviour. Despite it maintaining my physical strength, it destroyed my spirit. I was never happy. I would sit on the bottom step of my house with my hands on my face and my head on my lap.

School was tough as I was teased about my weight, the way I looked and the way I walked. I was always left out



and alone. I was placed in a unit where some of the kids had intellectual disabilities as well. I didn't fit in. My first electric wheelchair was ordered as it was becoming difficult to get around the large school campus.

At the age of 8 my parents decided to move me to another school in hope of a change for the better, and that it was. I was mainstreamed. I made some great friends at that school and the principal was very good to me.

At the age of 9 I was sitting on the bar stool in my house and needed to go to the toilet so I got off the stool without falling over for once but as I approached the bathroom door I tripped over. After that I never walked again. It was getting too hard and there was no point in walking when all I did was fall down.

At the age of 13 the muscles in my back deteriorated and I had to have a full spinal fusion. This was definitely the worst year I had. I struggled with anxiety and depression on top of that due to the surgery; however, it was worth it in the long run. I have not had a chest infection since the surgery. I have just completed trials for my school certificate and play wheelchair football and hockey. Thankfully, my brain is unaffected.

In closing. I would like to say one thing, I will never give in to this disgusting disease, otherwise Duchenne Muscular Dystrophy will get the better of me and what good is that?

*Jacob Lancaster.
6 October 2009*

Hi everyone, my name is Chloe...

I'm 17 years old and have a peripheral neuropathy known as CMT type 3. After numerous tests and a muscle and nerve biopsy, I was diagnosed with the condition at age 2. I walked unaided at age 3 and only showed signs of overall weakness and walking like I had a little too much to drink. My CMT didn't progress rapidly until I reached about 11. I had developed scoliosis from walking to a preferred side and at age 11 I had a spinal fusion to stop it increasing further. When I reached puberty and high school I started to use an electric wheelchair as I had a sudden decrease in strength and balance. The distance became too far to walk and my schoolbag became too heavy. This occurred between the ages 11-15 and since then my strength has plateaued.

Having CMT has not prevented me from experiencing many great times with family and friends. Over the last year I have been on a South-Pacific cruise, been a bridesmaid, had a helicopter joy flight over the Hawkesbury River and had my year 10 formal. These times mean a lot to me as the last two years I have spent time in hospital with pneumonia. Fortunately in one of my hospital stays I got to trial one of the cough assist machines purchased by INMR. This has helped make my hospital stays shorter and this year I haven't had an admission. I also sleep with a Bi-pap machine for sleep apnea.

Even though CMT prevents me from doing certain things, there is mostly an alternative and this is what I try to focus on. I feel that if your family and friends treat you like everyone else this helps to motivate you and gets you and them involved in things they might not normally do. I am currently

INMR PhD student profile: Dr Yemima (Mimi) Berman



on a trial of "Curcumin" which I take twice a day. It is an Indian spice and has showed improvement in the generation of the myelin sheath when trialled on rats and hopefully will help me and others with CMT type 3. Thankyou for taking the time to read my article and I hope it has helped you understand partly what living with CMT is like. I'll sign off for now with two quotes that I find inspiring:

"Life isn't always fair, but it's still good."

and

SMILE

"A smile costs nothing but gives much. It enriches those who receive it without making poorer those who give it. It takes but a moment, but the memory of it sometimes lasts forever. None is so rich or mighty that they can get along without it. and no-one is so poor that they cannot be made rich by it."

Mimi started her career in Science at The University of Sydney where she completed a Science degree with majors in Molecular Biology and Genetics, and Terrestrial Vertebrates and Evolution. Following an enjoyable Honours year working with fruit flies, she entered the first intake year of the graduate entry medical program to be offered at Flinders University in South Australia. Despite an avid exploration of the local vineyards, Mimi's interest in genetics continued during her medical studies, leading her to travel to Los Angeles in her final year of medical school for electives in Clinical Genetics. Mimi has now completed training in Clinical Genetics and works as a staff specialist at Royal North Shore Hospital.

Towards the end of specialty training in Clinical Genetics, Mimi commenced a PhD in Neurogenetics with Professor Kathryn North and Dr Nan Yang at The Institute for Neuroscience and Muscle Research. Her PhD has focused on defining the effects of a common polymorphism in the ACTN3 gene on metabolism. From studies in mice and humans Mimi has found that the 18% of the world's population who are completely deficient for the skeletal muscle protein alpha-actinin-3 appear to have improved insulin sensitivity, but may be at increased risk of type 2 diabetes. These findings have the potential to improve our understanding of normal

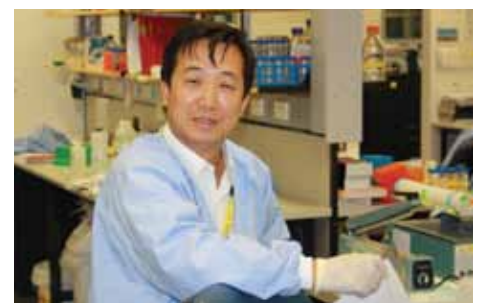


variation in glucose clearance in humans and the pathways involved in glucose clearance in muscle. Mimi plans to complete her PhD in 2009 but hopes to continue a career in research alongside her commitments in Clinical Genetics.

"My PhD has been challenging but incredibly rewarding," Mimi says. "Doing a PhD has opened lots of doors for me in my career. It has also reminded me how to be a good scientist and to apply that to my clinical work. I have enjoyed working with a lab full of enthusiastic young scientists who share my enjoyment of research and discovery. Hopefully I can continue to combine research and clinical work for many years to come."

Student Success

The INMR postgraduate students wowed the recent University of Sydney Discipline of Paediatrics and Child Health Student Conference held at the Novotel at Rosehill on August 14. Impressively, of the eight awards presented four INMR students were awarded for best presentations including Marshall Hogarth, Dr Mimi Berman, Frances Evesson and Frances Lemckert. Frances Lemckert was also presented with the 1st Year Encouragement Award.



The INMR would like to congratulate all students who participated in the meeting. The standard of their research and presentations was world-class and praised by the judges.

Multiple sclerosis in children

Multiple sclerosis (MS) is the most common cause of neurological disability in young adults and is an inflammatory disease of the brain and spinal cord. The inflammation attacks the myelinated white matter, a process called “demyelination”, and results in episodes of neurological attacks. These attacks can cause problems with walking, blindness and bladder control. Sadly, many patients suffer repeated episodes over the years, resulting in progressive neurological disability and premature death in some cases.

The neuroinflammation group at the INMR aims to investigate the earliest stages of demyelination in children with MS. Up to 10% of patients have the onset of disease in childhood. We have recently found an extremely increased immune response against myelin in half of children with MS. We expect this finding will help us improve the treatment of these children, aiming to stop the disease from progressing and causing neurological disability. The neuroinflammation group has seven active researchers and is led by Dr Russell Dale and Dr Fabienne Brilot.

Case history:

Megan was only four years of age when she had her first attack of brain demyelination. Having previously been well, one day she complained of seeing double and being unable to walk in a straight line. She was seen by a child neurologist who noted Megan was very unsteady whilst walking and had reduced vision. Her brain scan showed inflammatory lesions affecting the white matter of her brain (demyelination). She was treated with steroids and her symptoms resolved over two weeks. She was well until three months later when she suffered a further attack. This time, she had severe weakness of her legs, she could not walk and was bed-bound. A further brain scan confirmed new brain lesions. A diagnosis of multiple sclerosis was made. Again she was treated with steroids. Although she improved, she failed to return back to normal and has permanent difficulties with walking. Megan has to have injections of beta-interferon three times per week. This medicine aims to reduce the number of attacks in the future.

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Neurofibromatosis – What’s that?

In 1991 Professor Kathryn North began the first specialised clinic in Australia for children affected by Neurofibromatosis type 1 (NF1). NF1 is an inherited disorder affecting the nervous system. Children with NF1 can have serious health complications including optic gliomas (tumours around nerves to the eyes), other malignant tumours and skeletal abnormalities - pseudoarthrosis (‘fake’ joints). In addition, whilst most people with NF1 have normal intelligence, 50% of patients have specific learning difficulties. This can result in significant lifelong consequences including academic underachievement, behavioural problems, failure to complete higher education and limitation of career choice.

The NF1 team delivers a varied research program to address problems facing children with NF1. Our focus includes discoveries about learning disabilities and potential therapies, the incidence and better monitoring of malignancies in these children and identification of speech and language problems.

Dr Jonathan Payne, a Neuropsychologist with an interest in the relationship between how the brain works and human behaviour (especially in children with NF1), leads

a team assessing learning problems in these children. He works closely with Dr Richard Webster- Neurologist, TY Nelson Department of Neurology; Dr Belinda Barton - Head of Children’s Hospital Education Research Institute (CHERI) and psychologist; Jennifer Lorenzo- an educational psychologist; and Natalie Pride and Shelley Robertson - research assistants. In an exciting development, the team have just embarked on a clinical trial of the medication lovastatin to assess its effect on reducing the learning difficulties in these children. A new addition to the team is Dr Simone Ardern Holmes who works with Dr Mimi Berman and Speech Pathologist David Fitzsimons to determine the incidence of speech and swallowing problems for affected children and who also coordinates clinical trials of therapies that are becoming available to patients with NF1.

Our team needs to be vigilant in assessing the children that visit our clinic for the varied complications that this disorder may cause. We have coordinated research and clinic meetings and clinicians and therapists involved in the medical care of our patients also have active research interests to ensure that the latest discoveries are immediately available for affected Australian children.

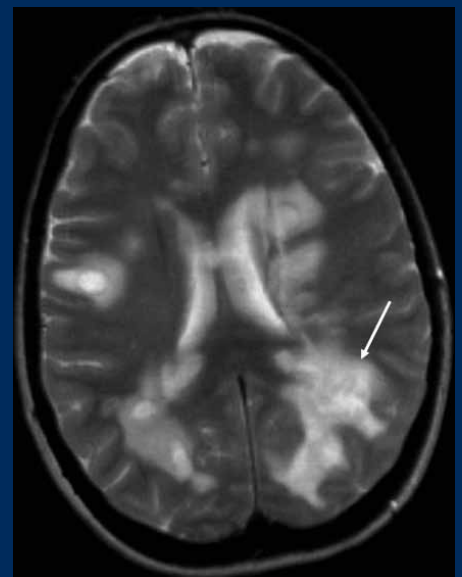


Figure shows Megan’s brain scan during her second attack. There are many inflammatory lesions in her brain white matter (arrow).

Improving diagnosis - a student's journey



Leigh Waddell, PhD student and Laboratory Diagnostic Coordinator, has received a 2009 Human Genetics Society of Australasia International Travel Award to attend the 2010 Summer School of Myology in Paris. Leigh will visit the Newcastle Muscle Centre and the Dubowitz Neuromuscular Unit in the UK – two specialist diagnostic and assessment services for Limb Girdle and Congenital Muscular Dystrophies.

The Summer School of Myology is an

internationally-recognised intensive 10-day training course in Myology, consisting of a series of lectures and interactive workshops led by leading clinicians and scientists in the field. The School addresses most aspects of muscle disease from basic science to cutting-edge therapies, clinical and genetic approaches to muscle disease. Attendance at this summer school will provide Leigh with world-class training in genetic muscle disease, assisting her in both the completion of her PhD as well as

her current and future career within the area of diagnosis of muscular dystrophies.

Visiting the UK Muscular Dystrophy Diagnostic Services will allow Leigh to bring back the most up-to-date knowledge and expertise to apply to the diagnostic service provided by the INMR. It will also strengthen the relationship of the INMR with large diagnostic centres around the world and result in improved diagnoses for our patients.

International Ankle Symposium



Kristy Rose, INMR PhD student and Clinical Trials Coordinator, recently attended the International Ankle

Symposium at The University of Sydney where she received the best student presentation award. The INMR would like to congratulate Kristy on her award and her demonstrated excellence in her research field. Since joining the INMR in 2006 Kristy has been awarded five awards for research excellence at local and International conferences and has received five financial awards including three conference travel awards.

In this study Kristy investigated factors associated with foot and ankle development in preschool-age children with Charcot-Marie-Tooth disease type 1A (CMT1A) and compared this with children of the same age who were not affected by CMT1A. She found that at this very young age

children with CMT1A had selective foot and ankle muscle weakness as well as imbalance in the strength of the muscles around the foot and ankle. She also found that children with CMT1A had reduced ankle flexibility. As none of the children with CMT1A were found to have pes cavus foot posture, which is a hallmark feature of this disease in older children, it suggests selective foot and ankle muscle weakness and imbalance as well as reduced ankle flexibility may have some influence in the development of cavus foot deformity. Future studies will tell us whether interventions which improve ankle flexibility and rebalance the strength of muscles around the foot and ankle can delay or prevent foot deformity in children with CMT1A.

Towards a brighter future

The INMR and the Duchenne Foundation have joined in partnership to host the "Towards a Brighter Future" conference in Sydney in 2010. The conference aims to provide sound and current medical and scientific information to reassure parents that whilst there is no "one size fits all" miracle cure for each disorder, the future is going to be much brighter for many of our children.

We know that world standards of care are changing every year via new drug therapies, practices and research findings and it is critical that we keep abreast of new information. The conference will deliver a stimulating, informative and topical program involving national and international speakers in the field of neuromuscular conditions. Speakers will present the latest information for researchers, students, health professionals (doctors,

allied health and nursing), educators (teachers, teacher's aides and special needs' educators), parents and people affected by these conditions.

Topics to be covered at the conference include diagnosis, management and the latest research. International speakers include Professor Jeffrey Chamberlain (USA), Professor Kate Bushby (UK -Co-Chair of TREAT-NMD), Dr Jos Hendriksen (The Netherlands - cognitive and behavioural expert), Dr John Bourke (UK - cardiac expert), Dr Jes Rahbek (a rehabilitation specialist from Denmark) and Louis Boitano (a respiratory specialist and NIV advocate from Seattle USA). Local speakers include Professor Kathryn North (NSW), Professor Robert Ouvrier (NSW), Dr Joshua Burns (NSW), Dr Monique Ryan (VIC), A/Professor Steve Wilton (WA), Professor Nigel Lang (WA) and many more.



The conference will be held at Eastern Avenue Auditorium, The University of Sydney, on February 26-27, 2010. For further information please refer to the conference website at www.towardsabrighterfuture.org.au