Dear SASHG members

Welcome to the first newsletter of 2019! This year has flown by, with the first quarter already behind us.

In this issue of the newsletter, we feature the Mitochondria Research Laboratory (MRL) of North-West University. Prof. Francois van der Westhuizen, who leads this group along with Prof. Roan Louw, gives us an overview of the focus areas and research of the MRL, which includes links to relevant publications from this group. We also have a feature on one of the MRL students, Ms Michelle Mereis (PhD candidate), which includes a personal profile and a summary of an article in her research area.

We would also like to draw attention to an article that was published on the 18th April 2018 in Nature News, ‘African scientists call for more control of their continent’s genomic data’, which should be of interest to members of our community. Link: https://www.nature.com/articles/d41586-018-04685-1

In other news, the abstract submission deadline for the SASHG 2019 conference, as well as the SASBiSC/SASHG Young Researchers’ Symposium, fast approaches. Don’t forget to submit your abstracts by the 12th April, via the SASHG congress website: https://sashg2019.co.za/call-abstracts/

We are also pleased to announce that all full-time or part-time students, interns, registrars, and postdoctoral fellows are eligible to apply for a SASHG conference travel bursary (deadline: 18th April). Please see the following link for more information: https://sashg2019.co.za/travel-bursaries/

We hope to see you there, and we wish you all the best for the year ahead!
**NWU Mitochondria Research Laboratory (MRL)**

**The Genetics of Energy Metabolism Diseases**

The Mitochondria Research Laboratory (MRL) at the North-West University was established in 2002, with the purpose of studying the involvement of energy metabolism and its genetics in rare inherited and non-communicable diseases. Bioenergetics - and especially the role of mitochondria - has been shown to greatly affect human health and contribute to many diseases on the background of the significant energetic changes of modern lifestyles. The primary focus of this group, led by Profs. Francois van der Westhuizen and Roan Louw with wide national and international collaboration, has been on studying mitochondrial disease (MD) and its aetiology in the diverse South African population. MD is a complex genetic disease of the OXPHOS system, affecting ~1/5000 people with a wide range of clinical features involving several tissues.

This research involves an interdisciplinary approach, studying the clinical and biochemical features, identifying the nuclear and mtDNA mutations in our population, as well as specialized investigations such as functional studies and metabolomics in patients and animal disease models.

This group also participates in a recently established global collaboration between six countries, called the International Centre for Genomic Medicine in Neuromuscular Disease.

The role of mtDNA variation in more common non-communicable disease has been an additional interest of the MRL, with studies investigating possible associations in cardiovascular disease, chronic fatigue syndrome and Parkinson’s disease.

Future plans are to focus on relevant disease models to study the effects of genetic variation that affects energy metabolism and the mechanisms that can be targeted in novel therapies for these disorders.

For more information go to: [http://natural-sciences.nwu.ac.za/mitochondrial-laboratory/research-focus](http://natural-sciences.nwu.ac.za/mitochondrial-laboratory/research-focus)

**Photo:** Prof. van der Westhuizen (far left) with the 2019 NWU Mitochondria Research Laboratory (MRL) group.
1. What is your current area of research?
For my PhD, I am currently researching inborn errors of fatty acid metabolism – in particular the genetic and biochemical presentation of multiple acyl-CoA dehydrogenase deficiency (MADD) in paediatric patients of South African descent. While MADD is well documented in most of the European population, little is known of its presentation in the diverse ethnic groups of South Africa.

2. What is your background and how did you become interested in your field of research?
I have been fascinated with human pathology from a very young age. My interest in Biochemistry and inborn errors of metabolism resulted from the passion and excitement demonstrated by two of my favourite lecturers (Professors Francois van der Westhuizen and Japie Mienie) during my undergraduate and postgraduate studies.

3. What piece of advice would you give to somebody beginning their career in global health?
Never be afraid to ask questions, no matter how trivial they may seem. It is the only way you learn how to ask the right questions.

4. Do you have any secret talents?
I love to draw. I’ve been sketching ever since I could hold a pencil.

5. How do you like to relax?
A book, movie or series with an exceptional plot is always a winner.

6. What would your superpower be?
The ability to teleport – I can only imagine how much I would get done. A little break on a tropical island in-between experiments doesn’t sound too bad either.

7. If you could go back in time where would you go (and why)?
Definitely America in the 80s, for the sole purpose of stalking my favourite bands.

Article summary compiled by Michelle Mereis
A Novel Truncating FLAD1 Variant, Causing Multiple Acyl-CoA Dehydrogenase Deficiency (MADD) in an 8-Year-Old Boy

Multiple acyl-CoA dehydrogenase deficiency (MADD), or glutaric aciduria type II (GAIi), is an autosomal recessive metabolic disorder affecting the fatty acid and amino acid metabolism. The disorder is clinically heterogeneous and may range from severe, neonatal-onset to mild, adult-onset forms. Traditionally, MADD results from mutations in the ETFA, ETFB or ETFDH genes, which respectively encode for the alpha and beta subunits of the electron transport flavoprotein (ETF) and the ETF-ubiquinone oxidoreductase (ETFQO). Since both ETF and ETFQO require flavin adenine dinucleotide (FAD) as a prosthetic group to function, mutations in the genes involved in FAD’s synthesis from riboflavin [via flavin mononucleotide (FMN)] are increasingly being recognized as MADD-causing. One such a gene, FLAD1, encodes FAD synthase (FADS) – the protein responsible for adenylating FMN to FAD.

In this article, the authors describe a novel truncating homozygous variant in FLAD1 (c.745C > T, p. Arg249*) resulting in MADD in an 8-year old Palestinian boy. To assess the associated biochemical parameters, the authors measured the quantity of riboflavin, FMN, FAD and the FADS protein in patient-derived fibroblasts (skin cells). Their findings indicate a drastic reduction in mature FADS with a corresponding decrease in the rate of FAD synthesis and cellular FAD content, thereby proving a functional deficiency. They further report a significant decrease in cellular FMN and riboflavin content, which suggests a possible regulatory metabolic response to the impairment of FADS. Finally, the authors comment on the use of riboflavin as a treatment for FLAD1-related MADD. The results presented in this article exceed those previously documented for MADD caused by FLAD1 variants and strongly advocate the inclusion of riboflavin metabolism in the differential diagnosis of MADD.

Article link: A Novel Truncating FLAD1 Variant, Causing Multiple Acyl-CoA Dehydrogenase Deficiency (MADD) in an 8-Year-Old Boy