SASHG NEWSLETTER; AUGUST 2018

Dear SASHG Members

Welcome to the first newsletter from the new SASHG YRF team. In the era of rapid technological advancements, we are in the midst of groundbreaking research, and this year has brought with it a multitude of new discoveries in the field of Human Genetics. In the incredibly busy life of a researcher, where we are presented with daily challenges to tackle, it is often difficult to find the time or energy to explore the plethora of exciting findings outside of our own niches. With this in mind, these newsletters will contain brief reports of current research in the broader field, to provide members with relevant information from different focus areas within Human Genetics. Personal profiles of young researchers will accompany each newsletter, highlighting their specific research interests. With this, we aim to lessen the gap between the many different working groups, helping us all to become better acquainted with the ongoing research in our community.

As the new Young Researchers' Forum Representative, I have decided to begin the cycle with students from Stellenbosch University, my home turf. I look forward to reaching out, and sharing with you the interests of young researchers from all over southern Africa. These newsletters can hopefully provide a quick mental break from your own consuming research questions, and I hope that you enjoy reading them!

Warm regards,

Ms Emma Frickel
Representative: Young Researchers' Forum

Systems Genetics Research Group

The Stellenbosch University Systems Genetics group was established in 2017 as a transdisciplinary research enterprise investigating complex biological phenomena with underlying genetic underpinnings. By moving away from more 'reductionist' methodological approaches, the research group aims to incorporate a systems biology perspective to better explain biological variation in form and function, by investigating various genetic and environmental factors, as well as the complex interactions between the two. The systems approach in particular seeks to provide a multidimensional framework to define a singular biological system within the ecological and evolutionary context of the organism by investigating the flow of biological information from the genome, transcriptome, proteome, and metabolome to the broader phenome. By incorporating a more holistic approach, it becomes possible to refine our understanding of functionality and the relationship between genotype and phenotype within complex biological systems.

The group is spearheaded by Drs Rhode and McGregor, both based at the Department of Genetics, Stellenbosch University. Although the focus is not exclusively on humans, current studies include investigating how the unique history of the South African human population influences the development of phenotypes in complex traits, using mental health disorders as a model. This includes exploring the utility of different genetic markers to characterize population substructure in the context of South Africa, examining heterogeneous genomic divergence between subpopulations at genes implicated in mental health disorders, as well as investigating the genetic merit behind the use of self-reported language to control for confounding in association analyses.

For more information go to:
https://www.sun.ac.za/english/faculty/agri/genetics/research/human-genetics

The Genetics of Depression

Recent results from an unprecedented global effort involving more than 200 scientists from 161 institutions working with the Psychiatric Genomics Consortium (PGC), has brought new hope for developing more effective treatments for major depression.

Major depressive disorder (MDD) is a common illness accompanied by considerable morbidity, disability, costs, and heightened risk of suicide. The identification of causal variants for MDD has proven difficult in the past, as a multitude of genetic loci with small-effects are believed to influence this disorder, implying that larger sample sizes are needed to detect specific loci.

By carefully combining seven separate datasets, this research has shed new light on the genetic underpinnings of this debilitating condition, which affects over 300 million people globally. The meta-analysis, which includes 135,458 individuals with depression and 344,901 controls, has identified 44 independent loci significantly associated with depression, of which 30 have not previously been linked to MDD or depressive symptoms.

The group found an overlap in the genetics that underpin depression and other mental health disorders such as anxiety, schizophrenia and bipolar disorder. The findings also suggest that having a higher body mass index (BMI) is linked to an increased risk of depression. The genetic architecture of major depression was also positively correlated with multiple measures of sleep quality (insomnia, daytime sleepiness, and tiredness).

Furthermore, the study found that some of the identified genetic variants are linked to neurotransmitters such as serotonin, which current antidepressants target. However, current antidepressant drugs have limited effect, and not all patients suffering from major depression draw benefit from current treatment avenues. As no major advances in the treatment of depression have been made since 1990, the implication of new gene variants, and possible biological mechanisms, holds particular value to therapeutic progress. Gerome Breen stated that "The hope is that in new data we identify new processes that can be targeted by newly developed types of drugs, which have different mechanisms of action to existing medications."

As with many other complex disorders, risk for depression is influenced by the amalgamation of both genetic and environmental effects. "By identifying the genetic factors, we're getting new tools for research into the interplay between genetics and the environment, so that we can gain a more complete understanding of the disease mechanisms", said Anders Børglum, one of the co-leaders of the study, in a recent interview.

More research will be needed to confirm that these newly discovered variants are indeed linked to MDD, as not all participants were clinically diagnosed, but instead were self-reporting. Nonetheless, better understanding the genetic causes of depression might allow for both the improvement of current, and the elucidation of new treatment strategies.

Article link: https://doi.org/10.1038/s41588-018-0090-3

Compiled by: Wilro van Niekerk

Green Tea and Wine for a Healthy Brain?

Researchers from Tel Aviv University have conducted a study investigating the potential use of compounds found in green tea and red wine to prevent the formation of toxic metabolites in inherited congenital metabolic disorders, that could otherwise contribute toward both developmental and mental disorders. The researchers considered two compounds: (1) epigallocatechin gallate (EGCG) and (2) tannic acid, from green tea and red wine respectively. Both compounds are already well known for potential health benefits, including the ability of tannins to prevent the formation of toxic amyloid structures that have been implicated in neurodegenerative disorders like Alzheimer's and Parkinson's disease.

The disorders in this study constitute a significant portion of pediatric genetic diseases. One such disease, phenylketonuria (PKU), produces an aggregation of phenylalanine. This metabolite must henceforth be avoided at all costs by those affected, otherwise they may face severe developmental problems. This research was initially based on two previous studies; the first demonstrating phenylalanine's ability for self-assembly and formation of amyloid structures, like those seen in Alzheimer's, Parkinson's, and other neurodegenerative disorders. The second study too, demonstrated an accumulation of metabolites found in other inborn congenital metabolic diseases to formation of toxic amyloid aggregates.

Up until this point, a viable course of 'treatment' has been suggestive of highly restrictive dietary requirements, hence the researchers investigated potential inhibitory effects exerted on metabolites amyloid formation by the two polyphenolic compounds mentioned above. Both these inhibitors have been previously shown to efficiently inhibit the formation of various protein amyloids *in vitro* and *in vivo*, displaying beneficial therapeutic and preventive effects in neurodegenerative diseases.

The researchers showed that the polyphenols successfully inhibited self-assembly of adenine, phenylalanine, and tyrosine into amyloid-like fibrils, known to accumulate in phosphoribosyltransferase deficiency, PKU and tyrosinemia metabolic disorders, respectively. The results were promising, with both tannic acid and EGCG effective in blocking the formation of toxic amyloid structures. The researchers also used computer simulations to verify the mechanism driving the compounds in conjunction with demonstration by *in vitro* assays and neuronal cell culture models.

This study has expanded on research pertaining to generic amyloid hypothesis, linking amyloid formation and metabolite amyloids in inborn error of metabolism disorders. The inhibition of metabolite amyloids by natural small polyphenolic compounds may lead to an innovative course of treatment for these less-explored metabolic disorders. This research has also uncovered many unknowns, as entering into a new era of understanding the role and the importance of metabolites in various diseases, including metabolic diseases, neurodegenerative diseases and even cancer can, provide ground-breaking tools and potential benefit to a wide range of patients.

Article link:
https://www.nature.com/articles/s42004-018-0025-z

Compiled by: Megan Hamilton

STUDENT PROFILE

Wilro van Niekerk

MSc (Genetics)

Stellenbosch University

1. ***What is your current area of research?***

   Currently I am investigating underlying genetic population substructure and heterogeneous genomic divergence in a South African cohort, using both microsatellite (STR) and Single Nucleotide Polymorphism (SNP) markers. I am interested in, and hope to contribute to, increasing the power to find associations in studies relating to mental health disorders.

2. ***What is your background and how did you become interested in your field of research?***

   I am, and have always been, passionate about both Psychology and Genetics. By investigating the methodological approaches we use to determine the genetic contribution to mental health disorders, I wish contribute to our knowledge in the field.

3. ***What piece of advice would you give to somebody beginning their career in global health?***

   Explore as many of the avenues as you are exposed to. Loving what you do sometimes relies on knowing the difference between an interest and a passion.

4. ***How do you like to relax?***

   I am a little bit of a foodie. I can play around in the kitchen for hours.

5. ***Has anyone in particular inspired you in your field or science in general?***

   After starting my postgraduate degree I faced the challenge of choosing between two very inspirational supervisors. Luckily for me, Drs N McGregor and C Rhode had decided to start the Systems Genetics Working Group together, and my dilemma turned to opportunity.

6. ***What would your superpower be?***

   Teleportation. Travel the world, be back in time for lunch.

STUDENT PROFILE

Megan Hamilton

MSc (Human Genetics)

Stellenbosch University

1. ***What is your current area of research?***

   Currently my research falls in the fields of pharmacogenetics and mental health. Specifically pertaining to schizophrenia and the optimization of treatment, I'm currently investigating miRNA-mediated regulation of regulatory genes in terms of antipsychotic treatment outcome.

2. ***What is your background and how did you become interested in your field of research?***

   I have a BSc background – but my passion has always been in the interest of human health – I wanted to be a doctor when I was in school but quickly found a passion for genetics when introduced in biology.

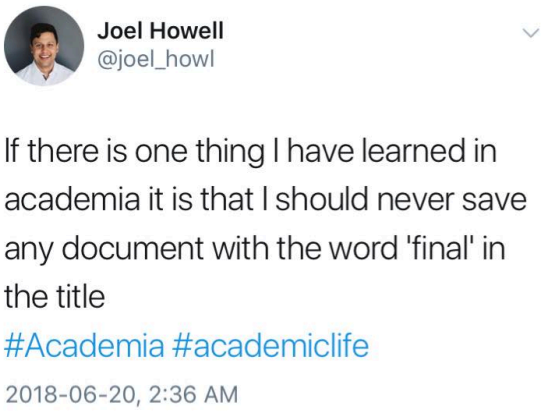
3. ***What piece of advice would you give to somebody beginning their career in global health?***

   My advice would be – don't be discouraged by failure! Each 'failure' is an opportunity to learn and grow further from that experience!

4. ***Do you have any secret talents?***

   I'm an avid yogi! I'm always upside down when I get the chance, or moving in some way.

5. ***Do you know any science jokes you can share?***



6. ***How do you like to relax?***

   I'm a very outdoorsy active person, so either a hike/run/walk/exercise of some kind – I also like to journal and draw.

7. ***Has anyone in particular inspired you in your field or science in general?***

   It sounds juvenile but when I was a child I would watch E.R non-stop, it was my favourite show and what initially inspired me to pursue science – that and my high-school biology teacher (Mr. Pete Le Roux) really encouraged me then too.

8. ***What would your superpower be?***

   To be able to 'translate' emotions via touch – when you can't explain how you feel? Being able to convey that simply through contact.

9. ***If you could go back in time where would you go (and why)?***

   Africa – before the time of 'modern' humans to see exactly what happened in our evolution!