Weill Cornell Medicine-Qatar

**WCM-Q and Sidra Medicine research boosts understanding of personalized medicine for Qataris**

**Doha – June 12, 2018:** Weill Cornell Medicine-Qatar researchers, working alongside peers from Sidra Medicine and Weill Cornell Medicine in New York, have made important new discoveries about genetic variations that affect the human metabolism, which could eventually help make diagnoses and treatments more effective.

The researchers analyzed the genetic material and the metabolisms of 1,000 Qatari subjects to identify links between genetic variations and metabolism. While similar research has previously been carried out in European populations, this is the first time that such a large study of this kind has focused on an Arab population.

The study, which has been published in the leading scientific journal *Nature Communications*, sheds light on the role of genetic differences between people and their ability to metabolize certain molecules from food. Some of these genetic differences may explain why people have different risks of developing metabolic disorders, such as diabetes and cardiovascular disease.

The research has established a high-quality data resource that will aid diagnosis of inherited diseases in Qatari and other Arab populations, as well as helping physicians identify targets for personalized treatments tailored to the individual genetic and metabolic profiles of patients.

The paper, titled 'Whole-exome sequencing identifies common and rare variant metabolic QTLs in a Middle Eastern population' has two joint first authors: Dr. Noha A. Yousri, adjunct assistant professor of genetic medicine at WCM-Q, and Dr. Khalid Fakhro, director of human genetics at Sidra Medicine and assistant professor of genetic medicine at WCM-Q.

Dr. Yousri said: "While previous studies of this type – known as Metabolomics Genome Wide Association Studies (mGWAS) – have been conducted in Caucasian populations, none had looked at Middle Eastern populations. Our motivation was to do a similar study for Qataris to understand how genetic variations affect metabolite levels in both health and disease states in this population. However, the use of an enhanced technology -whole exome sequencing- facilitated studying the effect of functional variants, in particular, on moderating metabolic pathways.

She added: "This study is the first of its kind to be done in a Middle Eastern population, and will benefit the whole region. It will eventually allow us to predict the likelihood that individuals will develop certain diseases, and also point the way towards more effective personalized medicine. It also paves the way to future collaborative efforts with key institutions in Qatar to integrate different omics data, as epigenetics and others, with genetic variants for enhancing disease treatment in this population."

The researchers used a technique called Whole-Exome Sequencing (WES) to analyze the exome - the part of the genome that contains all of the protein-coding genes. They then used a technique called high-resolution metabolomics profiling to map the metabolic processes taking place in each individual. In total, 1,303 metabolites were analyzed. The two datasets were then compared using high-performance computers to pinpoint associations between metabolic disorders and genetic variants in

particular positions on the chromosome, known as 'loci'. In total, the study discovered 21 common genetic loci and 12 rare loci, 45 percent of which were completely new discoveries, presumably specific to Qatar.

The study is the latest in a series of research projects led by WCM-Q and Weill Cornell Medicine in New York focusing on the Qatari genome. A previous study broke new ground by gathering vast amounts of genetic data from a large sample of the Qatari population and establishing a reference genome - an essential resource for understanding the nature of disease in a population and as a basis for personalized medicine.

Dr. Fakhro said: "The take-home message is that genetics alone may not give a complete picture of health and disease, and Metabolomic analysis can play a significant role in filling the gaps. Our work lays down an initial map of what a 'healthy Qatari metabolic profile' looks like, and can serve as a baseline for future studies against which 'disease states' can be compared."

He added: "Generating these profiles for 1,000 Qataris is a follow-up to our previous works studying Qatari genomes and performing large-scale analysis for the population. Our aim is to contribute these discoveries to the larger biomedical research enterprise in Qatar, which together will form the foundation on which precision medicine will be built in the country. This is also embedded in Sidra Medicine's approach to personalized care for the women, children and young people in Qatar. "

Other key contributors to the study were Dr. Karsten Suhre, professor of physiology and biophysics & director of the Bioinformatics Core at WCM-Q, and Dr. Ronald Crystal, professor and chairman of the Department of Genetic Medicine at Weill Cornell Medicine in New York.

Dr. Suhre, a pioneer in the field of metabolomics, said: "It is extremely pleasing to be able to unite the two disciplines of genomics and metabolomics in a single study in this way. By studying the associations between genes and the metabolism we are able to understand the nature of disease far more comprehensively."

Dr. Crystal, one of the world's leading genetic medicine experts, said: "Previous studies like this have mainly focused on Caucasian populations. While the Qatari population has essentially the same genes, the variations that cause disease are different from those of the Caucasian populations. As such, this study not only advances personalized medicine in the Middle East but also increases our understanding of how genetic diversity influences inherited disease."

The study was supported by the Biomedical Research Program at WCM-Q, with funding from Qatar Foundation. It was also supported by Qatar National Research Fund grants 09-740-3-192, and 09-741-3-793 and in part by 7-272-1-041.

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**Photos captions:**

**Photo1 & Photo2**: Dr. Noha Yousri of WCM-Q and Dr. Khalid Fakhro of Sidra Medicine and WCM-Q are joint first authors of research into genetic variations affecting metabolism among Qataris.

**Photo3**: WCM-Q's Dr. Karsten Suhre contributed his expertise as a pioneer in the field of metabolomics to the groundbreaking study.

**Photo4**: Dr. Ronald Crystal of Weill Cornell Medicine in New York, one of the world's leading genetic medicine experts, said the study increases understanding of the influence of genetic diversity on inherited disease.

**About Weill Cornell Medicine - Qatar**

Weill Cornell Medicine - Qatar is a partnership between Cornell University and Qatar Foundation. It offers a comprehensive six-year medical program leading to the Cornell University M.D. degree with teaching by Cornell and Weill Cornell faculty and by physicians at Hamad Medical Corporation (HMC), Aspetar Orthopedic and Sports Medicine Hospital, the Primary Health Care Corporation, the Feto Maternal Center, and Sidra Medicine, who hold Weill Cornell appointments. Through its biomedical research program, WCM-Q is building a sustainable research community in Qatar while advancing basic science and clinical research. Through its medical college, WCM-Q seeks to provide the finest education possible for medical students, to improve health care both now and for future generations, and to provide high quality health care to the Qatari population.

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