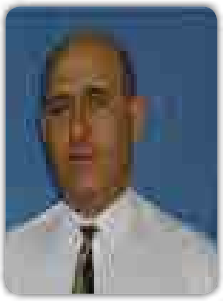

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Dissection the complexity of host susceptibility to type 2 diabetes development and the pharmacogenetics dilemma

Type-2 diabetes (T2D) is a complex metabolic disease characterized by impaired glucose tolerance. Despite environmental high risk factors, host genetic background is a strong component of T2D development. Identifying these genetic factors could contribute to developing new medical treatments and tools to identify most at risk individuals. Recently, a novel highly genetically diverse mouse resource population, named the Collaborative Cross (CC), was developed and aimed for studying complex traits, including T2D. The CC mice have more genetic diversity than human population. Here, we used this mouse population of mapping Quantitative Trait Loci (QTL) underlying impaired glucose tolerance phenotypic variations and associated diseases including liver fat accumulation in CC mice. Furthermore, we used Next generation RNA-sequencing (RNAseq) for studying gene expression variations and alternative splicing observation to identify genes that may underline the disease development. Our results have shown significant variations between the recorded phenotypes between the different CC lines and a sex was observed. QTL mapping results have identified number of small genomic regions associated with the tested traits.

Methods: A Cohort of 683 mice of 68 CC lines maintained on high-fat (42% fat) diet (HFD) for 12 weeks followed by biweekly body weight (BW), body length (BL), waist circumstance (WC), and body mass index (BMI) were measured. Subsequently, assessed by intraperitoneal glucose tolerance test (IPGTT), and liver weight (electronic balance) and fattiness (DEXA scanner) was assessed. Genomic DNA of the CC lines was genotyped with high-density single nucleotide polymorphic (SNP) markers and finally QTL mapping was conducted. Next generation RNA-sequencing (RNAseq) was performed for livers of diabetic and non-diabetic mice of CC lines following 12 weeks HFD, and DNA methylation assessed on blood for testing epigenetic effect of HFD.

Results & Discussion: Genome wide search for QTL analysis has revealed number of significant QTL associated with glucose tolerance test, which was defined as area under curve (AUC), as well QTL underline fatty liver accumulation as a results of T2D development. RNAseq approach of hepatic gene expression analysis has identified significant gene variations between the diabetic and no-diabetic mice, as well between both sexes.

Biography

Fuad A Iraqi is a Molecular Geneticist and world leader in the area of dissecting complex traits including hosts susceptibility to infection and chronic diseases. His current research is focused on understanding diseases etiology and host susceptibility to infectious and chronic diseases including type 2 diabetes and cardiovascular diseases (CVD) associated with obesity, Klebsiella pneumonia, Aspergillus fumigatus, dental infection (Periodontitis), and mapping modifiers for colon cancer development. His research projects are important for better understanding the host susceptibility to variety of infectious and chronic diseases, which will serve a step towards improving our knowledge of specific and general pathways and network systems, which can lead to establish better disease prevention and control strategies. He has studied for his BSc (Biology), MSc (Biochemistry) and PhD (Molecular Genetics) at the Hebrew University at Jerusalem. He worked as a Postdoctoral for two years at the Hospital for Sick Children at Toronto, Canada, and two more years at the USDA, ARS- East Lansing, MI, before joining the International Livestock Research Institute (ILRI), based in Nairobi, Kenya as Scientist. In 2007, he moved to his current position as Professor and Chairman of the Department of Clinical Microbiology and Immunology, at the Faculty of Medicine at Tel-Aviv University. He has more than 135 publications on per reviewed journals, and more than 25 book chapters. His current H-Index is 27.

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