Journal of Health Disparities Research and Practice

Volume 12, *Issue* 4 2018 *Article* 52

2019 STEP-UP SPECIAL ISSUE

Functional Analysis of Single Nucleotide Polymorphisms Associated with Type 2 Diabetes

Serdjan Rolovic* Zhongming Zhao, PhD†

Junfei Zhao, PhD‡

*

†The University of Texas Health Science Center at Houston

‡The University of Texas Health Science Center at Houston

Functional Analysis of Single Nucleotide Polymorphisms Associated with Type 2 Diabetes*

Serdjan Rolovic; Zhongming Zhao, PhD; and Junfei Zhao, PhD

Abstract

Type 2 diabetes (T2D), a metabolic disorder characterized by insulin resistance and relative insulin deficiency, is a life-long, common, complex disease of major public health importance. To date, there have been 86 published studies that have reported 639 associations between single nucleotide polymorphisms (SNPs) and T2D in the GWAS Catalog database, and others studies in literature. However, the majority ($\sim$93%) of the SNPs emerging from these studies are located within noncoding sequence, complicating their functional evaluation. Recently, several lines of evidence have suggested the involvement of a proportion of such variants in transcriptional regulatory mechanisms, including modulation of promoter and enhancer elements and enrichment within expression quantitative trait loci (eQTL). In this study, we downloaded T2D-associated SNPs from GWASdb, a derived database that included the data from GWAS Catalog. We then annotated them with transcription factor (TF) motif, promoter/enhancer, and eQTL information followed by the construction of a TF-target network module, in order to better detect the underlying mechanism of genetic variants involving in T2D. We found that T2D associated SNPs were significantly enriched with functional information. In addition, we found that functional annotations could significantly improve the power of detecting causal variants and understanding their pathogenesis. Using the data collected from the Gene-Tissue Expression Project (GTEx), we could further find the target genes for those eQTL SNPs. When cross-referencing with the Drug Bank database, we were able to discover certain drugs that might regulate the expression of these genes and fight against T2D.

KEYWORDS: Genetic variants; type 2 diabetes; association; functional roles; Genome-wide Association Studies

---

*The STEP-UP HS program is supported by the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health, Grant number: 1R25DK098067-01.

Journal of Health Disparities Research and Practice
Volume 12, STEP-UP Special Issue, Summer 2019, pp. 73

School of Public Health
University of Nevada, Las Vegas

Functional Analysis of Single Nucleotide Polymorphisms Associated with Type 2 Diabetes

Serdjan Rolovic
Zhongming Zhao, PhD, The University of Texas Health Science Center at Houston
Junfei Zhao, PhD, The University of Texas Health Science Center at Houston
Coordinating Center: University of Nevada, Las Vegas

ABSTRACT

Type 2 diabetes (T2D), a metabolic disorder characterized by insulin resistance and relative insulin deficiency, is a life-long, common, complex disease of major public health importance. To date, there have been 86 published studies that have reported 639 associations between single nucleotide polymorphisms (SNPs) and T2D in the GWAS Catalog database, and others studies in literature. However, the majority (~93%) of the SNPs emerging from these studies are located within noncoding sequence, complicating their functional evaluation. Recently, several lines of evidence have suggested the involvement of a proportion of such variants in transcriptional regulatory mechanisms, including modulation of promoter and enhancer elements and enrichment within expression quantitative trait loci (eQTL). In this study, we downloaded T2D-associated SNPs from GWASdb, a derived database that included the data from GWAS Catalog. We then annotated them with transcription factor (TF) motif, promoter/enhancer, and eQTL information followed by the construction of a TF-target network module, in order to better detect the underlying mechanism of genetic variants involving in T2D. We found that T2D associated SNPs were significantly enriched with functional information. In addition, we found that functional annotations could significantly improve the power of detecting causal variants and understanding their pathogenesis. Using the data collected from the Gene-Tissue Expression Project (GTEx), we could further find the target genes for those eQTL SNPs. When cross-referencing with the Drug Bank database, we were able to discover certain drugs that might regulate the expression of these genes and fight against T2D.

Keywords: Genetic variants, type 2 diabetes, association, functional roles, Genome-wide Association Studies

ACKNOWLEDGEMENTS

The STEP-UP HS program is supported by the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health, Grant number: 1R25DK098067-01.