

Genetics of Type 2 Diabetes, Obesity and Their Related Traits in Mexican Americans

Ravindranath Duggirala on behalf of the SAMAFS Research Group, South Texas Diabetes and Obesity Institute, University of Texas Rio Grande valley, Edinburg, Texas, US

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Introduction:

The twin epidemics of obesity and type 2 diabetes (T2D) have become global public health crises. Unfortunately, children and adolescents are not spared: the prevalence rates of obesity and T2D has increased dramatically among children and adolescents within the last few decades globally. In the US, minority groups such as Mexican-origin Hispanics (Mexican Americans [MAs]) have a disproportionate burden of T2D, obesity and their clinical correlates. Over the past 25 years, we have been examining the genetic factors that influence susceptibility to complex diseases including T2D, obesity and their related traits in MAs in San Antonio, Texas, using data from several well-characterized large family studies. Therefore, the objective of this presentation is an overview of our genetic investigations of T2D and its related traits in MAs, both adults and children.

Methods:

The phenotypic, genotypic, sequencing, and covariate data used represent the San Antonio MA Family Studies (SAMAFS), and their related study involving children and adolescents called the San Antonio Family Assessment of Metabolic Risk Indicators in Youth (SAFARI) study. All family data sets were analyzed using the statistical genetic analytical procedures as implemented in the computer program SOLAR. In addition, T2D-related genetic studies through our collaborations (e.g., T2D-GENES Consortium) were also discussed.

Results:

We localized susceptibility genes/variants for T2D and its related traits such as obesity, gallbladder disease, and metabolic syndrome (MS) using data from SAMAFS and genome-wide linkage and association studies. For example, we performed genome-wide association analysis of T2D, and the best hit which reached genome-wide significance was associated with marker rs2237888 (*KCNQ1* gene, an established T2D risk locus). A *TCF7L2* gene variant (rs7901695) also showed strong association signal, another established T2D risk locus, which was related to our previous T2D linkage finding on chromosome 10q in MAs. Several gene discovery activities related to various disease conditions are in progress. Our SAFARI data revealed that MA children were burdened with relatively high rates of overweight/obesity, pre-diabetes, and MS. A majority of the MS-related traits were found to be under strong genetic influences.

Conclusions:

Our ongoing genetic studies of T2D-related traits in MAs have direct relevance to Mexicans, given that Mexico is the largest contributor of immigrants to the US and that both the US and Mexico are highly burdened with the T2D-related traits, both in adults and children. Thus, findings from our studies would have tremendous relevance to both countries for developing effective strategies to prevent or treat persons at risk for T2D and its related diseases.

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