

PHYSIOLOGICAL GENOMICS ANALYSIS FOR DIABETES MELLITUS TYPE 2

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Key words: diabetes type 2, physiogenomics

SUMMARY

Diabetes type 2 is an endocrine disorder of highest prevalence. The disorder is present in all countries of the world. Although it has been determined for a long time there is no clear cut to define whether or not it is a genetic disorder. A systematic approach to the pathophysiology and genomics might provide useful information to better understand the pathogenesis of diabetes type 2. In this study, physiological genomics analysis for diabetes type 2 was performed. The results obtained pointed to 2 identified physiogenomic relationships on chromosome 18 (BW_32H) and chromosome 12 (GPD2).

INTRODUCTION

Since the Human Genome Project was completed, a new wave of bioinformatics has been launched and genomics has been widely used in medical research (1). Of several fields of genomics, physiological genomics is a new application tackling the formidable-

attaching function to genes within the human genome. In other words, the genome has to be linked to physiology (1). Physiogenomics can be helpful in the study of many complex diseases. Diabetes type 2 is an endocrine disorder that has highest prevalence all over the world. The disorder is detected in all countries of the world. Although it has been determined for a long time there is no clear cut to define whether or not it is a genetic disorder (2,3). A systematic approach to the pathophysiology and genomics might provide useful information to better understand the pathogenesis of diabetes type 2. In this study, physiological genomics analysis was performed for diabetes type 2.

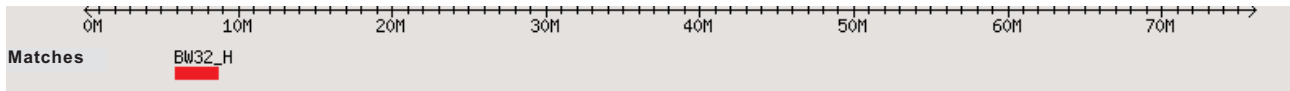
MATERIAL AND METHOD

The study was designed as a bioinformatics simulation study. The physiogenomics analysis by the consomics technique, i.e. the application of chromosomal substitution techniques in the gene-function discovery was used. Conceptually, consomic strain is the one in which an entire chromosome is introgressed into the isogenic background of another inbred strain using marker assisted selection (4,5). This concept is used for further development of many physiogenomic tools. The PhysGen tool was used for all simulations in this study. Briefly, this tool is used to test the functionality of relevant genes using a novel

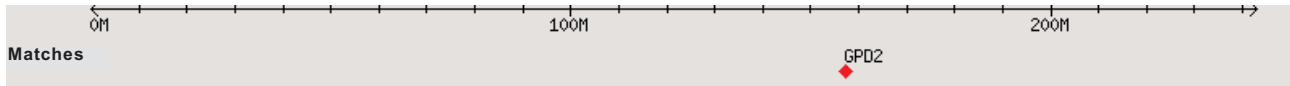
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Figure 1. **Physiogenome for diabetes type 2.**

Chromosome 18



Chromosome 12



strategy, TILLING (Targeting Induced Local Lesions in Genomes) assay (6). TILLING is a general reverse-genetic strategy that provides the ability to detect allelic series of induced point mutations in the genes of interest (7). The human genome was used as template. The input ontology term was “diabetes type 2”. The analysis was performed focusing on gene in range v 2.02. with length 1 Mbp.

RESULTS

Two physiogenomic relationships were identified on chromosome 18 (BW_32H) and chromosome 12 (GPD2). The number of basepairs for BW_32 H (2832134 bp) exceeded that of GPD2 (147001 bp). The GPD2 has a higher relationship score (13.09) than BW_32H (16.91). The physiogenome relationship is shown in Fig. 1.

DISCUSSION

The etiopathogenesis of type 2 diabetes is complex and still partially unknown. Its etiology is determined by the interaction of genetic and environmental factors (8). The genetic contribution is important, but has a polygenic origin (8). Evidence for a genetic component includes the finding of a variety of metabolic defects in various tissues in nondiabetic subjects with a genetic predisposition to diabetes type 2 and higher concordance rates for abnormal glucose tolerance including diabetes type 2 in monozygotic compared with dizygotic twins (9). Basically, hyperglycemia is related to a decrease in the peripheral

glucose uptake and an increase in hepatic glucose production due to reduced insulin secretion and insulin sensitivity (10). Multiple insulin secretory defects are present, including loss of basal pulsatility, lack of early phase of insulin secretion after intravenous glucose administration, decreased basal and stimulated plasma insulin concentrations, excess prohormone secretion, and progressive decrease in insulin secretory capacity with time (10).

Here, the author used the physiogenomic approach to study the physiogenome in diabetes mellitus type 2. According to the study, the simulation revealed that there are two genes that show genetic relationship to the etiopathogenesis of diabetes type 2. The two genes identified are concordant with the prediction from the metabolomics mapping technique in a recent report (11). However, the result from this study was discordant with Vionnet *et al.*, which indicated the susceptibility gene to be located on chromosome 11 (12). Concerning GDP2, it has been previously reported to be related to type 1 diabetes, but it was clearly demonstrated to have a pathophysiological relationship to type 2 diabetes (13). Concerning the BW_32H, it has already been reported to correlate with obesity. Indeed, obesity, especially when the fat mass is mostly located in the abdomen, is the main predisposing factor for type 2 diabetes, and almost 80% of diabetic patients are overweight or obese (14). The finding of BW-32H in the physiogenome of diabetes type 2 strongly implies the genetic component of diabetes type 2 and confirms the risk of obesity in diabetic patients.

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