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SIM1 and its Association with Diabetes

Elaine Vanterpool
Oakwood University, evanterpool@oakwood.edu

Gabrielle McIntosh
Oakwood University

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Gabrielle McIntosh and Elaine Vanterpool, PhD

Oakwood University

Department of Biological Sciences

Huntsville AL, 35896

ABSTRACT

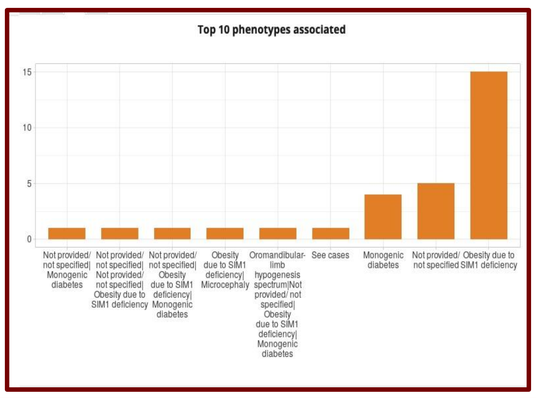
The significance of this CODE research is to assess the genes related to Diabetes, specifically the SIM1 gene and its variants. Diabetes is a chronic metabolic disorder characterized by elevated blood glucose levels. The body uses glucose from food or its own internal manufacture as its main energy source. The pancreas secretes insulin, which helps cells absorb glucose so they can use it as fuel. Your body produces insufficient insulin or uses it inefficiently if you have diabetes. Consequently, instead of entering your cells, glucose stays in your bloodstream. Simple ClinVar was utilized to identify the gene related to diabetes, SIM1, and provided a list of the variants associated with it. Specific SIM1 variants were analyzed using SIFT and Polyphen. The Swiss Model was used to illustrate a 3-Dimensional protein structure of the SIM1 gene. The missense mutations analyzed include Asp 707 His, Gln 704 Leu, and Lys708Arg. It was revealed that Asp 707 His and Gln 704 Leu were "probably damaging" and most likely pathogenic, while Lys708Arg was deemed as benign, likely having no impact on protein. The SIM1 gene, akin to the Drosophila sim gene, is associated with both monogenic and syndromic obesity. Understanding its role sheds light on the intricate relationship between obesity, genetics, and the increased risk of developing type 2 diabetes. Comprehending the genetic makeup of diabetes, particularly the function of the SIM1 gene, is essential for customized care, risk evaluation, medication development, and the influence on public health.

INTRODUCTION

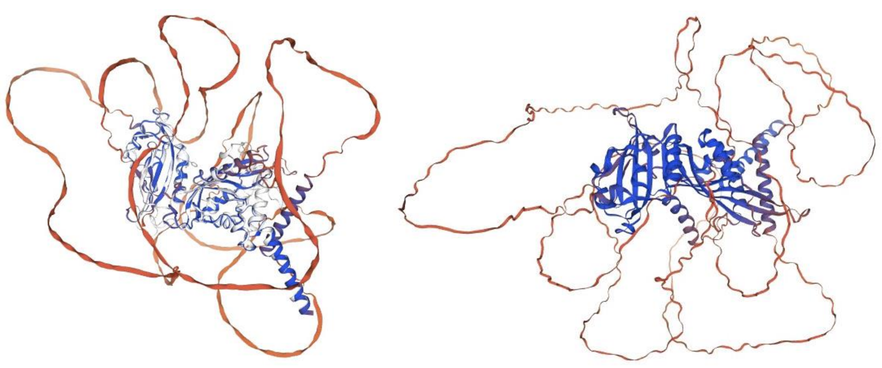
Diabetes is a chronic disease that occurs when your blood glucose (blood sugar) levels are too high. The main source of energy in the body is glucose, which is obtained from meals. For cells to absorb glucose and use it as fuel, the pancreas secretes insulin. If you have diabetes, your body uses insulin inefficiently or creates insufficient amounts of it. Therefore, glucose stays in your bloodstream rather than going into your cells. The three main types of diabetes include: Type 1, which is caused by an autoimmune reaction in which the immune system attacks the cells in the pancreas that produce insulin by mistake; Type 2, in which the body cannot maintain normal blood sugar levels due to insufficient insulin use; and Gestational Diabetes, which develops during pregnancy and typically goes away after giving birth. An estimated 2 million fatalities were attributed to diabetes and renal disease in 2019. Before the age of 70, 48% of all diabetes-related deaths took place. Approximately 8.5% of persons who were 18 years of age or older had diabetes. Sedentary lifestyle, high blood pressure, obesity, and family history are risk factors. All age groups are susceptible to diabetes, including adults (type 2) and children (type 1). Symptoms can differ, but typical indications include: An excessive amount of thirst, frequent urination, blurry vision, exhaustion, and unintentional loss of weight.

Diabetes is diagnosed using a number of tests: A1C Test, which determines the mean blood sugar levels throughout the previous two to three months, Random Blood Sugar Test that Identifies elevated blood sugar levels independent of meal timing, Blood sugar levels are measured via a fasting blood test following an overnight fast and the glucose tolerance test involves a two-hour fast, a sugary drink, and blood sugar readings. Diabetes can be prevented by eating healthy, exercising and avoiding any tobacco use. Treatments for diabetes include: Insulin injections (type 1) or oral medications (type 2), and/or regular blood sugar monitoring and screening for complications.

SIM1 is a gene known as "single-minded."It is essential for neurogenesis, especially in the hypothalamic paraventricular nucleus (PVN). Blood pressure control and energy balance depend on the PVN. SIM1 collaborates with the transcription factors Swi5 and Mcm1 to start CLN3 transcription, and its expression peaks during the G2 phase of the cell cycle. Hyperphagic obesity and increased sensitivity to a high-fat diet are the outcomes of Sim1 deficiency. According to a study, there is a consistent correlation between common variation in SIM1 and body mass index (BMI). Potential implications for metabolic health are suggested by SIM1's involvement in energy balance and obesity.



MODEL OF SIM1 PROTEIN



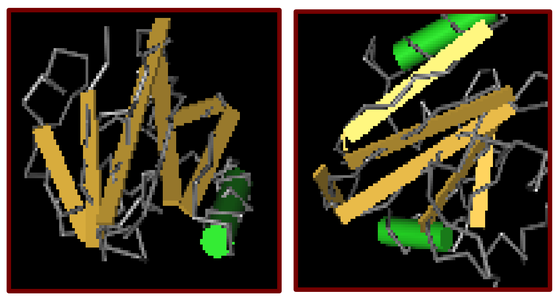
METHODS

- **Simple ClinVar to identify the genes associated with diabetes, as well as the variants of SIM1**
- **Polyphen and SIFT were used to analyze specific variants of SIM1**
- **SWISS model was used to illustrate the protein folding of the normal SIM1 gene and the mutated SIM1 gene**
- **NCBI was used to identify the organs where the gene is most expressed**

RESULTS

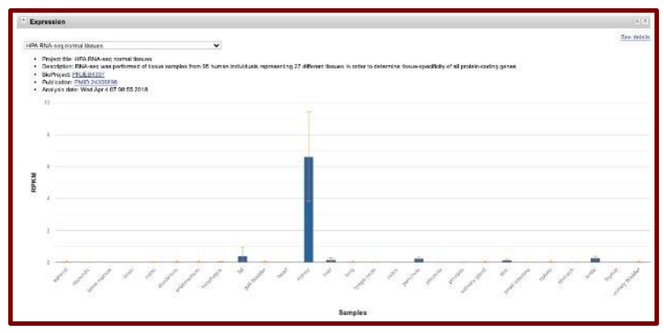
POLYPHEN

CONSERVED DOMAIN

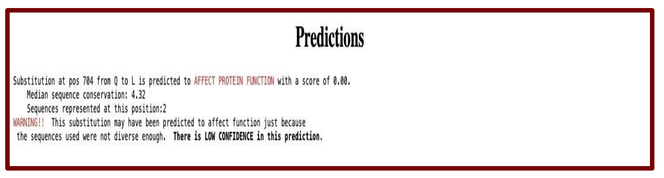


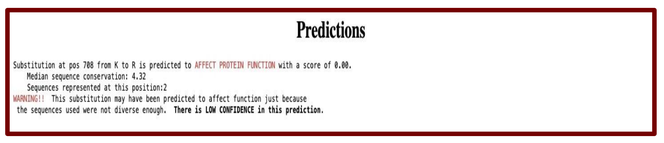
The PAS fold corresponds to the structural domain that has previously been defined as PAS and PAC motifs. The PAS fold appears in archaea, eubacteria and eukarya.

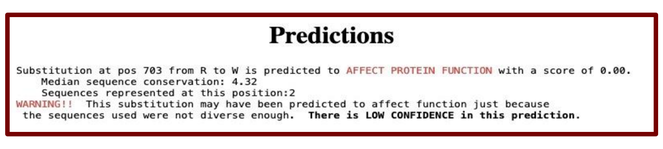
LOCATION OF EXPRESSION



SIFT







DISCUSSION AND CONCLUSION

According to the findings of this study it can be concluded that SIM1 can be associated with diabetes. The data collected from Polyphen predicts that these missense mutations, Asp 707 His and Gln 704 Leu, were "possibly/probably damaging," showing a strong possibility of protein modification. It was determined that Lys708Arg was benign, likely having no effect on protein.

Based on the results from SIFT all the missense mutations(Asp 707 His, Gln 704 Leu and Lys708Arg) are shown to "Affect protein function," despite the warning of low confidence, attributing to the possibility being pathogenic.

Diabetes is a common disease that affects many people on a daily basis. Currently, there is still no cure for Type 2 diabetes. SIM1 may not be directly connected to the disease based on the research done so far by others, but its primary association with obesity, and involvement in energy regulation and neurogenesis may indirectly impact diabetes. Knowing its function clarifies the complex interplay between heredity, fat, and the elevated risk of type 2 diabetes, potentially leading to a cure.

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