The Impact of the PCK1 gene and PPCK1 promoter polymorphism 232C→G on the incidence of TIIDM in Oji-Cree natives of Ontario

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Introduction

In 1999 the WHO predicted a 39% rate increase on the incidence of diabetes between 2000 and 2030. (1) Studies have calculated that Canada surpassed this astonishing rate last year in 2006. Worldwide more than 150 million people suffer from type II diabetes and it is calculated to cost an average of 5-15% of world health budgets budgets depending on the country.

The prevalence of TIIDM in Ojibwa-Cree Natives is approximately 2 in every 5. Highest from any subpopulation subpopulation in the world, the Oji-Cree desperately need need intervention strategies from a disease that “is killing [their] people”. Understanding the genetic component of this disease may help identify the different metabolic pathways pathways involved in diabetes and allow for faster intervention intervention strategies for the prevention and treatment of diabetes.

TIIDM is a heterogeneous disease where cells become glucose glucose intolerant and insulin resistant. Studies have shown that genetic predisposition plays a larger role than environment on the incidence of the disease. Most reported reported cases of TIIDM are polygenic and are causated when an individual’s environment (mainly diet and exercise) exercise(s) and genetic background interact. Chromosomes 1, 2, 1, 2, 3, 4, 5, 6, 7, 9, 10, 11, 12, 16, 19, 20, and X have been linked to the occurrence of type II diabetes. PCK1, located in chromosome 20q13, is among these candidate candidate genes.

Results

A literature review was conducted on the incidence of type 2 type 2 diabetes in the Ojibwa-Cree native population of Ontario, Canada. Particular attention was placed to the PCK1 gene and its location. During this time the significance significance of SNP 232C→G was also being evaluated. The PCK1 sequence was then acquired from NCBI and translated in six different ways by the EXPASY translation tool. The resulting sequences (those between stop stop codons) of 65 amino acids in length or greater greater were then evaluated. Subsequently amino acid and nucleotide homology searches were conducted on each of each of these sequences. An emphasis was placed on the different biochemical pathways of PCK1 involvement.

Methods

A literature review was conducted on the incidence of type 2 diabetes in the Ojibwa-Cree native population of Ontario, Canada. Particular attention was placed to the PCK1 gene and its location. During this time the significance significance of SNP 232C→G was also being evaluated. The PCK1 sequence was then acquired from NCBI and translated in six different ways by the EXPASY translation tool. The resulting sequences (those between stop stop codons) of 65 amino acids in length or greater greater were then evaluated. Subsequently amino acid and nucleotide homology searches were conducted on each of each of these sequences. An emphasis was placed on the different biochemical pathways of PCK1 involvement.

Conclusions

1. Due to the complexity of TIIDM, prevention and management strategies for type 2 diabetes should apply multi-tier treatment and prevention strategies.
2. Further research is needed to evaluate the different genes genes and their specific correlation with the incidence of type II diabetes.
3. Molecules fitting into the active site of cystolic phosphoenolpyruvate carboxykinease (PCK1) need to be engineered in order to develop future treatments for type II diabetes.
4. Alternate pathways, particularly with respect to transcription regulation need to be investigated to find alternative treatment strategies for type 2 diabetes.
5. The direct effect of Metformin on PEPCK translation is yet to be understood.

Literature cited

(4) Inoue, E. and Yamauchi, J. 2006. AMP-activated protein kinase regulates PEPCK gene expression by interactions between the PEPCK promoter and histone acetylation. Biochemical and Biophysical Research Communications 345, 564-571.

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For further information

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