Physiological Genomics Analysis for Central Diabetes Insipidus

Viroj Wiwanitkit

Abstract- Central diabetes insipidus (CDI) is a neuroendocrine disorder that has the highest prevalence. This disorder can be found in all countries around the world. Although CDI has been studied for a long time, it is still not clear whether this is a genetic disorder. Systemic approach on the pathophysiology and genomics might provide useful information to better understand the pathogenesis of CDI. In this work, physiological genomics analysis for CDI was performed. Based on this work, there are two genes identified with high physiogenomics relationship. They are Arginine vasopressin (AVP) on chromosome 20 and AVP receptor 2 (AVPR2) on chromosome X. Physiogenomics approach could be a novel and useful tool for researches.

Key Words: Diabetes, Insipidus, Physiogenomics

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INTRODUCTION

After the Human Genome Project was completed, a new wave of bioinformatics has been launched and genomics information is widely used in medical research[1]. Of several applied genomics, physiological genomics is a new application and it tasks at formidable-attaching function to genes within the human genome. In other words, the genome is linked to physiology[1]. The physiogenomics can be applied to study of many complex diseases. Central diabetes insipidus (CDI) is a common neuroendocrine disorde. This disorder can be found in all countries around the world. CDI has been researched for a long time but it is still unconcluded whether CDI is a genetic disorder[2,3]. Systemic approach on the pathophysiology and genomics might provide useful information to better understand the pathogenesis of CDI. In this work, physiological genomics analysis for CDI was performed.

MATERIALS AND METHOD

This work is a bioinformatics study. The physiogenomics analysis by consomics technique, an application of chromosomal substitution techniques in gene-function discovery, was used. Conceptually, a consomic strain is a strain that its entire chromosome is introgressed into an isogenic background of another inbred strain using marker-assisted selection[4,5]. This technique is used as a base for further development of many physiogenomics tools. In this work, the tool PhysGen was used for all simulations. Technically, PhysGen is a com-

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puterized tool (https://pga.mcw.edu) that is specifically designed based on data from consomic strains and it mainly focuses on manipulating specific genes on assessing the physiological results among different genetic backgrounds[7]. This bioinformatics tool is useful for testing functionality of relevant genes using a novel strategy, TILLING (Targeting Induced Local Lesions in Genomes) assay[6], a general reverse-genetic strategy which can provide the full ability to detect allelic series of induced point mutations in focused genes[7].

The human genome was used as templates. The input ontology term is "central diabetes insipidus". The author used this ontology term for searching because this term is directly matched with the interested disorder. Analysis was performed by focusing on gene in range v 2.02. with length 1 Mbp. The relationship score, which indicates the physiological correlation, in the term of an underlying contributing genetic factor, for each identified physiogenome was calculated.

RESULT

There are 2 identified physiogenomics relationship on chromosome 20, Arginine vasopressin (AVP) and on chromosome X, AVP receptor 2 (AVPR2). The number of basepairs for AVP (2169 bp) is less than that of AVPR2 (2272 bp). The AVP has an equal relationship score to AVPR2 (20.27). The relationship physiogenome is provided in Figure.

DISCUSSION

Diabetes insipidus is a heterogeneous disorder, characterized by polyuria and polydipsia. It is caused by a lack of secretion or physiological suppression of vasopressin following excessive water intake, or kidney resistance to vasopressin[8]. In many patients, it results from destruction or degeneration of the neurons that locate in the supraoptic and paraventricular nuclei of the hypothalamus[8].

CDI is an important disorder in neurological science. Etiopathogenesis of CDI is complex and still largely unknown. Its etiology should be attributed to the interaction of both genetic and environmental factors[9]. Whether there is hereditary CDI in humans is still uncertain[10]. The genetic contribution might be important, but CDI should be a polygenic disorder[9].

Although the relationship of some genes, especially AVP, and CDI has been well established, how those genes provide physiological impact to CDI has never been reported. In some cases, a few genes are documented as possible genetic factors for some disorders by some experiments or observations but that does not mean there must be a causal physiological correlation[1]. Here, we used the physiogenomics approach to study CDI in the physiogenome. This brief report introduced a physiogenomics tool, which is a new method in systemic biology for studying the physiological relationship between genes and disorders[1].

According to this work, there are two genes that contain high genetical relationship on the ethiopathogenesis

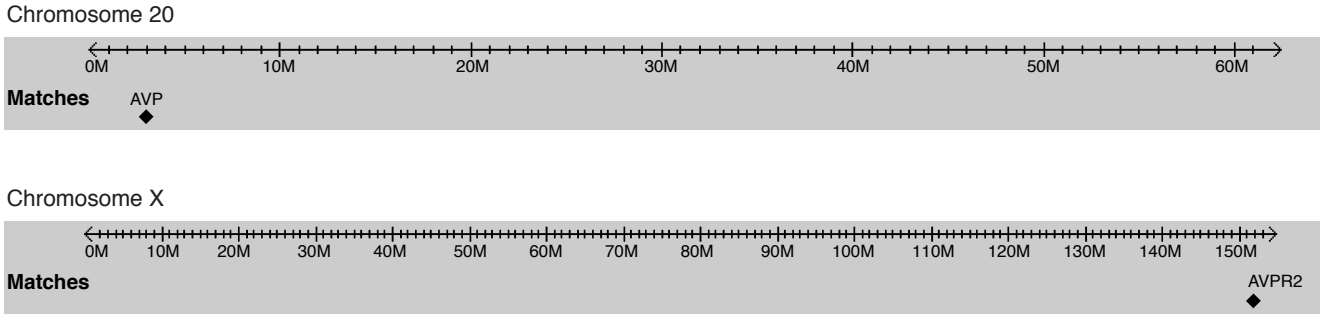

Figure . Identified physiogenomes for central diabetes insipidus (as red clubs).

of CDI. Using the physiogenomics technique, the author could also identify the relationship score which determines the quantified contribution of some gene to the studied disorder. This is an advantage that the simple gene name searching cannot provide. The two identified genes are similar in its phylogenomics property and equal in the degree of relationship. AVP has ever been reported to have a strong correlation with CDI[11]. A lack of AVP results in deficiency of tubular reabsorption of water and then low specific gravity of urine[12]. This facts validate the identified high relationship score and the strong linkage of AVP and CDI in this work. Containing a similar relationship score as AVP, AVRP2 is implied important in CDI and this should bring a large interest on AVRP2 in further study of the pathogenesis of CDI. Although AVRP2 was mainly mentioned in nephrogenic diabetes insipidus[13], it appears to be potentially important in physiogenome of CDI. Of interest, there are other documented genetic mutations in some diabetes insipidus cases but those ones do not confer any physiogenomics correlation and failed to figure out the role of these genes in the pathophysiological machinery of the disorder[14-16]. This also reflects the usefulness of physiogenomics approach to detect the genes with physiogemic correlation.

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