Diabetic Neuropathy – Future Genetic Prospects

Ramakrishnan V* and Akram Husain RS
Genetics Lab, Faculty of Allied Health Sciences, Chettinad Academy of Research and Education, India

*Corresponding author: Ramakrishnan V, Genetics Lab, Faculty of Allied Health Sciences, Chettinad Academy of Research and Education, Chettinad Health City, Kelambakkam - 603 103, Tamil Nadu, India, E-mail: rkgenes@gmail.com

Editorial

Diabetes Mellitus is a metabolic disease with high level of pancreatic insulin secretion, a condition where muscle, liver and fat cells poorly respond to insulin. According to the published reports by International Diabetes Federation (IDF), 387 million individuals were estimated to be with diabetes globally in 2014, and it has been predicted to raise to 592 million in the year 2035 [1]. In 70% of DM patients, diabetes is accompanied by neuropathies that can affect organs of the body and these complications are the main cause of mortality and morbidity among DM patients [2]. The microvascular complications damage small vessels and capillaries leading to clinical outcomes. Diabetic Neuropathy (DN) affects nerves leading to foot ulcers, loss of sensation and amputation as result of prolonged elevated blood glucose levels. The different types of DN include focal neuropathy, peripheral neuropathy, autonomic and proximal neuropathy [3]. Peripheral neuropathy is one of the most common microvascular complication affecting T2DM patients [4]. Obesity is also considered as the significant risk factor for DN development [5]. In spite of huge advances in DN, the exact mechanism of pain causation in neuropathy remains unidentified. The origin of pain could be from the peripheral nerves in the nervous system.

Genomic research tools have already provided us with a wealth of data on several genetic variants related with human metabolic disorders.

Likewise, candidate gene approach, Genome-wide association studies (GWAS), linkage analysis have identified genetic risk factors for diabetic microvascular complications including diabetic neuropathy [6]. Based on biological process the candidate genes (40) were studied for genetic association with diabetic microvascular complications such as Erythropoietin (EPO), Angiotensin 1 Converting Enzyme (ACE), Vascular Endothelial Growth Factor-A (VEGFA) and Aldo-keto reductase family 1, member B1 (AKR1B1) but most of the studies have documented inconsistent results, even though they were systematically investigated [7]. Most T2DM genes appear to be related with B-cell dysfunction, inflammatory response, involve in metabolic and vascular (Polyol pathway, Hexosamine) pathways, related to insulin resistance with obesity as risk factor. The obesity gene variants linked with pathways affecting the energy homeostasis. Although, several diabetes and obesity-associated genes have been identified till date, only 15% of the known genes predict T2DM and 5% obesity risk [8]. Earlier studies documented the genetic risk factors of DN, but they still remain scarce and nearly 60 loci have been identified to influence of developing T2DM risk [9]. (Figure 1) explains the risk factors leading to the development of diabetic neuropathy and its complications in human body.
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Figure 1: The risk factors leading to the development of DN and its complications.

DN is a multi-factorial disease affecting the function of all organs in the body due to alteration of glucose metabolism. In current state, the additional genes which play vital role in obesity associated DN should be discovered using high-throughput sequencing technologies leading to gene-gene, gene-environment and epigenetic interactions involving with diabetes. The identified DN targets (genes and proteins) can be more effectively used to determine the development and progression of neuropathies, an in-depth understanding of this disease etiology will be gained, enabling us to be more comprehensive in assessing an individual’s genetic risk profile.

References