The prevalence of type 2 diabetes mellitus (T2D) is increasing rapidly worldwide with figures being projected to reach 700 million and 366 million by 2030 respectively, according to the recent reports by the World Health Organization 2010 and the International Diabetes Federation 2010. T2D development has been shown to be driven by both environmental and genetic factors. Consanguinity among Middle-Eastern population, especially the Gulf region, has proved to play a major role in predisposing to multiple hereditary conditions such as cancer, hypertension, and T2D, the latter showing a moderately high prevalence (16.7%) among Qataris.

In this study we aim to identify novel genetic variants and clarify new molecular pathways of T2D in the Qatari population. We will take the advantage of the advanced technologies in genome wide scan and next generation sequencing to investigate a large three generation Qatari family with a history of early onset T2D for the initial stage of the study. More consanguineous families will be recruited for this project and will undergo the same investigational steps in order to identify shared novel mutations between the different family members.

To date, several approaches, such as candidate gene studies, linkage analysis, and genome-wide association studies (GWAS) have been used to identify genetic variants involved in the pathophysiology of T2D and glucose homeostasis. Among these, GWAS has been the most successful approach at the moment to uncovering common genetic variants involved in the disease susceptibility. Next generation whole exome sequencing is a promising approach to gather novel insights into genes and pathways involved in T2D susceptibility, also allowing the discovery of potential rare mutations. This study will use next generation sequencing technology to discover potential causative mutations segregating in diabetic inbred Qatari families, and possibly relevant to the Qatari population.

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Genetic and Epigenetic Investigations of SNCA in Parkinson’s Disease

Parkinson’s disease (PD) (OMIM168600) is the second most common age-related neurodegenerative disorder worldwide with a prevalence of more than 1% in people over 65 years old. The major hallmark of PD brain change is the formation of Lewy bodies, which are mainly composed of a protein called alpha-synuclein (encoded by the SNCA gene), aggregated together with other proteins. Genetic variants of SNCA have been reported to be involved in both familial as well as sporadic cases of PD. Many of these variants result in the over-expression of the encoded protein making it prone to aggregation.

This report describes investigation of methylation of the two CpG islands in SNCA in brain samples from PD patients. Fifty three DNA samples were made from cerebellum of PD brains, to add to 268 existing DNA samples. In the first part of the study, confirmation of suspected monogenic PD mutations was carried out using PCR and sequencing. However, no mutation was detected. Possible reasons for the discrepancy between predicted and observed results are discussed. In addition, 250 PD cases were screened for three monogenic mutations in SNCA using commercial service and found that none of these cases have the mutations.

In the second part of the study, DNA methylation of two SNCA CpG islands was assessed in seven different brain regions of ten PD cases using bisulfite sequencing. No significant difference was observed in DNA methylation of CpG 1, as well as CpG 2, when compared to the studied brain regions. Genetic and epigenetic studies on PD can help to provide better understanding of the mechanisms underlying the disease and its progression, enhancing our ability to discover and develop better treatment options for the future.