Understanding Modern Diagnoses with Unknown Gene Plays a Critical Role in Inherited Thrombophilia

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Protein C deficiency (PCD) is found in 1 out of 200 to 500 persons in the general global population. Inherited thrombophilia is characterized by an increased tendency of blood to clot in human blood vessels. It is caused by several factors including mutations in the genes involved in thrombin binding, protein c activation and numerous clotting factors. The purpose of this study is to identify the underlying genes that lead to PCD in patients with nationality in Saudi Arabia, so that a diagnosis can be potentially discovered. To begin the research, families with PCD were recruited. Targeting all coding exons of the human genome was performed using Illumina NextEra library preparation kits. This was followed by the paired-end sequencing on Illumina NextSeq500 instrument. Reads quality control was performed and the reads were aligned to the reference genome using Burrows-Wheeler Aligner (BWA). Variants calling and annotation were performed using Genome Analysis Tool Kit (GATK). All known genes involved in causing PCD were excluded by whole exome sequencing. The genes that were previously reported to be involved in inherited thrombophilia were checked for any causative variant. No mutation has been identified in known genes. Currently, data analysis is focusing on identifying a novel gene underlying PCD. The goal of this study will hopefully pave the way to better understanding the disease pathophysiology and help in developing DNA based diagnosis, carrier screening and somatic gene therapy.