

# **SCREENING OF *PCSK9* GENETIC VARIANTS IN FAMILIAL HYPERCHOLESTEROLEMIA (FH) PATIENTS IN A COHORT OF SRI LANKAN POPULATION**

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## **ABSTRACT**

### **Background:**

A hereditary predisposition for elevated serum levels of low-density lipoprotein cholesterol (LDL-C) leading to cardiovascular disease is a typical Familial hypercholesterolemia (FH) which affects approximately 1 in 250 individuals. In excess of thousand low-frequency variants in *LDLR*, *APOB*, and *PCSK9* have been implicated in **FH**, but only few studies have been conducted at the population level. The discovery of proprotein convertase subtilisin/kexin type 9 (*PCSK9*), a secretory protein that posttranscriptionally regulates levels of low density lipoprotein receptor (LDLR) by inducing its degradation, has opened a new era of pharmacological modulation of cholesterol homeostasis. Nevertheless, certain mutations of the *PCSK9* genes appear to hinder the expected results in certain patients. Thus, this study was aimed at designing of a novel PCR assay for the identification of *PCSK9* genetic variants in a cohort of patients in Sri Lanka diagnosed with FH.

### **Method:**

A comprehensive literature review was followed by designing of an allele specific PCR assay to genotype a total of 18 unrelated patients with a clinical diagnosis of familial hypercholesterolemia at the Human Genetics Unit, Faculty of Medicine, University of Colombo, Sri Lanka. The assay designed for the SNP *rs11591147* G>T variant was validated using Sanger sequencing.

**Results:**

The expected band sizes at 428bp, 285bp and 188bp indicated the wild type allele, heterozygous allele and the homozygous allele for the pathogenic variant respectively. Out of the 18 patients tested, no heterozygotes or homozygotes the pathogenic variant was detected.

**Conclusions:**

This study is first of its kind to screen the PCSK9 genetic variants in FH patients in Sri Lanka. However, no pathogenic variations were identified which shows *PCSK9* gene variants may be less significant in our population. Nevertheless, the designed assay will allow the application of precision medicine which will serve as paradigms for the prevention of premature atherosclerotic cardiovascular disease in all at-risk patients and families.

**Key words**

Familial Hypercholesterolemia, PCSK9, allele, genotype