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ASSOCIATION BETWEEN DYSLIPIDAEMIA AND MUTATIONS IN THE GENES *PCSK9, LDLR*

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INTRODUCTION

Coronary heart disease (CHD) is the main cause of death in developed countries. One of the main causes of CHD is atherosclerosis, in which pathogenesis dyslipidemia is a crucial factor. There are several genes involved in cholesterol metabolism, e.g. *PCSK9* and *LDLR*. Mutations and polymorphisms in these genes can be associated with hyper- or hypocholesterolemia, and can cause Familial hypercholesterolemia.

AIM

To determine the association of the polymorphism E670G in the gene *PCSK9* with dyslipidemia and to test patients with dyslipidemia for seven mutations in the gene *LDLR*.

MATERIAL

Group of patients: 38 patients with dyslipidemia (average age – 63.9±10.2 years, 21 males and 17 females).

Control's group: 66 healthy individuals (average age – 22±2.8 years, 10 males and 56 females).

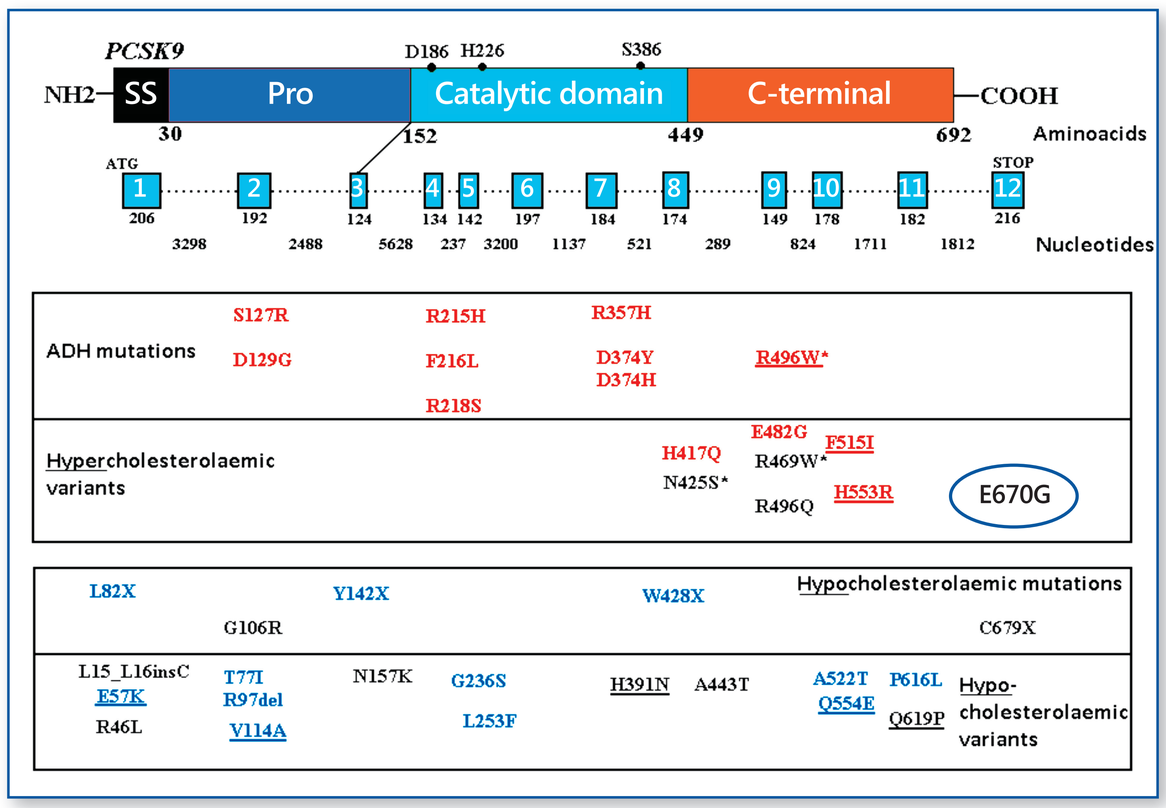

Figure 1. **Schematic localisation of the mutations in the gene *PCSK9* (in coding regions)** [adapted from Abifadel et al., 2009].

RESULTS

Table 1. **Frequency of *PCSK9* gene G allele in patients and control's group.**

Gene	Mutation	MAF patients	MAF control group	P value	OR	95% CI
PCSK9	**E670G**	**0.3947**	**0.1339**	**3.9×10^{-5}**	**4.217**	**2.069–8.597**

Staistically significant association with dyslipidemia was found with *PCSK9* gene E670G mutation – G allele was more common in patients, than in control's group.

Table 2. **Mutation found in the gene *LDLR* in patients with dyslipidemia.**

Mutations tested in gene *LDLR*						
D374Y	**P664L**	**L458P**	**R329X**	**E207X**	**D200G**	**E80K**
–	–	–	–	–	–	*

*** – found in 2 patients with dyslipidemia in one allele**

Mutation E80K in the gene *LDLR* was found in two individuals with dyslipidemia.

CONCLUSIONS

- Polymorphism E670G in the gene *PCSK9* is one of the genetic risk factors in development of dyslipidemia, but it is not associated with specific bio chemical markers;
- Mutation E80K in the *LDLR* gene suggests that two patients have Familial hypercholesterolemia, but to make precise diagnosis, the mutations should be confirmed by other molecular method.

METHODS

Molecular methods:

- DNA extraction
- The E670G polymorphism was detected by RFLP analysis
- The mutations: D374Y, P664L, L458P, R329X, E207X, D200G, E80K in the gene *LDLR* were detected by ELUCIGENE FH20 *(Tepnel Molecular Diagnostics)*.

Statistical analysis: PLINK and SPSS 16.0 were used.

Table 3.
Mutation E670G association with biochemical indices.

Gene	Mutation	Biochemical indices	BETA1	P value
PCSK9	**E670G**	Total cholesterol	0.7639	0.1246
		HDL	−0.2083	0.1703
		LDL	0.5556	0.1982
		TG	0.5598	0.1489
		APOB	5.457	0.6151
		APOA	5.408	0.6254
		ALAT	0.75	0.9384
		Glucose	−0.1548	0.7538
		ASAT	−1.833	0.6884

HDL – high density lipoprotein; LDL – low density lipoprotein; TG – triglyceride; APOB – apolipoprotein B, APOA – apoliporpotein A; ALAT – alanine transaminase; ASAT – aspartate transaminase.

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