LOW HDL-CHOLESTEROL LEVELS ARE ASSOCIATED WITH A DECREASED MONOCYTE ACTIVITY AND INFLAMMATION IN CARRIERS OF LCAT MUTATION

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BACKGROUND & AIM

Epidemiological studies have shown an inverse relationship between low HDL-cholesterol levels and CHD. Besides the capacity in promoting cholesterol efflux, HDL can contribute to atheroprotection through the modulation of the immune response. As monocytes are the major contributors to the underlying inflammation in atherosclerosis there is the need to study the effect of HDL on monocyte phenotype. Animal and in vitro data are already available, while *in vivo* data in human are lacking. Aim of this study is to evaluate the effect of genetic HDL deficiency, specifically determined by mutations in *LCAT* gene, on monocyte immunophenotype and function.

METHODS & RESULTS

- Carriers of *LCAT* mutation
- HDL-C < 1 mmol/L (40 mg/dL)
- Absence of cardiovascular disease, diabetes mellitus, CKD, metabolic syndrome

CLINICAL AND BIOCHEMICAL PROFILE OF STUDY SUBJECTS

Number of mutant <i>LCAT</i> alleles	Two (n=5)	One (n=7)	Zero (n=9)	p-value
Age (years)	44.0 ± 7.9	46.6 ± 6.4	41.2 ± 4.0	0.78
Gender (M/F)	1/4	4/3	5/4	0.37
BMI (kg/m ²)	25.1 ± 1.1	26.5 ± 1.8	24.5 ± 1.3	0.62
Smoking (n,%)	1 (20)	2 (29)	5 (44)	0.62
TC (mg/dl)	154.0 ± 25.9	189.4 ± 10.0	208.5 ± 9.6	0.05
TG (mg/dl)	173 (118-356)	125 (101-206)	113 (93-128)	0.09
LDL-C (mg/dl)	121.0 ± 23.9	134.2 ± 9.8	121.5 ± 7.7	0.71
HDL-C (mg/dl)	7.3 ± 1.7	37.9 ± 2.5	63.4 ± 5.9	<0.0001
ApoA-I (mg/dl)	27.0 ± 7.2	88.9 ± 3.5	121.1 ± 7.9	<0.0001
ApoB (mg/dl)	116.6 ± 22.9	103.6 ± 6.1	93.9 ± 2.9	0.33
Glucose (mg/dl)	93.2 ± 7.5	74.1 ± 2.1	87.1 ± 4.2	0.03

Data are expressed as mean ± SD and n (%) for categorical variable.

MONOCYTE SUBSET DISTRIBUTION

CD11c EXPRESSION ON BLOOD MONOCYTES

Data are shown as mean ± SEM. * < 0.05

MONOCYTE TRANSENDOTHELIAL MIGRATION

Data are shown as mean ± SEM; * < 0.05

ACTIVATION MARKERS

Data are shown as mean ± SEM; * < 0.05

CYTOKINE PRODUCTION CAPACITY

Data are shown as mean ± SEM; * < 0.05

PLASMA CYTOKINES

Data are shown as mean ± SEM; * < 0.05

CONCLUSIONS: Mutation in *LCAT* gene, despite leading to low HDL-C levels, are not associated with an increased inflammatory phenotype of monocytes