

Supplementary figures and legends

Figure S1. The effects of EGCG on circulating PCSK9 level in dose-dependent manner in rats. SD rats fed with HFD for 4 weeks and administered with EGCG by i.g. at different doses for another 4 weeks. The levels of plasma PCSK9 were analyzed by ELISA kit. **p <0.01, vs control, #p <0.05, ##p <0.01, versus HFD group (N=3).

Figure S2. EGCG modulates LDLR and LDL uptake through PCSK9-dependent pathway by regulating HNF1 α and FoxO3a in Huh7 cells. (A) Cells were added rhPCSK9 or transfected with siRNA negative control (si-Control) or stealth siRNA for the knockdown of PCSK9 (si-PCSK9). The levels of PCSK9 and LDLR were determined by western blot, GAPDH was used as the loading control. (B) The nuclear extracts from with or without EGCG (25 μ M) –treated Huh7 cells. The effects of EGCG on the nuclear HNF1 α and FoxO3a expression by western blot analysis, the normalized intensity of nuclear HNF1 α and FoxO3a protein, HDAC2 was used as the loading control. (C) Cells were transfected with siRNA negative control (si-Control) or stealth siRNA for the knockdown of HNF1 α , the level of PCSK9 and LDLR were determined by western blot, GAPDH was used as the loading control. (D) Cells were transfected with siRNA negative control (si-Control) or stealth siRNA for the knockdown of FoxO3a, the level of PCSK9 and LDLR were determined by western blot, GAPDH was used as the loading control. (E) Representative fluorescence microscopy images of cell - associated Dil-LDL (red), Hoechst - stained nuclei (blue) and the overlay (upper). Fluorescence of isopropanol - extracted Dil (520-570 nm, normalized to the cell protein) (lower). Data are presented as mean \pm SEM (N=3). **p <0.01 compared with control. ##p <0.01 compared with EGCG group.

Figure S3. Flow charts of the experiment. We studied the effects and underlying molecular mechanism of EGCG or green tea on regulating cholesterol from human, animal and *in vitro*, this chart shows the whole experiment process.

Figure S1.

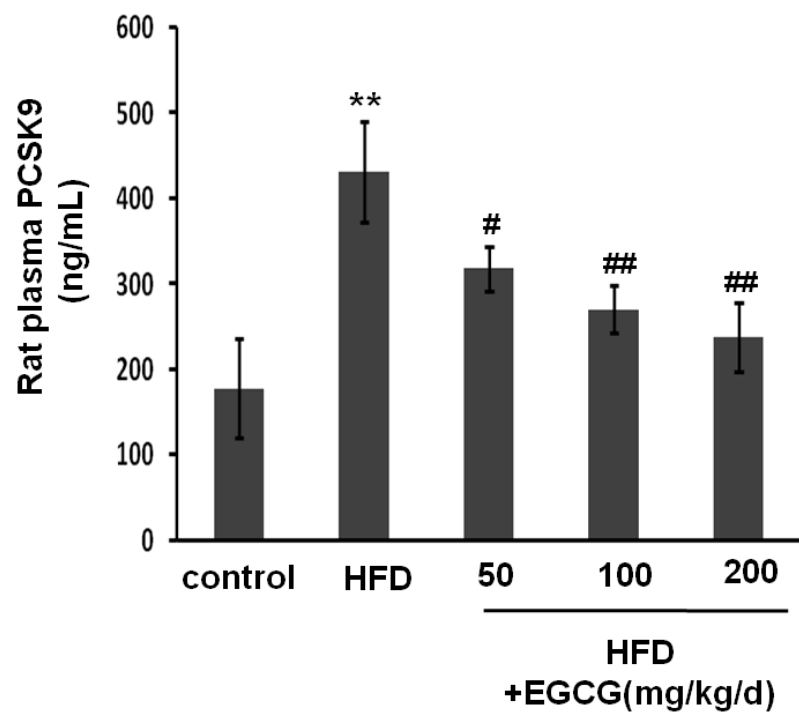
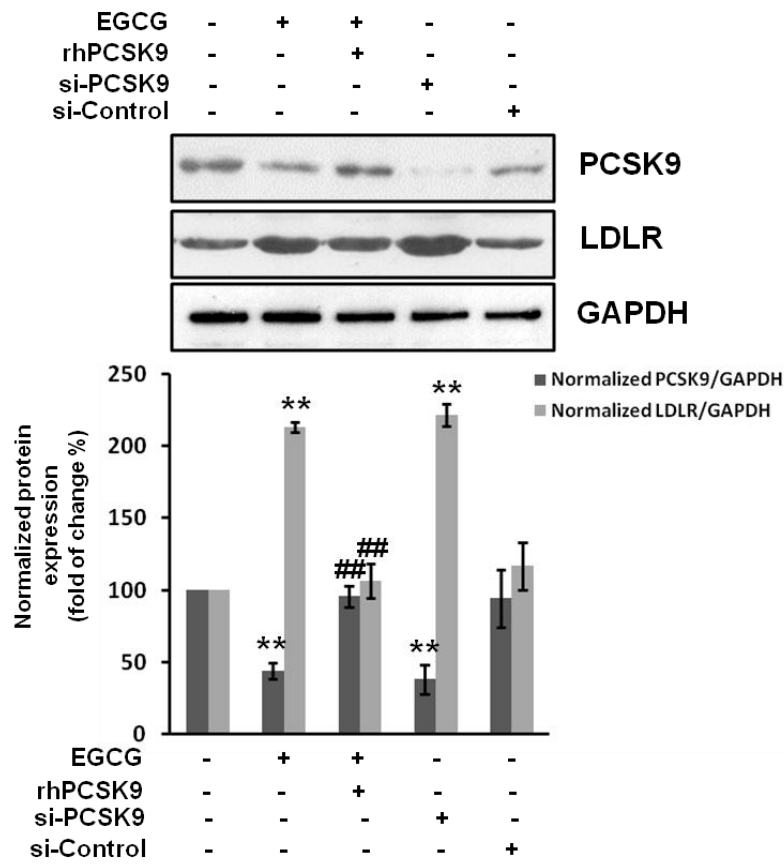
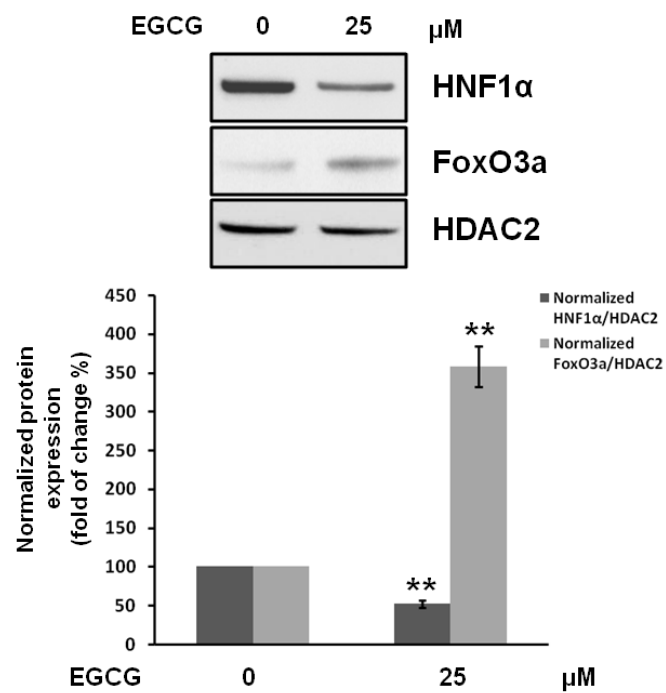


Figure S2.

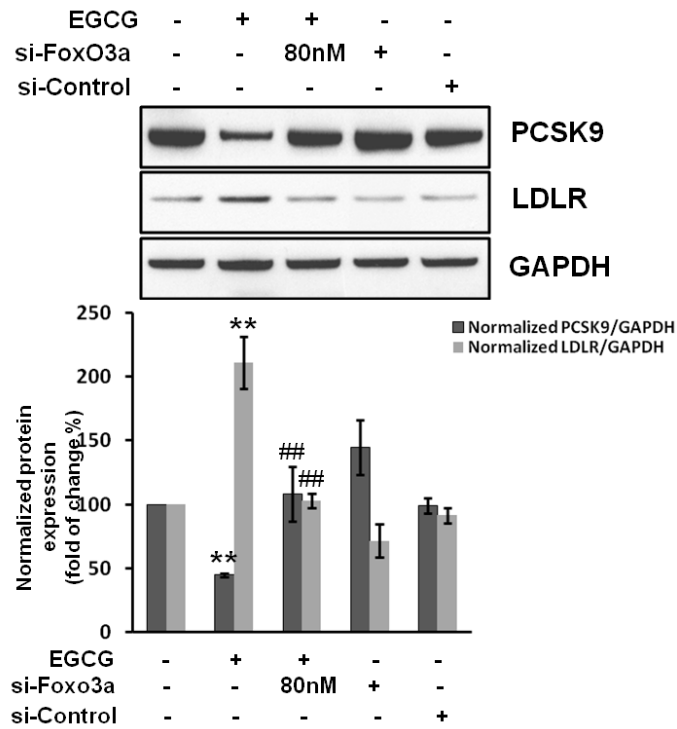
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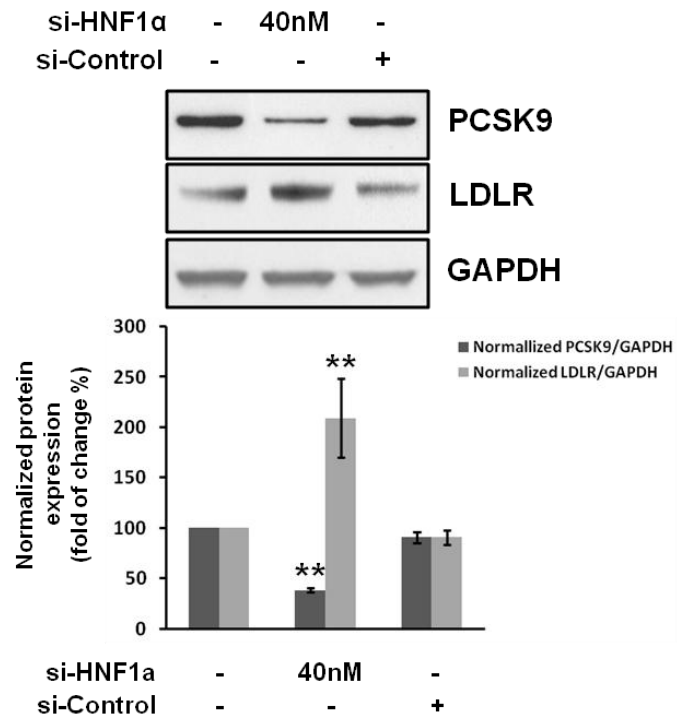
B.



C.



D.



E.

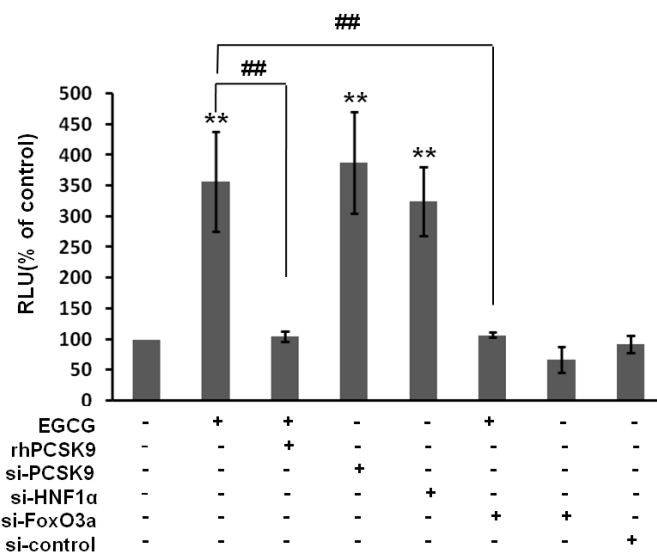
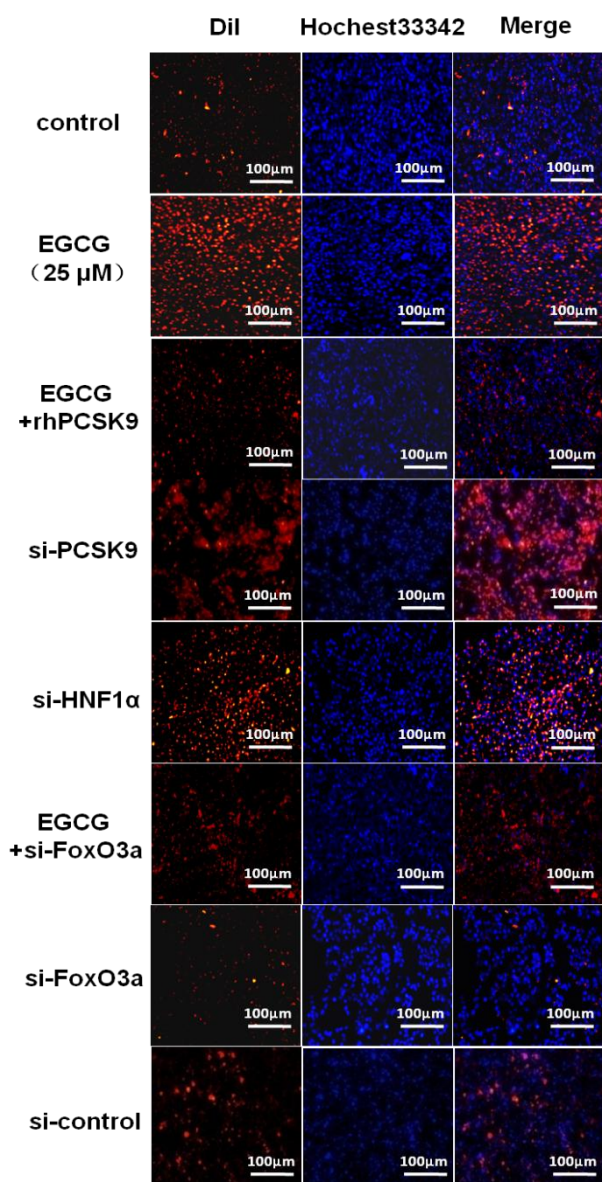


Figure S3.

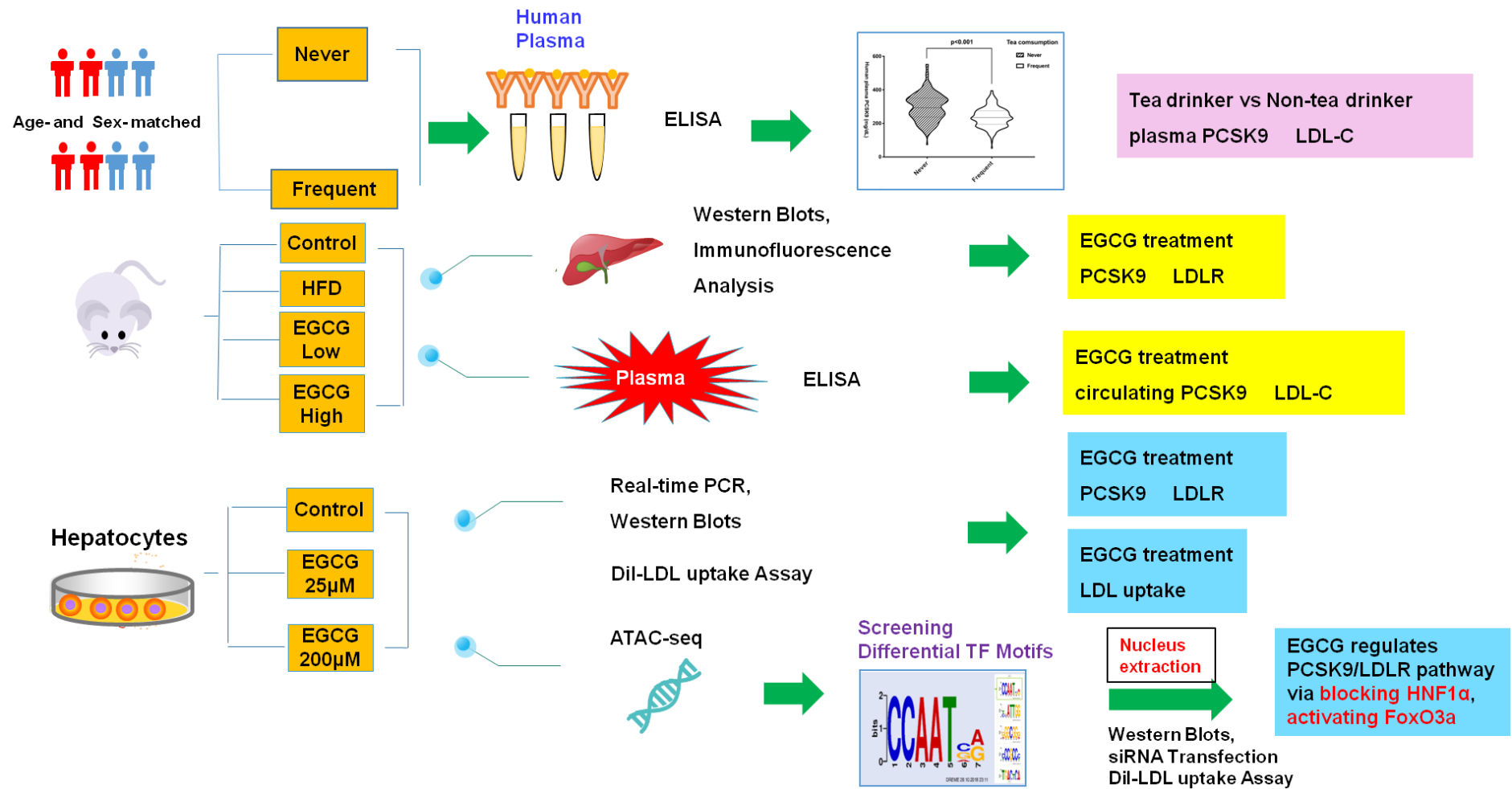


Table S1. Baseline characters of study population

Variables	Tea consumption		P
	Never, n=224	Frequent, n=224	
Age, years	53.7±10.5	54.3±10.6	-
Male, n (%)	155(69.2)	155(69.2)	-
BMI, kg/m ²	25.6±3.3	25.4±3.4	0.813
DM, n (%)	88(39.3)	80(35.7)	0.435
Hypertension	121(54.0)	110(49.1)	0.298
CAD, n (%)	123(55.8)	116(51.8)	0.394
Smoke, n (%)	95(42.4)	107(47.8)	0.255
Drink, n (%)	47(21.0)	53(23.7)	0.496
LDL-C (mmol/L)	3.05±0.92	3.26±1.02	0.025
HDL-C (mmol/L)	1.13±0.34	1.12±0.42	0.734
TG (mmol/L)	1.72(1.23-2.26)	1.70(1.14-2.50)	0.739
PCSK9 (mg/dL)	236.8±57.7	297.4±81.6	<0.001

Data were expressed as mean ± SD, median with 25th and 75th percentile or n (%).

BMI: body mass index; DM: diabete mellitus; CAD: coronary artery disease; TG: triglyceride; LDL-C: low density lipoprotein cholesterol; HDL-C: high density lipoprotein cholesterol.

Table S2. Univariate and multivariate linear regression analyses for the relationship of PCSK9 and tea consumption

Variables	Univariate regression		Multivariate regression	
	Standard Coefficients	P	Standard Coefficients	P
BMI	0.075	0.146	0.043	0.382
Hypertension	0.090	0.057	0.025	0.617
DM	0.050	0.295	-0.013	0.778
Smoke	-0.006	0.900	0.012	0.810
Drink	-0.018	0.705	-0.032	0.527
CAD	0.163	0.001	0.114	0.026
TG	-0.022	0.643	0.030	0.527
HDL-C	0.100	0.034	0.046	0.350
LDL-C	0.271	<0.001	0.136	0.008
Tea consumption	-0.362	<0.001	-0.330	<0.001