ARTICLE

'C   [7], Sa   E. R   a a   [12], Ma   A   [13],
A Ma   a [14], W. C   J   [15], Ja   A. P   [7], T   P   ba[3,8], C   S   [3,8], L L. S   a   a[12],
T   E   [13], Sa   R   a [12], V   Sa   aa   [12], A   C   a   [16], Ra a a   S. Va a   [17,18,19],
Ma   K   [3,20], B   ja   M. N   a   [1,2,3,8], E   S. La   [3], G   a   Ab   a [21], B a   M   [7],
S   S. R   [14], Ja   G. W   [16,22], L. A   C   [4,19], J   I. R   [23]
NHLBI TOPM   W   G   , C   J. W   [24] & S   a Ka   a   [1,2,3]

P . . . . (LDL-C), ... (HDL-C), ... , ... [1,2] U(
. . . .

A . . . . DNA . . . . . .
(. . , S . . . . #X . . . .

. . . . DNA . . . .
. . . . . H . . . . #X . . . .

. . . . . . I(. . . . .
DNA . . . . #N

I . . . .
fi . . . . (>20- . . . .), . . .
. . . . (WGS) . . . .
(SNP), ...
T . . . . WGS .

M ... (TOPM) ... >20 ... EST ... FIN (... F . 2). T ... (SD) ... >30 ... 37.1(5.4) ... >20 ... 29.8(5.4)X.

A ... 189 ... T ... (F. 2). A ... MESA ... OOA ... (S ... T 3). T ... 19 ... 3,391,000, ... 4878 ...

Common plus low-frequency variant association study. W f ... (MAF) >0.1% ... WGS ... (... >16 ... FHS/

T ... MAF ... 0.25% ... 0.090–0.69% (S ... F ... 8). T ... M ... S ... K ... A ... (T ... (SKAT)[11,12]. S ... ($\alpha = 0.05/$ 20,000 ... ($ = 2.5 \times 10^{-6}$) (*LDLR, APOB, PCSK9,* ... *APOE* ... LDL-C, *LCAT* ... HDL-C, ... *APOC3* ...). E ... M ... (S ... T ... 9).

Rare variant association study of non-coding variants. N ...
... W ... ... (F ... 3). F ... ... 3 ... ... [13,14]. S ... 20 ... ... 5 ... TSS ...). T ...
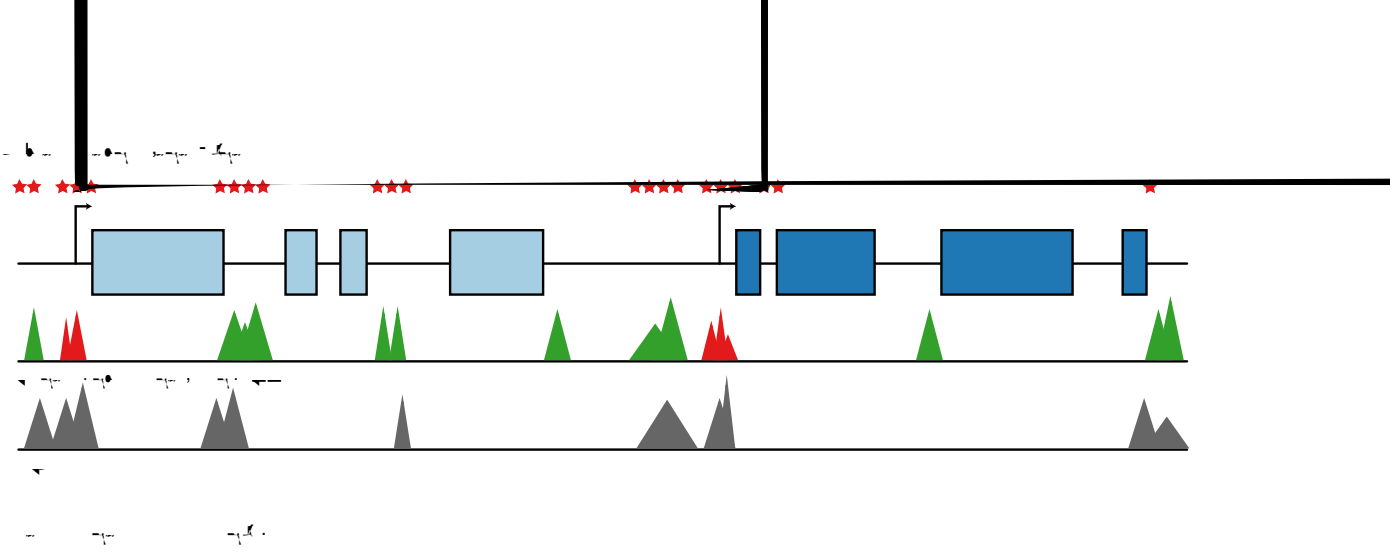
A (	AA 	(	) – 	((	 	(–
– 	÷	 – (	 7.43 (95% CI 3.01–18.35) 	
 #	 	 LDL-C, 	 – 	(	 	
– ÷	 – 	 3.2 (95% CI 2.1–4.89). I(	AA
 (	 	 	 	(	 (	;
41 	/	 LDL-C (	(	 – 	 	(	;
$P = 2.3 \cdot 10^{-7}$), 	 (	 	 – 	(EA 	(	–
 	(	 	 	(	 	 17 	/
 	LDL-C (	(	 	 	; $P = 6.4 \cdot 10^{-10}$),
 	 	 	 – 	(EA 	(	 O 	217 AA
 	(	 #	 	 LDL-C, 3% 	 – 	((
 	(	(	13% 	 – 	(	 	A 	
 	 	 LDL-C 	(	 , 	 SD 	 LDL-C
– 	(	 	 – 	÷	 	 15.5 	/ LDL-C
– (	EA ($P = 4 \cdot 10^{-277}$) 	(	8.7 	/ LDL-C 	(	AA
($P = 1 \cdot 10^{-47}$).
W 	 	 – 	 – 	÷	(	 	((	 	(
– (	#	 	 LDL-C (	(	(	 	((	 	 ,	 ARIC

 	A 	(ARIC-EA ($N = 7755$) (	 	 	 	 	(
 	 – 	 	÷	 – (	 	 	7.35 (95% CI 5.95–9.10;
$P < 2 \cdot 10^{-16}$) 	 #	 	 	 LDL-C (	42.8 	/ (95% CI
40.0–47.5; $P < 2 \cdot 10^{-16}$

MA), 3266 JHS ... U(... W ...
N ... G ... C ... (S... , WA). A ... 4601 MESA ...
... B... I(... H ... MIT ...
TOPMED P... 2. A ... 1180 F... FINRISK ... 2281 E. ...
B... ... B... I(... H ... MIT
(C ... , MA). T ...
TOPMED 1 BAM fi ...
TOPM I(... R ... C ... (IRC) ...
... I(... ...
G ... 37 5 ... 37 ... R ...
... "G . C " ...

18. H... O. L... S... ... TM6SF2 ... *Nat. Genet.* **46**, 345–351 (2014).

19. K..., M. ... A ... *Nat. Genet.* **46**, 310–315 (2014).

20. B... D. ... FUN-LDA: ...

Additional information

Ra a Ma a[35], Pa M A[31], M -L M D a[38], S a M Fa a[87], S M Ga[69], Ha M[33], D b a A M[88], J M a[34], Na M[33], M M a[34], R a L M[71], S M a[33], Sa M a g D[33], J C M a j[55], G Na a[65], R Na[35], S g N a[89], D b a N[32], Ka N[66], T O'C[31], H a O -Ba[90], Ja Pa[91], G g Paa a[34], Mag a Pa[54], A Pa a[31], Sa a P[49], J a Ma P a a[67], Ma P[39], U P[70,32], Pa a P[46], La P[30], Sa P[32], T P[31], W P[35], J a P B[42], M P B g a[42], M a P[65], D P[87], B P a[32], Pa aj Qa ba[34], Da Q a[54], Z a Q[30], N a Ra a[42], La a Raffi[66], D.C. Ra[68], La a Ra -T[92], A Ra a[55], S a R[54], R b R[31], E ab Rg a[49], A R[70,32], K R[32], Da R[63], Ca a R[57], Ig R[35], Pa a R[42], Sa a R a[93], Ka Ra[31], P a a Sa a a[54], S ab a Sa[31], S Sa b g[35], K Sa[56], V'ja Sa a a