Supporting Information

Kenny et al. 10.1073/pnas.0907336106

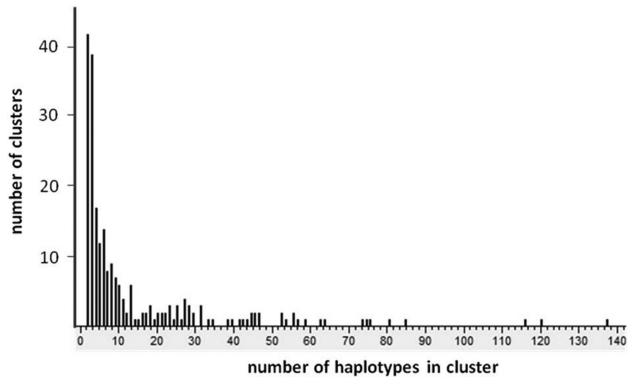
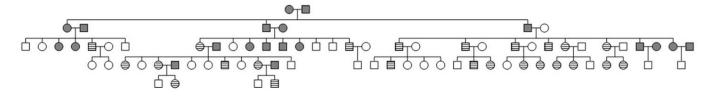
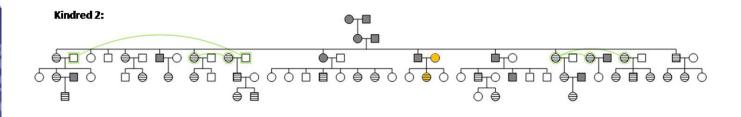


Fig. S1. Histogram of haplotype cluster sizes. The x-axis shows the haplotypes binned by the number of haplotypes in each cluster and the number of clusters for each bin is shown on the y-axis.

Kindred 1:





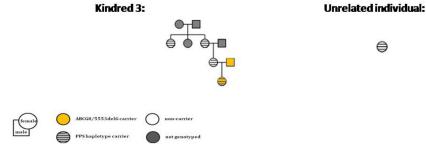
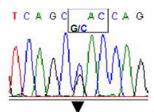


Fig. S2. Segregation of PPS haplotype in three kindreds from one village. The pedigree structure of 146 individuals forming three kindreds and one unrelated individual from the same village on Kosrae. PPS haplotype carriers are shown in horizontal strips. ABCG8 nonsense mutation carriers are shown in orange. Noncarriers are shown in white. Thirty-six nongenotyped individuals (shown in solid gray) are included to preserve the kindred structure.



	D 450 H	
Human	NAVNLFPVLRAVSDQESQDGLYQKWQMMLAYALHVLPFSVVATMIFSSVCYWTLGLHPEV	496
Chicken	NAAALFPPLRAISDQESKDGLYQKWQMLLAYIIHFLPFSILSVVIFSTFMYWTVGMYPDP	407
Frog	NAVALFPTLRAIGDQEGKDGLYQKWQMLLAYIIHIVPFSILSVVIFSGFIYWVIGLYPDI	394
Lizard	NALALFPALRAVADQESKDGLYQKWQMLLAYIVHFLPFSIIGVALYSVFIYWTMGLYPEV	402
Rhesus	NAVNLFPVLRAVSDQESQDGLYQKWQMLLAYVLHVLPFSVIATMIFSSVCYWTLGLHPEV	496
Dog	NAVNLFPVLRAVSDQESQDGLYQKWQMLLAYVLHALPFSVLATIIFSSVCYWTLGLYPEV	496
Horse	NAVNLFPVLRAVSDQESQDGLYQKWQMLLAYVLHVLPFSILATVILSSVSYWTLGLYPEA	496
Mouse	NAVNLFPMLRAVSDQESQDGLYHKWQMLLAYVLHVLPFSVIATVIFSSVCYWTLGLYPEV	496
Platypus	NAVAL	393
Opossum	NAVAFFPALRAISDQESQDGLYQKWQMLLAYILHILPFALISVVIFSSVLYWTVGLYPEA	492
Stickleback	NAVALFPALRAIGDQESQDGLYSKWQMFLAYIFHILPFSILSVFIFTSFLY	439

Fig. S3. D450H missense mutation in exon 10 of the ABCG5 gene. The sequencing chromatograph showing the G to C mutation that results in a coding change from aspartic acid (D) to histidine (H) at codon 450 in exon 10 of the ABCG5 gene. The aspartic acid is highly conserved in vertebrates.

Table S1. Linkage equilibrium between the ABCG8 nonsense mutation and rs12185607/G allele

		rs12185607	
ABCG8 nonsense mutation		GG	GT
	GG	2512	64
	GC	321	2
	CC	5	0

Table S2. Lathosterol:cholesterol and other plasma lipid levels. ANOVA analysis of lathosterol:cholesterol and plasma lipid levels comparing carriers of the ABCG8 mutation and 526-kb haplotype and individuals who are wild type for both mutations

	Total Population	Noncarriers	ABCG8 mutation carriers	PPS haplotype carriers	Non- carriers vs. ABCG8 mutation carriers	Non- carriers vs. PPS haplotype carriers	Non- carriers vs ABCG8 carriers vs. PPS carriers
Lath:Chol	1.50 ± 0.66 (1,900)	1.52 ± 0.67 (1.687)	1.33 ± 0.55 (213)	0.84 ± 0.38 (44)	1.08×10^{-4}	3.68×10^{-11}	< 0.0001
TC, mg/dL	166.09 ± 34.43 (2,819)	165.48 ± 34.35 (2.452)	170.2 ± 34.48 (315)	167.55 ± 34.92 (52)	0.022	N.S.	N.S
LDL-c, mg/dL	102.1 ± 29.54 (1,899)	101.63 ± 29.3 (1.645)	105.42 ± 30.63 (210)	100.84 ± 30.73 (44)	N.S.	N.S.	N.S
ApoB, mg/dL	86.97 ± 21.32 (1,884)	86.65 ± 21.31 (1.621)	88.53 ± 21.64 (219)	89.7 ± 19.8 (35)	N.S.	N.S.	N.S
HDL-c, mg/dL	38.28 ± 11.04 (1,899)	38.09 ± 10.95 (1.645)	38.77 ± 11.36 (210)	42.00 ± 9.93 (44)	N.S.	N.S.	N.S
ApoA1, mg/dL	116.87 ± 24.39 (1,875)	116.64 ± 24.07 (1.621)	118.07 ± 26.5 (219)	122.21 ± 25.3 (35)	N.S.	N.S.	N.S
TG, mg/dL	99.94 ± 46.16 (2,817)	100.94 ± 45.91 (24.50)	95.58 ± 39.02 (315)	93.26 ± 36.32 (52)	0.05	N.S.	N.S

N, number of individuals; Lath:Chol, lathosterol/cholesterol ratio; TC, total cholesterol; LDL-c, low density lipoprotein cholesterol; HDL-c, high density lipoprotein cholesterol; TG, triglycerides. All numbers are averages \pm standard deviation and the sample size is shown in parentheses.