

U.S. Genome Variation Estimates

MTHFR Allele and Genotype Frequencies

AVAILABLE POLYMORPHISM(S)

rs number	Common Designations		Genotyping method
	Nucleotide change	Amino acid change	
rs1801131	Ex8-62A>C 1298A>C	Glu429Ala	TaqMan
rs1801133	Ex5+79C>T 677C>T	Ala222Val	MGB Eclipse
rs2066470	Ex2-120C>T	Pro39Pro	MGB Eclipse

BY RACE/ETHNICITY

Variant	Race-Ethnicity	Allele % (95% CI)		Chi-Square P-Value†	Genotype % (95% CI)			Chi-Square P-Value†	HW P-Value‡
rs1801131		A	C		AA	AC	CC		
	Non-Hispanic White	68.9 (65.9, 71.8)	31.1 (28.2, 34.1)	<0.001	48.2 (44.1, 52.4)	41.3 (38.2, 44.4)	10.5 (8.4, 12.9)	<0.001	0.07
	Non-Hispanic Black	82.1 (81.1, 83.1)	17.9 (16.9, 18.9)		67.6 (65.9, 69.2)	29.0 (27.4, 30.7)	3.4 (2.7, 4.2)		0.42
	Mexican American	81.2 (77.8, 84.2)	18.8 (15.8, 22.2)		66.0 (61.0, 70.6)	30.5 (27.2, 34.1)	3.5 (2.2, 5.6)		0.77
	Total*	71.6 (69.2, 73.9)	28.4 (26.1, 30.8)		52.2 (48.8, 55.6)	38.8 (36.1, 41.5)	9.0 (7.4, 10.9)		
rs1801133		C	T		CC	CT	TT		
	Non-Hispanic White	67.4 (64.8, 70.0)	32.6 (30.0, 35.2)	<0.001	46.4 (42.5, 50.3)	42.1 (38.8, 45.5)	11.5 (9.7, 13.5)	<0.001	0.10
	Non-Hispanic Black	88.4 (87.5, 89.2)	11.6 (10.8, 12.5)		77.9 (76.2, 79.5)	20.9 (19.2, 22.7)	1.2 (0.7, 1.9)		0.49
	Mexican American	55.4 (52.5, 58.3)	44.6 (41.7, 47.5)		30.7 (27.5, 34.1)	49.4 (46.3, 52.5)	19.9 (16.7, 23.5)		0.93
	Total*	69.2 (67.2, 71.2)	30.8 (28.8, 32.8)		49.3 (46.3, 52.4)	39.8 (37.2, 42.5)	10.9 (9.4, 12.5)		

rs2066470		C	T		CC	CT	TT		
	Non-Hispanic White	90.4 (88.6, 92.0)	9.6 (8.0, 11.4)	0.042	81.9 (78.7, 84.8)	17.0 (14.4, 20.0)	1.1 (0.6, 1.8)	0.057	0.32
	Non-Hispanic Black	91.3 (90.0, 92.4)	8.7 (7.6, 10.0)		83.5 (81.2, 85.6)	15.6 (13.6, 17.8)	0.9 (0.5, 1.6)		0.25
	Mexican American	93.5 (92.2, 94.6)	6.5 (5.4, 7.8)		87.4 (85.1, 89.5)	12.1 (10.1, 14.4)	0.5 (0.2, 1.2)		0.84
	Total*	90.3 (88.9, 91.5)	9.7 (8.5, 11.1)		81.9 (79.4, 84.2)	16.8 (14.7, 19.2)	1.3 (0.9, 1.7)		

* Includes all U.S. race/ethnic groups.

† "other" race/ethnicity category was not included in chi-square tests.

‡ P-values from unweighted chi-square goodness-of-fit tests to test for deviations from Hardy-Weinberg (HW) proportions.

BY AGE*

Variant	Age (Years)	Allele % (95% CI)		Chi-Square P-Value	Genotype % (95% CI)			Chi-Square P-Value
rs1801131		A	C		AA	AC	CC	
	12-19	74.8 (71.5, 77.8)	25.2 (22.2, 28.5)	0.030	55.9 (50.7, 61.0)	37.8 (32.9, 42.9)	6.3 (4.4, 9.1)	0.041
	20-39	72.5 (69.5, 75.4)	27.5 (24.6, 30.5)		52.7 (48.2, 57.1)	39.7 (35.9, 43.7)	7.6 (5.7, 10.1)	
	40-59	69.8 (65.9, 73.4)	30.2 (26.6, 34.1)		51.1 (46.1, 56.1)	37.3 (33.5, 41.4)	11.5 (8.6, 15.2)	
	>=60	70.1 (68.2, 72.0)	29.9 (28.0, 31.8)		50.3 (46.7, 54.0)	39.6 (35.4, 44.0)	10.0 (8.4, 12.0)	
	Total	71.6 (69.2, 73.9)	28.4 (26.1, 30.8)		52.2 (48.8, 55.6)	38.8 (36.1, 41.5)	9.0 (7.4, 10.9)	
rs1801133		C	T		CC	CT	TT	
	12-19	69.3 (64.7, 73.5)	30.7 (26.5, 35.3)	0.764	49.8 (42.5, 57.1)	39.0 (32.2, 46.4)	11.2 (8.4, 14.7)	0.551
	20-39	69.9 (67.1, 72.5)	30.1 (27.5, 32.9)		50.4 (46.4, 54.4)	38.9 (35.2, 42.7)	10.7 (8.6, 13.2)	
	40-59	69.1 (65.5, 72.5)	30.9 (27.5, 34.5)		49.1 (44.3, 54.0)	40.0 (35.6, 44.6)	10.9 (7.9, 14.7)	
	>=60	68.1 (65.1, 70.9)	31.9 (29.1, 34.9)		47.1 (43.5, 50.8)	41.9 (39.2, 44.6)	11.0 (8.6, 13.9)	
	Total	69.2 (67.2, 71.2)	30.8 (28.8, 32.8)		49.3 (46.3, 52.4)	39.8 (37.2, 42.5)	10.9 (9.4, 12.5)	
rs2066470		C	T		CC	CT	TT	
	12-19	91.3 (88.6, 93.4)	8.7 (6.6, 11.4)	0.017	83.1 (78.0, 87.2)	16.5 (12.5, 21.4)	0.4 (0.1, 1.3)	<0.001
	20-39	91.7 (89.6, 93.4)	8.3 (6.6, 10.4)		84.2 (80.6, 87.3)	15.0 (12.1, 18.4)	0.8 (0.4, 1.9)	
	40-59	89.0 (87.0, 90.8)	11.0 (9.2, 13.0)		80.1 (76.8, 83.0)	17.8 (15.4, 20.6)	2.1 (1.2, 3.5)	

	>=60	88.8 (87.2, 90.1)	11.2 (9.9, 12.8)		79.1 (76.0, 81.8)	19.4 (16.4, 22.7)	1.6 (0.9, 2.6)	
	Total	90.3 (88.9, 91.5)	9.7 (8.5, 11.1)		81.9 (79.4, 84.2)	16.8 (14.7, 19.2)	1.3 (0.9, 1.7)	

* Includes all participants, regardless of race/ethnicity.

BY SEX*

Variant	Sex	Allele % (95% CI)		Chi-Square P-Value	Genotype % (95% CI)			Chi-Square P-Value
rs1801131		A	C		AA	AC	CC	
	Male	71.4 (68.0, 74.6)	28.6 (25.4, 32.0)	0.784	52.1 (47.6, 56.7)	38.6 (34.9, 42.4)	9.3 (6.8, 12.6)	0.935
	Female	71.8 (69.7, 73.8)	28.2 (26.2, 30.3)		52.3 (49.2, 55.4)	39.0 (36.2, 41.8)	8.7 (7.2, 10.6)	
	Total	71.6 (69.2, 73.9)	28.4 (26.1, 30.8)		52.2 (48.8, 55.6)	38.8 (36.1, 41.5)	9.0 (7.4, 10.9)	
rs1801133		C	T		CC	CT	TT	
	Male	69.6 (66.6, 72.5)	30.4 (27.5, 33.4)	0.628	50.2 (45.5, 54.9)	38.8 (34.5, 43.3)	11.0 (8.9, 13.5)	0.731
	Female	68.9 (66.7, 70.9)	31.1 (29.1, 33.3)		48.5 (45.4, 51.6)	40.7 (38.1, 43.3)	10.8 (9.2, 12.5)	
	Total	69.2 (67.2, 71.2)	30.8 (28.8, 32.8)		49.3 (46.3, 52.4)	39.8 (37.2, 42.5)	10.9 (9.4, 12.5)	
rs2066470		C	T		CC	CT	TT	
	Male	90.2 (88.4, 91.8)	9.8 (8.2, 11.6)	0.777	81.9 (78.6, 84.8)	16.7 (14.0, 19.7)	1.4 (1.0, 2.1)	0.731
	Female	90.4 (89.1, 91.6)	9.6 (8.4, 10.9)		81.9 (79.6, 84.0)	17.0 (15.0, 19.2)	1.1 (0.6, 2.0)	
	Total	90.3 (88.9, 91.5)	9.7 (8.5, 11.1)		81.9 (79.4, 84.2)	16.8 (14.7, 19.2)	1.3 (0.9, 1.7)	

* Includes all participants, regardless of race/ethnicity.

BY RACE/ETHNICITY AND AGE

Variant	Race-Ethnicity	Age (Years)	Allele % (95% CI)		Genotype % (95% CI)		
rs1801131			A	C	AA	AC	CC

	Non-Hispanic White	12-19	72.5 (67.8, 76.9)	27.5 (23.1, 32.2)	52.8 (46.2, 59.2)	39.5 (33.8, 45.5)	7.7 (4.5, 12.8)
		20-39	68.9 (64.8, 72.8)	31.1 (27.2, 35.2)	47.0 (41.3, 52.8)	43.8 (39.1, 48.6)	9.2 (6.5, 12.8)
		40-59	67.6 (63.7, 71.3)	32.4 (28.7, 36.3)	48.0 (43.0, 53.1)	39.2 (35.1, 43.4)	12.8 (9.7, 16.7)
		>=60	68.6 (66.4, 70.6)	31.4 (29.4, 33.6)	48.2 (43.9, 52.4)	40.8 (35.9, 45.9)	11.0 (9.2, 13.1)
	Non-Hispanic Black	12-19	82.7 (79.2, 85.8)	17.3 (14.2, 20.8)	68.9 (62.9, 74.3)	27.7 (22.3, 33.8)	3.4 (1.8, 6.5)
		20-39	81.7 (79.2, 83.9)	18.3 (16.1, 20.8)	67.1 (62.9, 71.1)	29.1 (25.5, 33.1)	3.7 (2.7, 5.1)
		40-59	82.2 (78.8, 85.1)	17.8 (14.9, 21.2)	67.0 (61.5, 72.2)	30.3 (25.6, 35.5)	2.6 (1.3, 5.3)
		>=60	82.4 (75.8, 87.5)	17.6 (12.5, 24.2)	68.3 (57.5, 77.5)	28.1 (19.9, 38.1)	3.6 (1.6, 7.6)
	Mexican American	12-19	82.9 (76.8, 87.7)	17.1 (12.3, 23.2)	70.6 (62.5, 77.6)	24.7 (19.7, 30.4)	4.8 (2.1, 10.5)
		20-39	81.5 (78.4, 84.2)	18.5 (15.8, 21.6)	66.2 (61.5, 70.5)	30.7 (27.0, 34.5)	3.2 (1.7, 5.7)
		40-59	79.4 (73.0, 84.6)	20.6 (15.4, 27.0)	62.1 (51.4, 71.7)	34.6 (25.9, 44.5)	3.3 (1.6, 6.5)
		>=60	80.1 (77.2, 82.7)	19.9 (17.3, 22.8)	63.6 (58.0, 68.8)	33.0 (26.8, 39.7)	3.4 (1.6, 7.2)
rs1801133			C	T	CC	CT	TT
	Non-Hispanic White	12-19	67.4 (60.3, 73.8)	32.6 (26.2, 39.7)	46.9 (36.7, 57.3)	41.0 (32.2, 50.4)	12.1 (8.0, 18.0)
		20-39	68.4 (64.6, 71.9)	31.6 (28.1, 35.4)	47.7 (41.8, 53.7)	41.4 (35.6, 47.3)	10.9 (8.3, 14.3)
		40-59	67.0 (62.7, 71.0)	33.0 (29.0, 37.3)	46.1 (40.8, 51.4)	41.8 (36.7, 47.0)	12.1 (8.3, 17.4)
		>=60	66.5 (63.6, 69.3)	33.5 (30.7, 36.4)	44.2 (40.7, 47.9)	44.5 (41.5, 47.6)	11.3 (8.8, 14.4)
	Non-Hispanic Black	12-19	87.9 (84.8, 90.5)	12.1 (9.5, 15.2)	77.4 (72.2, 81.8)	21.1 (17.1, 25.8)	1.5 (0.5, 4.3)
		20-39	88.3 (86.8, 89.5)	11.7 (10.5, 13.2)	77.7 (75.3, 79.9)	21.2 (19.1, 23.5)	1.1 (0.5, 2.6)
		40-59	89.6 (87.2, 91.6)	10.4 (8.4, 12.8)	79.9 (75.7, 83.6)	19.3 (15.8, 23.4)	0.8 (0.2, 3.2)
		>=60	87.3 (83.8, 90.1)	12.7 (9.9, 16.2)	76.0 (69.6, 81.3)	22.6 (17.3, 29.0)	1.4 (0.5, 3.9)
	Mexican American	12-19	51.9 (46.3, 57.5)	48.1 (42.5, 53.7)	28.4 (22.6, 35.0)	47.0 (37.9, 56.4)	24.6 (17.2, 33.8)
		20-39	55.5 (53.2, 57.7)	44.5 (42.3, 46.8)	31.1 (28.1, 34.2)	48.8 (45.5, 52.3)	20.1 (17.7, 22.7)
		40-59	58.8 (53.4, 64.1)	41.2 (35.9, 46.6)	33.1 (26.8, 39.9)	51.6 (47.2, 56.0)	15.4 (11.1, 20.8)
		>=60	54.5 (51.0, 57.9)	45.5 (42.1, 49.0)	28.2 (23.9, 32.9)	52.7 (46.1, 59.1)	19.2 (14.7, 24.6)
rs2066470			C	T	CC	CT	TT
	Non-Hispanic White	12-19	92.4 (88.8, 94.9)	7.6 (5.1, 11.2)	84.7 (77.8, 89.8)	15.3 (10.2, 22.2)	0.0 (NA)
		20-39	91.5 (88.7, 93.7)	8.5 (6.3, 11.3)	83.9 (79.1, 87.8)	15.2 (11.6, 19.6)	0.9 (0.3, 2.7)
		40-59	89.8 (87.8, 91.5)	10.2 (8.5, 12.2)	80.9 (77.5, 83.8)	17.8 (15.1, 20.9)	1.3 (0.7, 2.5)
		>=60	88.4 (86.6, 90.0)	11.6 (10.0, 13.4)	78.4 (75.0, 81.5)	19.9 (16.6, 23.8)	1.6 (0.8, 3.2)

	Non-Hispanic Black	12-19	90.9 (87.2, 93.5)	9.1 (6.5, 12.8)	82.8 (76.6, 87.7)	16.0 (11.6, 21.8)	1.1 (0.3, 3.7)
		20-39	91.6 (90.1, 92.8)	8.4 (7.2, 9.9)	83.6 (80.6, 86.1)	16.0 (13.4, 19.1)	0.4 (0.1, 1.1)
		40-59	91.7 (88.8, 93.8)	8.3 (6.2, 11.2)	84.5 (79.6, 88.4)	14.4 (10.8, 18.9)	1.2 (0.4, 3.2)
		>=60	90.5 (85.9, 93.7)	9.5 (6.3, 14.1)	82.5 (74.9, 88.2)	15.9 (10.8, 22.7)	1.6 (0.6, 4.2)
	Mexican American	12-19	94.3 (91.0, 96.5)	5.7 (3.5, 9.0)	89.6 (84.4, 93.2)	9.5 (6.5, 13.8)	0.9 (0.2, 4.3)
		20-39	94.2 (93.0, 95.3)	5.8 (4.7, 7.0)	88.7 (86.2, 90.8)	11.0 (8.9, 13.7)	0.3 (0.1, 1.2)
		40-59	91.4 (88.8, 93.5)	8.6 (6.5, 11.2)	83.6 (78.2, 87.9)	15.6 (11.1, 21.5)	0.8 (0.2, 2.8)
		>=60	92.3 (90.6, 93.7)	7.7 (6.3, 9.4)	84.6 (81.3, 87.4)	15.4 (12.6, 18.7)	0.0 (NA)

BY RACE/ETHNICITY AND SEX

Variant	Race-Ethnicity	Sex	Allele % (95% CI)		Genotype % (95% CI)		
			A	C	AA	AC	CC
rs1801131							
	Non-Hispanic White	Male	68.6 (64.5, 72.5)	31.4 (27.5, 35.5)	48.3 (42.8, 53.8)	40.7 (36.2, 45.3)	11.0 (7.9, 15.1)
		Female	69.1 (66.2, 71.9)	30.9 (28.1, 33.8)	48.2 (44.1, 52.3)	41.9 (38.3, 45.5)	9.9 (7.7, 12.7)
	Non-Hispanic Black	Male	81.3 (79.4, 83.1)	18.7 (16.9, 20.6)	66.3 (63.3, 69.2)	30.0 (27.5, 32.7)	3.6 (2.6, 5.0)
		Female	82.7 (81.3, 84.1)	17.3 (15.9, 18.7)	68.7 (66.1, 71.1)	28.2 (25.7, 30.8)	3.2 (2.3, 4.4)
	Mexican American	Male	81.6 (78.3, 84.6)	18.4 (15.4, 21.7)	66.0 (60.3, 71.2)	31.3 (26.8, 36.3)	2.7 (1.8, 4.0)
		Female	80.8 (76.8, 84.2)	19.2 (15.8, 23.2)	65.9 (60.7, 70.8)	29.6 (26.5, 32.9)	4.4 (2.5, 7.9)
rs1801133			C	T	CC	CT	TT
	Non-Hispanic White	Male	68.4 (64.7, 71.9)	31.6 (28.1, 35.3)	48.0 (42.4, 53.6)	40.8 (35.7, 46.2)	11.2 (8.6, 14.3)
		Female	66.5 (63.6, 69.3)	33.5 (30.7, 36.4)	44.8 (40.7, 49.1)	43.4 (39.9, 46.9)	11.8 (9.8, 14.1)
	Non-Hispanic Black	Male	88.1 (86.3, 89.6)	11.9 (10.4, 13.7)	77.3 (74.0, 80.3)	21.5 (18.4, 24.9)	1.2 (0.6, 2.4)
		Female	88.7 (87.6, 89.7)	11.3 (10.3, 12.4)	78.4 (76.3, 80.4)	20.5 (18.3, 22.8)	1.1 (0.6, 2.0)
	Mexican American	Male	54.8 (50.6, 58.9)	45.2 (41.1, 49.4)	29.3 (25.7, 33.2)	50.9 (47.2, 54.6)	19.8 (15.1, 25.5)
		Female	56.1 (53.9, 58.3)	43.9 (41.7, 46.1)	32.2 (28.7, 35.9)	47.8 (43.9, 51.8)	20.0 (18.0, 22.2)
rs2066470			C	T	CC	CT	TT
	Non-Hispanic White	Male	90.0 (87.6, 92.0)	10.0 (8.0, 12.4)	81.3 (77.0, 85.0)	17.4 (13.9, 21.4)	1.3 (0.7, 2.4)

		Female	90.9 (89.2, 92.3)	9.1 (7.7, 10.8)	82.5 (79.6, 85.1)	16.7 (14.2, 19.5)	0.8 (0.3, 1.9)
	Non-Hispanic Black	Male	92.2 (90.6, 93.6)	7.8 (6.4, 9.4)	84.9 (81.8, 87.6)	14.6 (12.0, 17.7)	0.5 (0.2, 1.2)
		Female	90.5 (88.6, 92.2)	9.5 (7.8, 11.4)	82.3 (79.0, 85.2)	16.4 (13.7, 19.5)	1.2 (0.6, 2.7)
	Mexican American	Male	93.6 (91.9, 94.9)	6.4 (5.1, 8.1)	87.7 (84.7, 90.1)	11.8 (9.5, 14.6)	0.6 (0.2, 1.9)
		Female	93.4 (91.5, 94.9)	6.6 (5.1, 8.5)	87.2 (83.4, 90.3)	12.4 (9.3, 16.3)	0.4 (0.1, 1.4)