GENETIC VARIANT ANALYSIS

SUBJECT	Yanlene Torres
REFERENCE DATE	23 September 2016
SPECIMEN MODEL	Peripheral blood / DNA
CASE ID	HX-2016-0923
REPORT CATEGORY	Population distribution and genetic origins

GENETIC MARKERS COVERED

ABO / RHD	O-positive blood group
CCR5	Delta32 deletion variant
FMR1	Fragile X-associated CGG repeat
HBB	Sickle cell-associated HbS variant

GENETIC VARIANT DISTRIBUTION ATLAS

Population genetics | CCR5-Delta32 | FMR1 | HBB | ABO/RhD

Subject: Yanlene Torres **date:** September 23, 2016

Specimen model: Peripheral blood / DNA

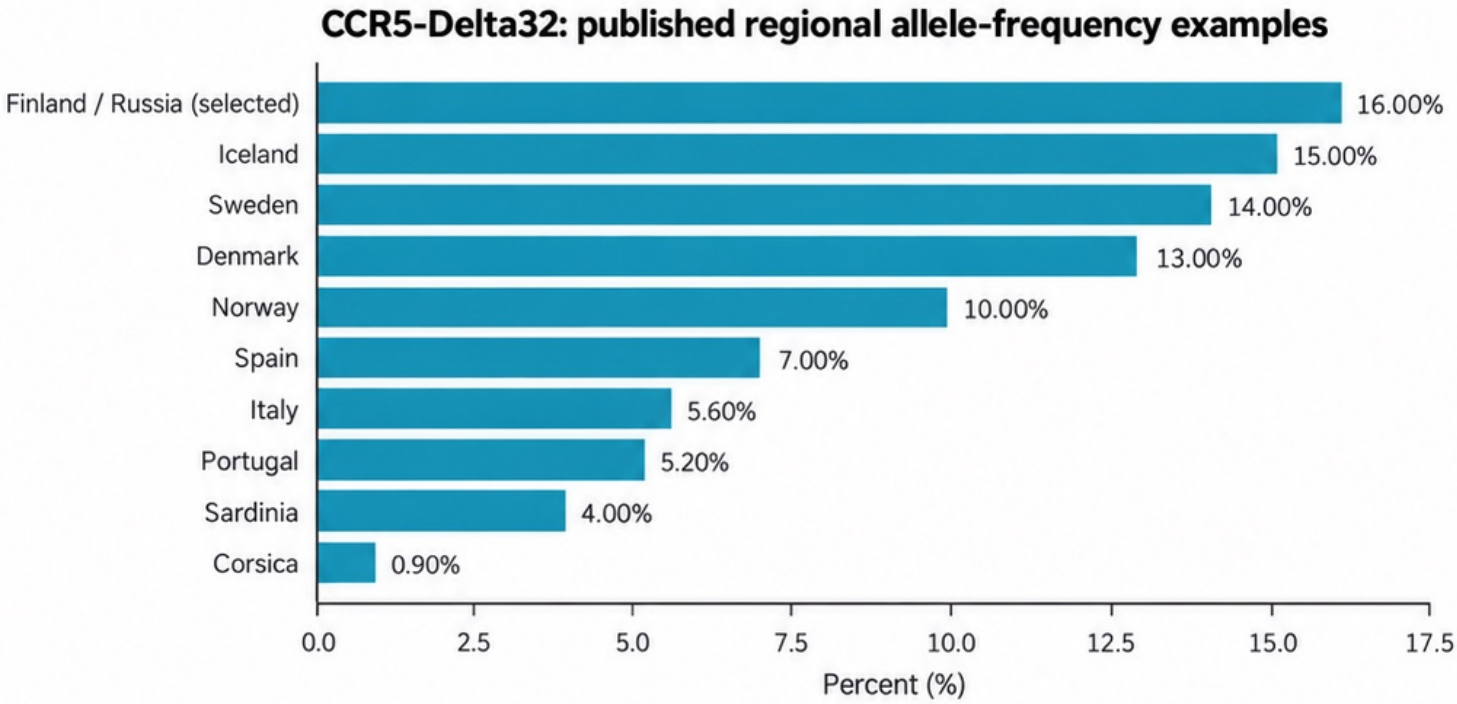
DNA extraction method: Standard silica-based column extraction (e.g., QIAamp DNA Blood Mini Kit, Qiagen).

Variant inventory and interpretation

Marker	Molecular locus	What would be required to confirm
O positive	ABO / RHD	Blood typing, not a sequence-based ancestry test
CCR5-Delta32	CCR5, rs333; 32-bp deletion	Deletion-specific assay; one versus two copies
Fragile X carrier	FMR1 CGG-repeat expansion	Repeat count, AGG interruptions, methylation
Sickle cell trait	HBB, HbS (rs334)	Hemoglobin electrophoresis / HPLC and/or DNA

CCR5-Delta32: where is it most common?

CCR5-Delta32 is a deletion variant in the CCR5 chemokine-receptor gene. Its allele frequency generally increases toward northern Europe, with notable geographic peaks in northeastern Europe, Scandinavia, the Baltic region, and selected Russian populations. The chart uses published regional examples, not a single harmonized worldwide survey.

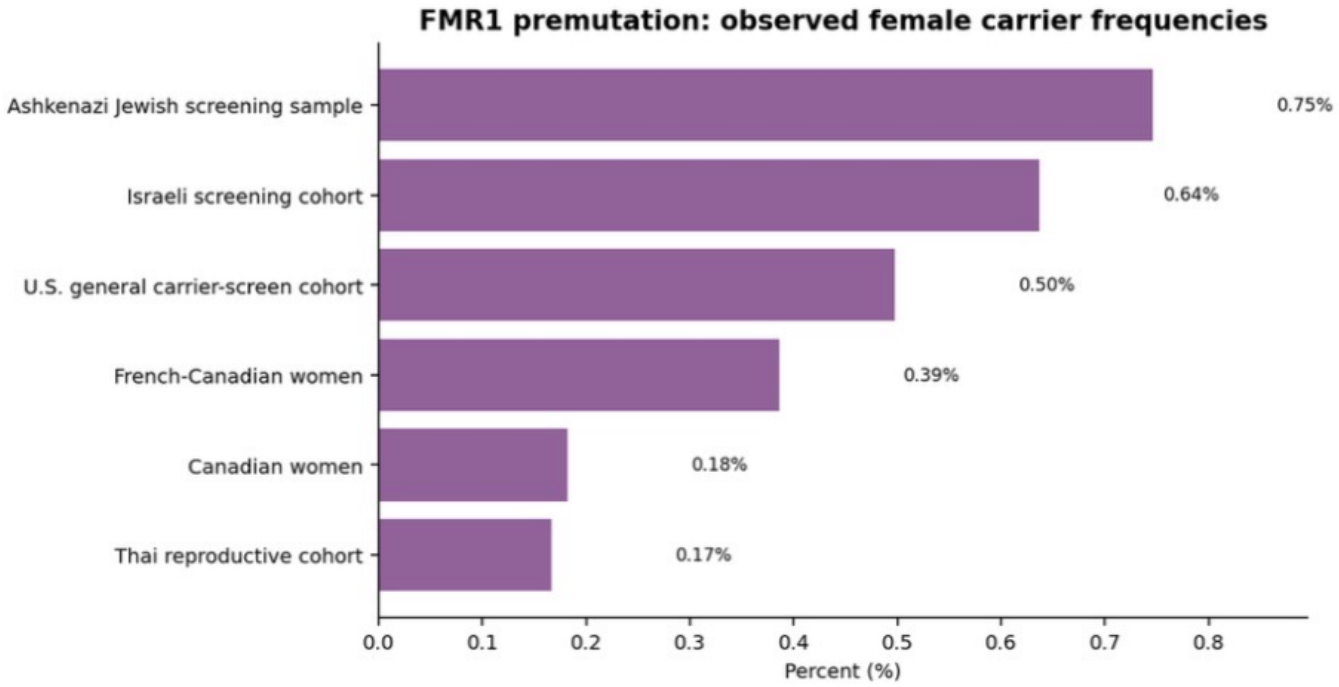


Critical distinction: An allele frequency of 16% does not mean 16% of people have two deleted copies. Under Hardy-Weinberg assumptions, 16% allele frequency predicts ~26.9% heterozygotes and ~2.6% homozygotes. For a 10% allele frequency, the corresponding estimates are ~18% and ~1%.

Northern Russia is not accurately described by a universal 1% carrier rate; the estimate varies by region, sample, and whether one means allele frequency, heterozygote, or homozygote frequency.

FMR1 PREMUTATION: COMPARATIVE POPULATIONS

FMR1 is on the X chromosome. Fragile X syndrome is usually associated with a **full mutation** (>200 CGG repeats), while a **premutation** typically spans 55-200 repeats. These are distinct from intermediate alleles (45-54 repeats). The chart compares reported **female premutation carrier** frequencies, not fragile X syndrome diagnoses.



Reading the ranking: The Ashkenazi Jewish sample (1 in 134), Israeli screening cohort (1 in 157), diverse U.S. screening cohort (1 in 201), French-Canadian cohort (1 in 259), Canadian cohort (1 in 549), and Thai cohort (1 in 600) were studied in different settings. This is a comparison of study results, **not** a definitive global ranking of ethnicities. Differences in sampling and screening criteria matter.

Origin, selection, and ancestry: what can actually be inferred?

CCR5-Delta32: Its geographic pattern supports a European evolutionary history, but its exact place and time of origin are disputed. Scandinavian/Viking dispersal is one historical hypothesis, not an established point of origin. The variant also occurs in some Ashkenazi Jewish populations; it is not a Jewish-specific ancestry marker.

FMR1: CGG repeat expansions can arise in many ancestral backgrounds. A carrier finding alone cannot determine Sephardic, Ashkenazi, or other Jewish ancestry, and it cannot assign an ancestry percentage.

HBB sickle cell trait: HbS occurs in multiple regions historically affected by malaria, including sub-Saharan Africa, parts of the Mediterranean, the Middle East, and India. Selection against severe malaria helped maintain HbS in those populations. HbS does not establish a single geographic ancestor.

O-positive: Blood group frequencies vary widely among populations. O-positive is common, not intrinsically a rare blood type; blood type is not a reliable ancestry-percentage assay.

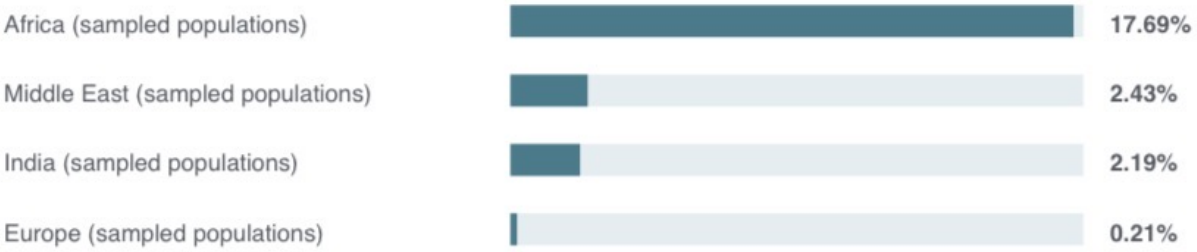
Combined rarity

A defensible combined frequency cannot be calculated from these four labels alone. It requires validated individual genotypes, comparable population reference data, ancestry context, and an explicit statistical model; multiplying unrelated published percentages would produce a misleading number.

GLOBAL DISTRIBUTION AND COMBINED GENOTYPE RARITY

HBB sickle-cell trait | Geographic distribution

Worldwide sickle-cell trait (HbAS) is most prevalent in regions with historical malaria exposure. A 2023 systematic review reported regional pooled estimates of 17.69% for studied African populations, 2.43% for Middle Eastern cohorts, 2.19% for Indian cohorts, and 0.21% for European cohorts. These are study-derived regional estimates, not fixed national or ethnic frequencies.



Where the four findings may overlap

The requested combination is O-positive (ABO/RhD), CCR5-Delta32, an FMR1 premutation and HbAS sickle-cell trait. These markers have different inheritance patterns. The CCR5-Delta32 allele is relatively enriched in northern and northeastern Europe; HbAS is enriched in malaria-endemic ancestry groups; FMR1 premutations occur in multiple populations; O-positive is widespread.

Geographic overlap is plausible in people with mixed ancestry connecting northern or northeastern Europe (for example Sweden, Finland, Estonia, Lithuania or parts of Russia) and regions with historic HbS prevalence (for example West/Central Africa, the Mediterranean, the Middle East or India). Migration and intermarriage make this possible worldwide. No published population has been established as the most common source of the exact four-marker combination.

Combined worldwide frequency

Not established. No defensible worldwide percentage or country-specific ranking can be assigned from separate population studies. A numerical estimate would require jointly sampled individual genotypes, a specified FMR1 repeat range, CCR5 copy count, and population-specific ancestry weighting. Multiplying four unrelated prevalence figures would falsely imply precision.

Selected references

Colombatti et al., Journal of Clinical Medicine (2023), global SCT systematic review.

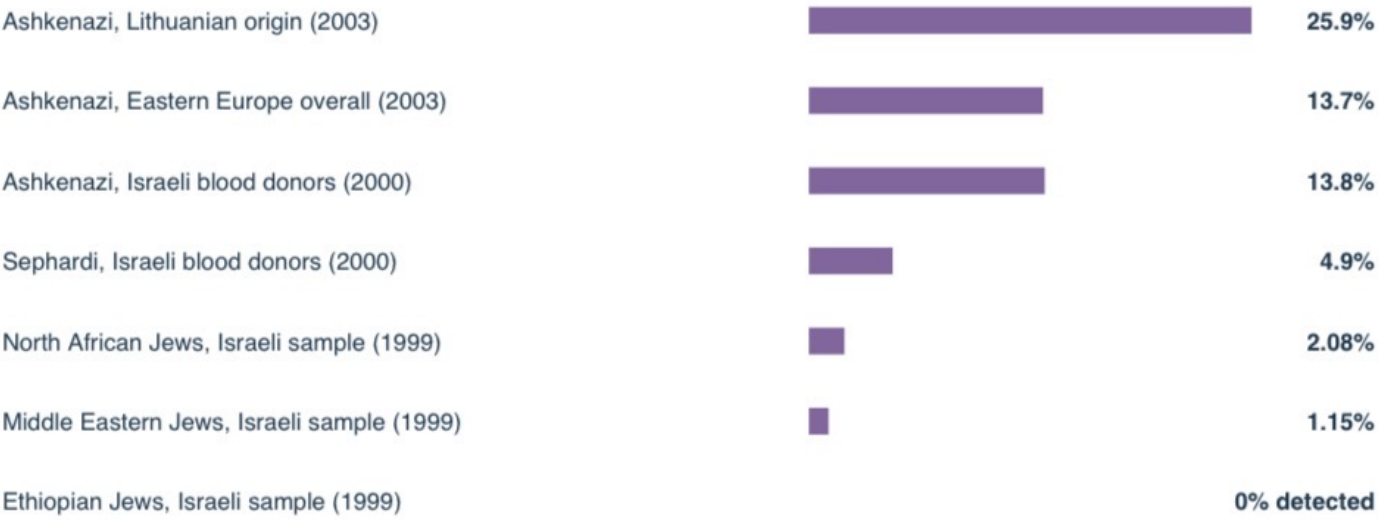
Novembre et al., PLOS Biology (2005), CCR5-Delta32 geographic spread.

Lucotte & Mercier, JAIDS (1998), CCR5-Delta32 frequencies in Europe.

CCR5-DELTA32 IN JEWISH POPULATIONS

Published allele-frequency observations | Jewish diaspora and Kohanim context

Selected population studies (allele frequency, not carrier prevalence)



Comparisons combine different samples, years and ascertainment methods. The Lithuanian-origin subgroup estimate is not a national prevalence estimate. A zero means none detected in that particular sample.

Kohanim (Cohen) lineage: a separate genetic question

Kohanim are families with a tradition of hereditary Jewish priestly descent. Research on the Cohen Modal Haplotype examines Y-chromosome paternal markers, not CCR5-Delta32.

CCR5 is an autosomal gene on chromosome 3. The Delta32 deletion is found in some Jewish and non-Jewish populations. It cannot identify Cohen descent or establish a Jewish ancestry percentage.

No reliable Kohanim-specific CCR5-Delta32 allele frequency was established by the cited studies. A person with a Cohen surname cannot be assigned a CCR5 genotype from that surname.

Primary research references

Lucotte & Smets (2003), Genetic Testing 7:333-337. PMID: 15000812.

Maayan et al. (2000), Genes & Immunity 1:358-361. PMID: 11196681.

Kantor & Gershoni (1999), JAIDS 20:81-84. PMID: 9928734.

Klitz et al. (2001), Human Immunology 62:530-538. PMID: 11334678.

REFERENCE NOTES & INTERPRETATION

Selected scientific references (frequencies in figures correspond to the populations and cohorts discussed in these publications):

CCR5 distribution review
https://pmc.ncbi.nlm.nih.gov/articles/PMC8829453/

CCR5 geographic spread, PLOS Biology
https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.0030339

ACMG FMR1 laboratory standard
https://www.nature.com/articles/s41436-021-01115-y

FMR1 population screening
https://pubmed.ncbi.nlm.nih.gov/21116185/

FMR1 diverse carrier cohort
https://pubmed.ncbi.nlm.nih.gov/29603880/

FMR1 Thai cohort
https://pubmed.ncbi.nlm.nih.gov/39320553/

Scientific summary

The most striking scientifically supported pattern is the strong north-to-south European gradient in CCR5-Delta32, contrasted with the broad, study-dependent distribution of FMR1 premutations. Neither variant can establish an individual's exact ancestral percentages without appropriate genome-wide ancestry analysis.