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Blood groups of Neandertals and Denisova decrypted

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Blood groups of Neandertals and Denisova decrypted

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Background

- Red cell blood group systems are relevant to transfusion medicine and anthropology
- Sporadic knowledge of their gene variation in archaic populations

Aims

- To explore the archaic gene variation of the key blood groups
- To shed light on the late evolutionary history of Neandertal and Denisova

Selection of the 4 probands

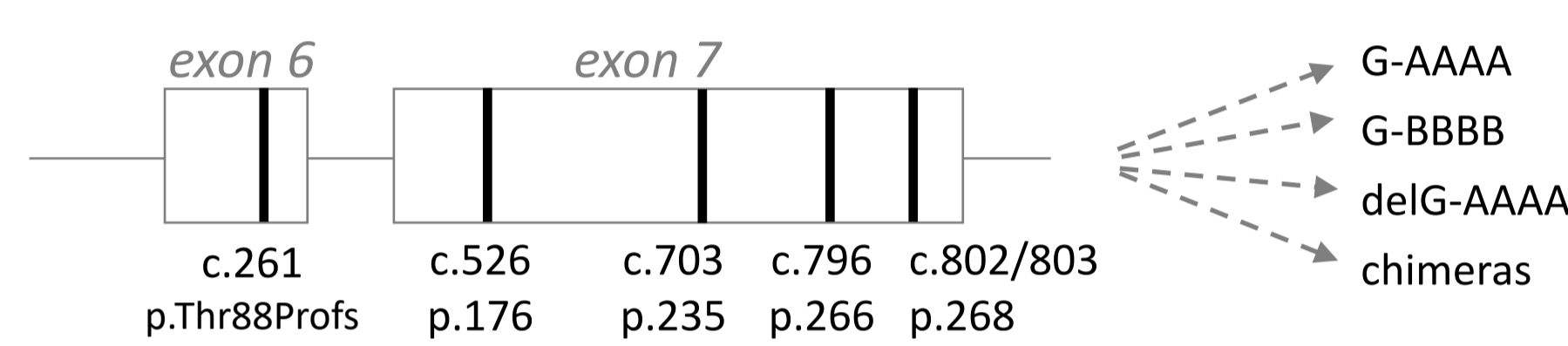
- High coverage
- Low contamination
- Unadmixed
- Few uncalled snps

Altai Neandertal
Vindija 33.19
Chagyrskaya 8
Denisova 3

Caution items

- HG19: 5' strand and alignment with blood group *Locus Genomic References*

- ABO genotype calls : 5 key snps → enzyme activity



- *RHD* and *RHCE* haplotypes : The Human RhesusBase,



- Key indels: *ABO* c.261delG, c.1061delC, and *RHCE* 209bp

- Low-mapped variants : IGV → Mapping Quality threshold

Allele exploration procedure

- Tabix
- Vcftools
- IGV Integrative Genomics Viewer

Key snps & exons browsing:
*bam & *vcf files



- GT:DP:GQ:A:C:G:T:PL & PP
- Mapping quality 25
- Amino-acid changes

- ISBT International Society of Blood Transfusion
- ClinVar Genomic variation as it relates to human health
- ERYTHROGENE

Alleles and inferred phenotypes

Key blood group systems and their genes

ABO, H, Se (secretor)	<i>ABO, FUT1, FUT2</i>
Rh	<i>RHD, RHCE</i>
Kell, Kx	<i>Kell, XK</i>
Duffy	<i>DARC</i>
Kidd	<i>SLC14A1</i>
MNS	<i>GYPB</i>
Diego	<i>SLC4A1</i>

Probable phenotypes from functional genotypes

Altai Neandertal (130-90 ky)

ABO > A¹ (G-BAAA / G-BAAA), **SeSe**
partial RhD > *RHD*DIII type4 (602G, 733C) / RHD*DIII type4 (602G, 733C)*
partial Rhce > *RHCE*ceEK / RHCE*ce(48C, 410T, 712G)*
K- k+, **Js(a+, b-)** > *KEL*02/*02, KEL*06/*06*
Fy(a-, b+) > *FY*02/*02*
Jk(a+, b-) > *JK*01/*01*
S-, s+ > *GYPB*04/*04*
Di(a-, b+) > *DI*01/*01*

Vindija 33.19 (65-50 ky)

ABO > B (delG-AAAA / G-BABB), **SeSe** (*rs1800028, c.571T, p.191stop*)
partial RhD > *RHD*DIII type4 (602G, 733C) / RHD*DIII type4 (602G, 733C)*
partial Rhce > *RHCE*ceEK / RHCE*ce(48C, 744C, 787G)*
K- k+, **Js(a+, b-)** > *KEL*02/*02, KEL*06/*06*
Fy(a-, b+) > *FY*02/*02*
Jk(a+, b-) > *JK*01/*01*
S-, s+ > *GYPB*04/*04*
Di(a-, b+) > *DI*01/*01*

Chagyrskaya 8 (51-45 ky)

ABO : A¹ (delG-AAA / G-BAAA), **se** (*rs1800028, c.571T, p.191stop*)
partial RhD > *RHD*DIII type4 (602G, 733C) / RHD*DIII type4 (602G, 733C)*
partial Rhce > *RHCE*ceEK / RHCE*ce(48C, 410T, 800A)*
K- k+, **Js(a+, b-)** > *KEL*02/*02, KEL*06/*06*
Fy(a-, b+) > *FY*02/*02*
Jk(a+, b-) > *JK*01/*01*
S-, s+ > *GYPB*04/*04*

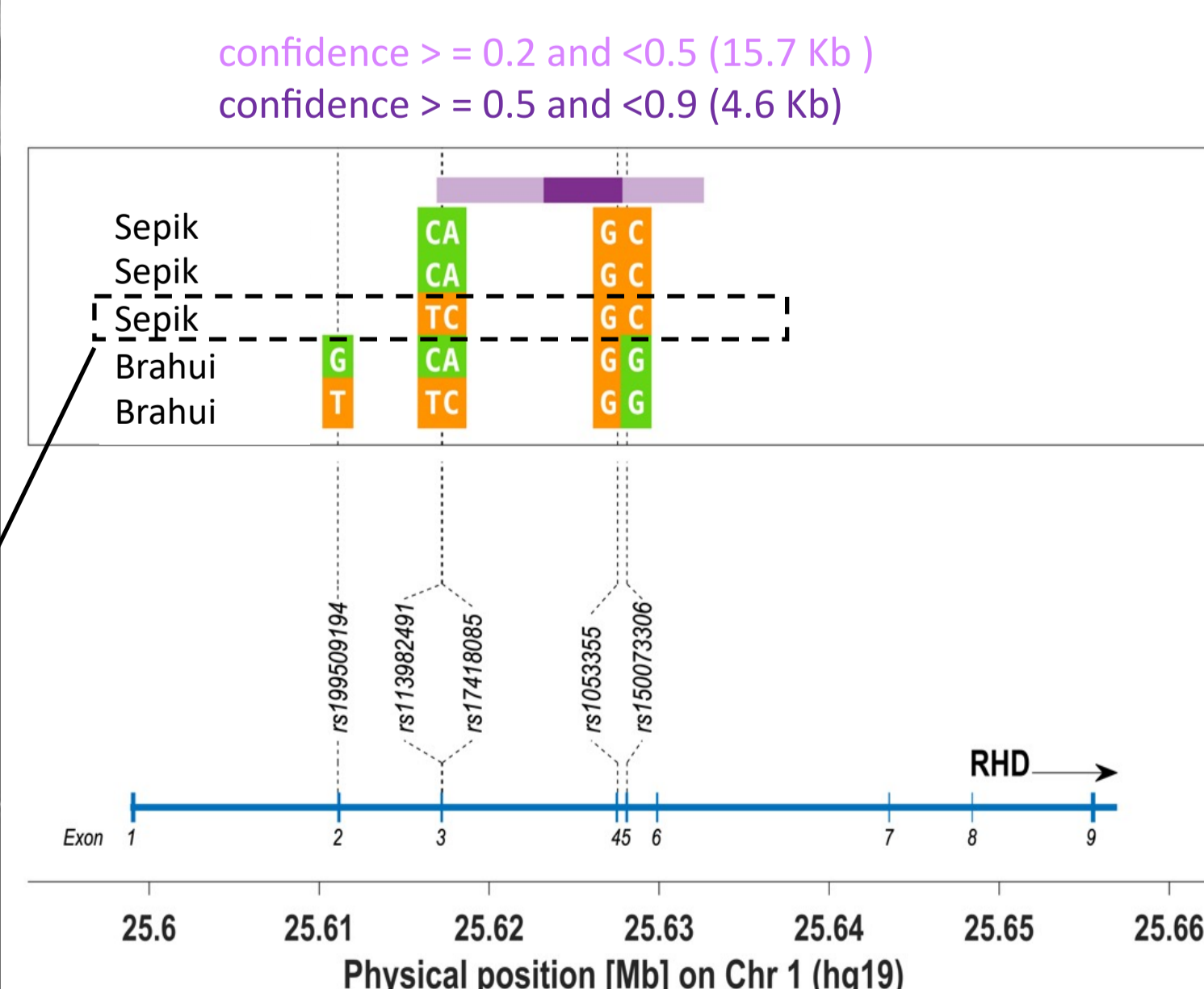
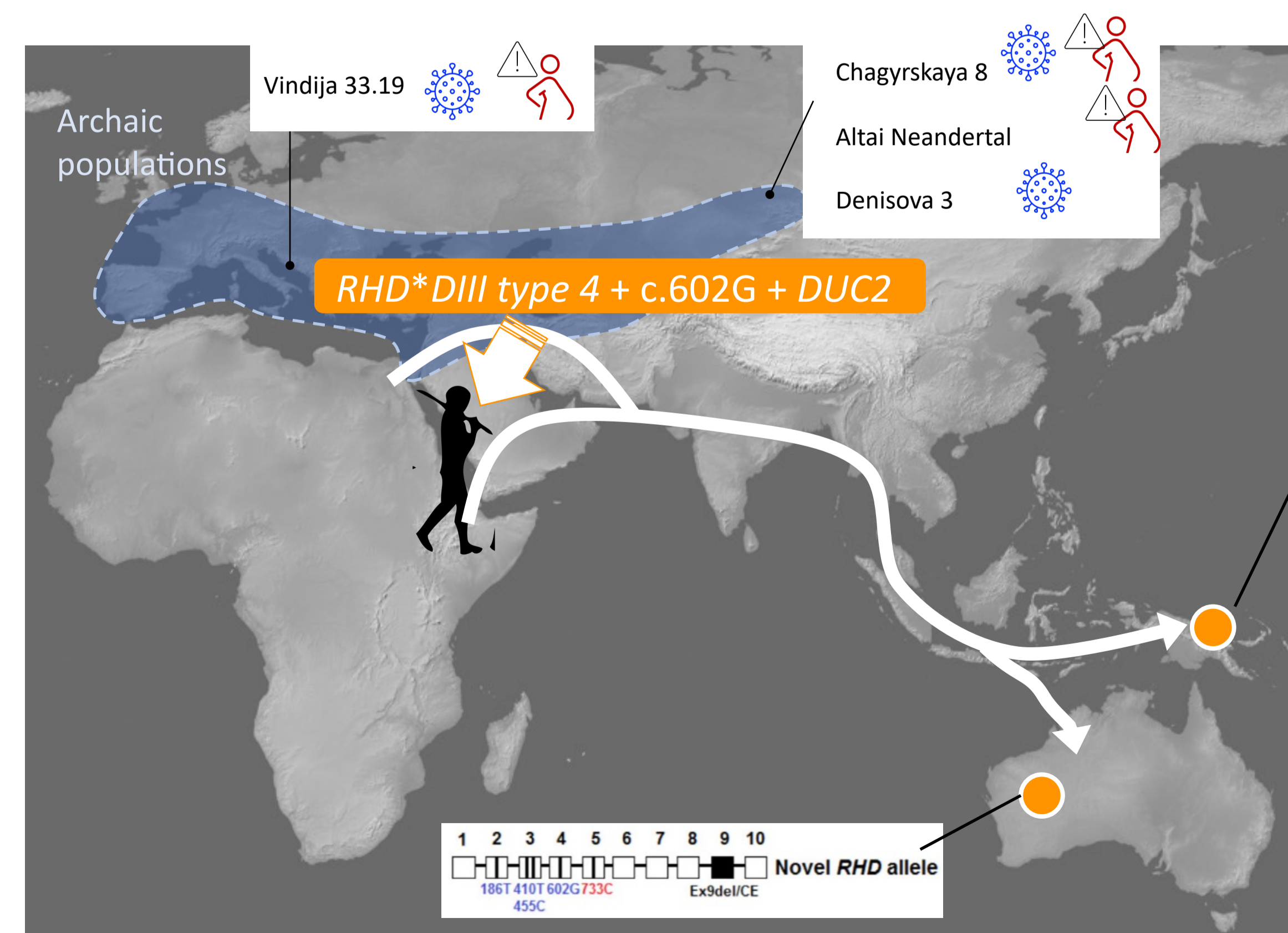
Denisova 3 (76-52 ky)

ABO > O¹ (delG-AAAA / delG-AAAA), **Se/se** (*c.714A, p.237stop, undescribed*)
RhD > *RHD*D / RH*D(19G, 186T, 410T, 929G)*
Rhce > *RHCE*ce(48C) / RhCE*ce(48C)*
K- k+, **Js(a-, b+)** > *KEL*02/*02, KEL*07/*07*
Fy(a-, b+) > *FY*02/*02*
Jk(a+, b-) > *JK*01/*01*
S-, s+ > *GYPB*04/*04*
Di(a-, b+) > *DI*01/*01*

Highlights

- Presence of the 3 ABO phenotypes
- Non-secretor alleles
- *DIII type 4, *ceEK* → sub-Saharan background, → partial D, partial ce (RH:-18)
- Neandertal-specific *RHD* haplotype
- Denisova : unknown *RHD* (c.929A>G, Pro310Arg)
- Homozygous at 6 loci: K-k+, Fy(a-b+), Jk(a+b-), S-s+, Di(a-b+)
- Ancestral alleles: *DARC* (rs12075 "Fy^b", c.125A, p.42Asp), *SLC4A1* (rs5036 "Memphis", c.166G, p.56Glu), *Kel* (rs8176038 "Js^b", c.1790T>C, p. 597Pro)

Evolutionary outcomes



- 1. Consolidation of an African origin**
Ancestral forms for RH, Kell, Duffy, Kidd, MNS and Diego
African clusters of *RHD*, *RHCE* variants
Absence of the antigen combination RhC, RhE, K, Fya, Jkb and S
- 2. Admixture before expansion towards Oceania**
*RHD*DIII type4* with c.602G and *DUC2* : only 2 cases in Australia & Papua New Guinea
- 3. Genetic signature of environmental pressure**
Polymorphism at the ABO level → balanced selection
Non-secretor *FUT2* snps → exposition to « Norovirus-like »
- 4. Neandertal demography at risk**
High level of homozygosity
Partial RhD, Rhc and Rhe antigens → risk of hemolytic disease of the foetus and the new born

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