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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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Scan me for data and more!

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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

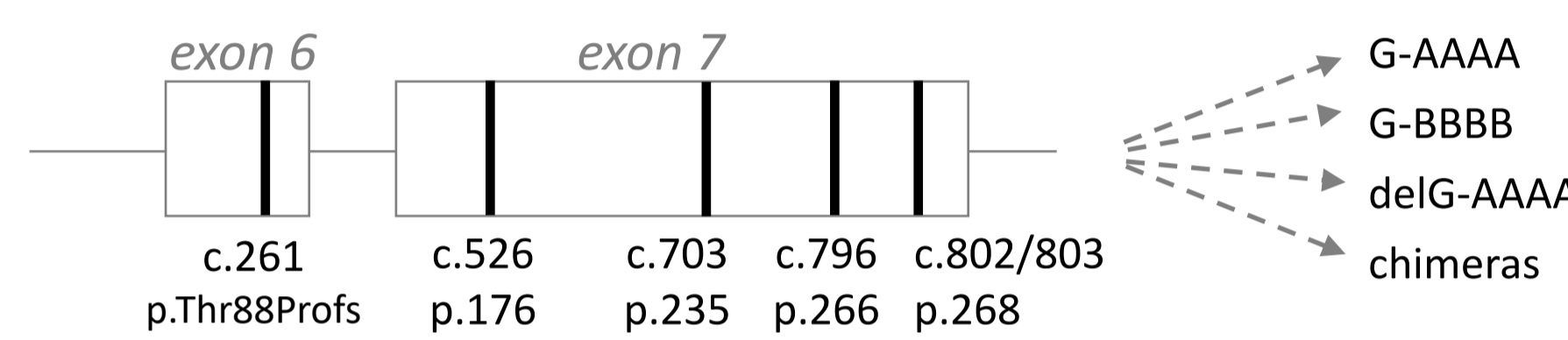
- High coverage
- Low contamination
- Unadmixed
- Few uncalled snps

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
- Integrative Genomics Viewer

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

Department of Evolutionary Genetics

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

- 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** > A<sup>1</sup> (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** : A<sup>1</sup> (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*

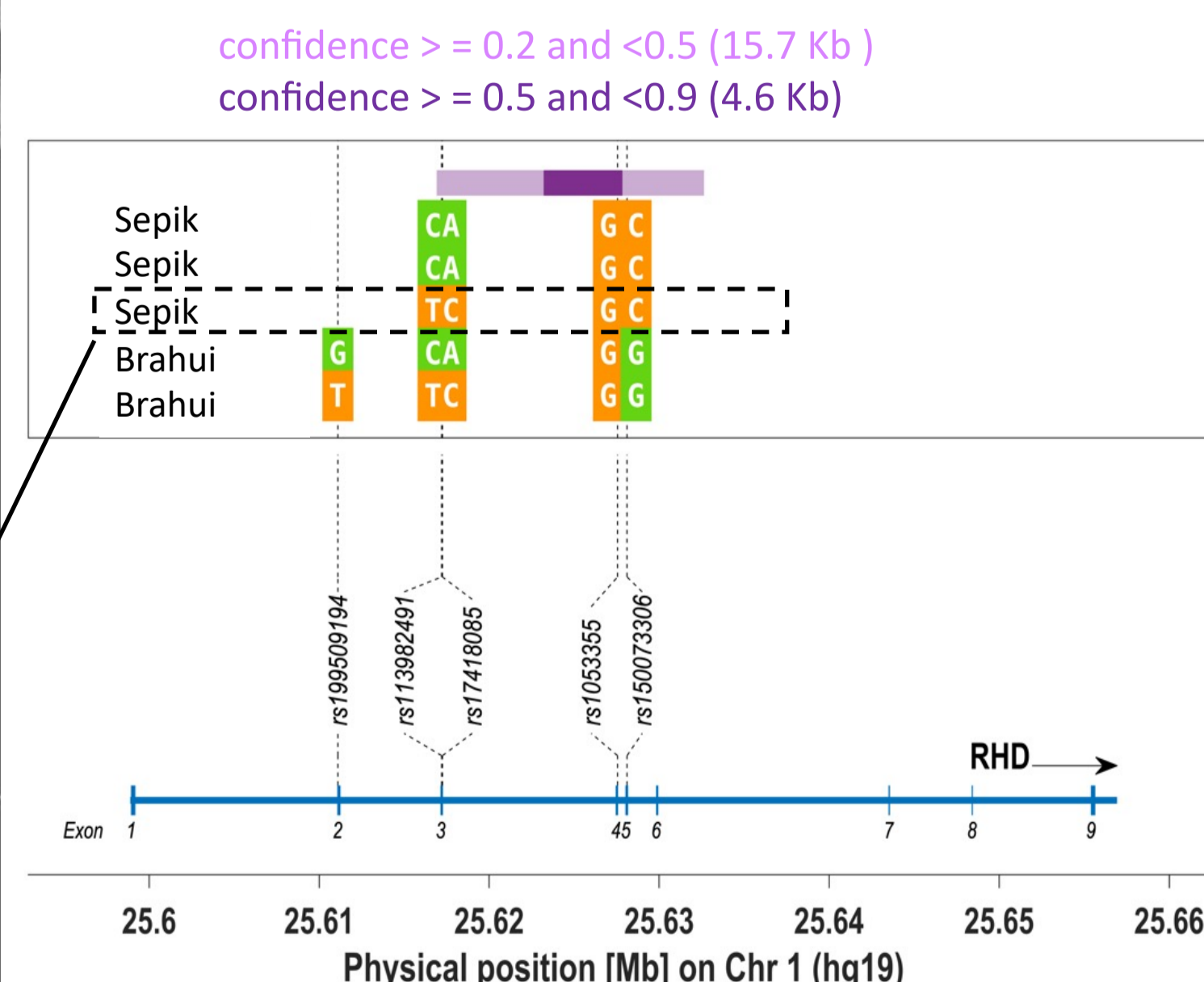
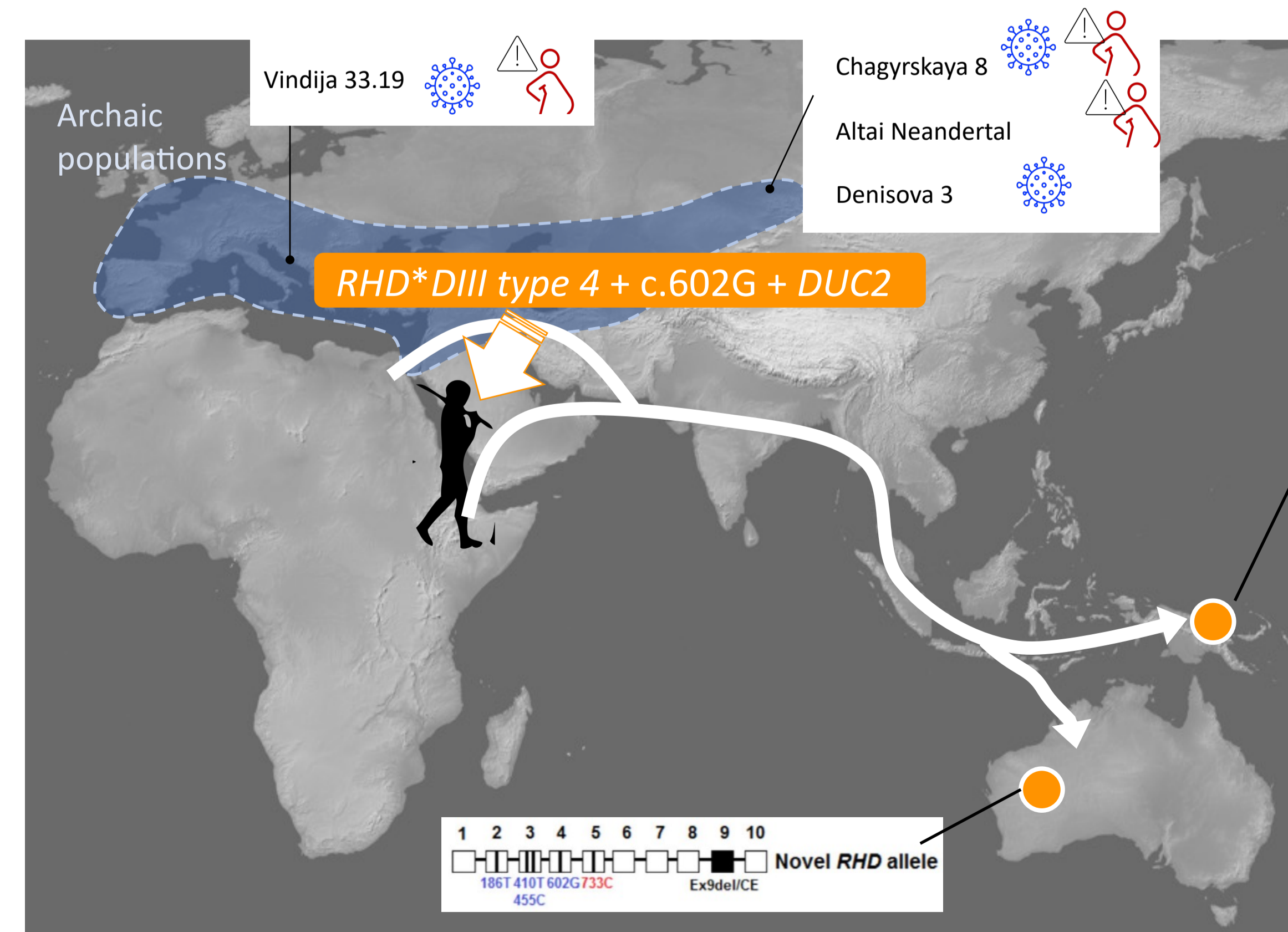
### Denisova 3 (76-52 ky)

**ABO** > O<sup>1</sup> (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<sup>b</sup>", c.125A, p.42Asp), *SLC4A1* (rs5036 "Memphis", c.166G, p.56Glu), *Kel* (rs8176038 "Js<sup>b</sup>", 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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