DISCOVERY AND PHASING OF A NOVEL NULL ALLELE IN A *FY*A/FY*B* INDIVIDUAL WITH NANOPORE SEQUENCING

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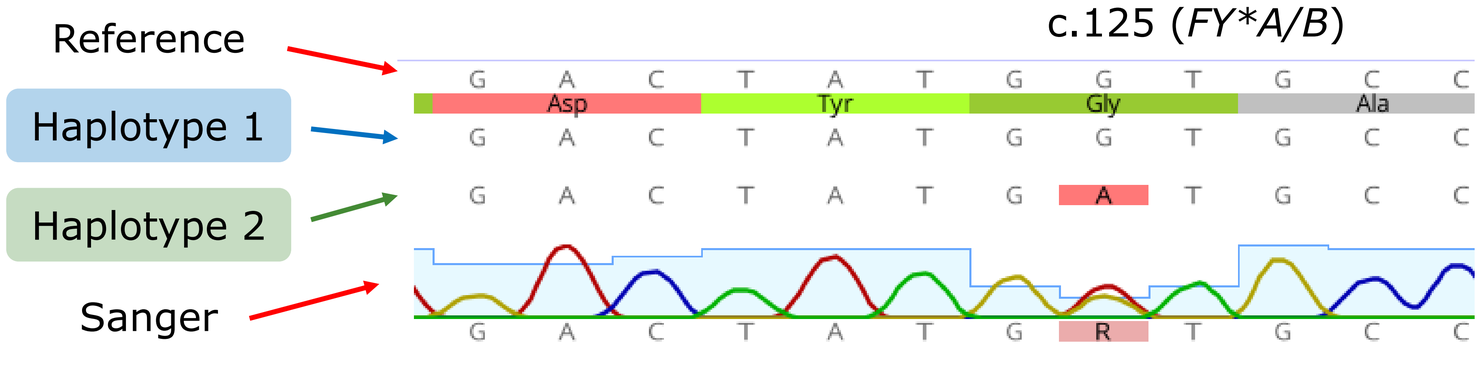
Sequencing new blood group **alleles** as **complete** gene **haplotypes** could become the **emerging standard**

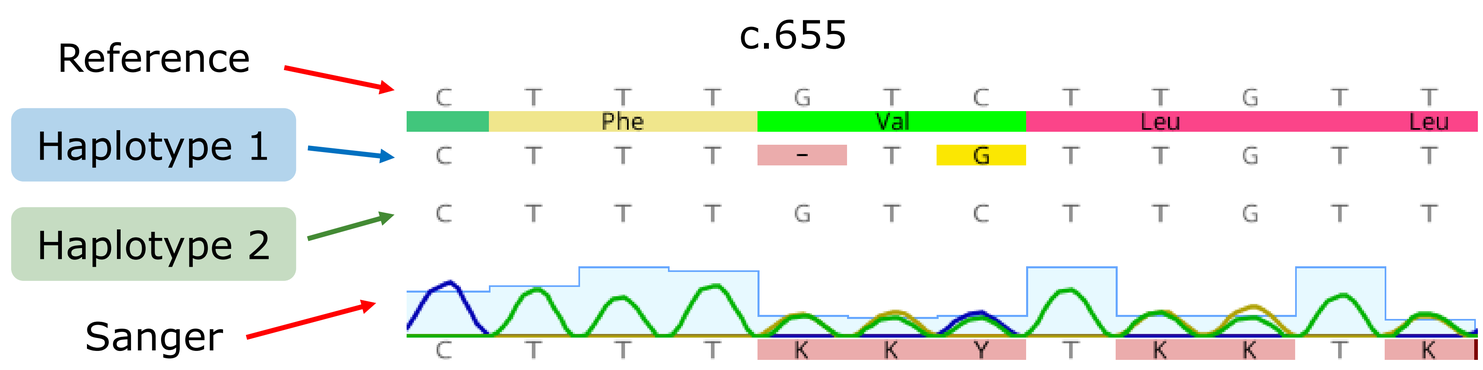
Background

The Duffy (Fy) blood group is encoded by *ACKR1*. The *FY*A/FY*B* alleles are defined by the SNV c.125G>A. We resolved a rare discrepant case between serology and genotyping using long-read Nanopore sequencing.

Methods

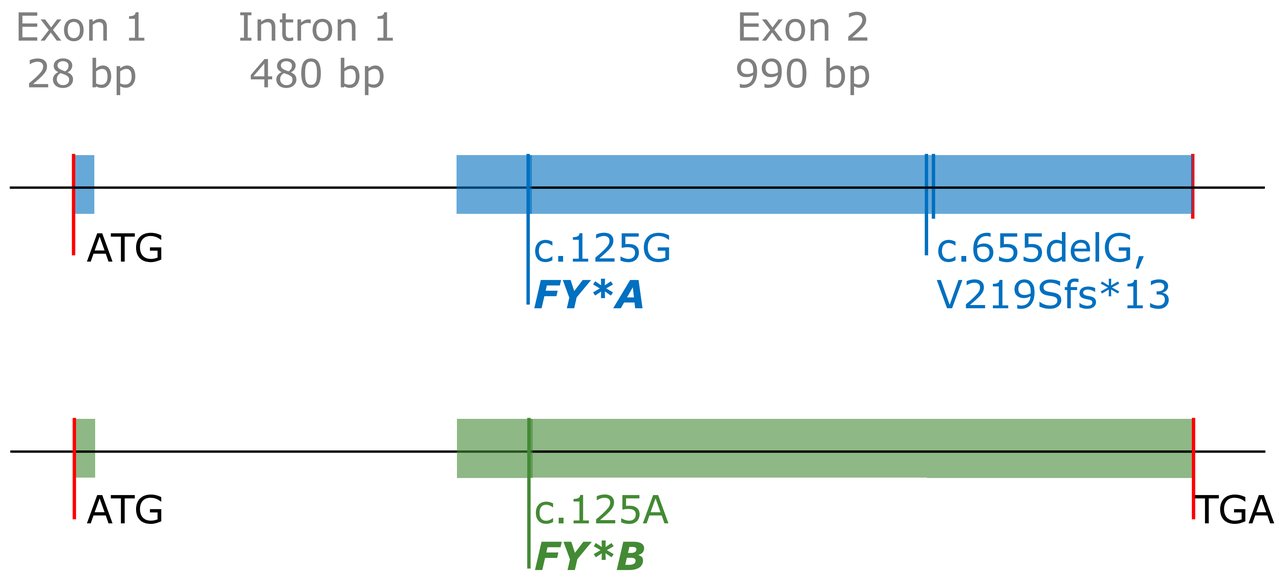
- > 40’000 donors genotyped with MALDI-TOF MS for 3 SNVs on *ACKR1*
- Fy phenotyping for ~ 13’200 donors
  → 1 discrepancy investigated:
- Nanopore sequencing
- Confirmation with Sanger sequencing





Results

- Heterozygous *FY*A/FY*B* individual expressing Fy(a-b+) phenotype
- Nanopore sequencing revealed a 1bp deletion located on the *FY*A* allelic background (c.655delG, V219Sfs*13)
- This frameshift mutation is yet undescribed



Direct phasing of novel variant to *FY*A* allelic background by Nanopore sequencing

Conclusion

In this proof-of-principle study, we showed that Nanopore sequencing, which, unlike Sanger sequencing, allows haplotype generation along the whole gene, proved well-suited to resolve a discrepancy between Duffy blood group genotype and phenotype.

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Abstract