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A Rare KEL Compound Null Heterozygote Defines A K_0 Phenotype In A Patient With Anti-Ku and Discovery Of A New Silenced KEL*02 In A k– Donor

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INTRODUCTION

- The Kell null phenotype (K_0) is rare, with most individuals identified after they have made anti-Ku.
- To date, more than 57 alleles are known to encode for a K_0 phenotype with the majority (n=54) on a *KEL*02* background.
- We investigated *KEL* in a:
  - African American (AA) patient whose plasma contained anti-Ku
  - Caucasian donor with a k phenotype/genotype discordance.

MATERIALS AND METHODS

Serological Testing

- RBC and plasma testing was performed by standard tube methods.
- Kell system antigen typing was performed using licensed commercial reagents or unlicensed single donor source antibodies.

DNA Testing

- Genomic DNA was isolated from WBCs.
- HEA PreciseType BeadChip (Immucor) was performed.
- *KEL* exons 1 to 19, including flanking intron regions were Sanger sequenced.

CASE STUDIES

Table 1: Referral of the two samples for Kell investigation

Sample	Serology Results	HEA PreciseType
Patient Sample was from a 46-year-old AA female patient.	K–, k–Kp(b–), Js(b-), Ku–	*KEL*k/k, KEL*Kp^b/Kp^b, KEL*Js^a/Js^b*
Donor Sample was from a Caucasian female donor.	K+, k–	*KEL*K/k, KEL*Kp^b/Kp^b, KEL*Js^b/Js^b*

RESULTS

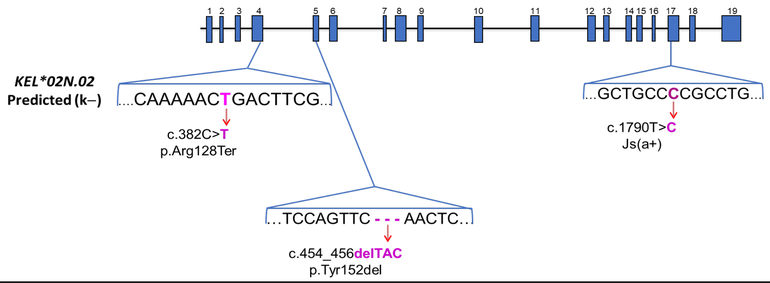
PATIENT SAMPLE

Serology

- Patient's plasma reacted by IAT with all RBCs except her own, DTT treated RBCs, and K_0 RBCs.
- RBCs were group A+ with a negative DAT and typed K–, k–, Kp(b–), Js(b–) and Ku–.
- Results are consistent with a K_0 phenotype with anti-Ku in the plasma.

DNA Testing

- By HEA, the RBCs were predicted K–k+, Kp(a–b+), Js(a+b+).
- *KEL* gene sequencing found:
  - heterozygosity for changes on *KEL*02*:
    - c.382C>T change in exon 4 encoding premature stop codon (p.Arg128Ter) designated by ISBT as *KEL*02N.02* and c.1790T>C (p.Leu597Pro) in exon 17.
    - a novel deletion of three nucleotides, c.454_456delTAC in exon 5 that results in the loss of one codon (p.Tyr152del).
  - No other changes were found.



RESULTS

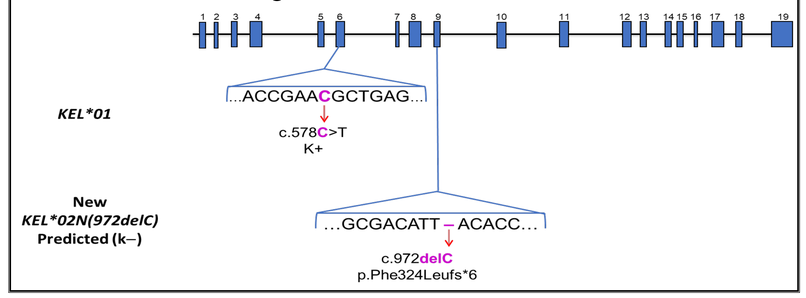
DONOR SAMPLE

Serology

- RBCs typed K+k– using commercial reagents.
- The sample was insufficient for adsorption and elution studies.

DNA testing

- By HEA the RBCs were predicted:
  - K+k+, Kp(a–b+), Js(a–b+)
- *KEL* sequencing found:
  - Confirmed KEL*01/02
  - Identified heterozygosity for a novel deletion of 1 nucleotide, c.972delC, in exon 9, predicted to cause a frameshift and premature stop codon (p.Phe342Leufs*6), presumed on a *KEL*02* background.
  - No other changes were found.



CONCLUSIONS

- We report two new *KEL*02* null alleles:
  - A novel c.454_456delTAC (p.Tyr152del) *in-trans* to *KEL*02N.02* in a patient who made anti-Ku
  - A c.972delC (p.Phe342Leufs*6) *in-trans* to *KEL*01* in a k– donor.
- The c.454_456delTAC is found in Africans with a frequency of 0.0002297 (gnomAD v2.1, rs1241298894).
- The p.Phe342Leufs*6 is not currently found on dbSNP or gnomAD databases.
- Autologous donation or avoidance of transfusion is recommended for persons with a Kell null phenotype because K_0 donors are exceedingly rare.
- These cases highlight the value of serological testing for identifying rare null phenotypes that otherwise may be missed by SNP-based DNA testing and the need for gene sequencing for the characterization of such phenotypes.