A NOVEL HIGH FREQUENCY ANTIGEN IN THE LUTHERAN BLOOD GROUP SYSTEM (LUNU)

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Case study

• 31 year old female of Caucasian origin

• Presented with an unidentified alloantibody to a high frequency antigen

• Pregnant, gestational week 13

• B, R₁R₁, Ss, Lu(a-b+), Fy(a+b+), Jk(a+b+)

• DAT negative
Initial findings; Berlin

- Plasma positive with all panel cells tested, except several In(Lu) examples
- Plasma weakly reactive with red cells of a patient with auto-AnWj
- Antibody was successfully inhibited with soluble recombinant Lutheran protein

Suspected: antibody against a high frequency antigen of the Lutheran system
Serology; Bristol

• Confirmed the presence of a Lu-related antibody, reacting with all tested untreated and papain treated cells, except one example of In(Lu)

• Confirmed that antibody was successfully inhibited with soluble recombinant Lu protein

• Lu phenotype was Lu(a-b+), LU:3,5,6,8,13,20,21

Antibody recognising epitope on Lu-glycoprotein ⇒ new Lu antigen?
Lu-glycoprotein is encoded by a single gene BCAM (LU) described in 1996

LU locus on chromosome 19 q13.3, 2.5 kb in size, organised in 15 exons

Two isoforms due to alternative splicing of intron 13
Two isoforms due to alternative splicing
Sanger sequencing

• Sanger sequenced all 15 BCAM exons
• Confirmed LU*B and LU*18 (Au\textsuperscript{a})

BCAM exon 2:

c.121G>A
p.Val41Met

gnomAD frequency: 3.98x10\textsuperscript{-6}
Family study

Cells from father, mother and 2 siblings incompatible with patient’s plasma

- No c.1340C>T, Ser447Leu associated with LU:-13
• 25 antigens in the system
• All encoded by single nucleotide mutations (encoding single amino acid changes)

• 4 pairs are antithetical antigens: Lu\textsuperscript{a}/Lu\textsuperscript{b} (LU1/LU2), Lu6/Lu9, Lu8/Lu14, Au\textsuperscript{a}/Au\textsuperscript{b} (LU18/LU19)

• Remaining 17 antigens are of high frequency

Burton & Brady. *Blood Cells Molecules & Diseases* 2008; **40**: 446-448
Lutheran domain 1 model

Comparison of top 5-ranking clusters of wild-type (blue) and V41M mutation (red/amber)

Wild-type Val

Val41Met
Comparison of start clusters (left) end-of-calculation cluster representatives (right)

Blue = wild-type
Amber = Val41Met

N-terminal Val41Met β-strand becomes de-structured over the duration of calculation.
**Close-up on end-of-calculation comparison**

Met41 is exposed to exterior solvent whereas Val41 is stably embedded in protein interior.
The absence of this high frequency antigen arises from a rare mutation in $BCAM$ exon 2, encoding an amino acid change in Lu-glycoprotein: $c.121G>A$, p.Val41Met

Antigen was named LUNU (LU = Lutheran, NU = initials of the patient)

Anti-LUNU in patient’s plasma presumed to have been made as a result of previous pregnancy

**Summary**

New antigen of the Lutheran blood group system

LUNU = LU28