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

Institute of Transfusion Medicine
Charité-Universitätsmedizin
Berlin, Germany

- Presented with an unidentified alloantibody to a high frequency antigen

- Pregnant, gestational week 13

- B, R_1R_1, 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 $\Rightarrow$ new Lu antigen?
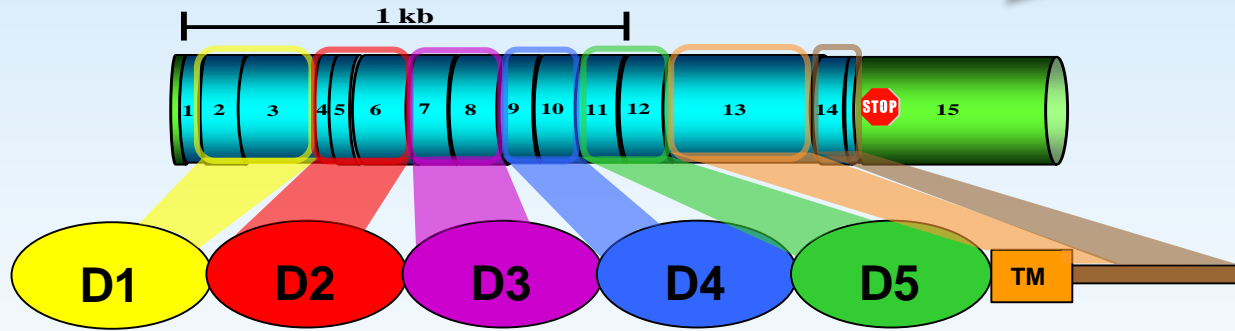
Sanger sequencing of *BCAM* gene (*LU*)

- 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

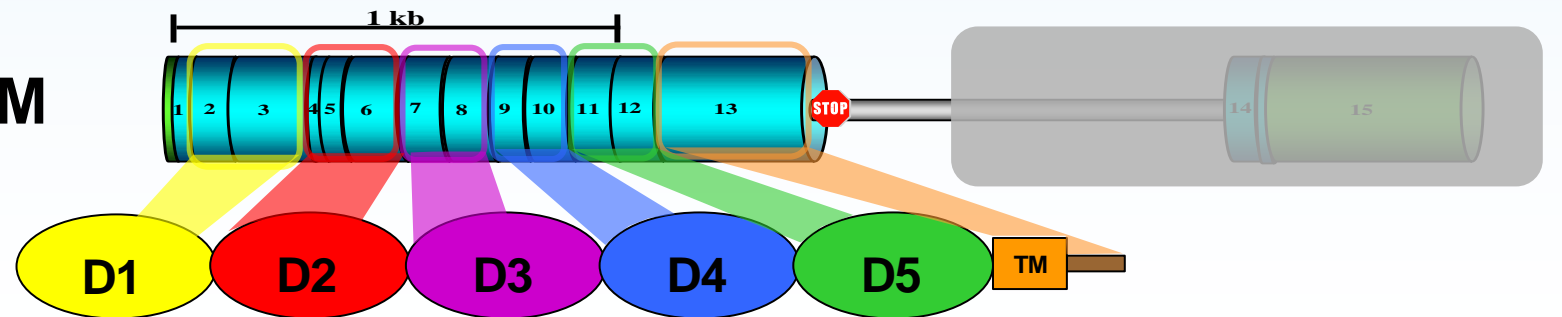- Two isoforms due to alternative splicing of intron 13
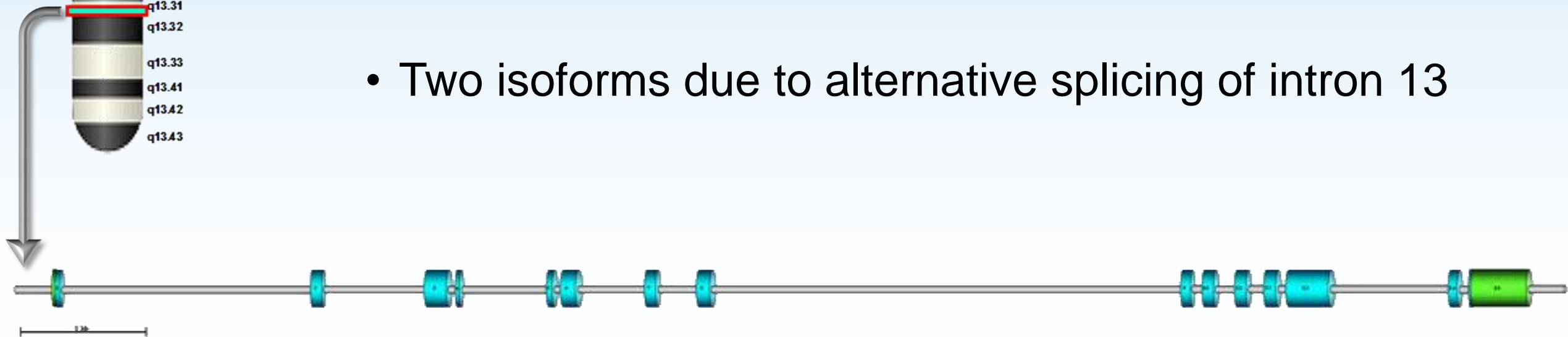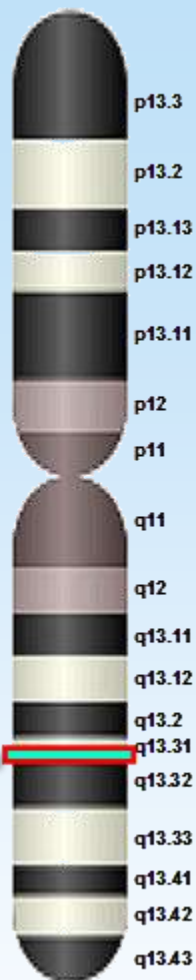
Two isoforms due to alternative splicing
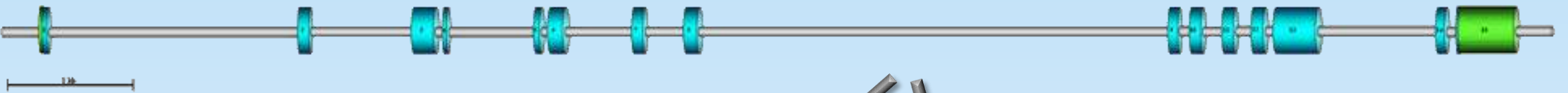
Sanger sequencing
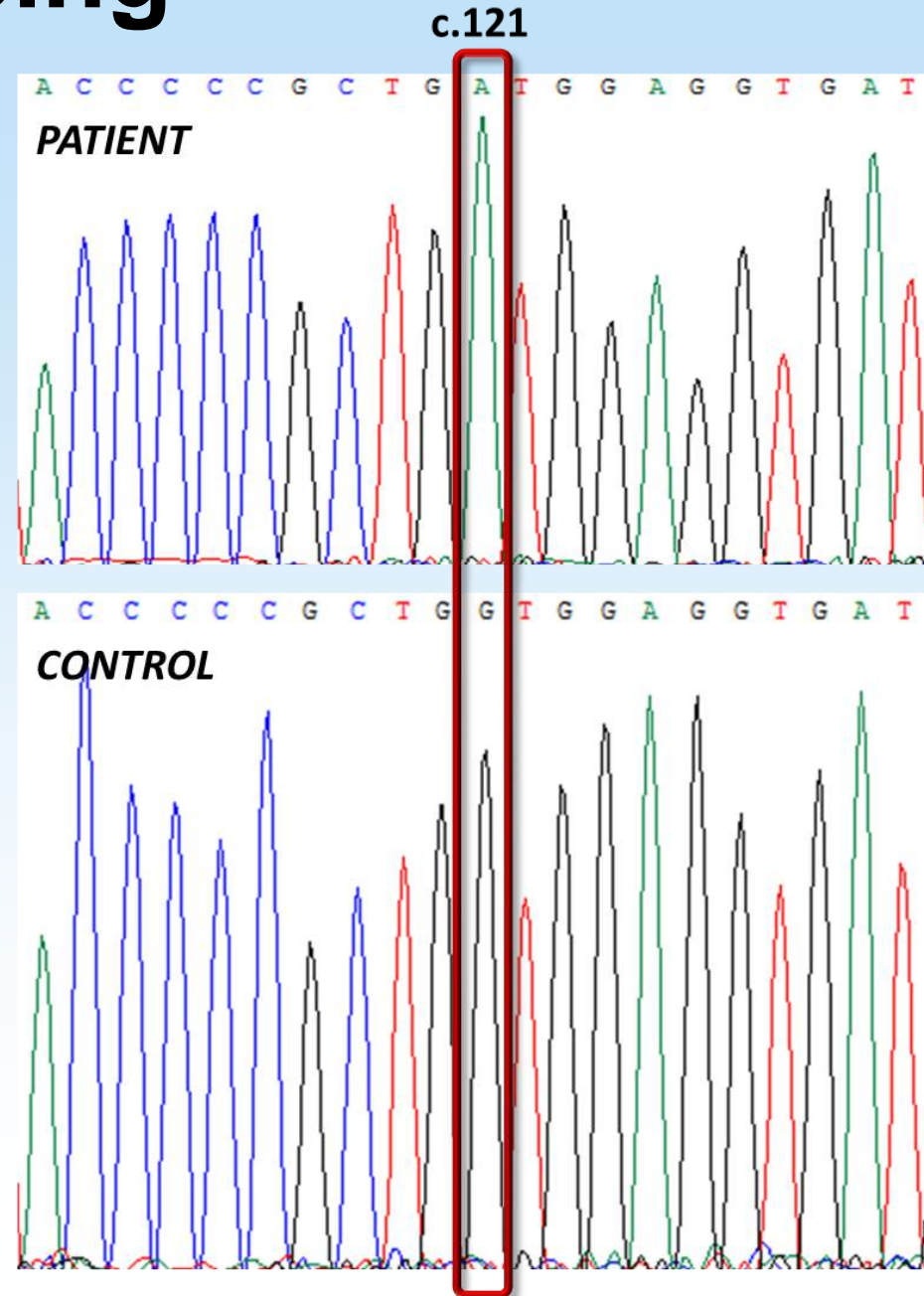

- Sanger sequenced all 15 *BCAM* exons

- Confirmed *LU*B* and *LU*18* (Au[a])

BCAM exon 2:

c.121G>A

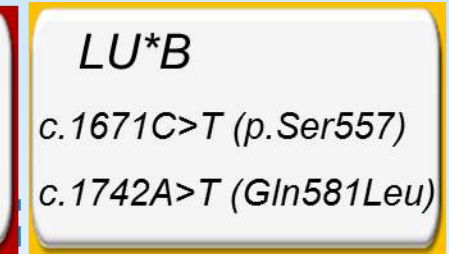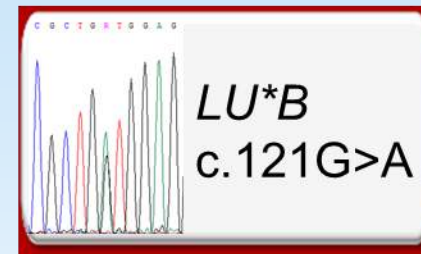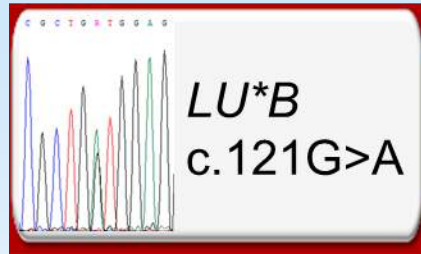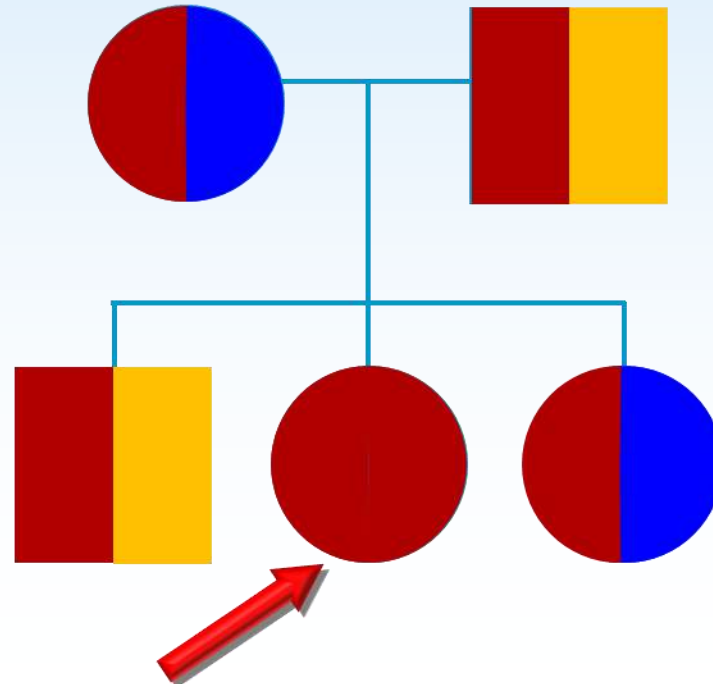**p.Val41Met**

gnomAD frequency: 3.98×10^{-6}

Family study

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

Lu-glycoprotein model

- 25 antigens in the system

- All encoded by single nucleotide mutations (encoding single amino acid changes)

- 4 pairs are antithetical antigens: Lu^a/Lu^b (LU1/LU2), Lu6/Lu9, Lu8/Lu14, Au^a/Au^b (LU18/LU19)

- Remaining 17 antigens are of high frequency

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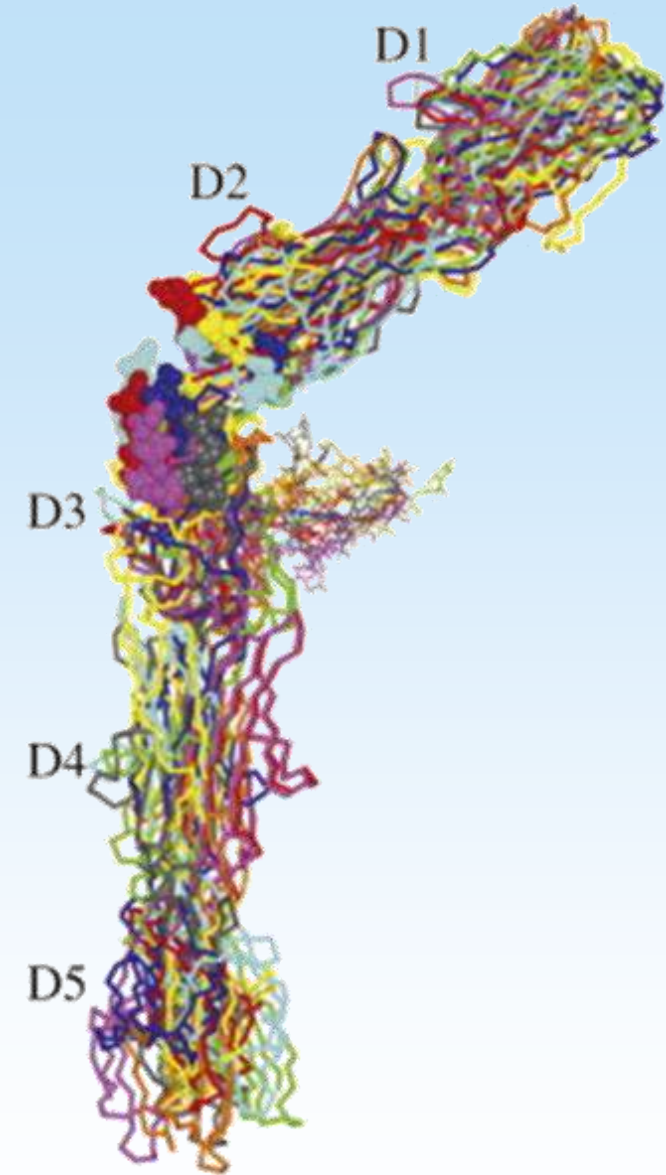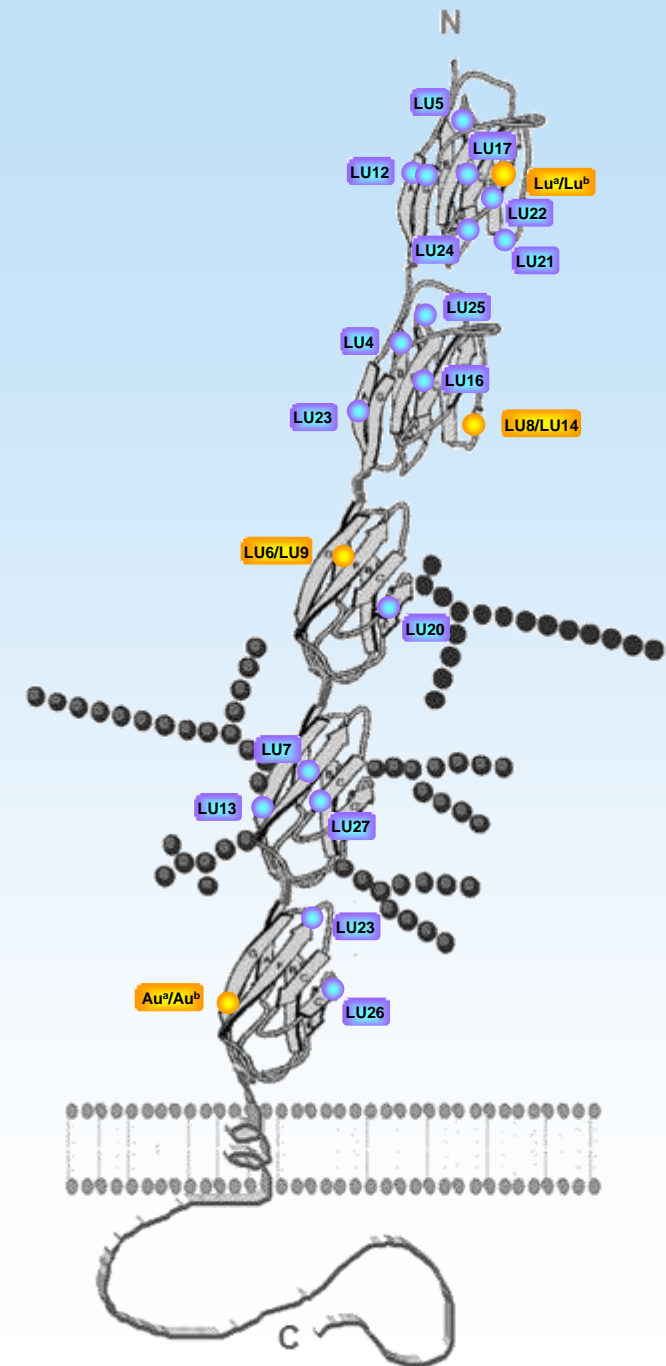
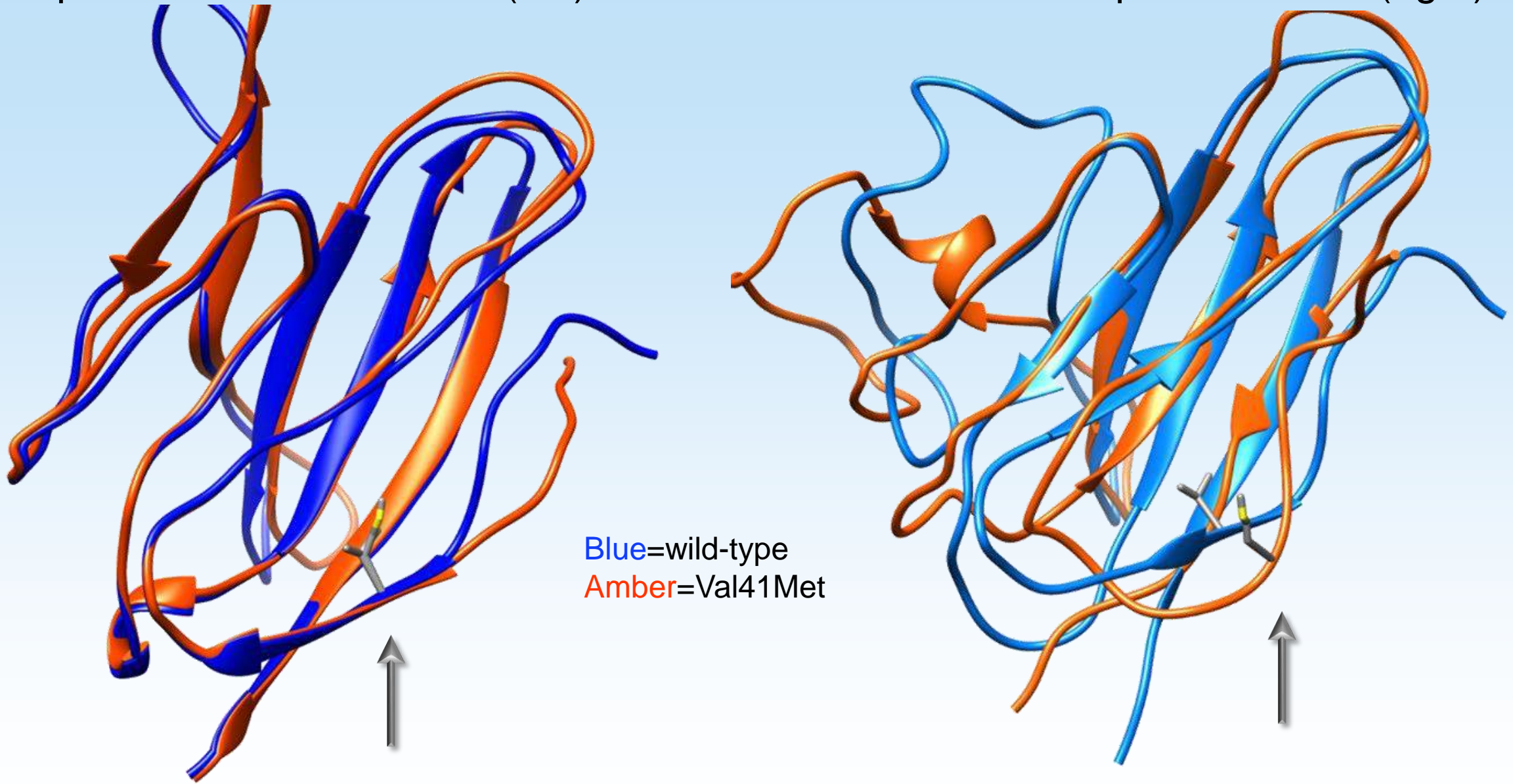# Lutheran domain 1 model

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

Wild-type Val
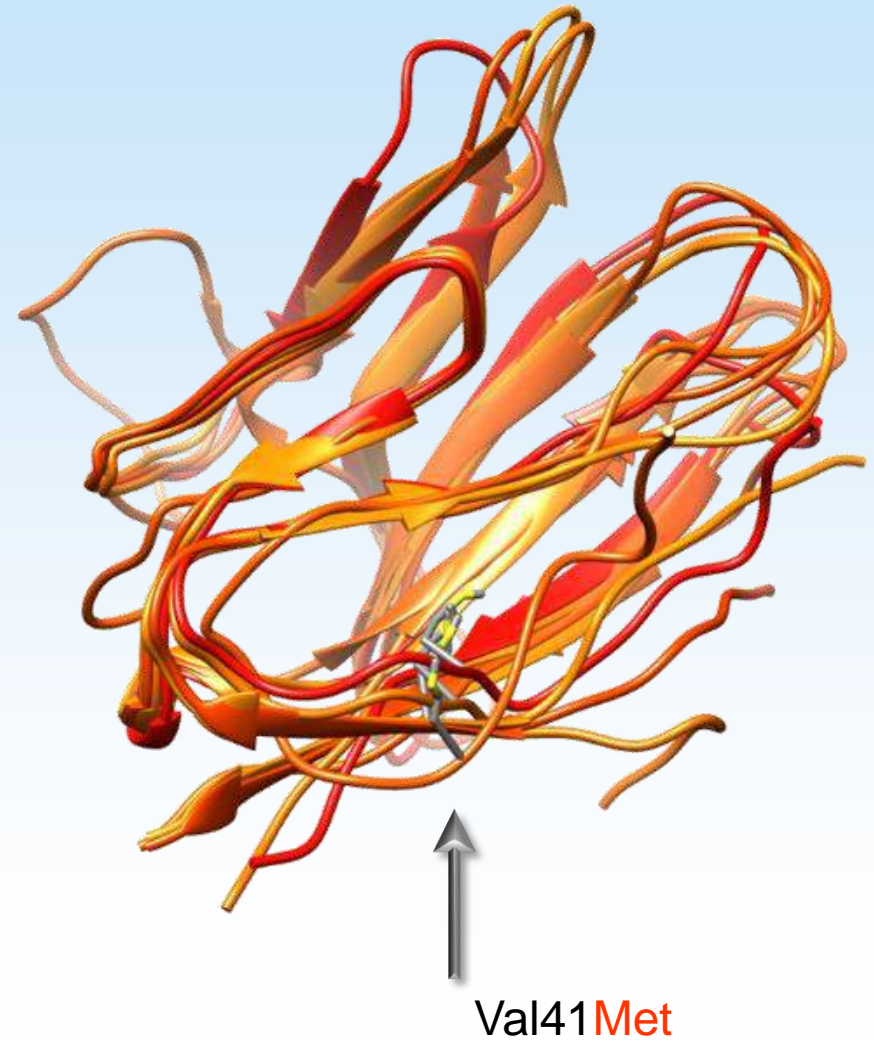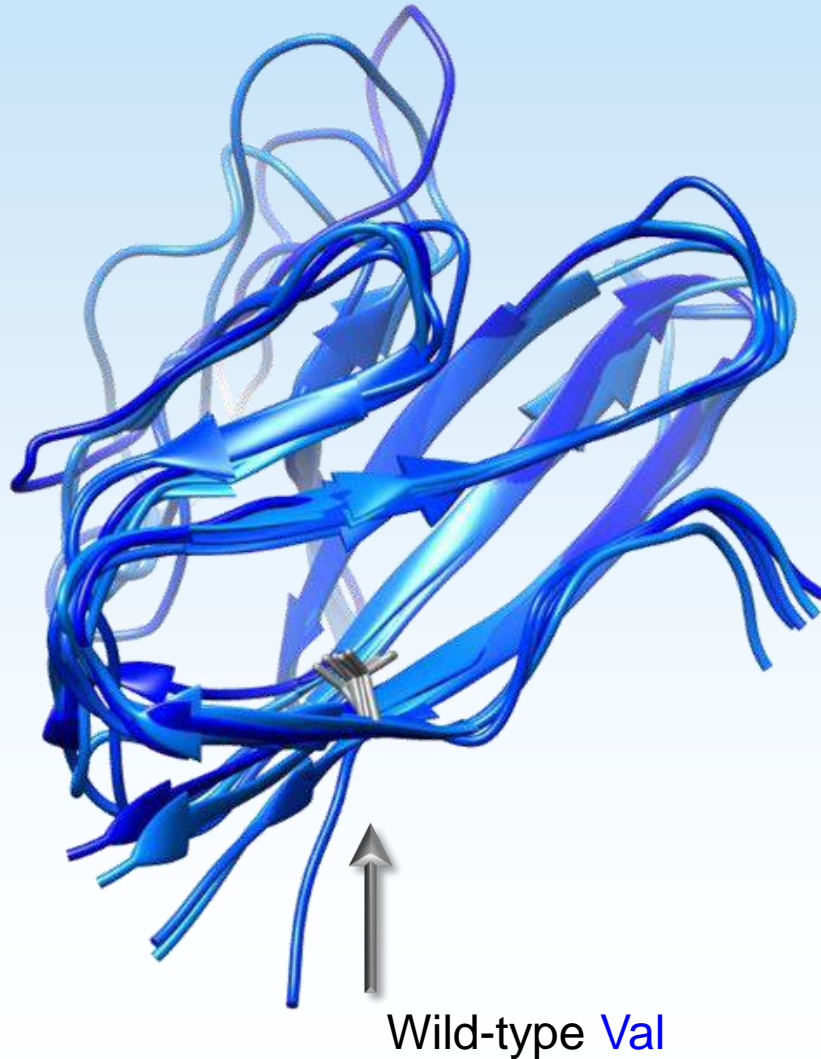
Val41Met

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
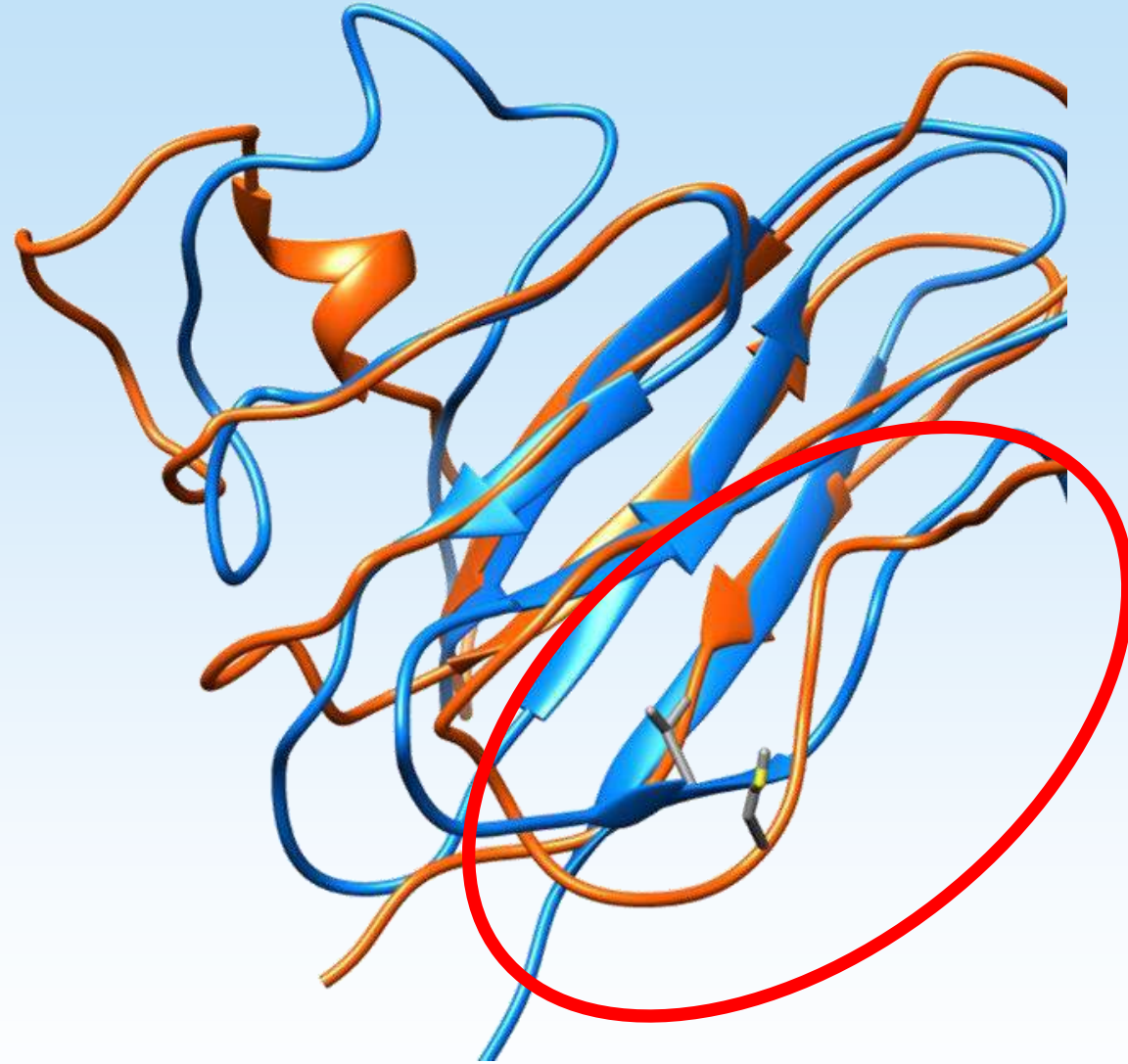
Met41 is exposed to exterior solvent whereas Val41 is stably embedded in protein interior

Summary

New antigen of the Lutheran blood group system

- 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

LUNU = LU28

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Thank You