

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

**Vanja Karamatic Crew<sup>1</sup>, Beate Mayer<sup>2</sup>, Laura Baglow<sup>1</sup>, Salih Yürek<sup>2</sup>,  
Thilo Bartolmäs<sup>2</sup>, Piers Walser<sup>3</sup>, Nicole Thornton<sup>1</sup>**

<sup>1</sup>The International Blood Group Reference Laboratory, NHSBT, Bristol, UK

<sup>2</sup>Institute of Transfusion Medicine, Charité-Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Germany

<sup>3</sup>Clinical Biotechnology Centre, NHS Blood and Transplant, Bristol, United Kingdom



**Blood and Transplant**



# Case study



Institute of Transfusion Medicine  
Charité-Universitätsmedizin  
Berlin, Germany

- 31 year old female of Caucasian origin
- Presented with an unidentified alloantibody to a high frequency antigen
- Pregnant, gestational week 13
- B, R<sub>1</sub>R<sub>1</sub>, 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**

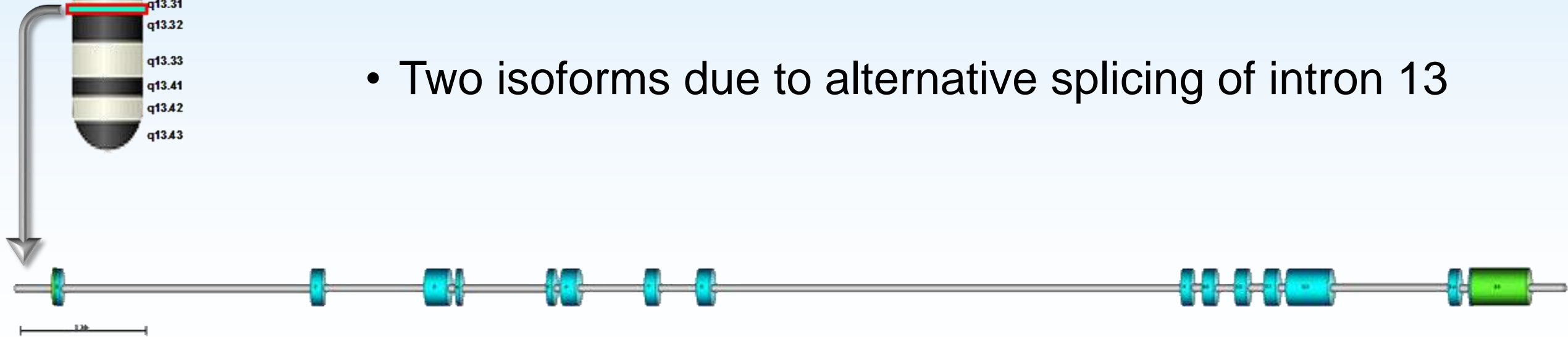
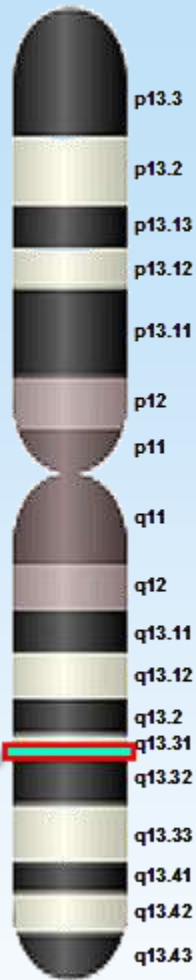
# Serology; Bristol

- 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

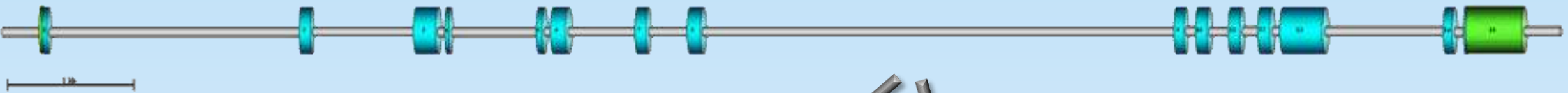
**Antibody recognising epitope on Lu-glycoprotein  $\Rightarrow$  new Lu antigen?**

# Sanger sequencing of *BCAM* gene (*LU*)

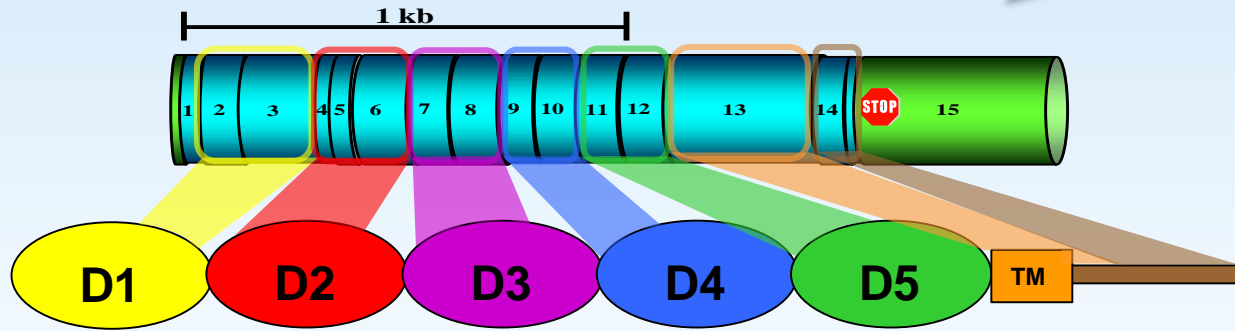
- Lu-glycoprotein is encoded by a single gene *BCAM* (*LU*) described in 1996
- *LU* locus on chromosome 19 q13.3, 2.5 kb in size, organised in 15 exons
- Two isoforms due to alternative splicing of intron 13



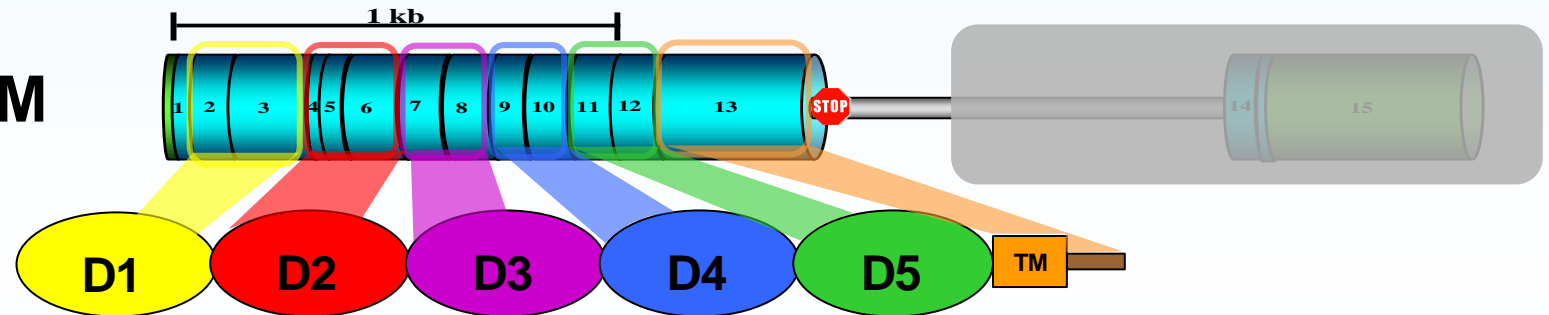
# Two isoforms due to alternative splicing



Lu-glycoprotein



B-CAM



# Sanger sequencing

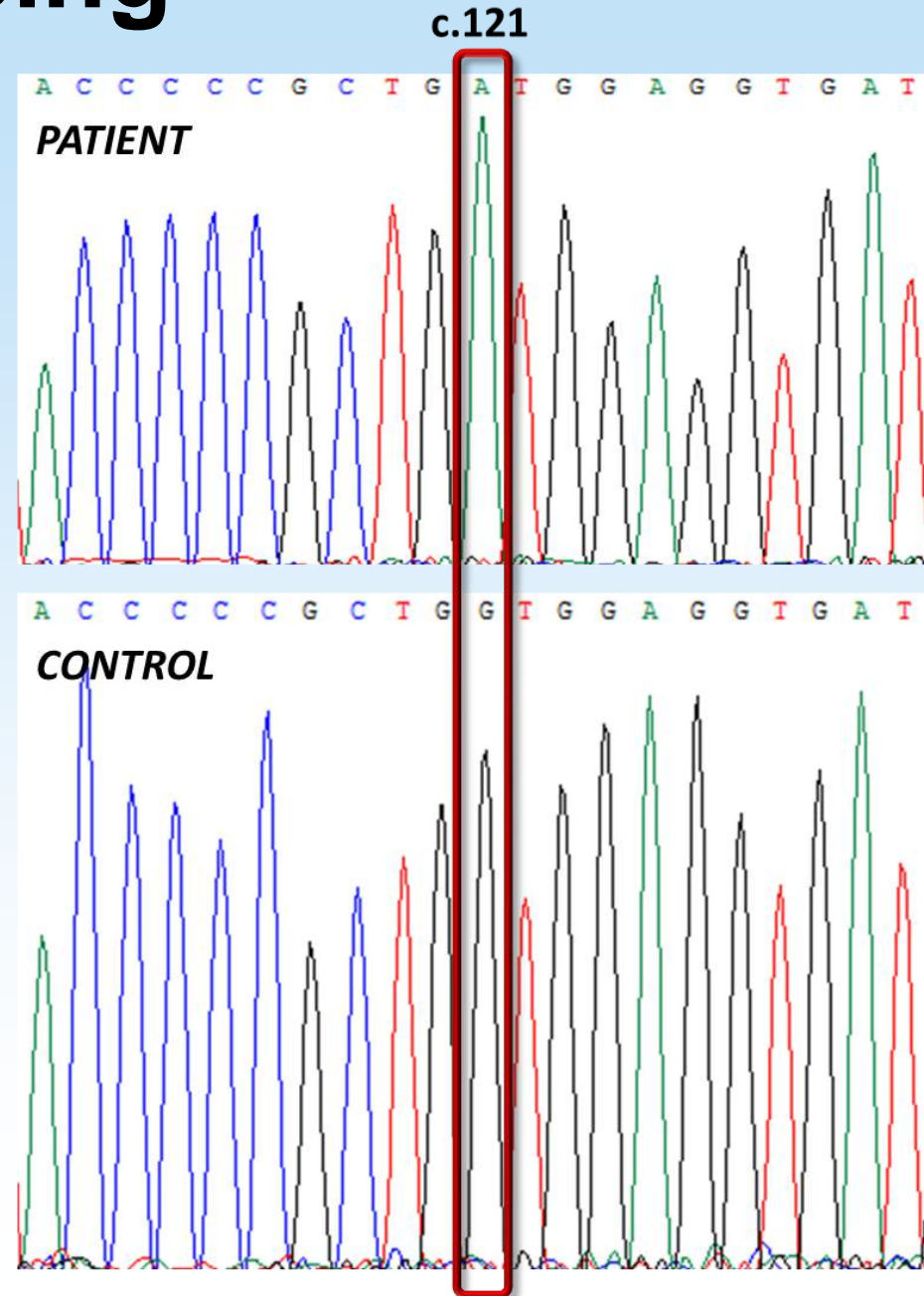
- Sanger sequenced all 15 *BCAM* exons
- Confirmed *LU\*B* and *LU\*18* (Au<sup>a</sup>)

*BCAM* exon 2:

**c.121G>A**

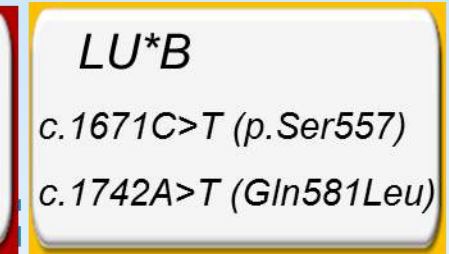
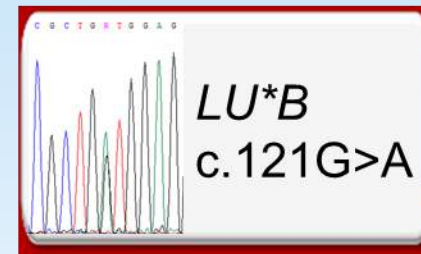
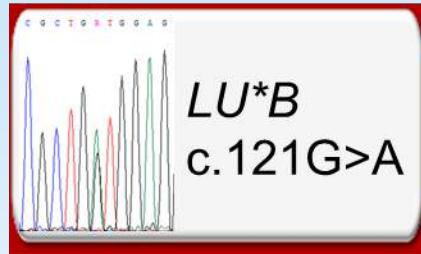
**p.Val41Met**

gnomAD frequency:  $3.98 \times 10^{-6}$

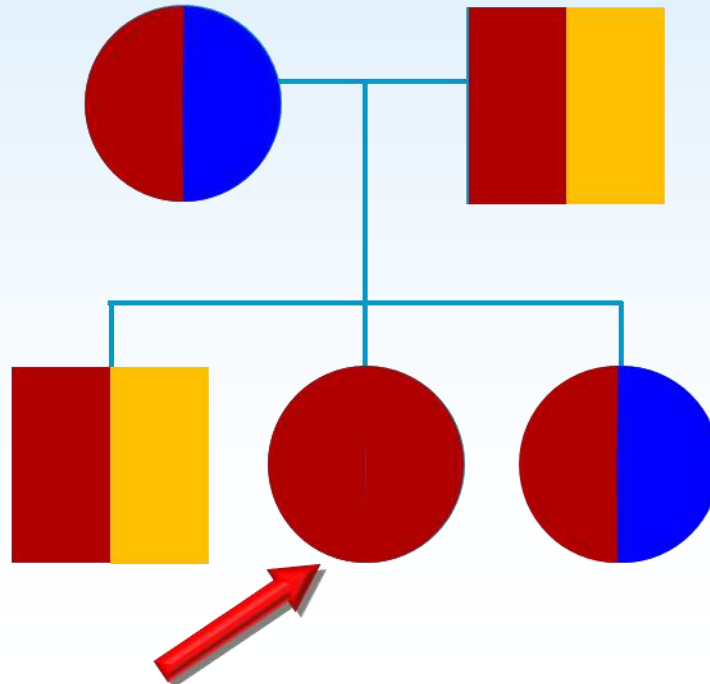


# Family study

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



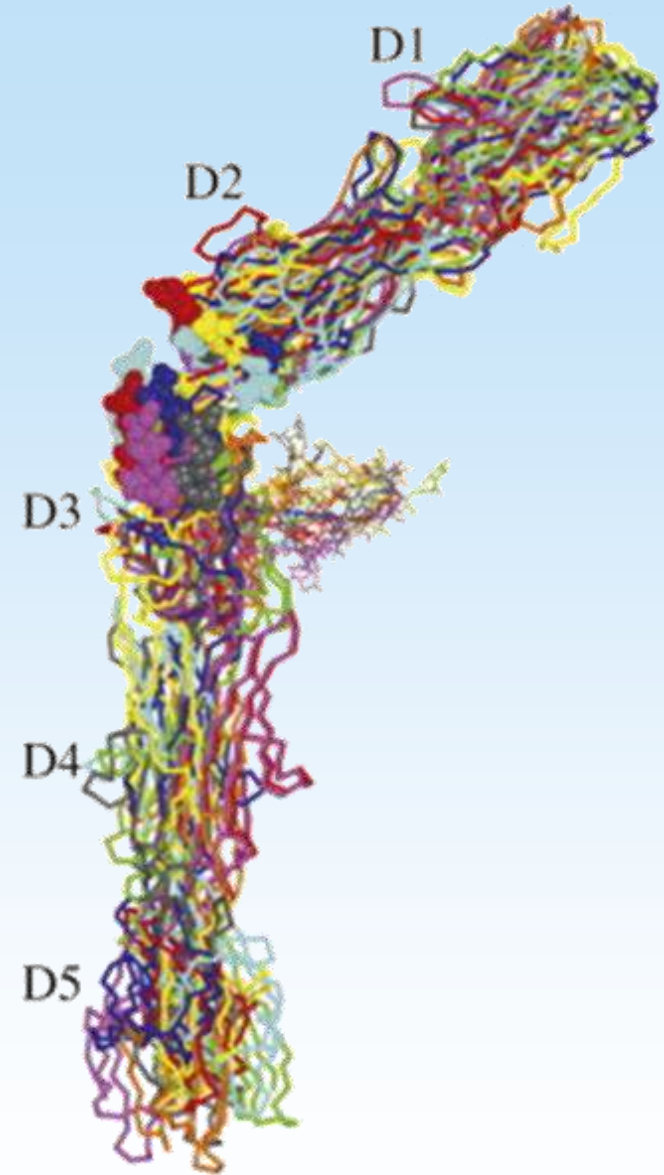
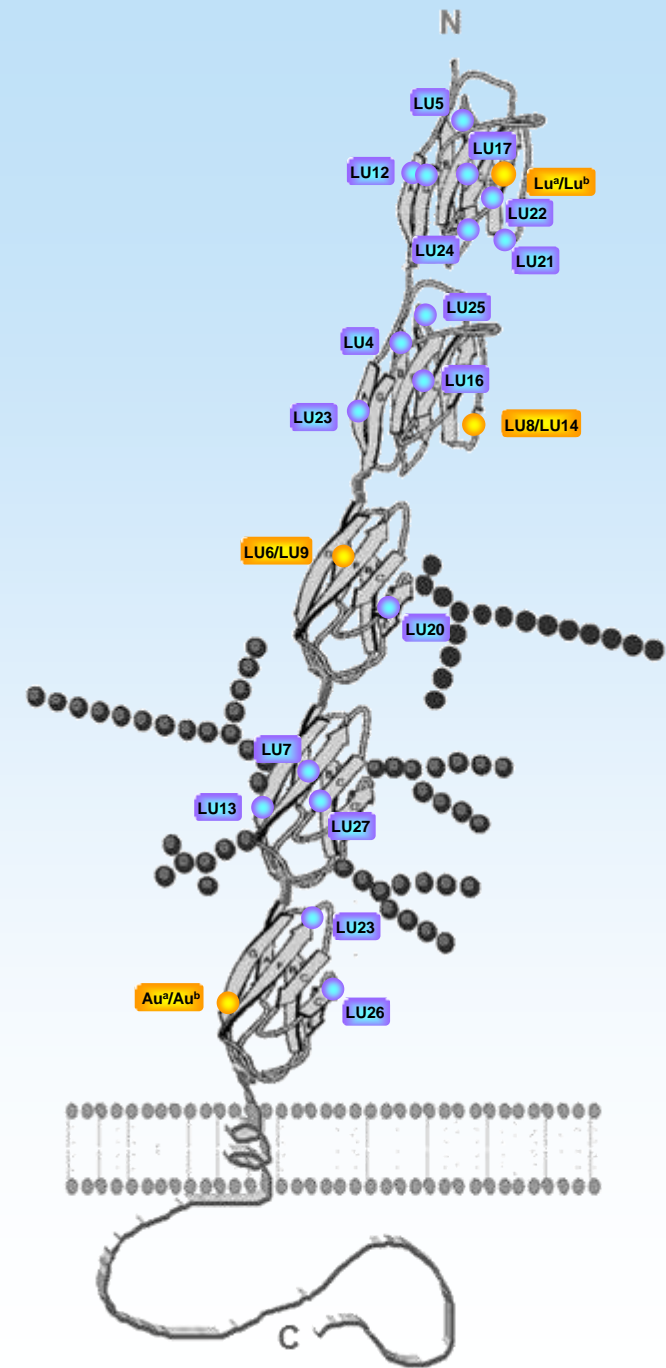
No c.1340C>T, Ser447Leu  
associated with LU:-13





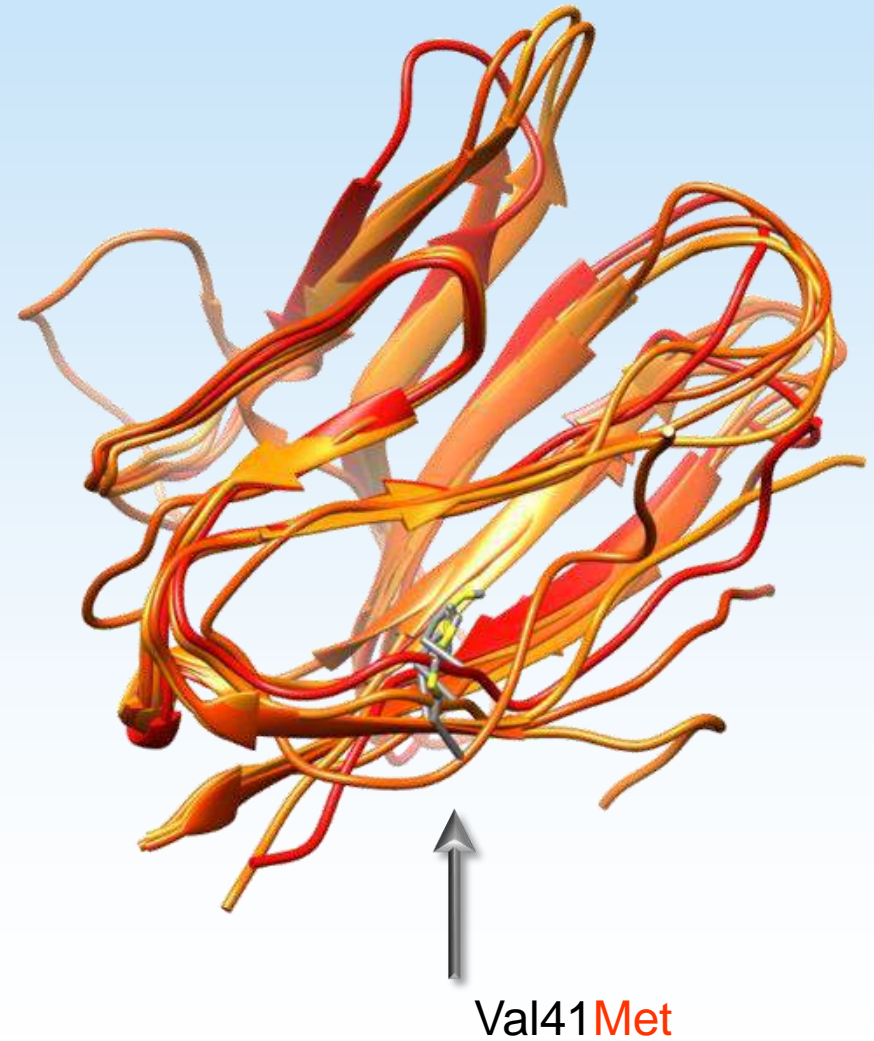
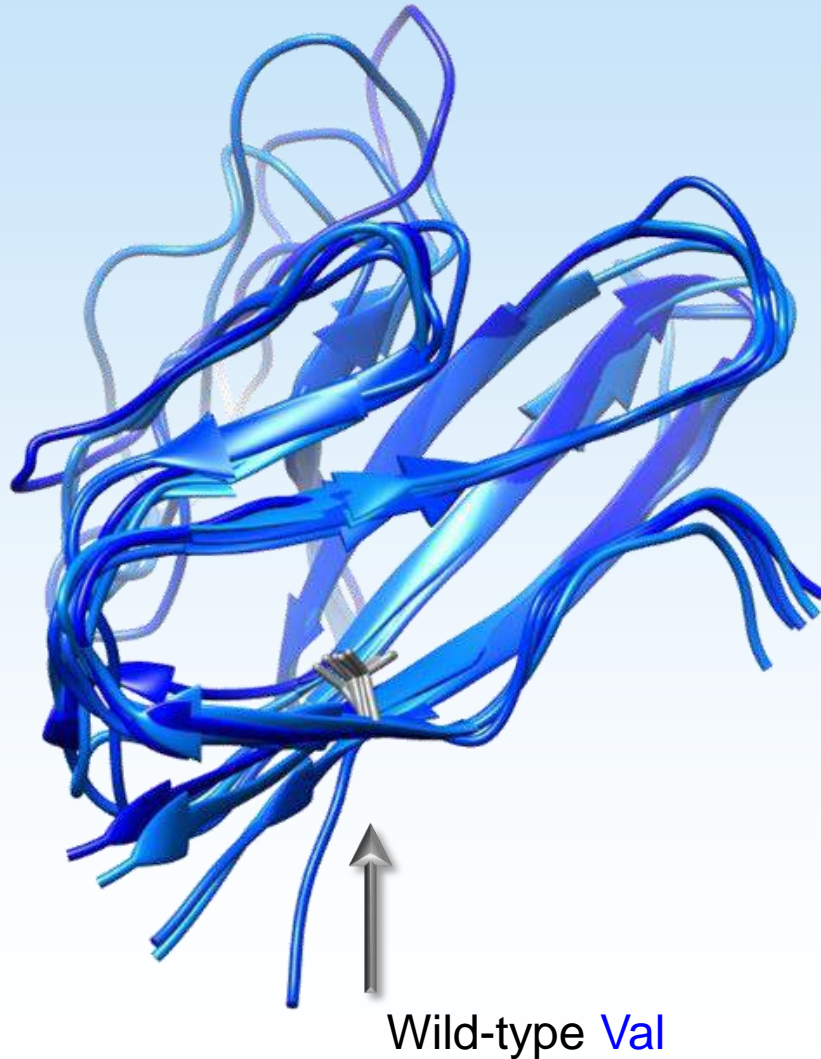
# Lu-glycoprotein model

- 25 antigens in the system
- All encoded by single nucleotide mutations (encoding single amino acid changes)
- 4 pairs are antithetical antigens:  $\text{Lu}^a/\text{Lu}^b$  (LU1/LU2), Lu6/Lu9, Lu8/Lu14,  $\text{Au}^a/\text{Au}^b$  (LU18/LU19)
- Remaining 17 antigens are of high frequency

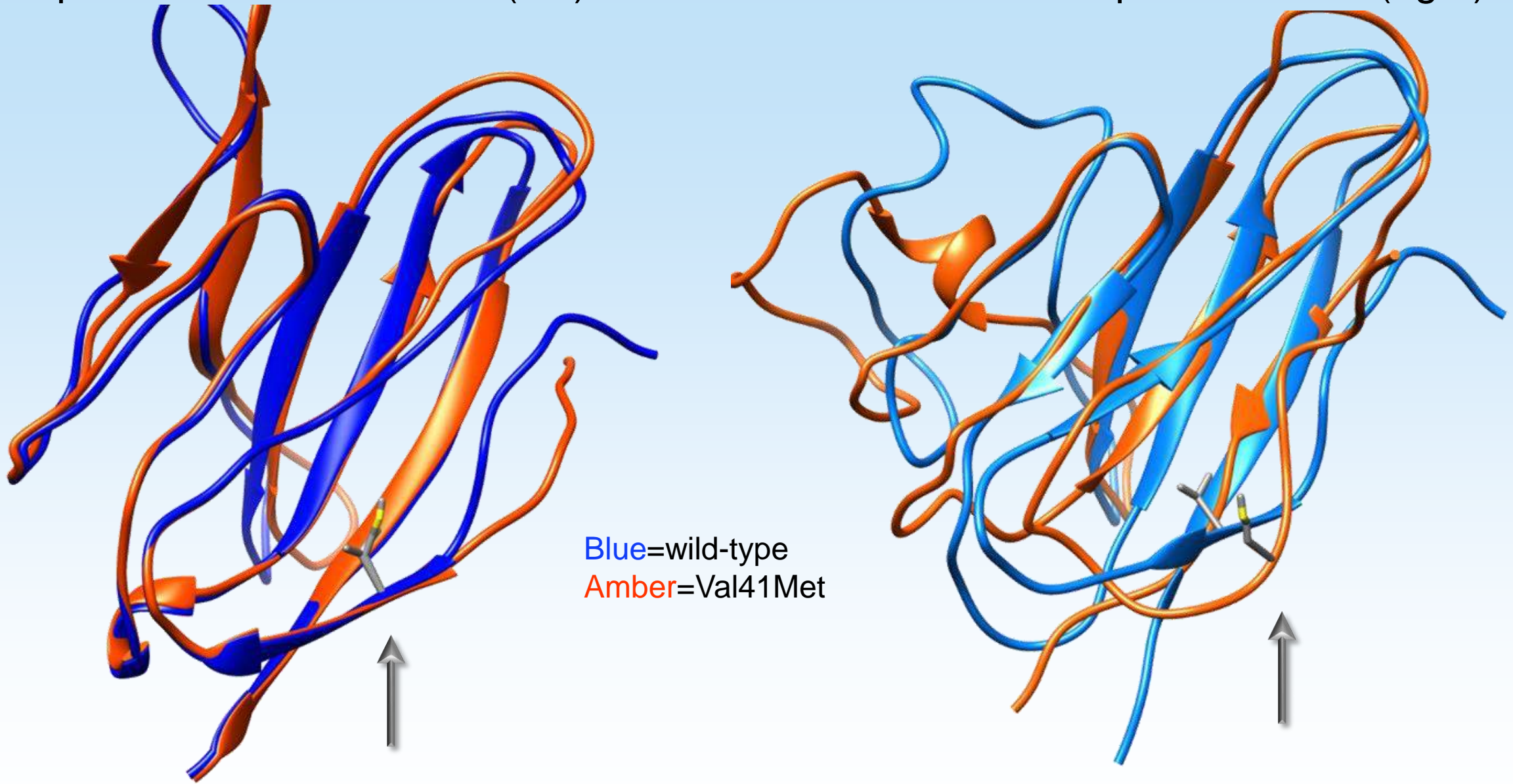


# Lutheran domain 1 model

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

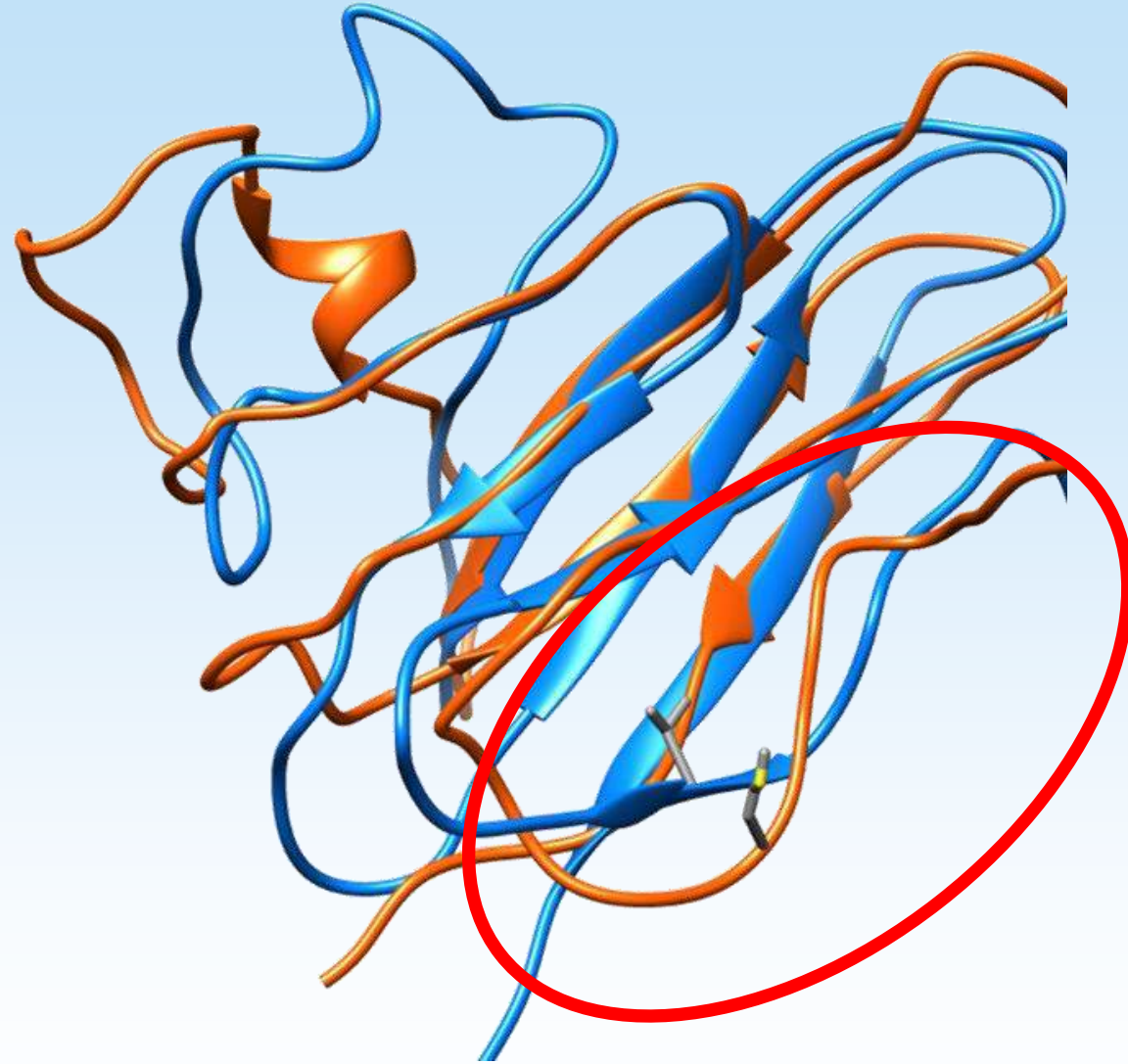


Comparison of start clusters (left) end-of-calculation cluster representatives (right)



N-terminal Val41Met  $\beta$ -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**

**IBGRL/BITS Bristol:**

Nicole Thornton

Laura Baglow

Vanja Crew

Institute of Transfusion Medicine,  
Charité-Universitätsmedizin Berlin,  
corporate member of Freie Universität  
Berlin, Humboldt-Universität zu Berlin,  
and Berlin Institute of Health, Germany

Beate Mayer

Salih Yürek

Thilo Bartolmäs

**CBC, NHSBT, Bristol:**

Piers Walser

**Thank You**

