The high frequency antigen KANNO is located on prion protein, encoded by the \textit{PRNP} gene, as a new blood group system
Characteristics of anti-KANNO

- First example of anti-KANNO was reported in 1991

- First case of non-Japanese individual with anti-KANNO was reported in 2018 (Jones et al. ISBT Toronto)
Characteristics of anti-KANNO

- Against unknown HFA (reactive with $K_o, Jr(a-), Rh_{null} ...$)
- Like a HTLA antibody
- Mainly detected in female with pregnancy history
- Clinical significance of anti-KANNO is unknown

Incompatible transfusion: 7 cases
Pregnant women: 15 cases

No cases showed HTR or HDFN

Characteristics of KANNO antigen

- Sensitive to proteases Ficin, Trypsin, \( \alpha \)-Chymotrypsin...

- Resistant to disulphide bond reducing agents AET and DTT

- KANNO- frequency is 0.44% (10 in 2,260)
What is the carrier molecule?

- IP, blotting, and MAIEA assays were failed...
- Genome-based approaches to identify the causal gene of KANNO antigen  
  (Omae et al. *Transfusion* 2019)

Genome-Wide Human SNP array 6.0 (Affymetrix)
Genome-Wide Association Study (GWAS)
4 KANNO- individuals vs. 415 healthy Japanese

Whole-Exome Sequencing (WES)
Sanger Sequencing
What is the carrier molecule?

Significant association on Chromosome 20p13
rs6116471

c.655G>A (p.Glu219Lys)

Manhattan plot from the GWAS

**PRNP**

- NG_009087
- Exon 1
- Intron 1 (12.7 kb)
- ATG
- Exon 2
- STOP

Japanese Red Cross Society
Central Blood Institute, Blood Service Headquarters
**PRNP** genotype of the 4 probands and their family members

Proband-1

- **KANNO-**

Father

- **KANNO+**

Mother

- **KANNO+**

Husband

- **KANNO+**

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c.655G>A  rs1800014

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Family-1

Family-2

Family-3

Family-4

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*Japanese Red Cross Society*

**Central Blood Institute, Blood Service Headquarters**
Monoclonal antibody-specific immobilization of erythrocyte antigen (MAIEA) assay

- KANNO antigen is on the prion protein
- Confirmed by transfection and expression study using CHO-K1
The *PRNP*\(^{*655A}\) frequencies in the ExAC database and in the Tohoku region

<table>
<thead>
<tr>
<th>Population</th>
<th>Allele Frequency (c.655G&gt;A, rs1800014)</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Asian</td>
<td>4.11% (677 in 16,472)</td>
</tr>
<tr>
<td>East Asian</td>
<td>4.03% (348 in 8,642)</td>
</tr>
<tr>
<td>Latino</td>
<td>0.19% (22 in 11,560)</td>
</tr>
<tr>
<td>African</td>
<td>0.03% (3 in 10,374)</td>
</tr>
<tr>
<td>European</td>
<td>0.004% (3 in 66,660)</td>
</tr>
<tr>
<td>Tohoku (Japan)</td>
<td>5.80% (58 in 1,000)</td>
</tr>
</tbody>
</table>
## Correlation between KANNO phenotype and PRNP genotype

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Agglutination strength</th>
<th>Number of samples*</th>
<th>c.655 genotype</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>GG</td>
</tr>
<tr>
<td>KANNO+</td>
<td>(2+-3+)</td>
<td>100</td>
<td>89</td>
</tr>
<tr>
<td></td>
<td>(w+)</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>KANNO—</td>
<td>(0)</td>
<td>10</td>
<td>0</td>
</tr>
</tbody>
</table>

*Obtained from blood donors living in the Kanto-Koshinetsu region
Summary

- Anti-KANNO may be stimulated by pregnancy or by transfusion
- Anti-KANNO appears to be clinically insignificant
- HFA KANNO is located on prion protein encoded by the PRNP gene
- Recessive inheritance of KANNO- is caused by the PRNP*655A with c.655G>A (p.Glu219Lys) mutation
- The PRNP*655A allele is more frequent in Asians than in other populations
Thank you for your attention!