The high frequency antigen KANNO is located on prion protein, encoded by the *PRNP* gene, as a new blood group system

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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: 7cases

Pregnant women: 15 cases

→ No cases showed HTR or HDFN

(Kawabata et al. *Transfus Med Rev* 2014; 28: 23-8)

Characteristics of KANNO antigen

- Sensitive to proteases Ficin, Trypsin, α-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)

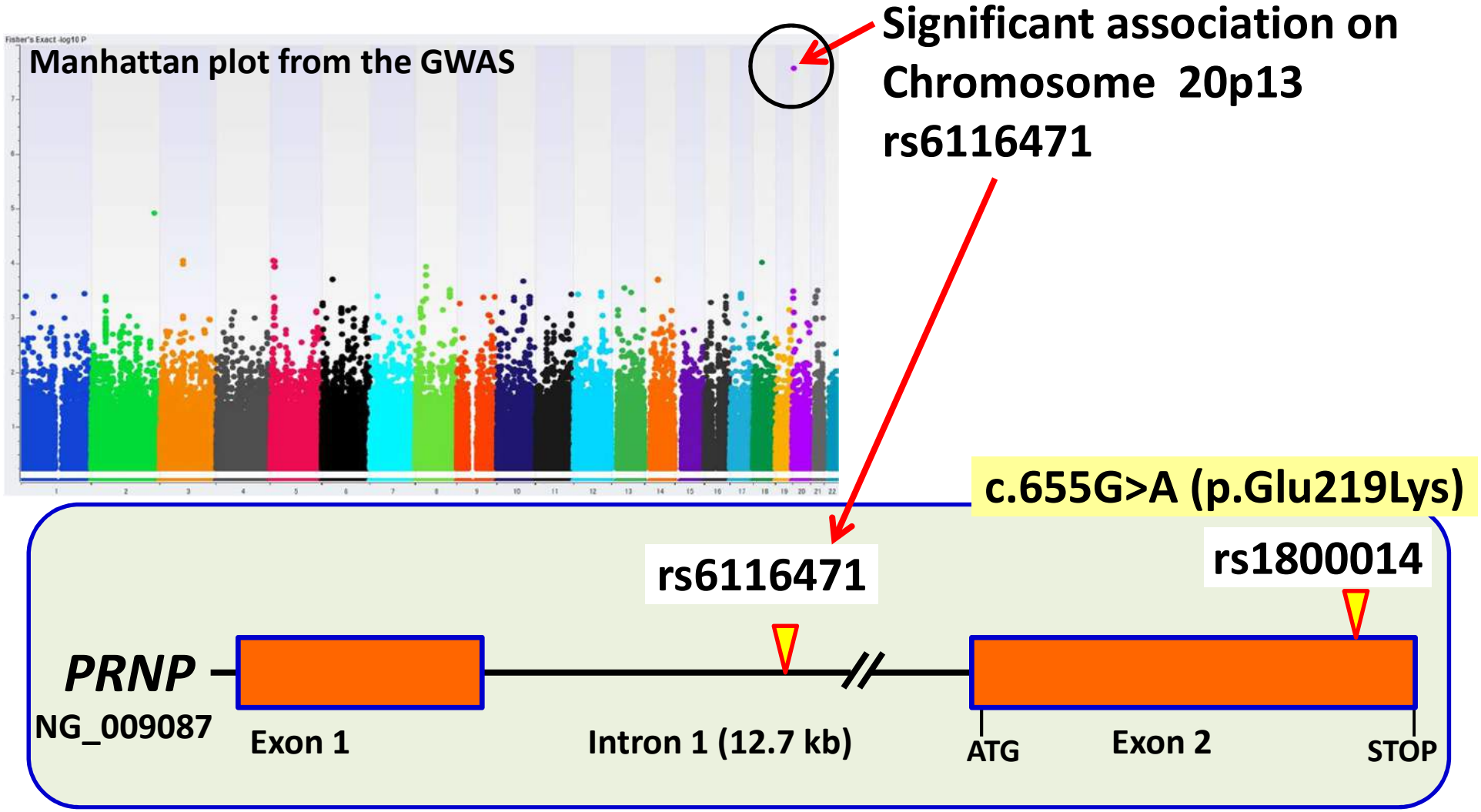
Genome-Wide Association Study (GWAS)

→ 4 KANNO- individuals vs. 415 healthy Japanese

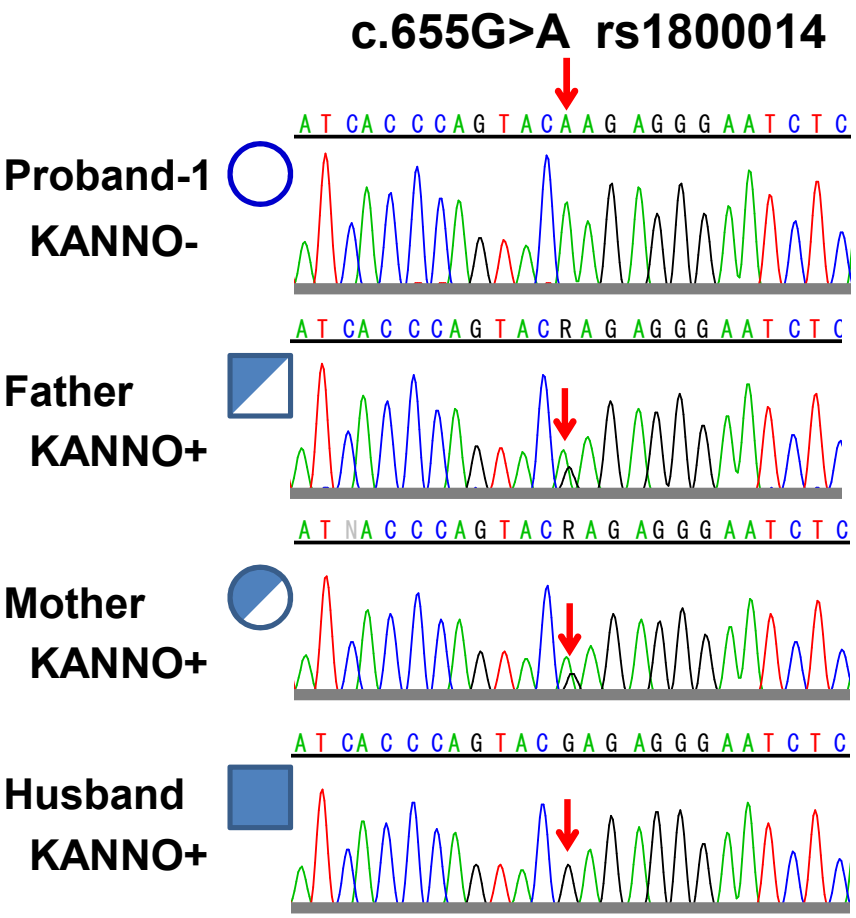
Whole-Exome Sequencing (WES)

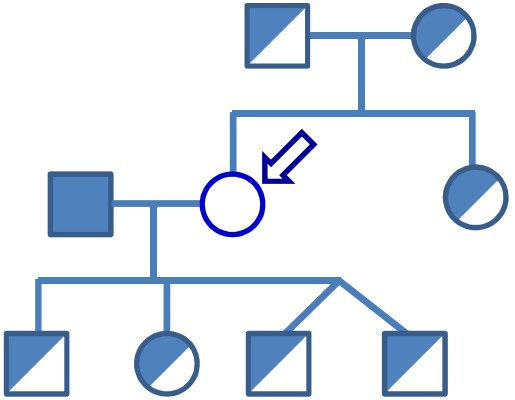
Sanger Sequencing

What is the carrier molecule?

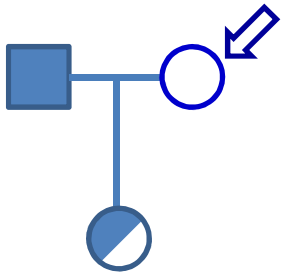


PRNP genotype of the 4 probands and their family members

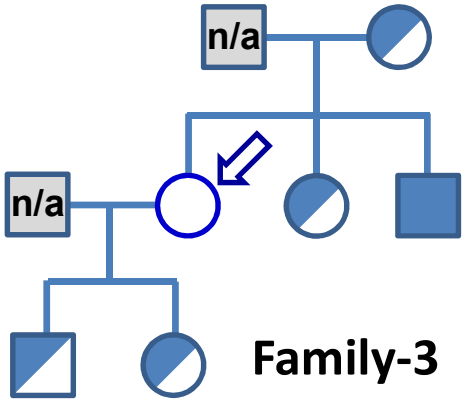




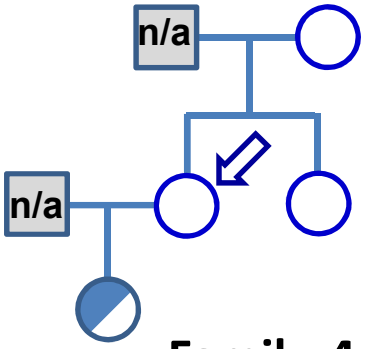
Family-1



Family-2

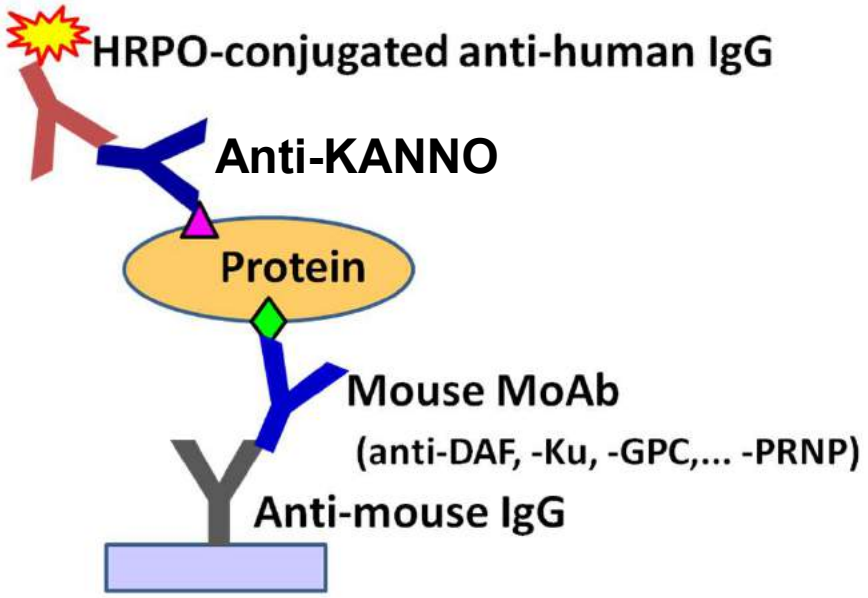


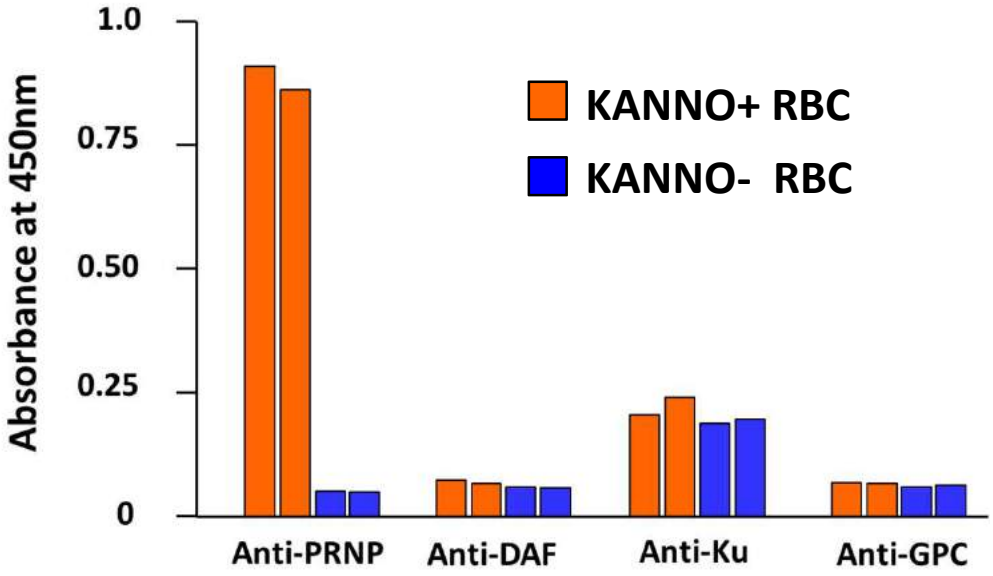
Family-3



Family-4

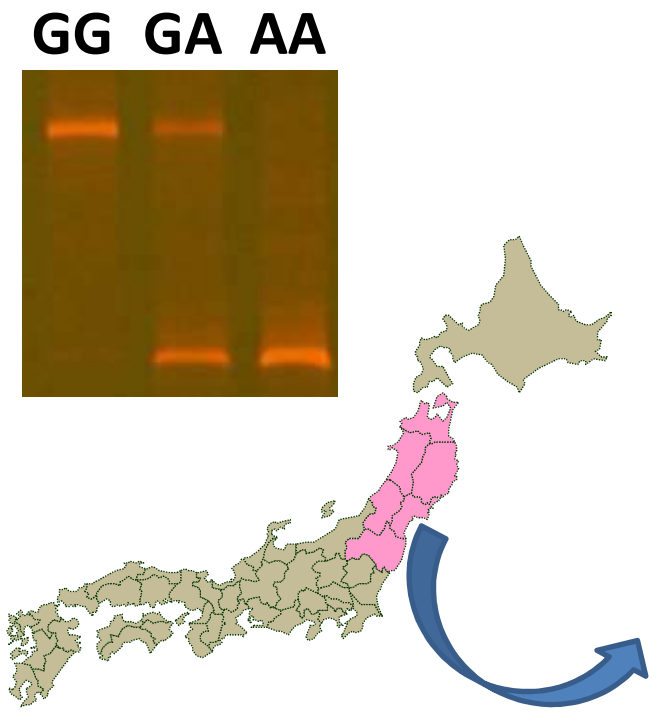
Monoclonal antibody-specific immobilization of erythrocyte antigen (MAIEA) assay





- <u>KANNO antigen is on the prion protein</u>
- Confirmed by transfection and expression study using CHO-K1

The *PRNP**655A* frequencies in the ExAC databese and in the Tohoku region

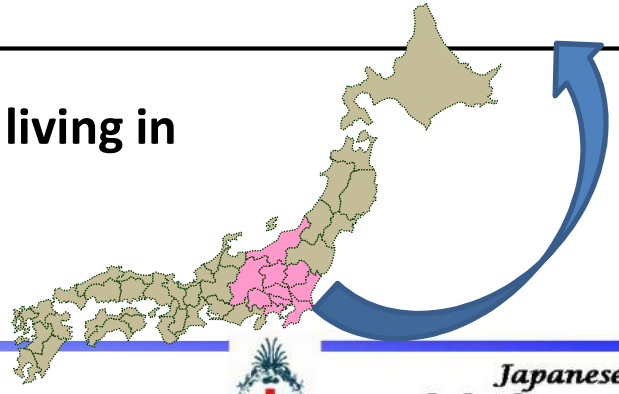


Population	Allele Frequency (c.655G>A, rs1800014)
South Asian	4.11% (677 in 16,472)
East Asian	4.03% (348 in 8,642)
Latino	0.19% (22 in 11,560)
African	0.03% (3 in 10,374)
European	0.004% (3 in 66,660)
Tohoku (Japan)	5.80% (58 in 1,000)

Correlation between KANNO phenotype and *PRNP* genotype

Phenotype	Agglutination strength	Number of samples*	c.655 genotype		
			GG	GA	AA
KANNO+	(2+-3+)	100	89	11	0
	(w+)	12	1	11	0
KANNO－	(0)	10	0	0	10

*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!

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