

Genome-wide association study identifies major effect on natural antibodies in chickens



Tom Berghof MSc
PhD Candidate
E-mail: Tom.Berghof@wur.nl

Tom V.L. Berghof^{1,2}, Henk K. Parmentier², Joop A.J. Arts², Alex A. Hulzebosch¹, Jan J. van der Poel¹, Addie Vereijken³, Marleen H.P.W. Visker¹, Henk Bovenhuis¹

Objective

Identify genes involved in genetic variation of NAb levels by means of genome-wide association studies (GWAS)

Background

- Natural antibodies (NAb) are antibodies present in individuals without previous exposure to the recognized antigen
- NAb binding Keyhole Limpet Hemocyanin (KLH) are
 - heritable ($h^2 = 0.07-0.14$) (Berghof et al., 2015, PLOS ONE)
 - associated with increased chance to survive laying period: more NAb = longer survival (Star et al., 2007, Poultry Science)

Conclusion

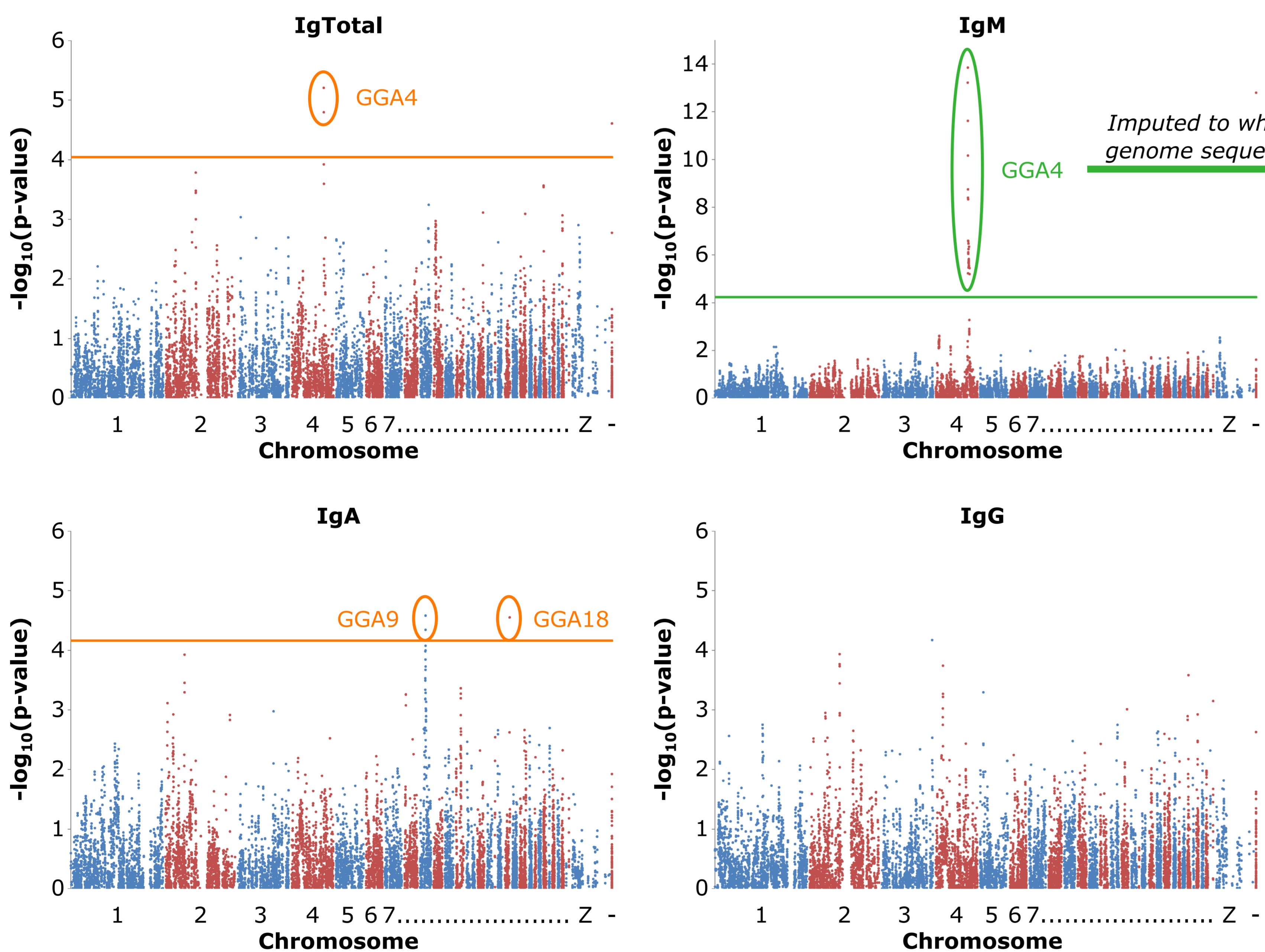
- Major effect on IgM NAb by genomic region on GGA4
→ Most likely candidates: *TLR1A*, *TLR1B*, *KLF3*, *FAM114A1*
- No other genetic regions significantly associated to IgTotal, IgM, IgA, or IgG NAb levels

Material & Methods

- 1,628 layer chickens around 16 weeks of age were:
 - phenotyped for KLH-binding IgTotal, IgM, IgA, and IgG NAb
 - genotyped and imputed to 57,636 SNPs
 - region(s) of interest imputed to whole genome sequence

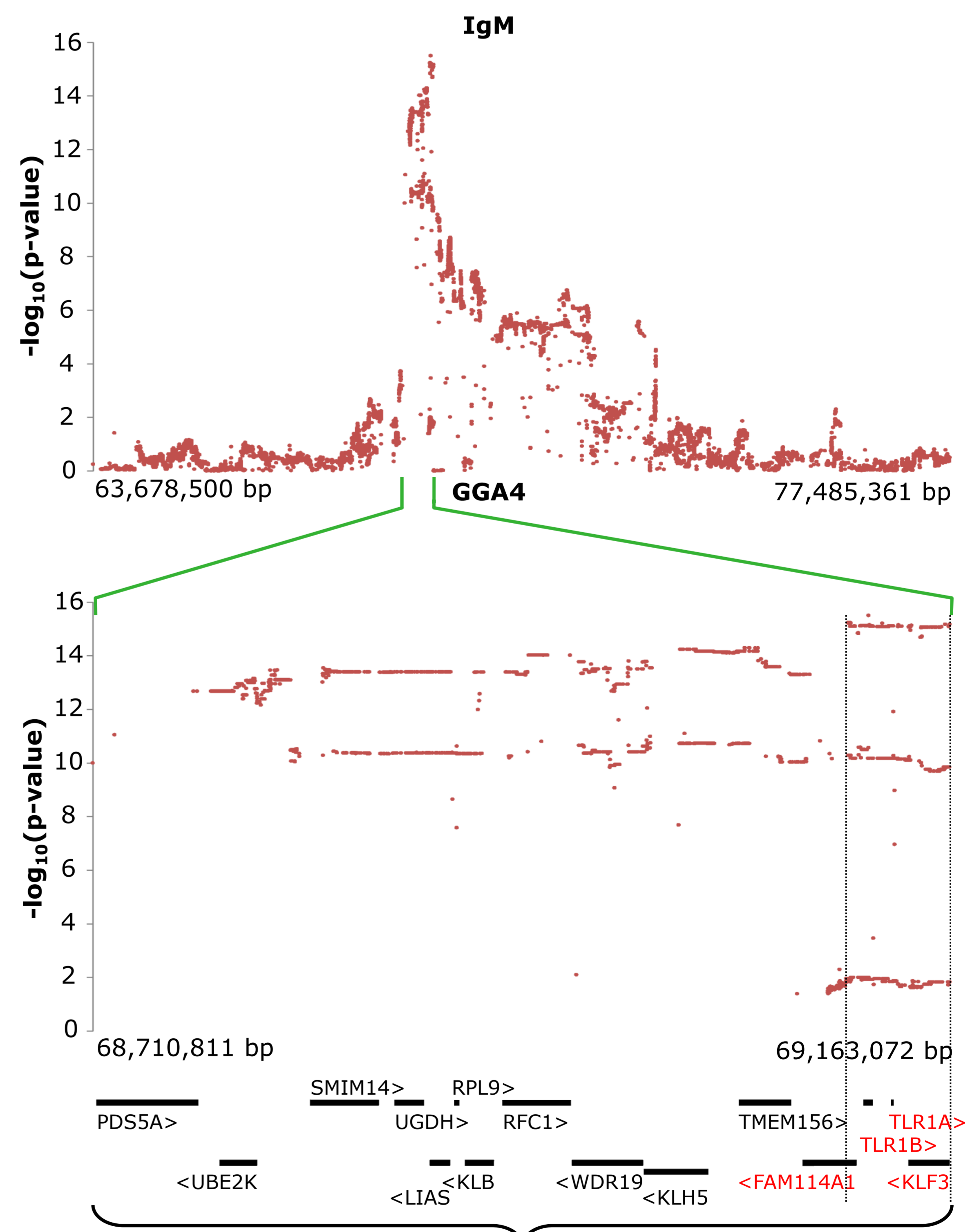
Results

Manhattan plots of GWAS. X-axis: physical position across the chicken genome based on Gallus_gallus-5.0 (chromosomes 1-28, linkage groups LGE22C19W28_E50C23 and LGE64, chromosome Z, and unplaced represented by "-"). Y-axis: $-\log_{10}(p\text{-value})$ for association of SNP with NAb type. Green threshold: significant association. Orange threshold: suggestive association.



IgM association on GGA4

- Full dominance
- Explains ~60% of IgM genetic variation



15 candidate genes for IgM association: 4 most likely

- Toll-like receptor 1 family member A } → Recognition of bacterial lipoproteins and peptidoglycan (with TLR2A/B)
- Toll-like receptor 1 family member B }
- Krüppel-like factor 3 } → Adipose tissue development
- FAM114A1 } → ???; Neuronal cell development (?)

Acknowledgements

We thank Ger de Vries Reilingh (Adaptation Physiology) for determining IgA titers. We thank Tessa Brinker (Animal Breeding and Genomics) for her help in selecting key ancestors of the used populations for sequencing. This research is supported by Institut de Sélection Animale (ISA) - a Hendrix Genetics company, and the Dutch Technology Foundation STW, which is part of the Netherlands Organisation for Scientific Research (NWO), and which is partly funded by the Ministry of Economic Affairs (grant number 12208 and grant number 12654).