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Genome-wide association studies of morphometry, gaits, cardiac function and behavior in endurance horses

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Background

- Arabian and crossed Arabian horses are well adapted to run long distances up to 160 km endurance race in bouts of 30-40 km

- This level of performance is based on:
  - -intense aerobic metabolism
  - -adaptation of the cardiorespiratory system
  - -effective body heat dissipation
  - -maintenance of homeostasis

Hard to evaluate

GenEndurance project:

Determine phenotypic criteria that are:

1/ easily measurable

2/associated with endurance performance

3/sufficiently inheritable

GenEndurance

Background

Phenotypic criteria evaluated on GenEndurance:

Body measurements, morphometry, gaits, cardiac dimension, behavior traits

Phenotypic criteria	Correlation with endurance performance	h^2
Body measurements	0.1<r	High
Morphometry	0.11<r<0.17	Low to medium
Gaits	0.08<r<0.15	Low to medium
Cardiac dimension	0.18<r<0.20	Medium

Robert et al., 2017

→ Endurance performance was suspected to be **multifactorial**

Objective

Perform GWAS to identify genetic determinants (SNPs) associated with :

- body measurements
- 2D-morphometry
- gaits (walk and trot)
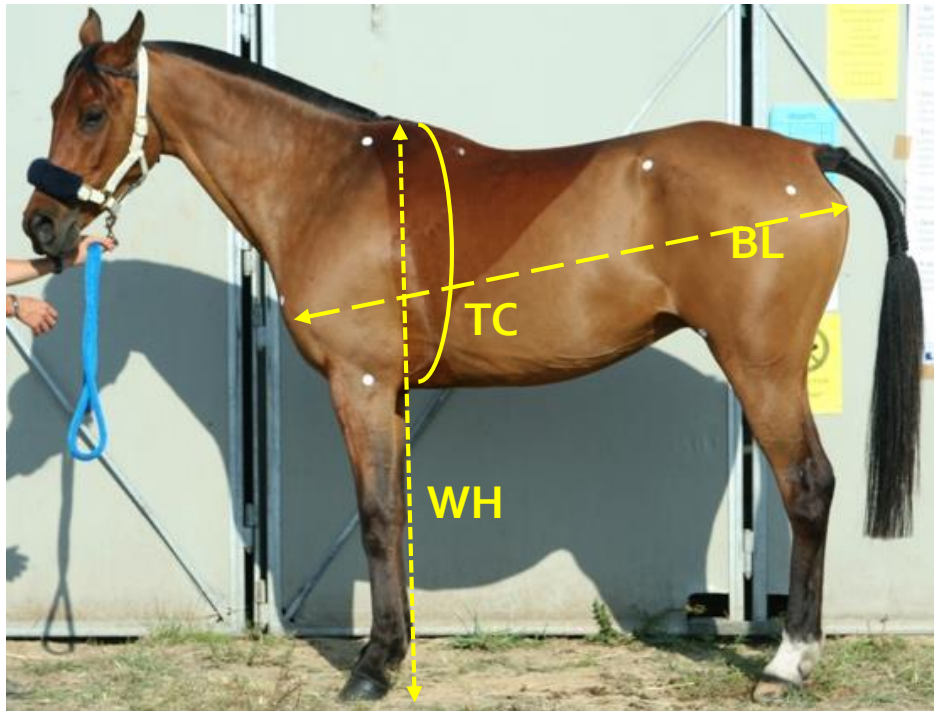- cardiac function
- behavior traits

Animals and phenotypes

63 phenotypic traits measured on 1,013 **Arabian horses**

- Body measurements (n=1,012 horses):

Withers height (WH), thoracic circumference (TC), body length (BL), weight, **skin thickness**

Animals and phenotypes

63 phenotypic traits measured on 1,013 **Arabian horses**

- 2D-Morphometry (n=716):

Angular measurements, bones length, body surface (calculated), …

Animals and phenotypes

63 phenotypic traits measured on 1,013 **Arabian horses**

- Walk (n=673) and trot (n=668) characteristics:

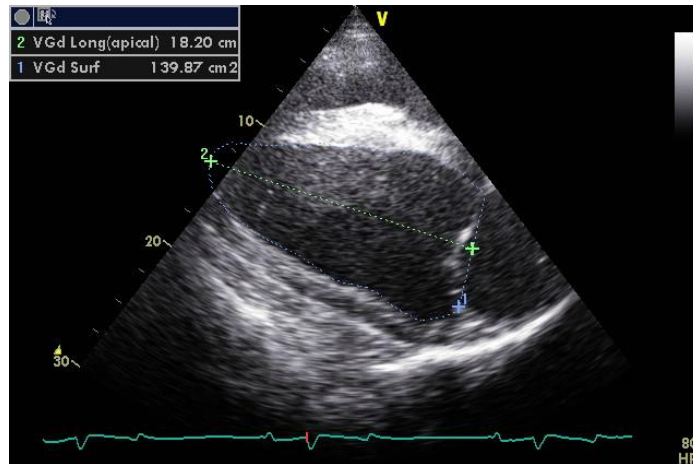Stride frequency, regularity, symmetry, dorso-ventral, lateral and longitudinal activities, propulsion power, …

Gait analysis on the track with an accelerometric device: Equimetrix™

Animals and phenotypes

63 phenotypic traits measured on 1,013 **Arabian horses**

- Cardiac dimensions (n=326)

Pulmonary artery and aortic diameters, area of left ventricle, stroke volume, …

Transthoracic, two-dimensional echocardiography

Animals and phenotypes

63 phenotypic traits measured on 1,013 **Arabian horses**

- Quantitative behavior traits (n=370)

- Behavior score when measuring :
  - skin thickness
  - withers height
  - weight
  - taking blood sample

- Number of trials to step on the weighting platform

Animals and phenotypes

1,013 Arabian horses:	
Age	4-12 years
Sex	9% male, 44% gelding, 47% female
Places	17 Endurance competition or Field exercise test
Years	2011-2014

1,309 horses genotyped (1,013 phenotyped horses + ancestors):
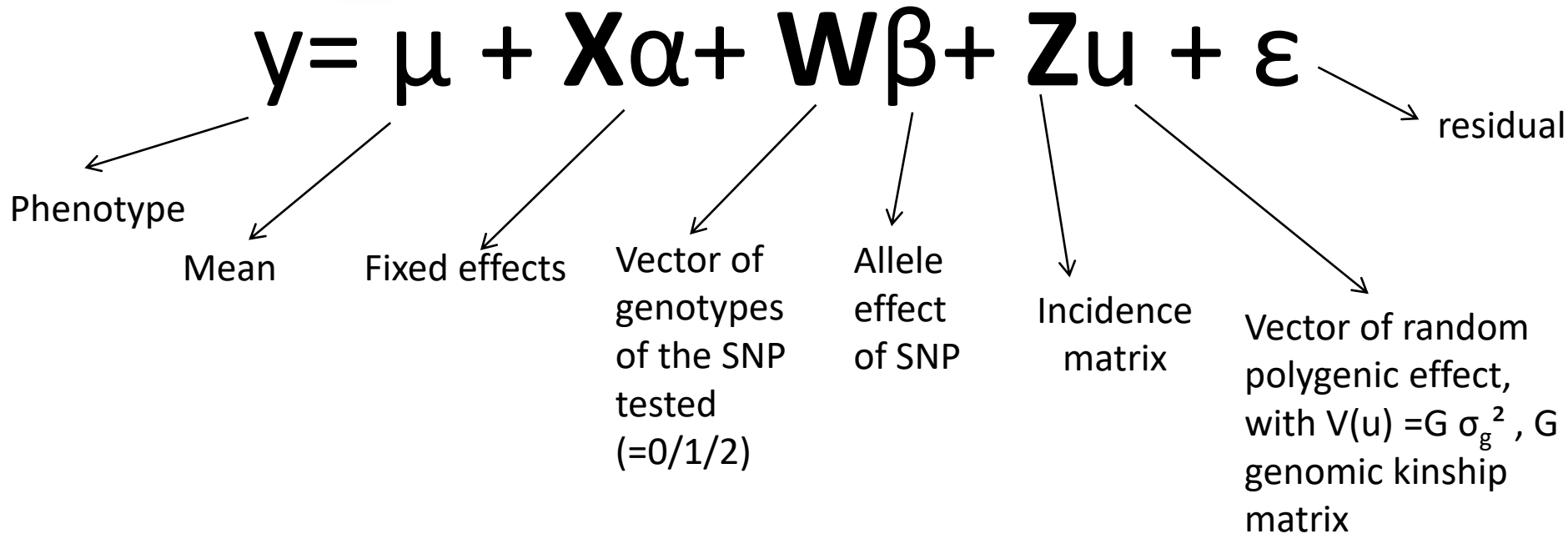
86% MD chip (Illumina)   &   **14% HD chip** (Affymetrix)

Imputation (Fimpute 2.2 software)
allowed to merge all the genotyping data
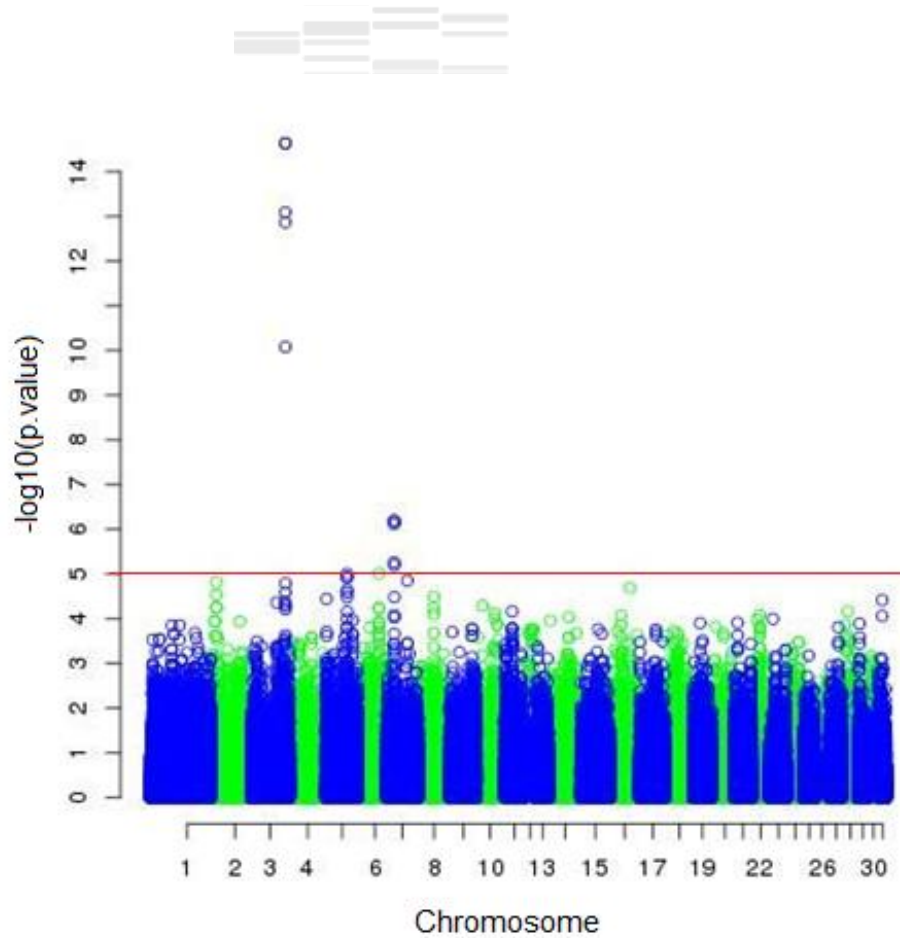**100% HD chip**

Genome-wide association studies

Linear mixed model with a single allele SNP effect:

$$y = \mu + X\alpha + W\beta + Zu + \varepsilon$$

Phenotype

Mean   Fixed effects   Vector of genotypes of the SNP tested (=0/1/2)   Allele effect of SNP   Incidence matrix   Vector of random polygenic effect, with $V(u) = G\sigma_g^2$, G genomic kinship matrix   residual

Using GenABEL package in R (Aulchenko *et al.* 2007)

Threshold p-value: 10^{-5}

INRA SCIENCE & IMPACT

Results: Withers Height

HG

OPEN ACCESS Freely available online

PLoS one

A Genome-Wide Association Study Reveals Loci Influencing Height and Other Conformation Traits in Horses

Heidi Signer-Hasler[1], Christine Flury[1], Bianca Haase[2,3], Dominik Burger[4], Henner Simianer[5], Tosso Leeb[2], Stefan Rieder[4]*
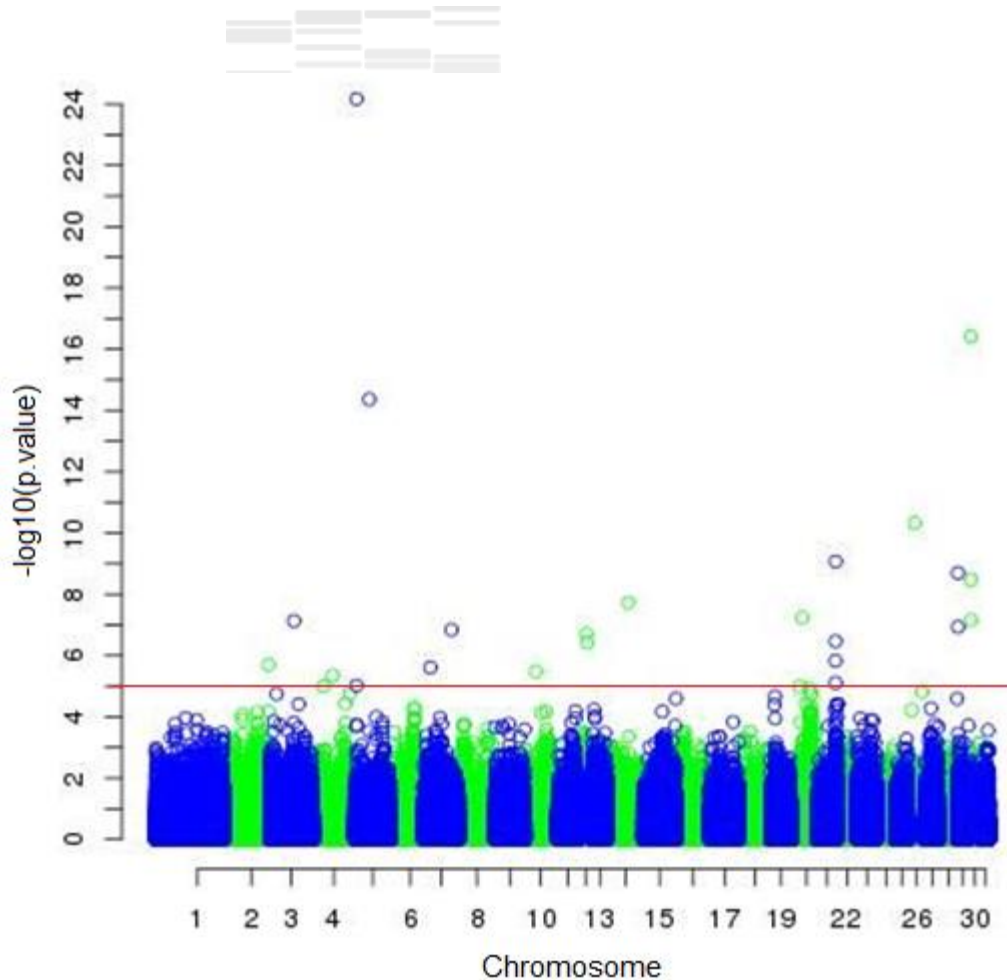
2 SNPs on ECA3:
 - BIEC2-808543, 3: 105547002,
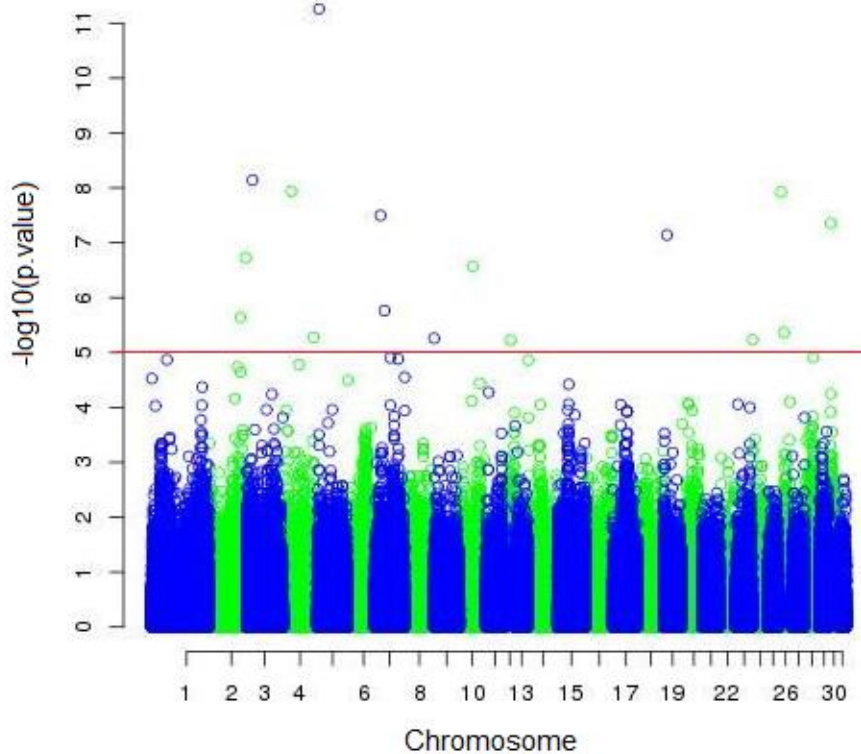 - BIEC2-808466, 3: 105163077
9 SNPs on ECA9

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Results: Skin thickness

21 SNPs distributed on 13
chromosomes
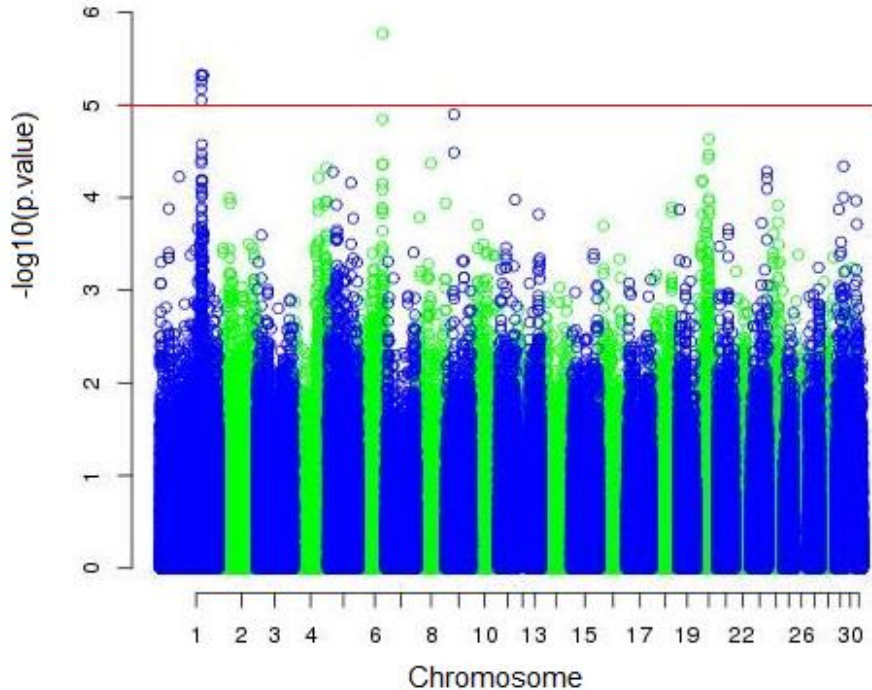$10^{-5} <$ p.value $<10^{-24}$

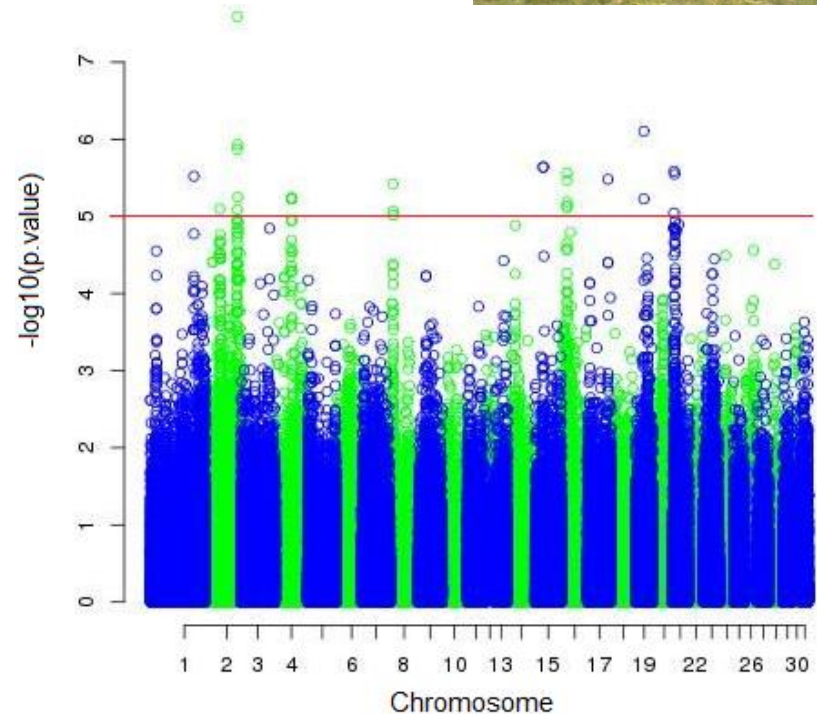# Results: Cardiac dimensions

Pulmonary artery diameter (PA)

31 SNPs distributed on 18 chromosomes
$10^{-5} < $ p.value $< 10^{-11}$

Results: Gaits and behavioral traits

Propulsion power (Trot)

Number of trials to step on the weighting platform

SNPs 10^{-5} < p.value < 10^{-8}
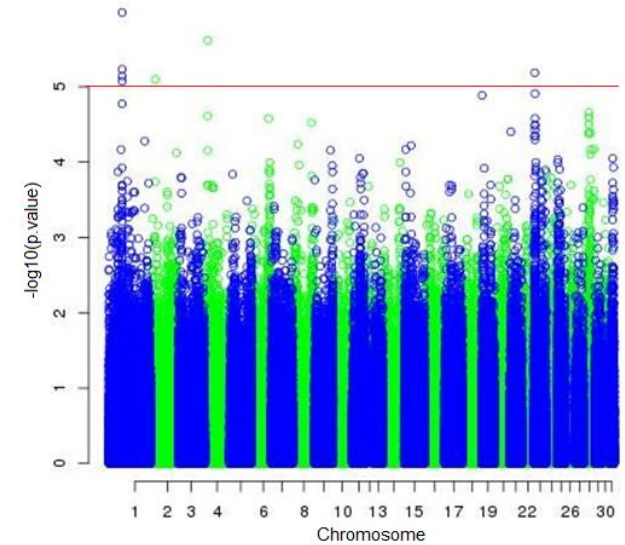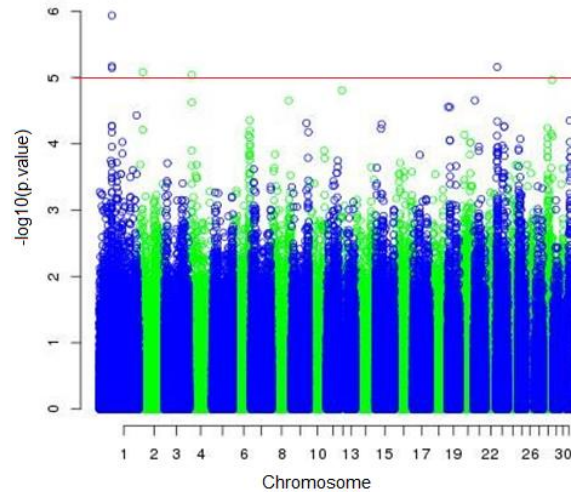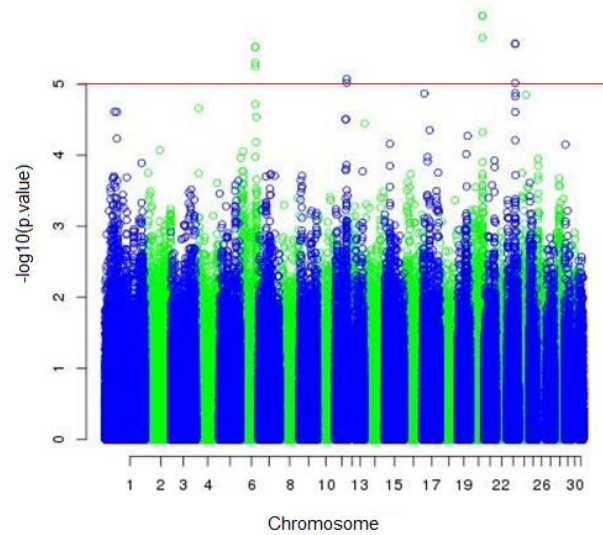
Results: Endurance racing performance

Assessed with 3 performance traits:

speed **total distance covered** **finishing status**

SNPs $10^{-5} <$ p.value $< 10^{-6}$

Conclusion:

GWAS:

- **Skin thickness**
  Pulmonary artery diameter — High/Medium SNP significance: $10^{-5} <$ p.value $< 10^{-24}$

- **Gaits** & **Behavioral traits** → Low SNP significance: $10^{-5} <$ p.value $< 10^{-8}$

- **Endurance racing performance** → Low SNP significance: $10^{-5} <$ p.value $< 10^{-6}$

Polygenic determinism of the endurance ability

Candidate genes will be investigated in the main QTL regions

Thank you for your attention

CHASSIER Marjorie

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