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landwirtschaftliche fakultät

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Bundes Hybrid Zucht Programm
Sau solide.

70th Annual Meeting of the European Federation of Animal Science, 26. – 30.08.2019 Ghent (Belgium)
Session 30: Neonatal survival in pigs

Genome-wide association studies on stillbirth, birth weight and postnatal growth in pigs

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Introduction – Piglet Survival

Production system: →

– Management[1]
– Infection pressure[1]

Breeding: →

– Litter size[2] ↑
– Piglets birth weight[3] ↓
– Variance of birth weights[4] ↑

Piglet survival

adisagroblog.wordpress.com

→ **Politics and society:**

- Animal welfare[1]
- Health status[2]
- Public acceptance[3]

→ **Farmer:**

- Economic viability[4]
- Public acceptance[3]

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[1] Edwards and Baxter, 2015; [2] Rutherford, 2013; [3] Roehe und Kalm, 2000; [4] Milligan et al., 2002

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Current situation and challenges

- In the past: Increased litter size[1] (plus one piglet every three years[2])
- Decreased individual birth weights[3]
- High variation of birth weights within litter[4]

➡ Reduced piglet survival[5]

➡ Reduced fattening performance[6]

[1]Tribout et al.,1998 and 2003, [2]VanEngen et al. 2010, Hortmann Scholten 2012, [3]Roehe and Kalm, 2000, [4]Milligan et al., 2002,[5]Roehe et al., 2014, [6]Fix et al., 2010

Estimated (co)variance components for individual piglet traits (Heuß et al. submitted)

Landrace				**Correlations with BW**	
Trait	h^2	m^2	c^2	r_g	r_p
SB	0.02^{b}	0.05^{a}	0.12^{b}	0.22^{c}	-0.20
BW	0.03^{a}	0.20^{b}	0.12^{a}		
PWL	0.02^{a}	$< 0^{a}$	0.07^{a}	-0.50^{c}	-0.38
BW	0.02^{a}	0.24^{b}	0.13^{a}		
Large White					
SB	0.00^{a}	0.04^{a}	0.10^{b}	n.e.	-0.22
BW	0.04^{a}	0.09^{b}	0.15^{a}		
PWL	0.02^{a}	$< 0^{a}$	0.08^{a}	-0.70^{c}	-0.36
BW	0.04^{a}	0.22^{b}	0.14^{a}		

BW= Individual birth weight, PWL= Pre-weaning loss, SB = Stillbirth, h^2=Heritability, m^2=Maternal genetic effects, c^2=Common environment effects (biological litter in SB and BW and foster litter in PWL), r_g=Genetic correlation, r_p=Phenotypic correlation. n.e.=not estimable. Results for SB and PWL are presented on the underlying liability scale. ^{a}: se<0.008, ^{b}: se 0.008 – 0.010, ^{c}: se 0.120 - 0.300

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Objective of this study

- **Genome-wide Association Study (GWAS) for piglet survival**
  - in a Landrace (LR) and a Large White (LW) population

- **Piglet survival traits:**
  - Birth weight
  - Intermediate weight
  - Stillbirth


Allaboutfeed.net

➡ **Aim: Identification of relevant genetic markers and candidate genes**

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Investigated animals, traits and genotypes

- 5´662 animals with genotypes, born between 2015 and 2017
- Birth weight
  - recorded immediately after birth
  - LR: 2´808 and LW: 2´854
  - LR: 1.44kg (± 0.33) and LW: 1.41kg (± 0.31)
- Intermediate weight
  - recorded between 2nd to 3rd week of life
  - LR: 1´864 and LW: 1´902
  - 5.14kg (± 1.14) and LW: 4.53kg (± 1.22)

Quality control genotypes:
Call Rate > 95%, MAF > 5%, No. sig. HWG < 0.01
LR: 37´407 and LW: 38´717

Pictures: BHZP GmbH

Genome-wide association study (GWAS)

- normal distributed traits: birth weight and intermediate weight

$$y_{ijkl} = \mu + S_j + G_k + L_l + \beta_1 TN_{ijkl} + \beta_2 age_{ijkl} + \delta_1 SNP_{ijkl} + e_{ijkl}$$

y_{ijkl}	Birth weight	Intermediate weight
μ	Population mean	
S_j	Season	
G_k	Gender	
L_l	Litter number	
TN	Number total born	Number piglets after cross fostering
age	-	Age at weighting
SNP	Investigated SNP {-1, 0, 1}	
β, δ	Regression coefficients of covariable or SNP	
e_{ijkl}	residuals	

Linear model:

- normal distribution

Likelihood ratio test:

- Genomic control
- Bonferroni correction

GWAS results for weight traits

- Birth weight (direct genetic effects)
  - LR: 2 chromosome-wide significant SNPs on SSC 1 and SSC 15
  - LW: 0 associations

➡ **Keep in mind:** Important contribution of maternal genetic and litter effects (Heuß et al. submitted)

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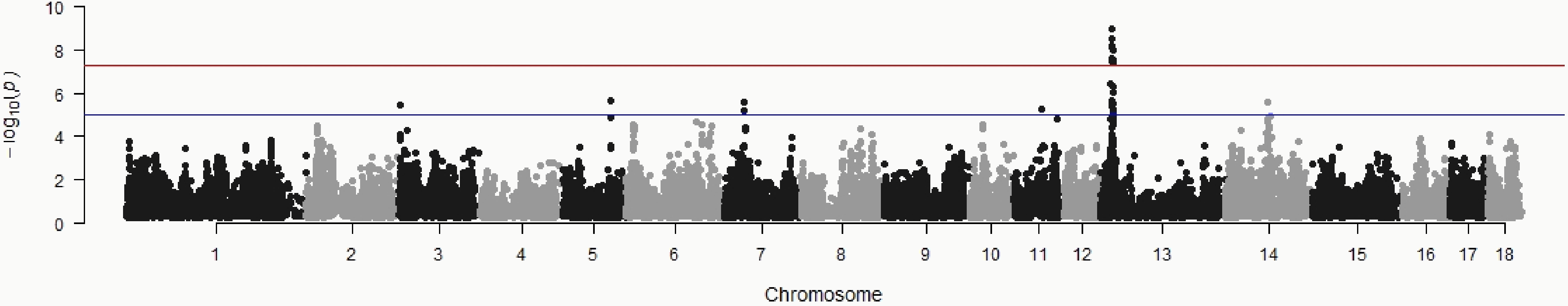
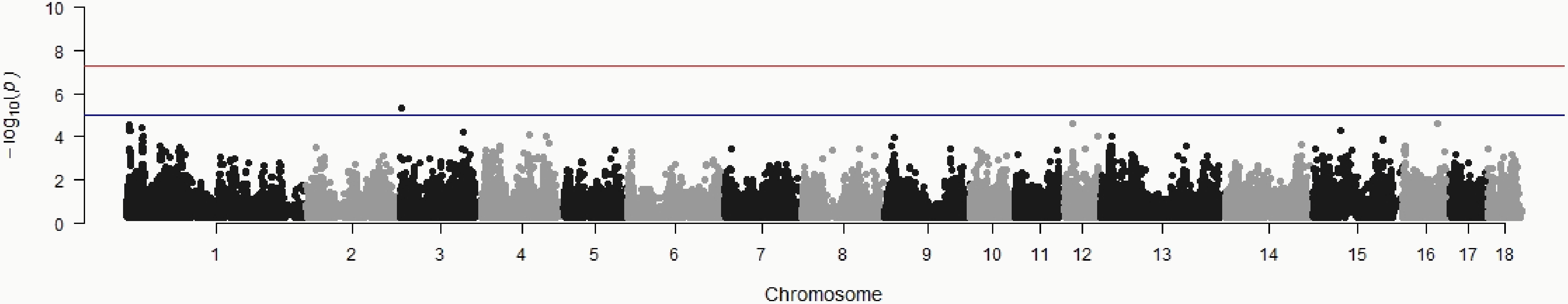
- Intermediate weight
  - LR: 47 significant associations
  - LW: 3 significant associations

Intermediate weight

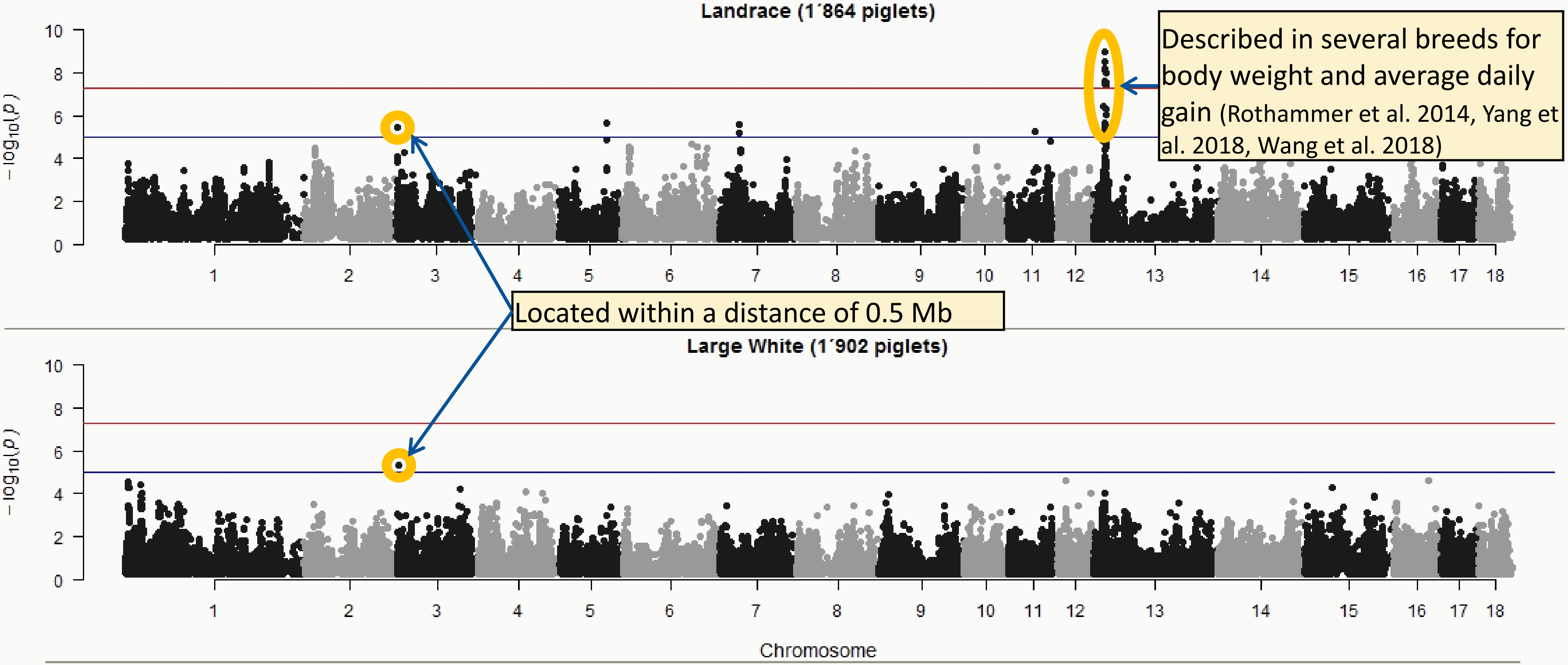
Landrace (1´864 piglets)



Large White (1´902 piglets)



Intermediate weight



Described in several breeds for body weight and average daily gain (Rothammer et al. 2014, Yang et al. 2018, Wang et al. 2018)

Located within a distance of 0.5 Mb

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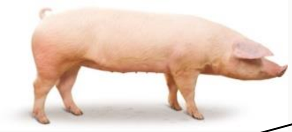
Experimental set-up for stillbirth (pigFit project)



2 x 250 **dams**

1-2 **dead piglet**

full sibs

N=2x750

2 **piglets born alive** (♂/♀)

Blood/tissue samples (N=1500/500)

BS0: Sows (Ø 7d p.p.)
BS1: Piglets (Ø 35d p.p.)

Genotyping (N=2´000 + 3´662)

Extended by animals of the routine genotyping

DNA isolation from blood and tissue samples

Genotyping with porcineSNP60 Illumina BeadChip

Pictures: BHZP GmbH

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Analysis of stillbirth: fullsibs

		Landrace		Large White	
No. Piglets		Born alive	Stillborn	Born alive	Stillborn
		654	285	564	239
No. litter		271		217	
No. SNP		37´712		38´859	
Birth weight	Average (kg ± sd)	1.46 (±0.30)	1.08 (±0.35)	1.43 (±0.28)	1.08 (±0.35)
	Range (kg)	0.40 – 2.26	0.21 – 2.01	0.64 – 2.34	0.24 – 1.87

Genome-wide association study (GWAS)

Binary trait: stillbirth

$$y_{ijkl} = \mu + S_j + G_k + L_l(bw_{ijkl}) + \beta_1 TN_{ijkl} + \delta_1 SNP_{ijkl} + e_{ijkl}$$

y_{ijkl}	**Stillbirth**
μ	Population mean
S_j	Season
G_k	Gender
$L_l(bw)$	Birth weight nested within litter number
TN	Number total born
SNP	Investigated SNP {-1, 0, 1}
β, δ	Regression coefficients of covariable or SNP
e_{ijkl}	residuals

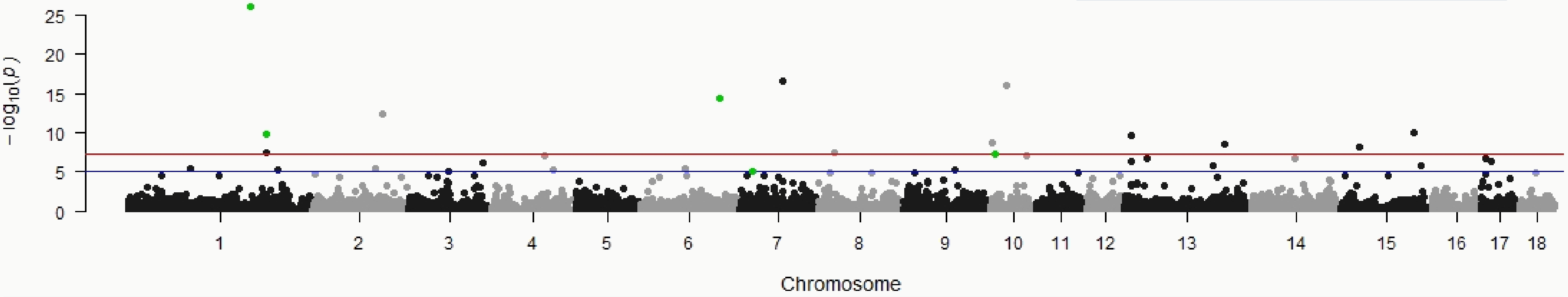
Generalized linear model:

- binominal distribution
- logit-function

$\mathbf{X^2} - \boldsymbol{Test}$

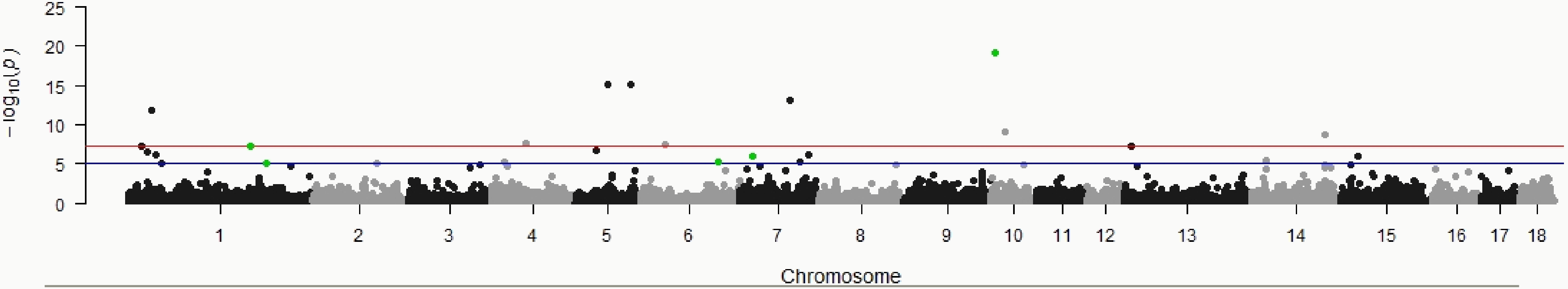
- Genomic control
- Bonferroni correction

GWAS of the binary trait: stillbirth



Landrace (654 born alive, 285 born dead)

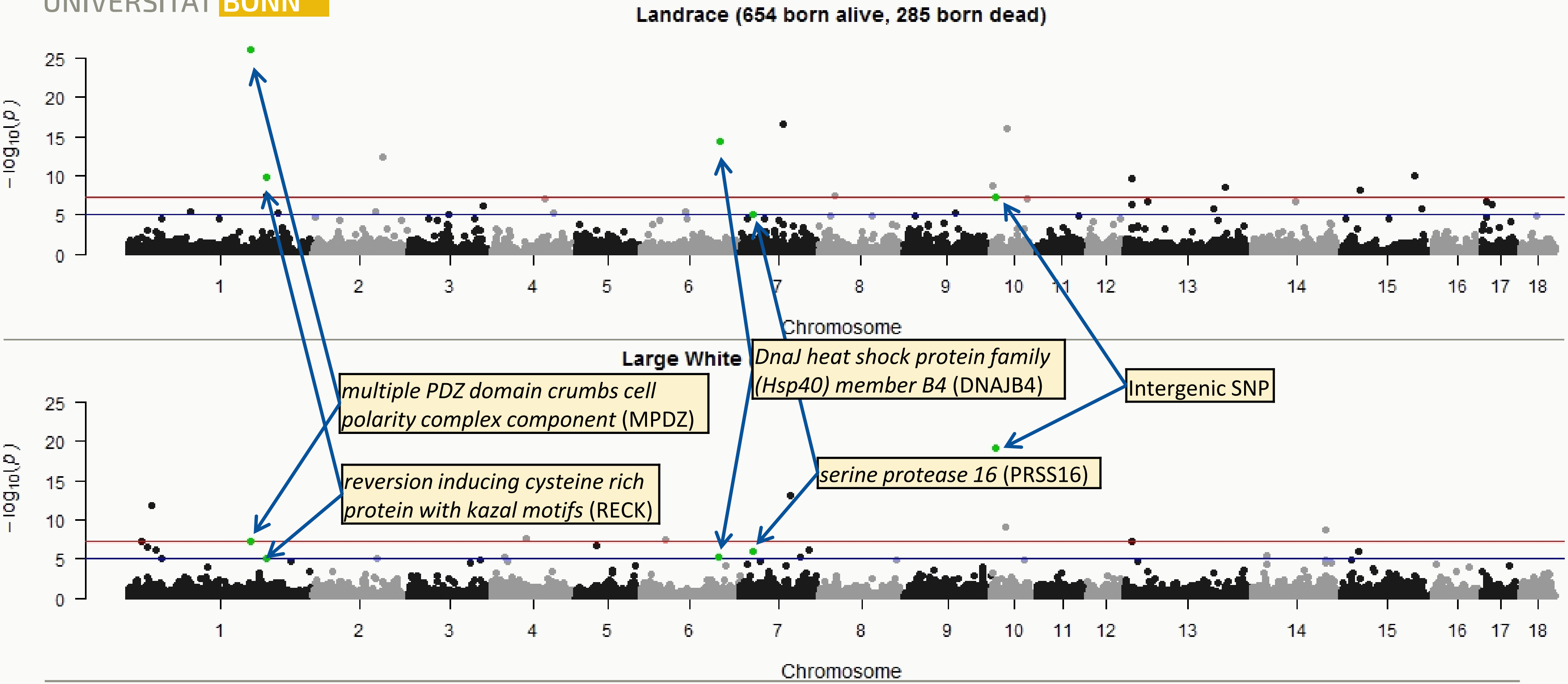
41 significant associations



Large White (564 born alive, 239 born dead)

31 significant associations

GWAS of the binary trait: stillbirth



Landrace (654 born alive, 285 born dead)

Large White

multiple PDZ domain crumbs cell polarity complex component (MPDZ)

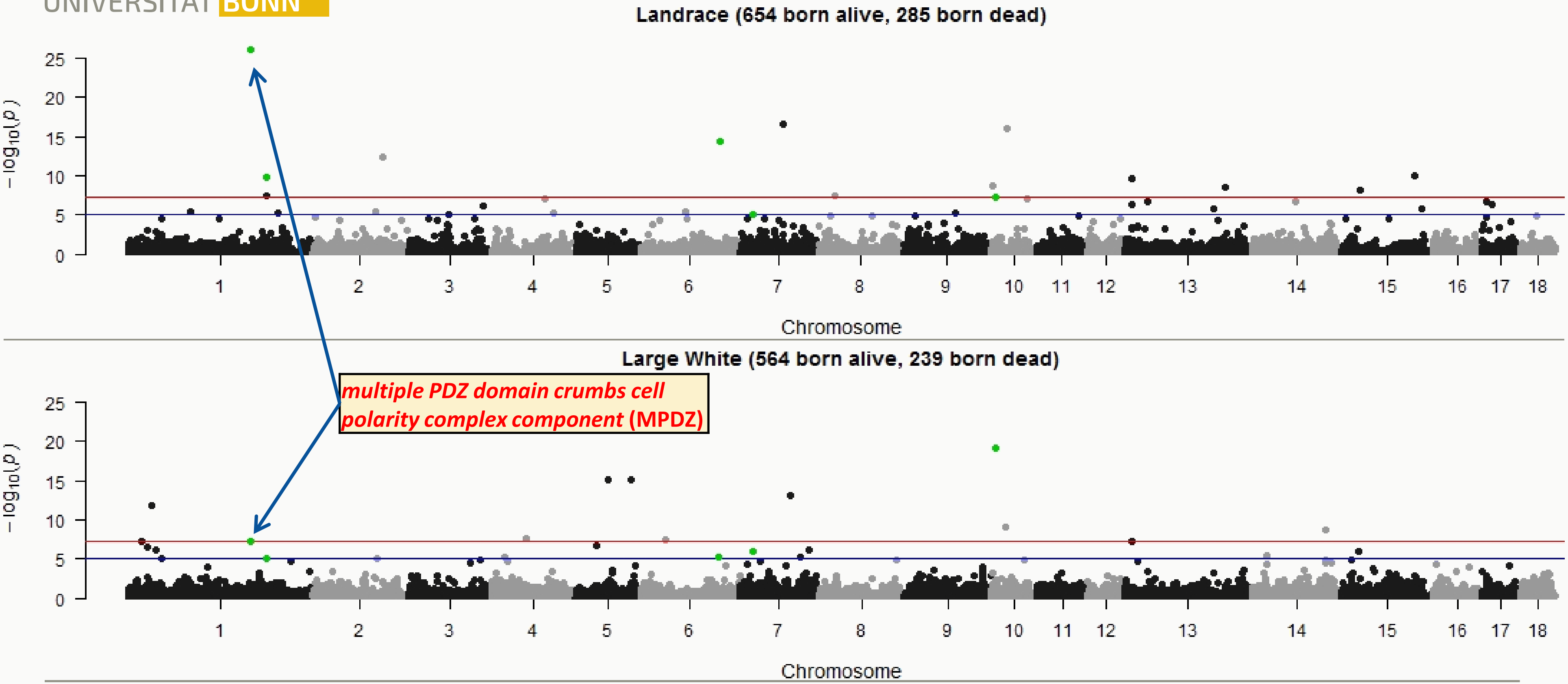
reversion inducing cysteine rich protein with kazal motifs (RECK)

DnaJ heat shock protein family (Hsp40) member B4 (DNAJB4)

serine protease 16 (PRSS16)

Intergenic SNP

GWAS of the binary trait: stillbirth



Landrace (654 born alive, 285 born dead)

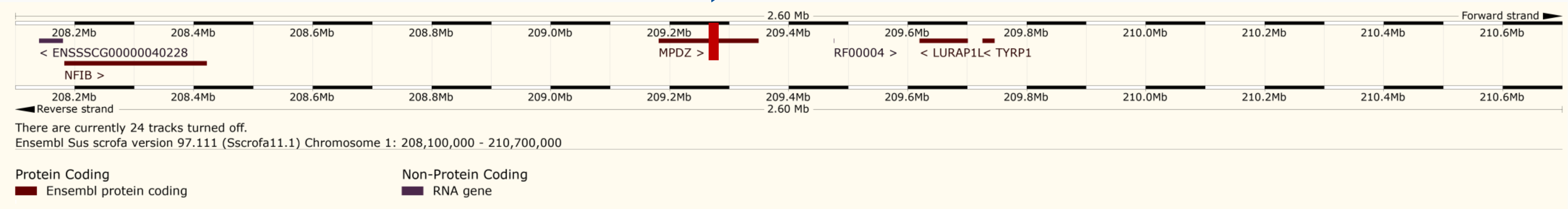
Large White (564 born alive, 239 born dead)

multiple PDZ domain crumbs cell polarity complex component (MPDZ)

Candidate gene: MPDZ

- *multiple PDZ domain crumbs cell polarity complex component*
  - Involved in the *“notch signaling pathway”*
  - Important for embryonic tissue development (animal specific)
  - Autosomal recessive diseases in human and mouse (Felder et al. 2017)

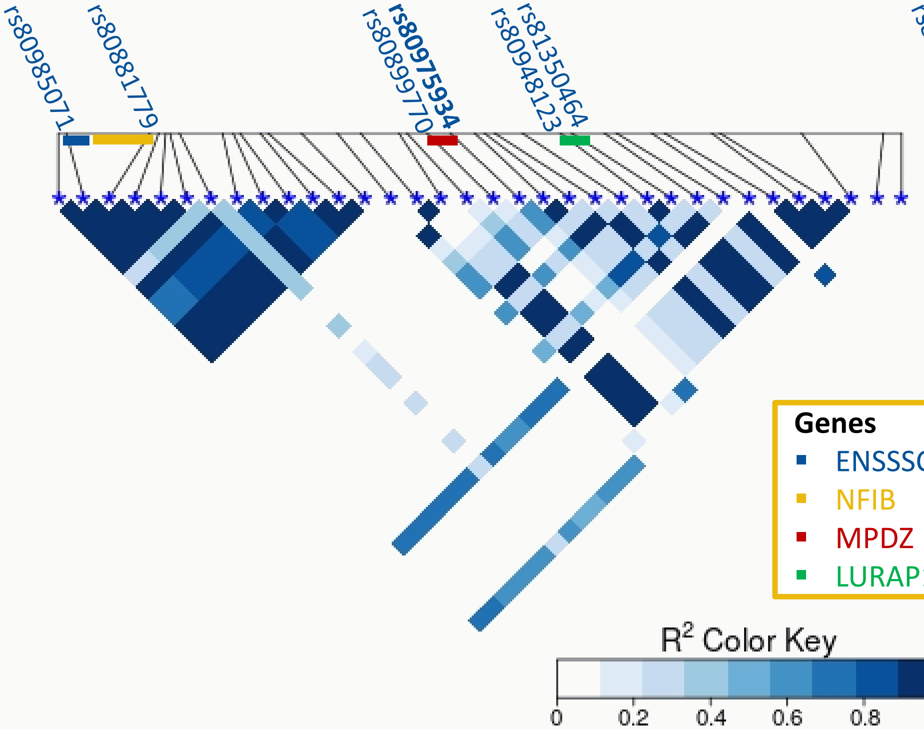
***multiple PDZ domain crumbs cell polarity complex component* (MPDZ)**



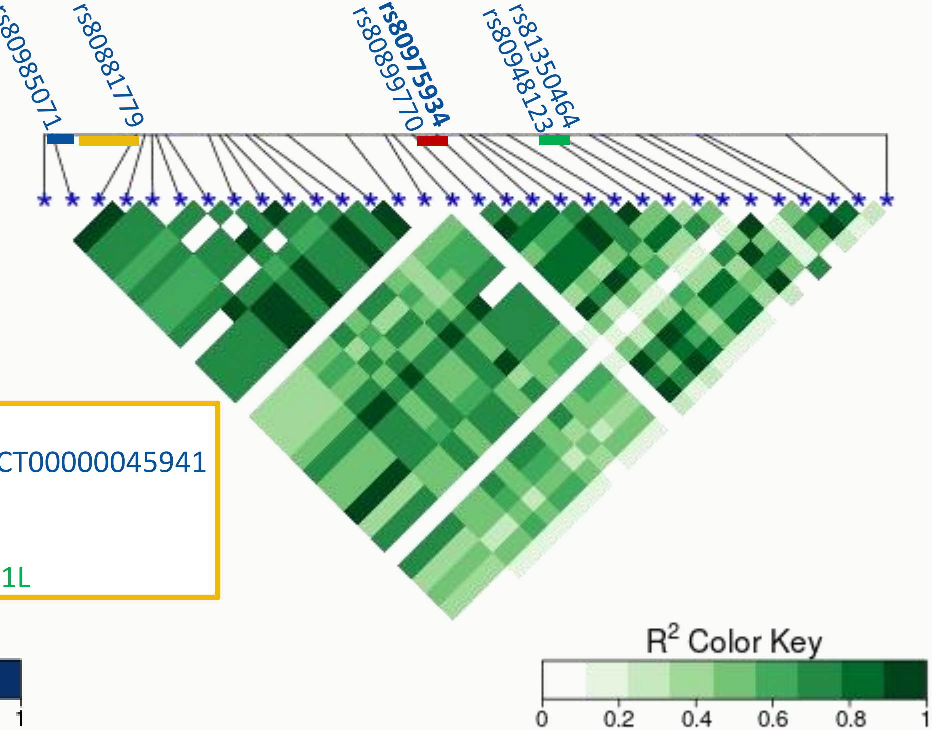
There are currently 24 tracks turned off.
Ensembl Sus scrofa version 97.111 (Sscrofa11.1) Chromosome 1: 208,100,000 - 210,700,000

Linkage disequilibrium on SSC 1 208.1 Mb – 210.7 Mb (2538.4 kb)

Landrace (32 SNP)



Large White (34 SNP)



Genes

- ENSSSCT00000045941
- NFIB
- MPDZ
- LURAP1L

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Summary and conclusion

- Two significant associations for birth weight
  - Polygenic inherited
  - Strong influences of maternal effects (Heuß et al. 2019)

- One interesting genome-wide significant QTL region on SSC 13 for intermediate weight in LR

- Detection of novel (five) interesting associations for stillbirth
  - Relevant in both breeds
  - MPDZ: Involved in autosomal recessive diseases in human

Ongoing steps

- Inclusion of the maternal genetic effect in the analysis of birth weight
- Investigation of maternal reproduction traits
  - (Abstract page 410, Theatre Session 40, Brinke et al.)
- Fine mapping of the identified region using sequence data
  - (Abstract page 255, Theatre Session 18, Dauben et al.)
- Implementation of the identified genetic marker within the breeding program

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Thank you for your attention!

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Bundesanstalt für
Landwirtschaft und Ernährung

rentenbank

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