

A Large X-Chromosomal Haplotype is Associated with Small Body Size of Minipigs



C. Reimer¹, A.R. Sharifi, C.-J. Rubin², S. Weigend³, K.-H. Waldmann⁴, O. Distl⁴, S.D. Pant⁵, M. Fredholm⁵, H. Simianer¹

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² Science for Life Laboratory, Department of Medical Biochemistry and Microbiology, Uppsala University, Sweden

³ Institute of Farm Animal Genetics of the Friedrich-Loeffler-Institut, Neustadt-Mariensee, Germany,

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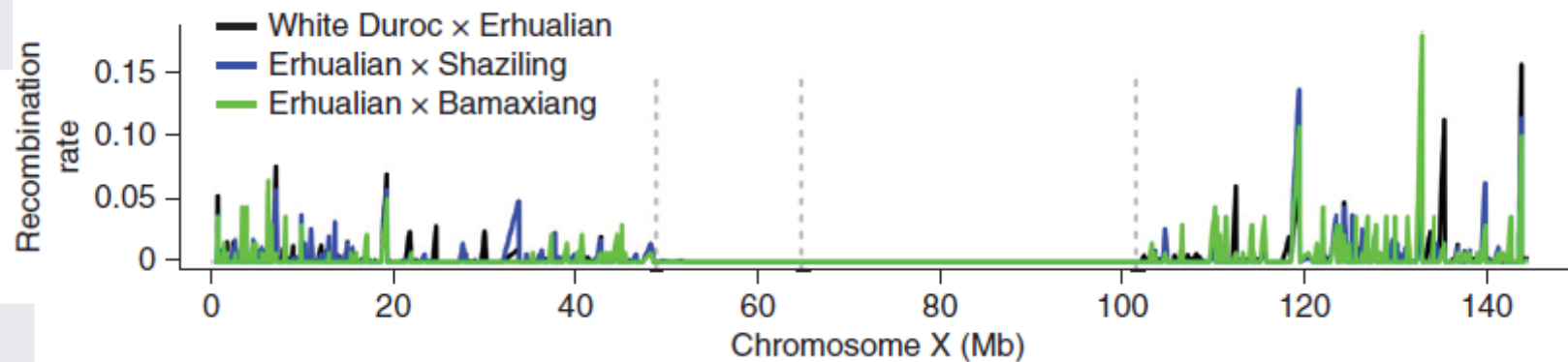
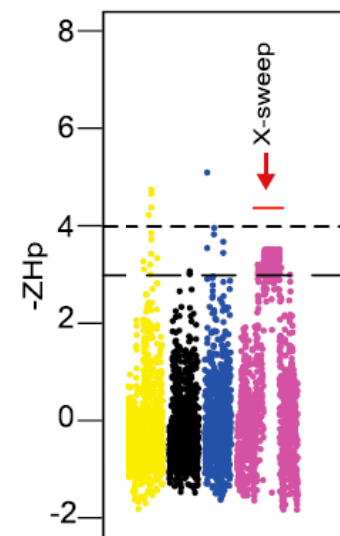


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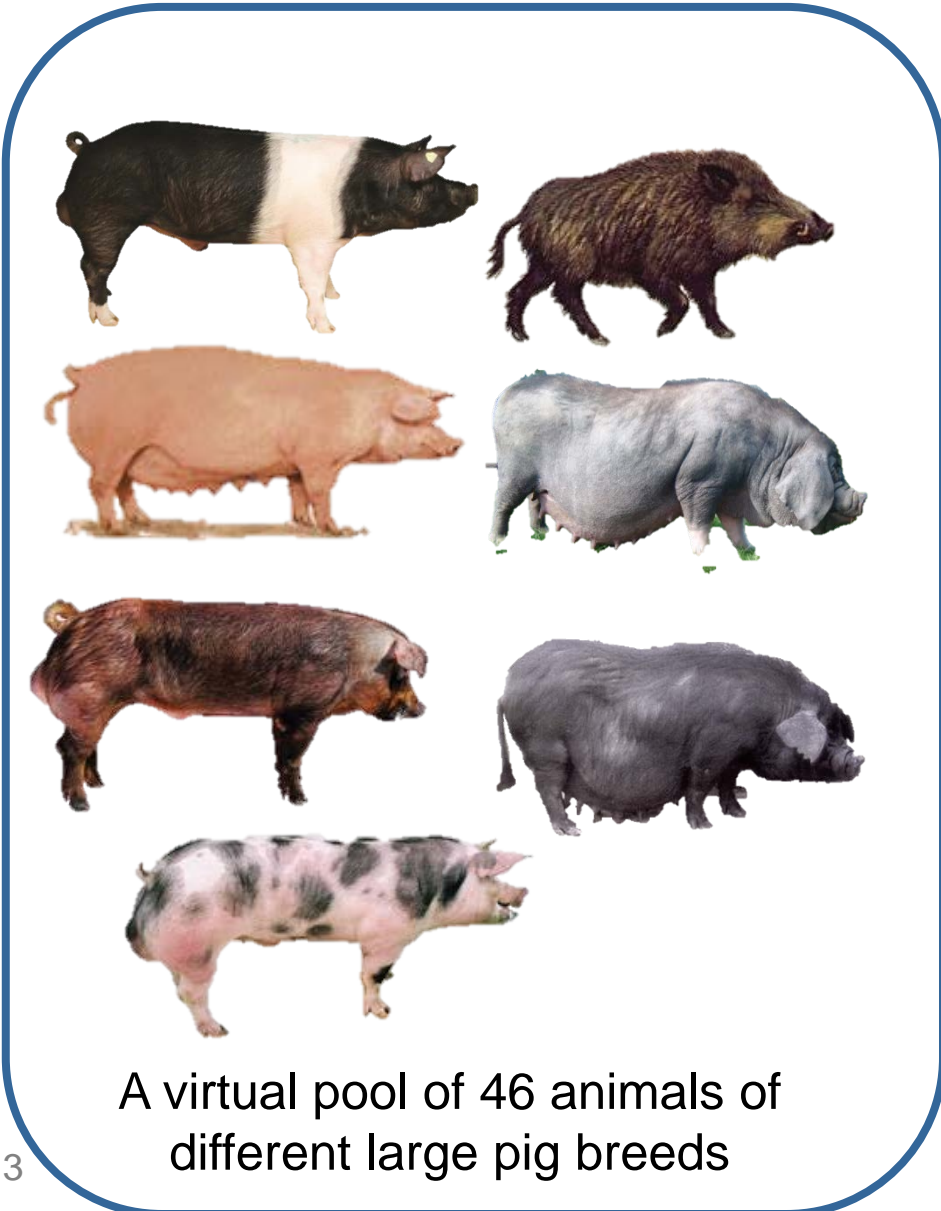


- Large selective sweep on chromosome X between 50 and 100 Mb (Rubin et al., 2012)
- Highly differentiated between European and Asian pig breeds
- Only three different haplotypes (Ai et al., 2015)

➔ What is the haplotypic state in the Minipig and does it influence body size?



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A virtual pool of 46 animals of different large pig breeds

VS.



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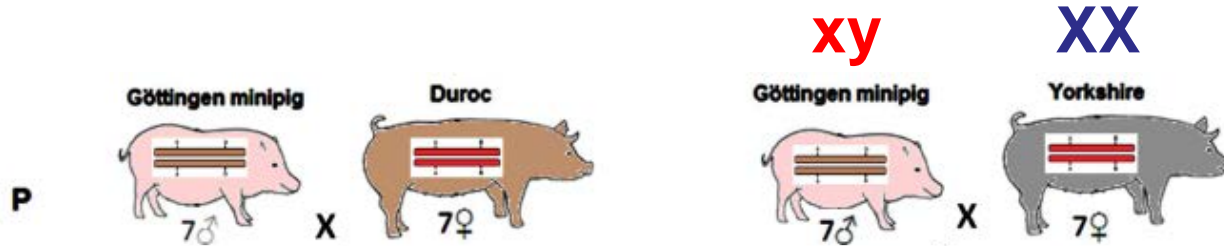


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Analysis of SNP array data



Chromosome of

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Statistical modelling

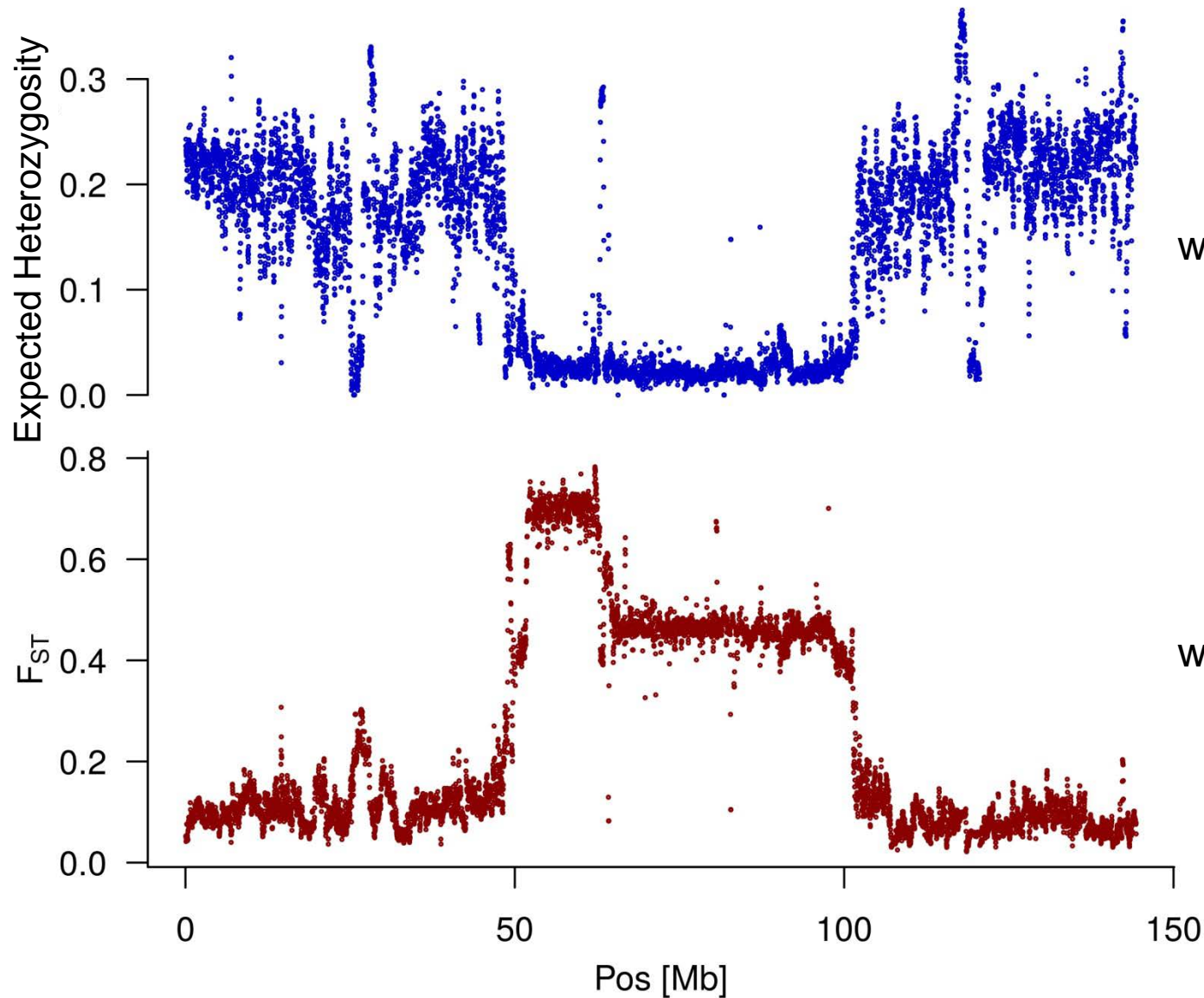


Linear model, Proc GLM, SAS (SAS Institute, Cary, NC)

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Signature of selection on Chromosome X



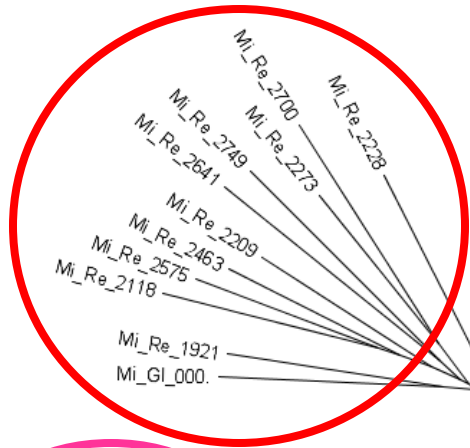
Minipig
without Wushizhan

Minipig
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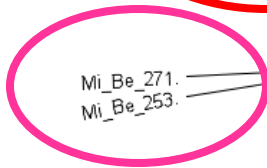
Phylogeny – Genome wide



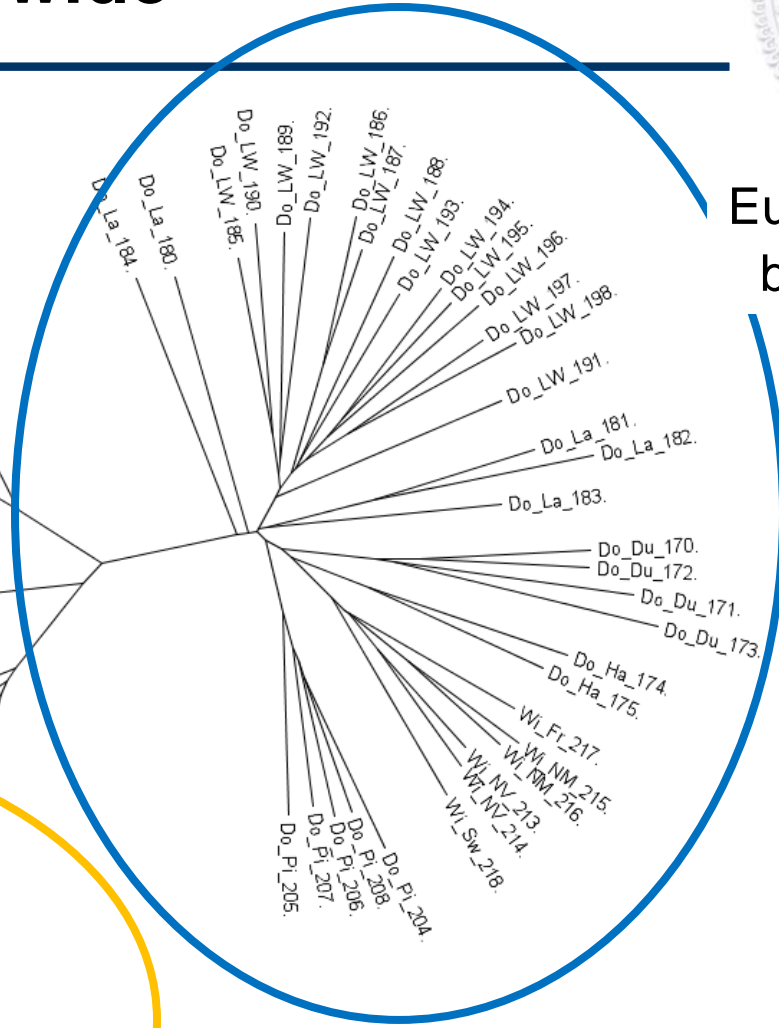
Goettingen
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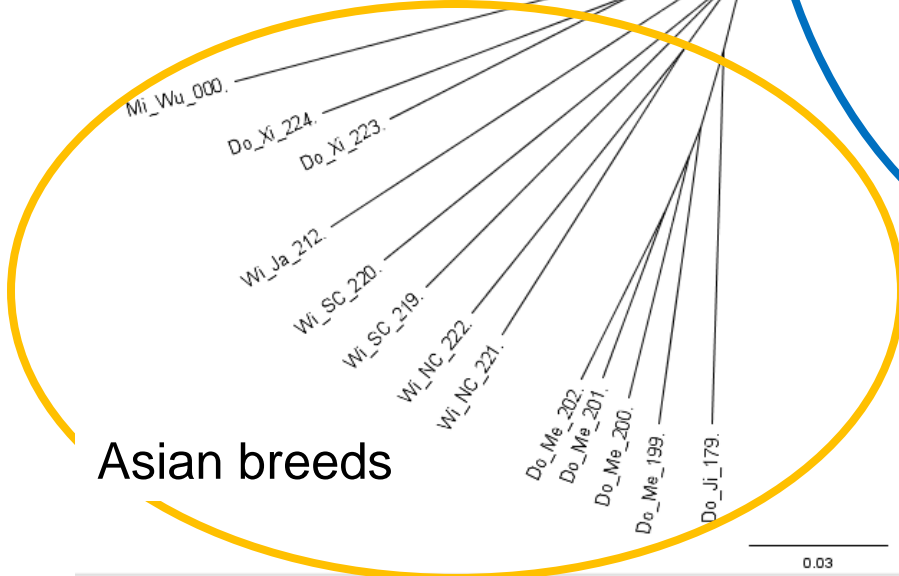
Berlin
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European
breeds



Asian breeds



Software: PHYLIP (Felsenstein,1989)

0.03

Phylogenie – X:53-61

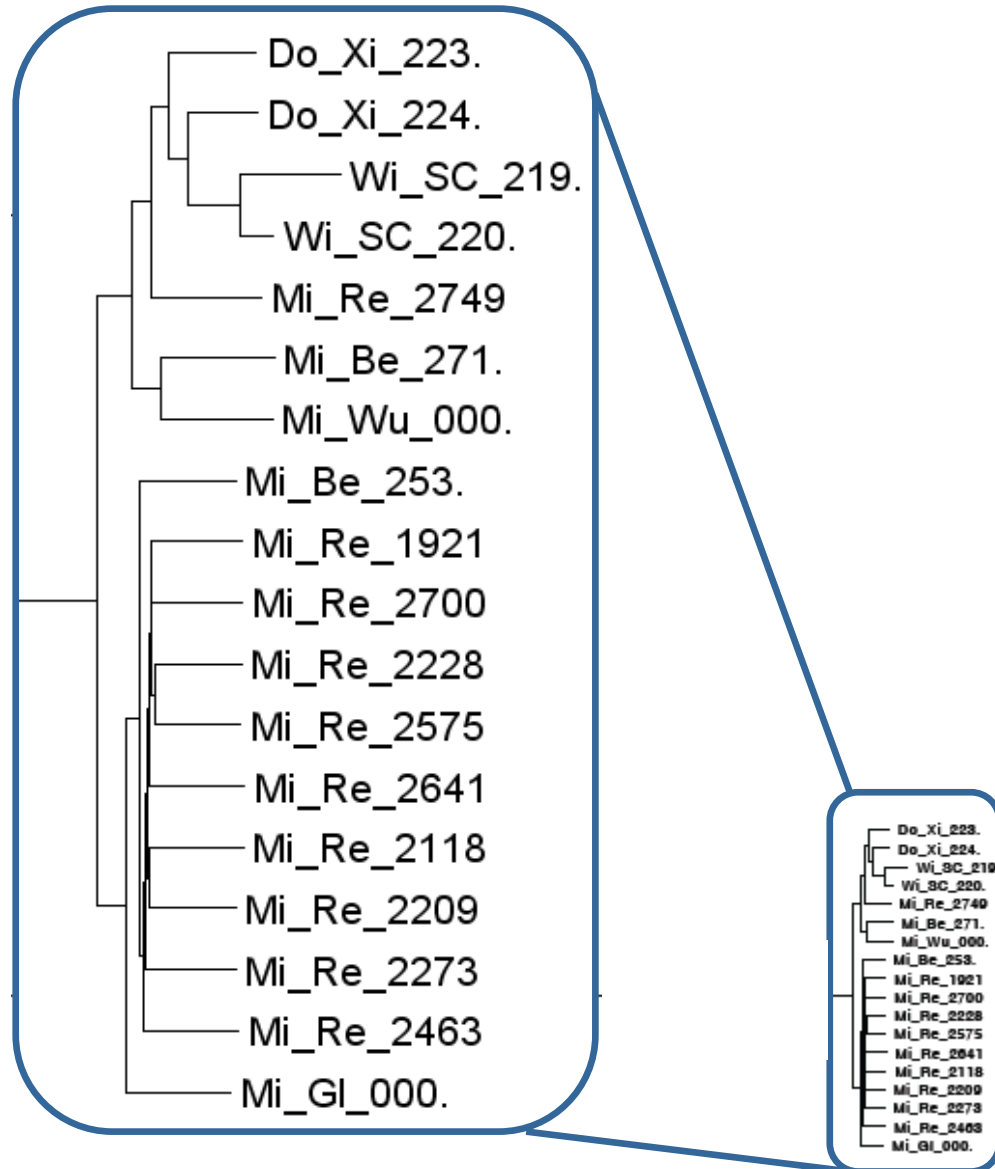


Xiang

South-chinese wild boar

Wushizhan
Berlin Minipig

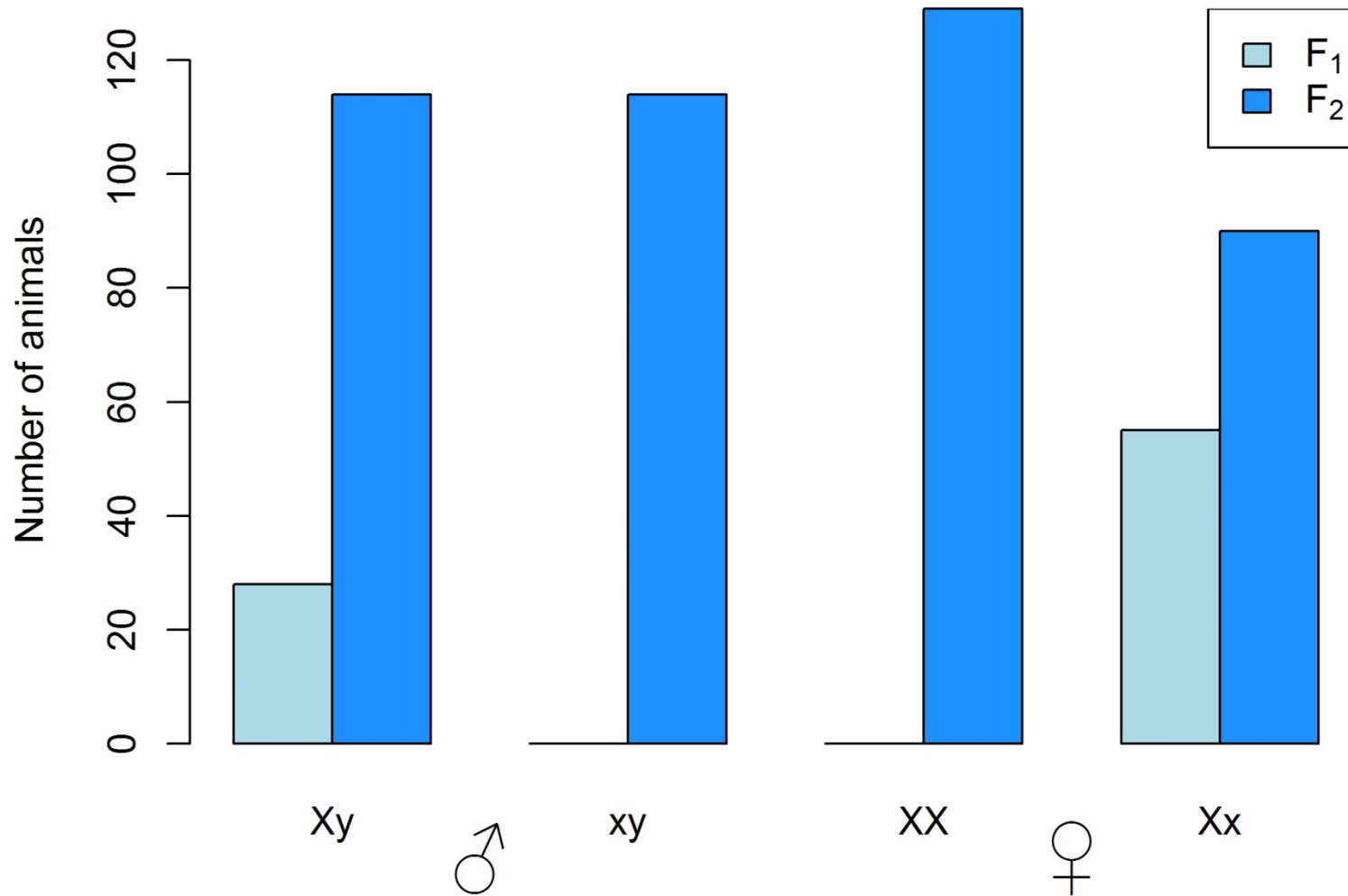
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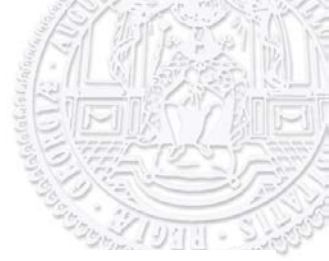
Distribution of haplotypes in cross-breeds



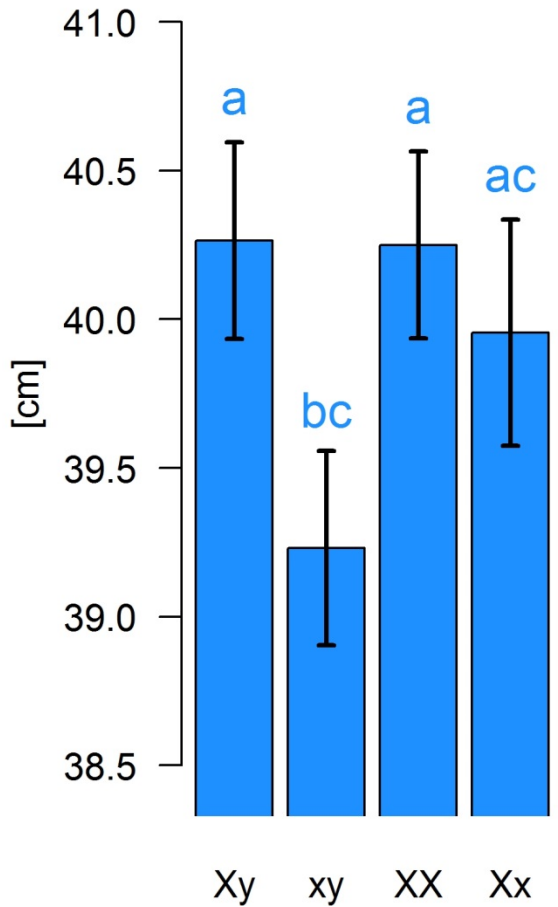
- Genotypes segregate as expected in F_1 and F_2



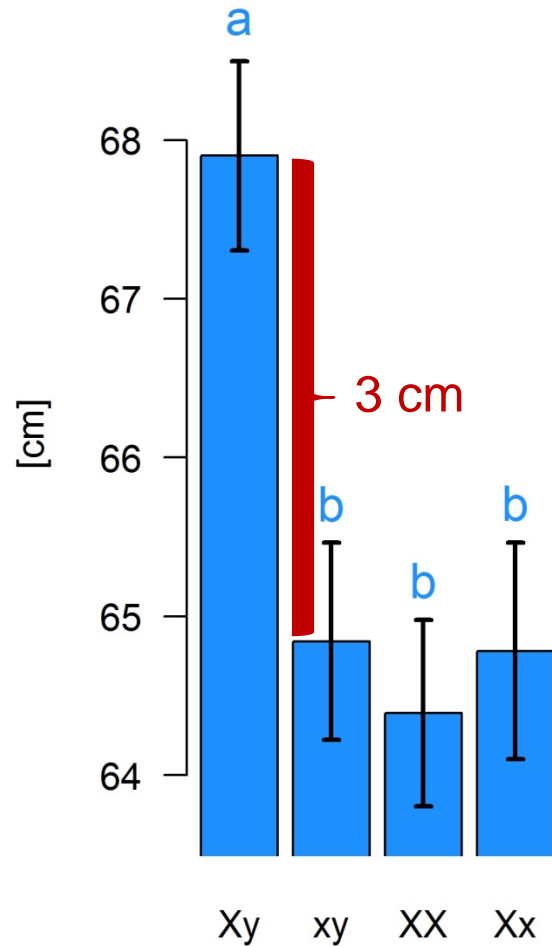
Significant haplotype effects



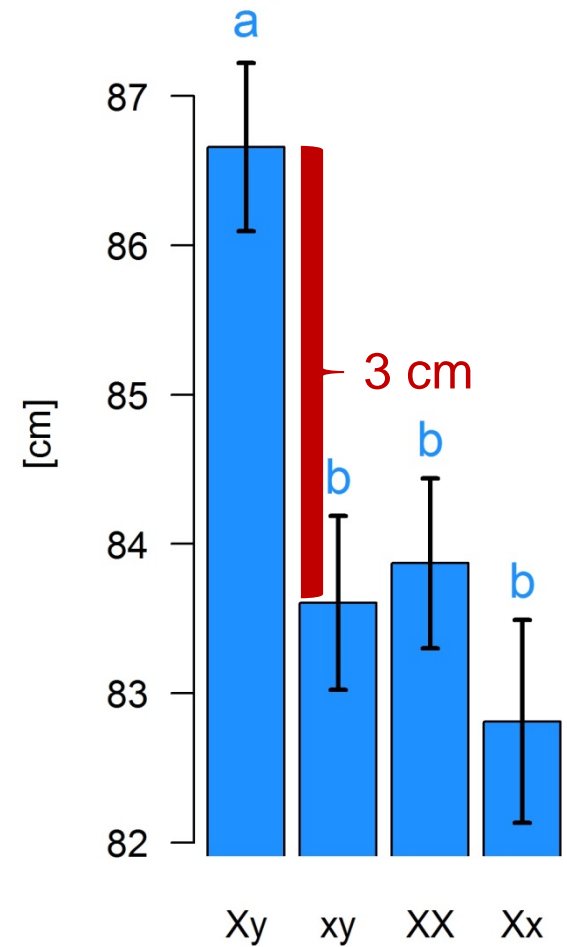
Height at scanning



Height at slaughter



Length at slaughter



Conclusion



- All minipigs carry the same X-chromosomal haplotype
 - Female cross-breds can carry both haplotypes
 - Boars carrying the minipig haplotype are significantly smaller than boars carrying the large pig haplotype (3% shorter and 3% less high)
- The X-chromosomal sweep region explains a considerable part of the total variability of body size**

Acknowledgement



Thank you for your attention!



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References



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- Gaerke C, Ytournal F, Sharifi a. R, Pimentel ECG, Ludwig A, Simianer H. 2014. Footprints of recent selection and variability in breed composition in the Göttingen Minipig genome. *Anim Genet* 381–391.
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- Reimer C, Rubin C-J, Weigend S, Waldmann K-H, Distl O, Simianer H. 2014. The Minipig Genome Harbors Regions of Selection for Growth. *10th World Congr Genet Appl to Livest Prod Proceedings; Vancouver, BC, Canada*

Filtering with GATK



- Sequencing depth lower 90 X or higher 840 X
- BaseQualityRS lower -5.5 or higher 5.5
- MappingQualityRS lower -11 or higher 11
- ReadPositionRankSum lower -6
- FisherStrand higher 45
- Mapping Quality lower 30
- SNP Clusters with more than 5 SNP within 20 Basepairs

- Individual filtering
 - Genotyping Quality lower 20
 - Depth higher lower 5

Used Samples



Breed	Individual sequence		DNA pool sequence	
Duroc	4	6X		
Hampshire	2	6.5X		
Jiangquhai	1	8.2X		
Large White	14	6.5X		
Landrace	5	6.4X		
Meishan	4	6.8X		
Pietrain	5	5.6X		
European Wildboar	6	6.4X		
Asian Wildboar	5	6.3X		
Göttingen Minipig	11	12.8X		
Berlin Minipig	2	13.9X	1 (10)	13.1X



Re-sequenced breeds



Whole genome re-sequencing (Illumina HiSeq2000)

	Large pigs	Minipigs
Wild boars	European Wild boars Asian Wild boars	
Hausschweine	Land Race Hampshire Duroc Pietrain Jiangquhai Large White Meishan	Goettingen Minipig (GMP) MiniLEWE (Berlin) Xiang Wuzhishan MiniLEWE-Pool
	46 Individuals	16 Individuals 1 DNA Pool of 10

Publically available WGS data:

Rubin et al., 2012; Fang et al., 2012; Vamathevan et al., 2013

Distribution of haplotypes in cross-breeds



- Distribution of F_1 and F_2 follow expectation

F_1	Sum	Boars	Sows	Sex	Boars	Sows	Sum	F_2
				Haplotype				
	28	28		XX, Xy	114	129	243	
	55		55	xX	0	90	90	
				xy	114	0	114	
	83	28	55	Sum	228	219	447	



	Mean	SD	min	max
Height at scan	39.93	4.39	24.00	55.00
Height at slaughter	65.3	5.05	45.0	79.0
Length at scan	48.56	5.91	34.50	69.00
Length at slaughter	84.16	6.21	65.00	108.00

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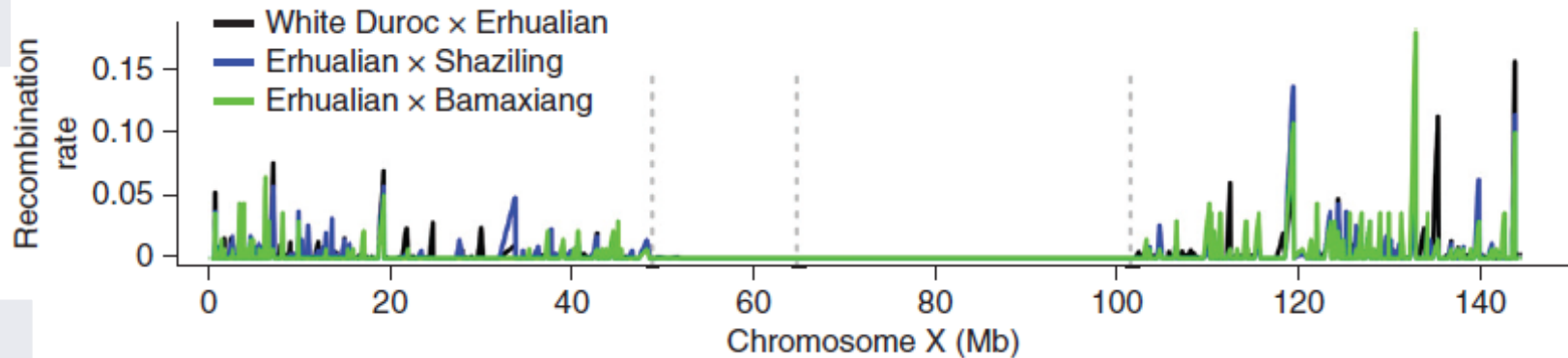
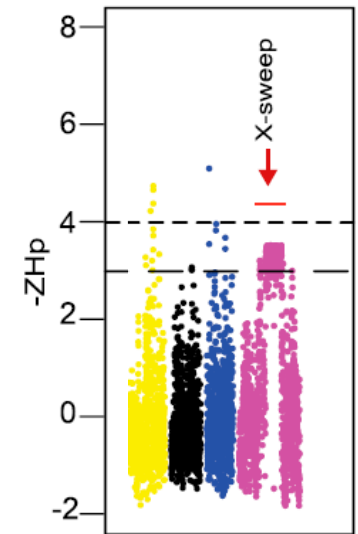
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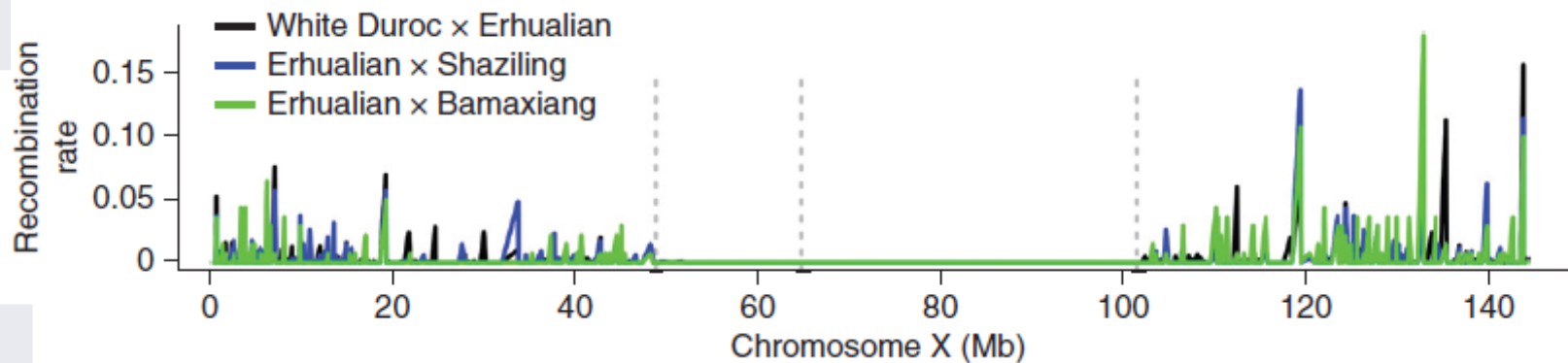
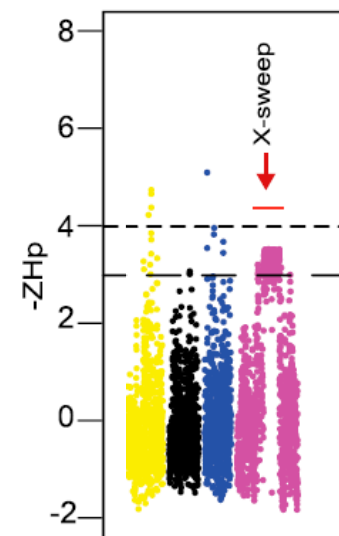
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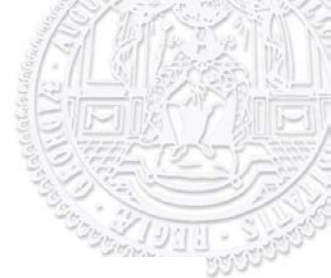
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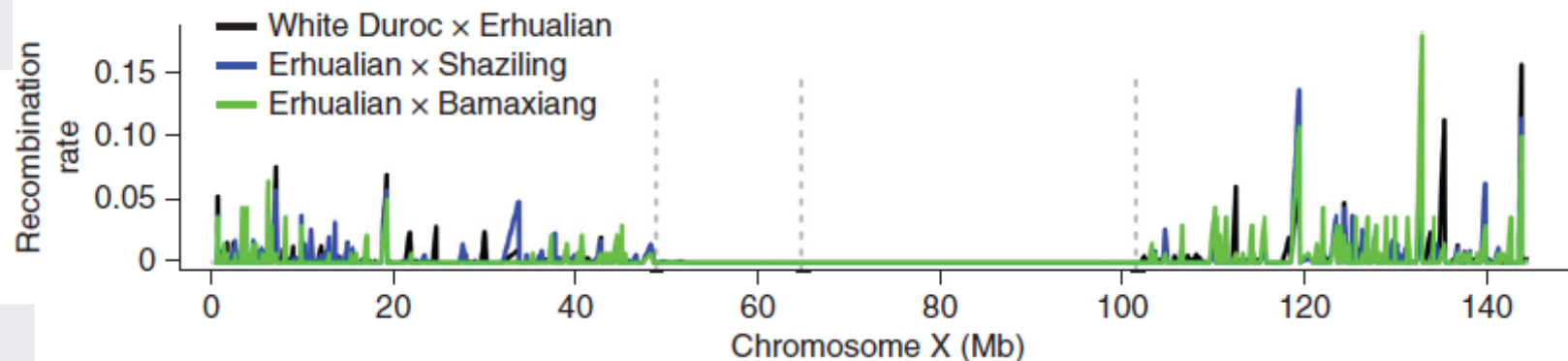
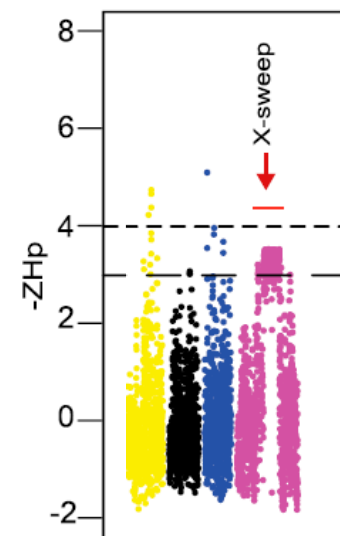


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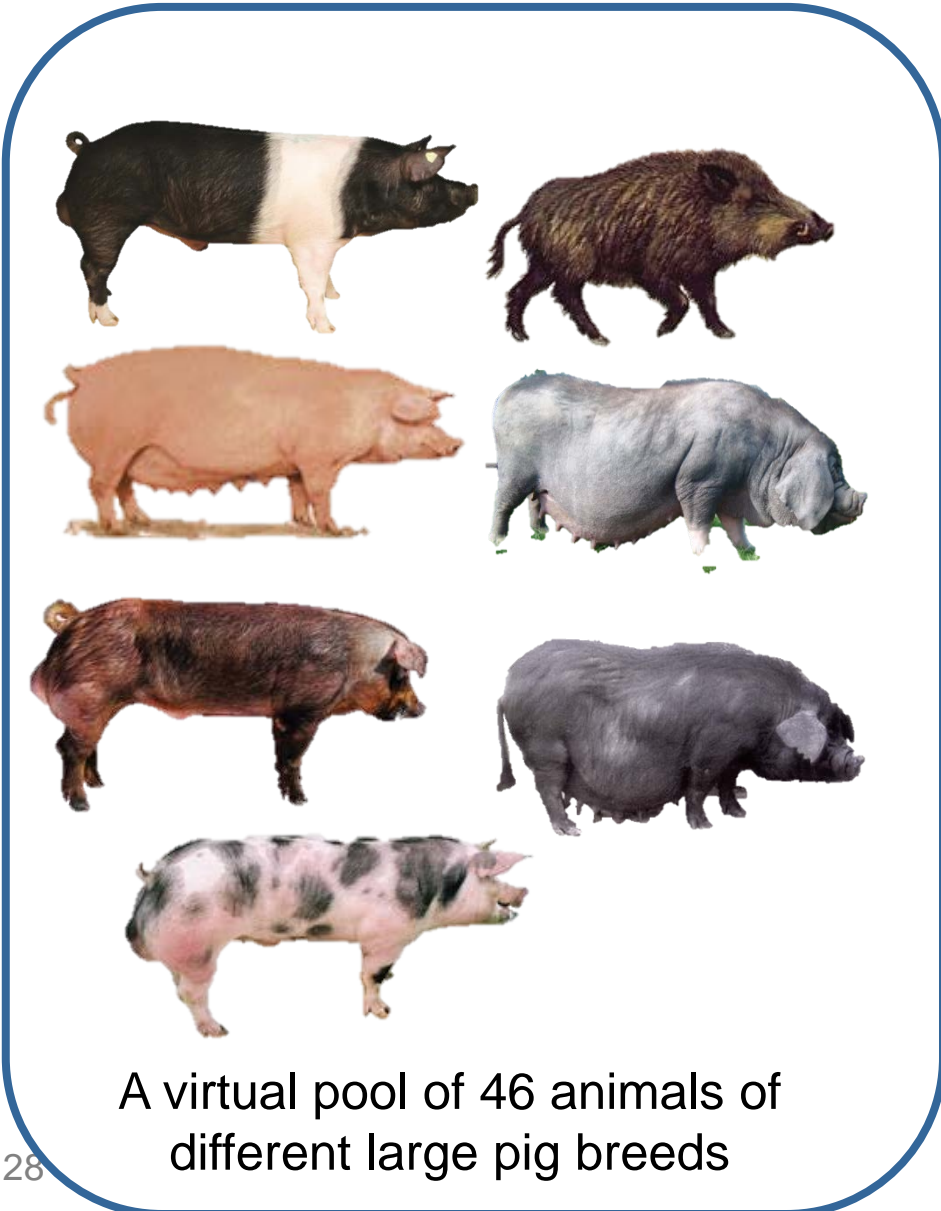


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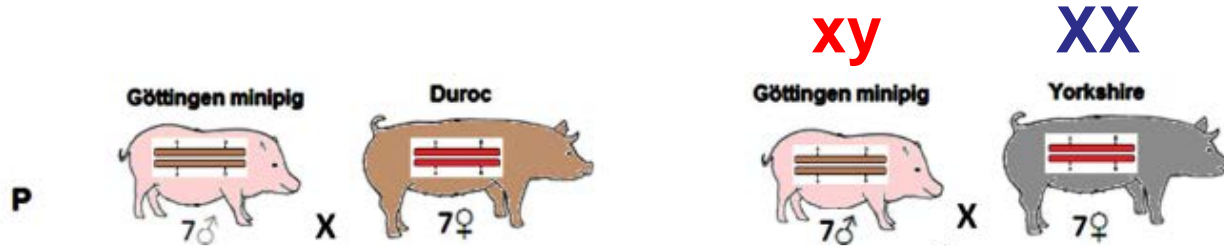


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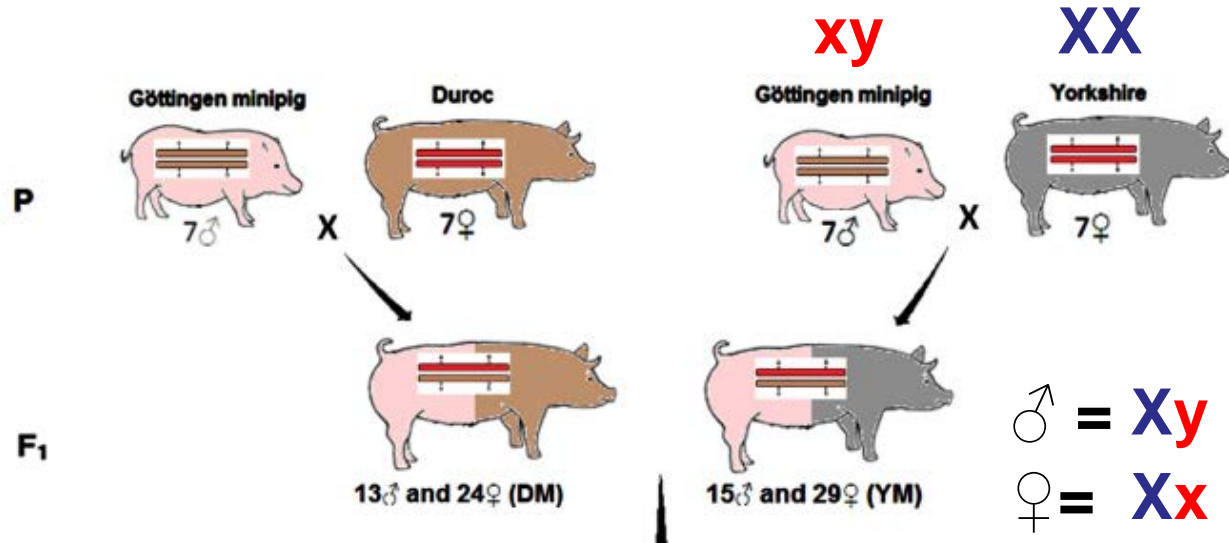
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Chromosome of

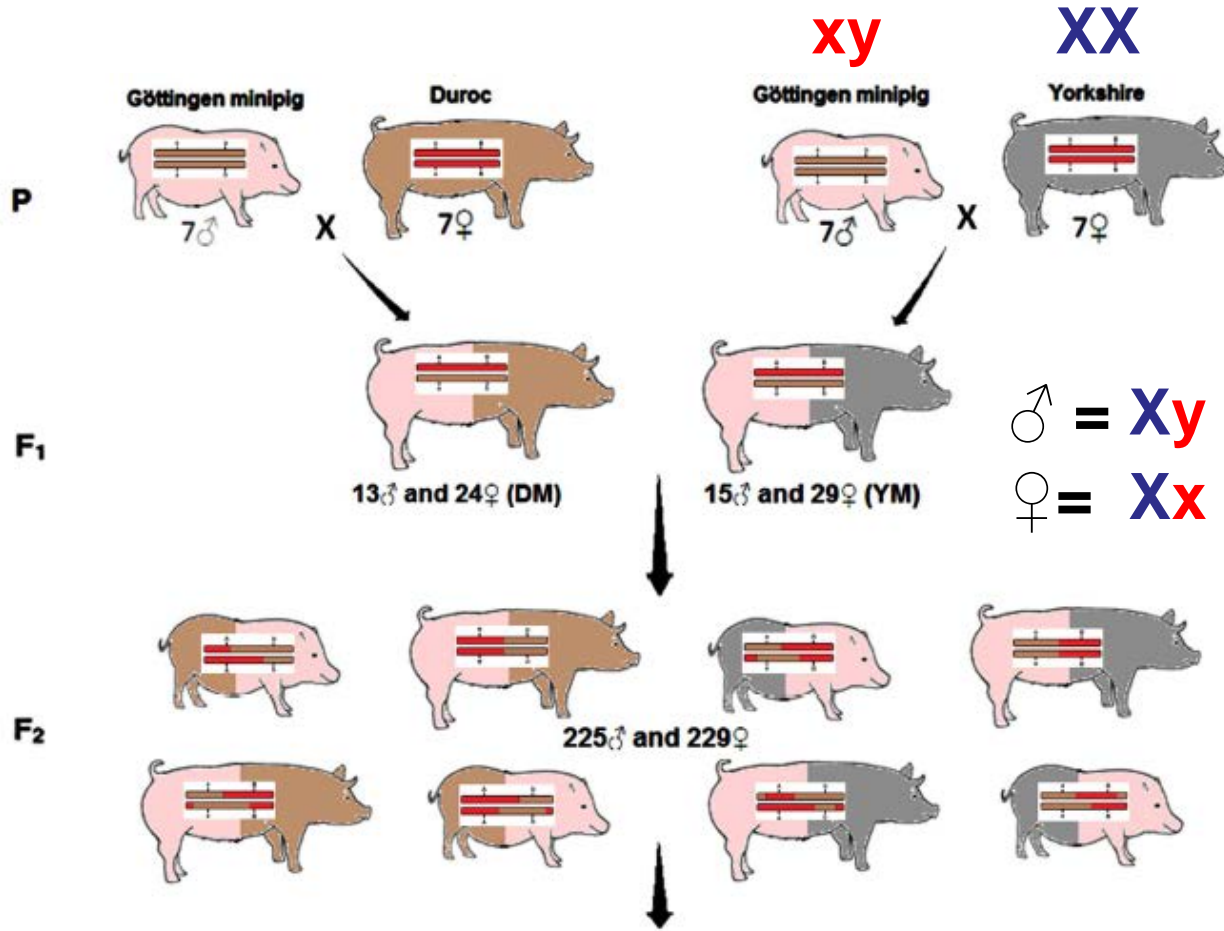
Large Pigs
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Analysis of SNP array data



Chromosome of
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Determination of the haplotypic state of F_2 animals

→ **XX, Xy = 1; Xx = 2; xy = 3**

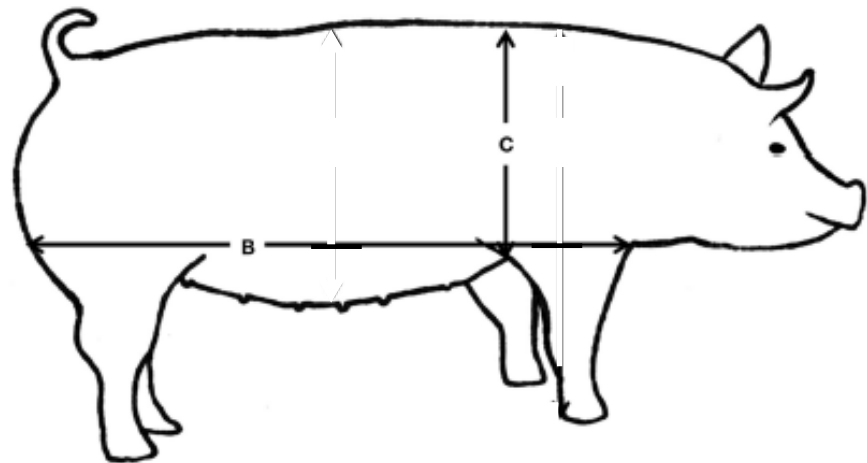
Statistical modelling



Linear model, Proc GLM, SAS (SAS Institute, Cary, NC)

$$y_{ijk} = B_i + S_j + b_1(A_{ij}) + b_2(A_{ij}^2) + H_k(S_j) + B_i * S_j + b_3(B_i * A_{ij}) + b_4(B_i * A_{ij}^2) + e_{ijk}$$

y_{ijk} Body length/ height
 B_i Breed of dam in P_0
 S_j Sex
 A_{ij} Age at recording
 H_k Haplotype state
 b_x Regression coefficients



Recording at	1) routine scanning	Ø 63 days
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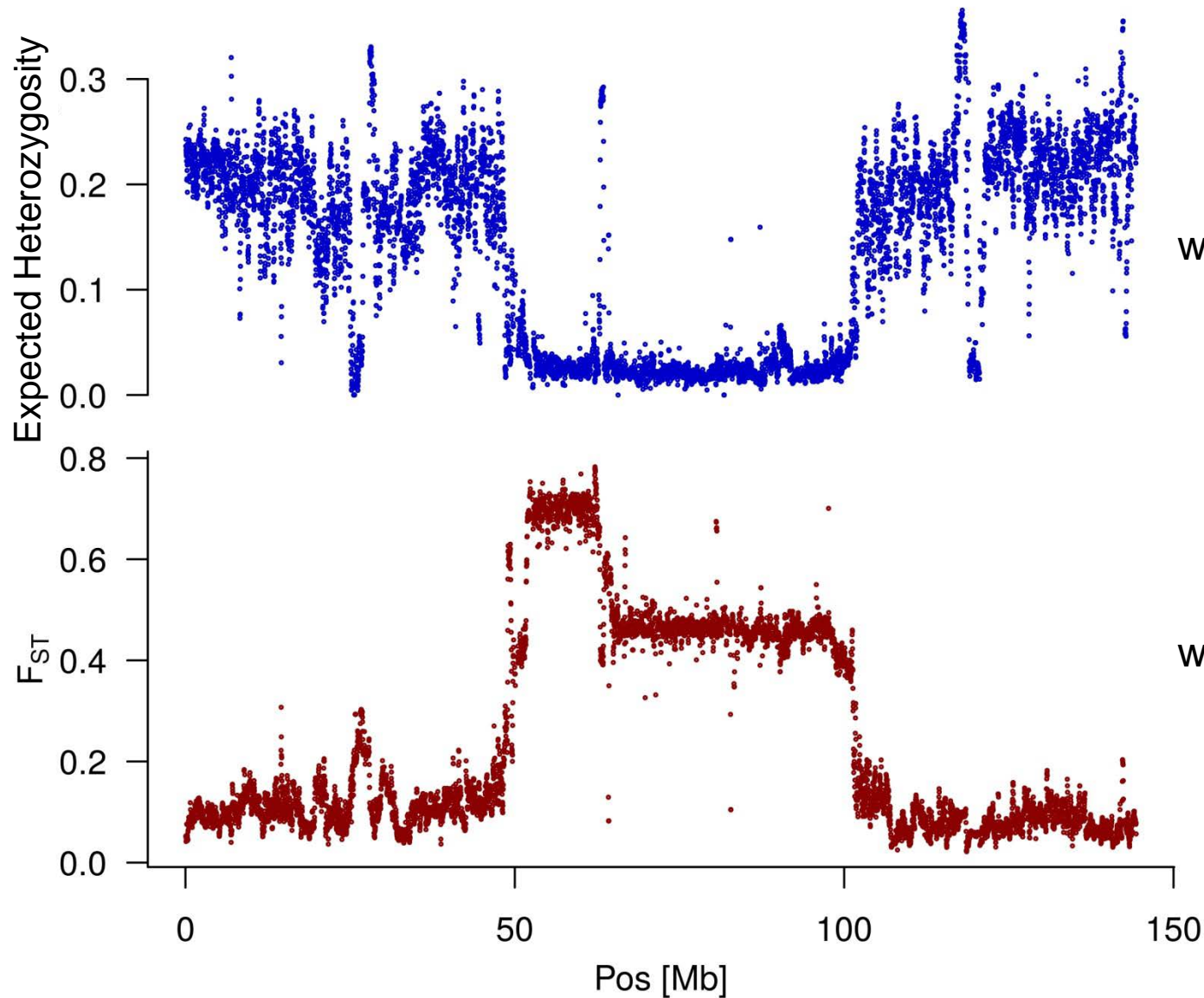


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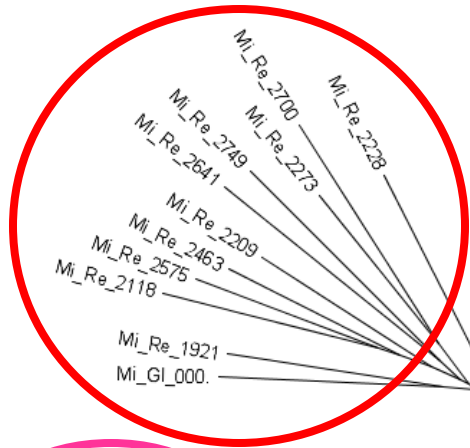
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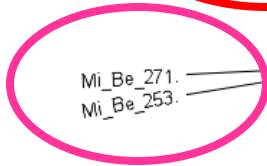
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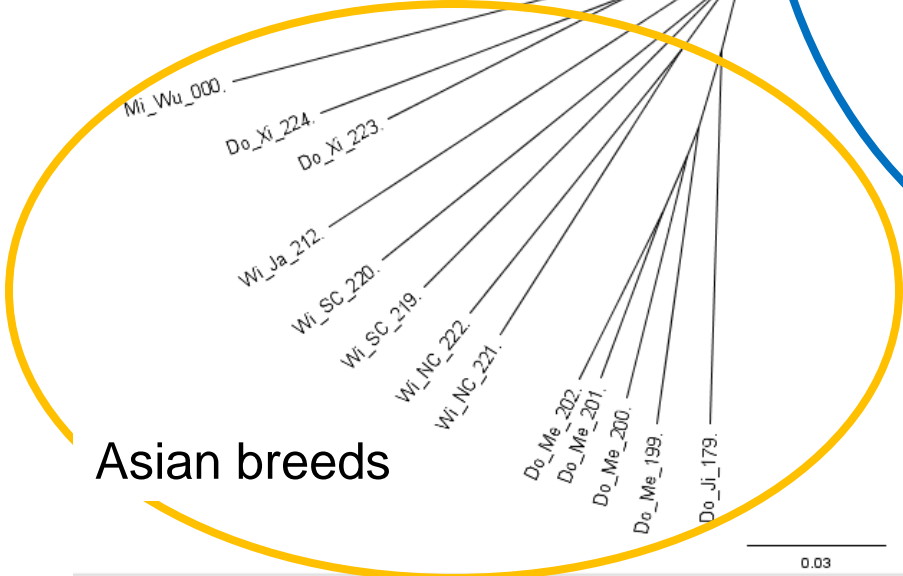
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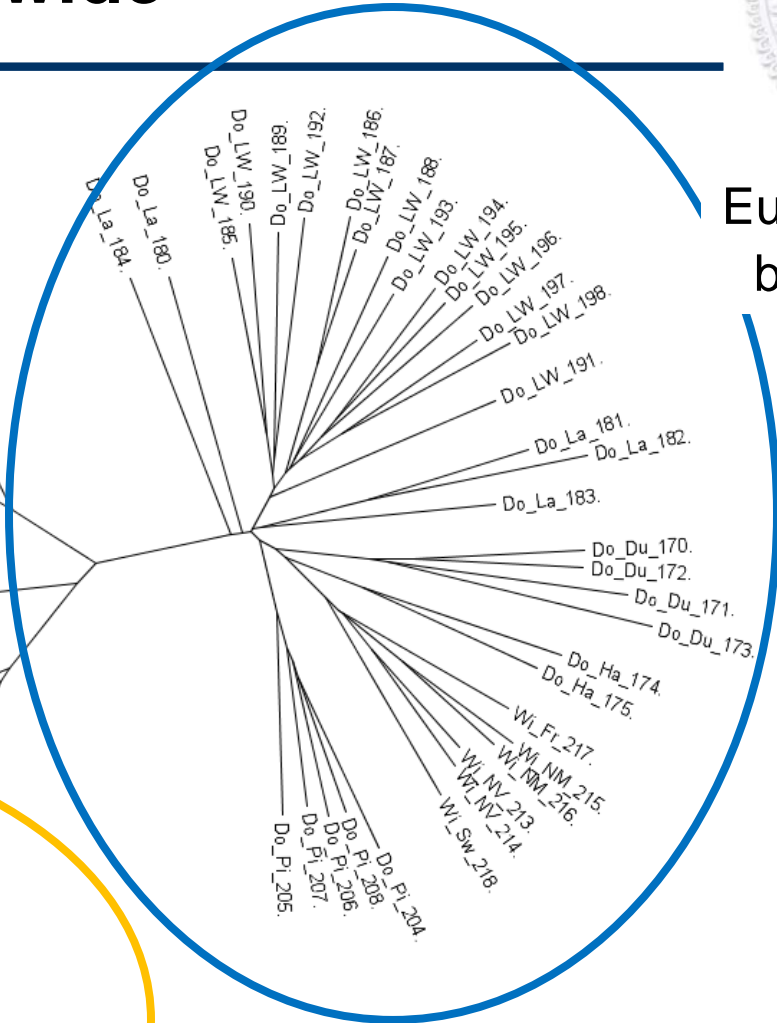
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Asian breeds

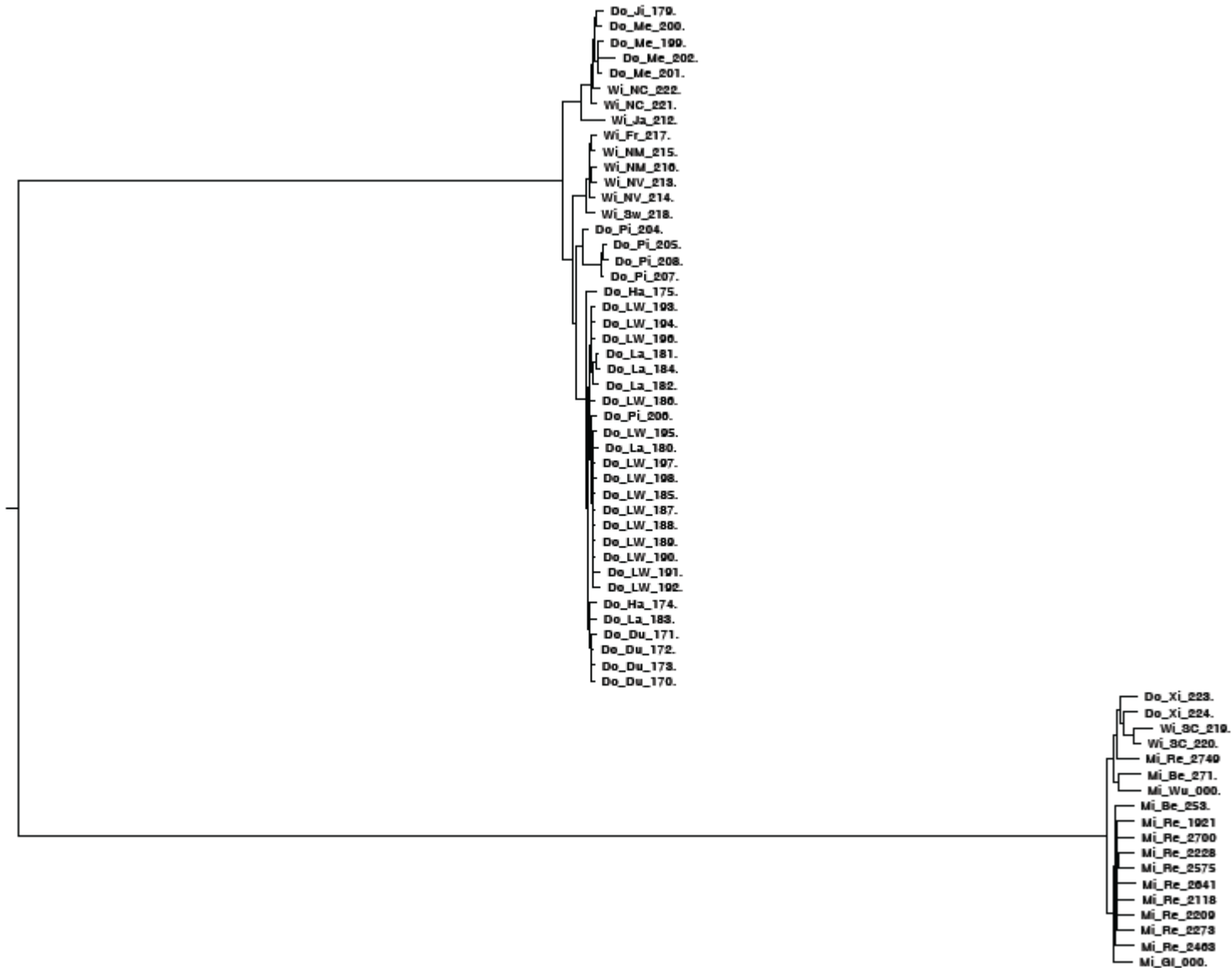


European
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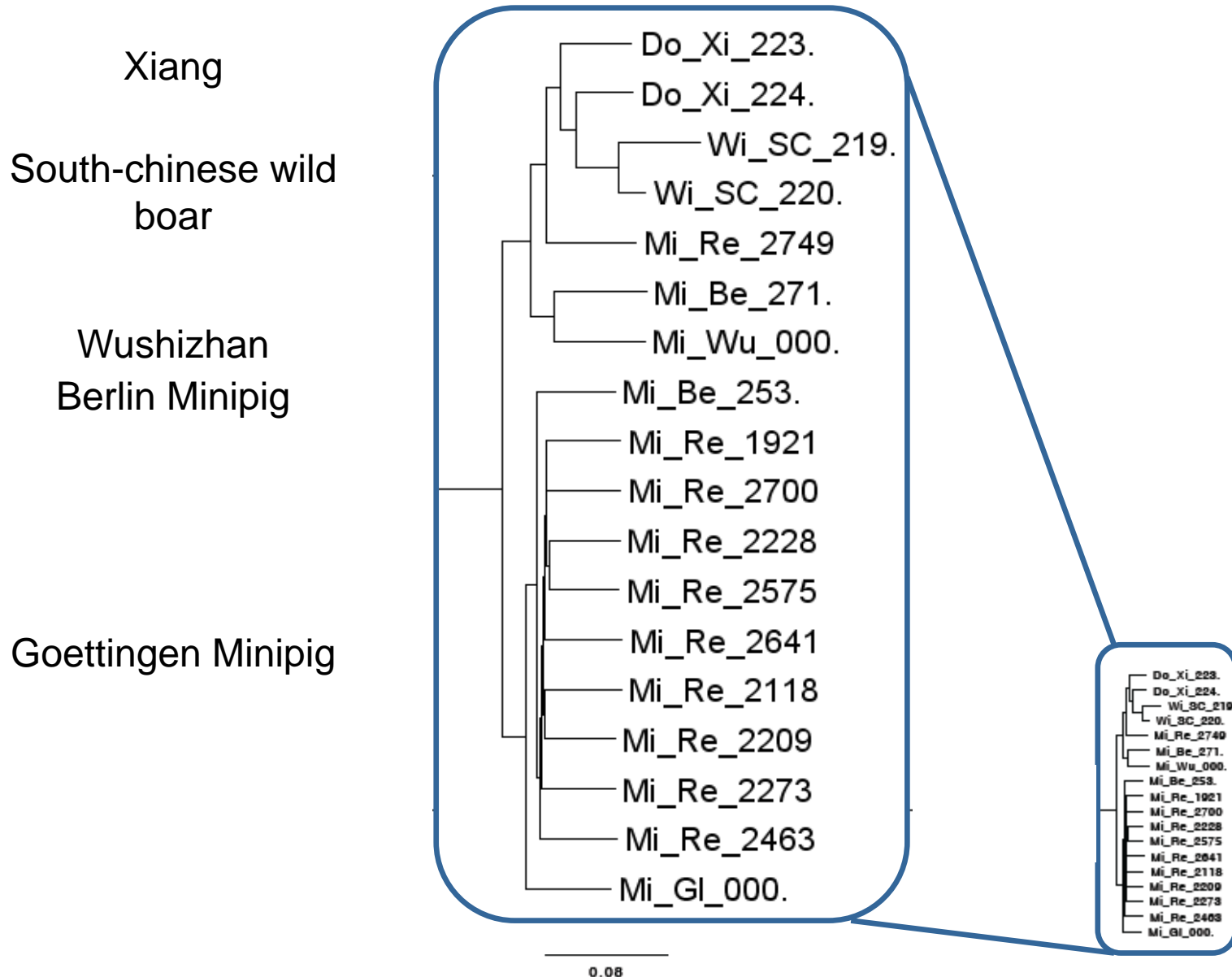
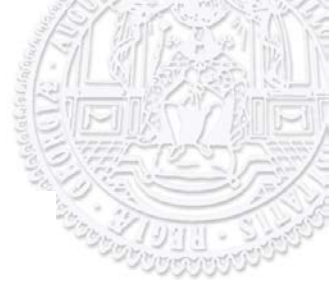


Software: PHYLIP (Felsenstein,1989)

Phylogenie – X:53-61



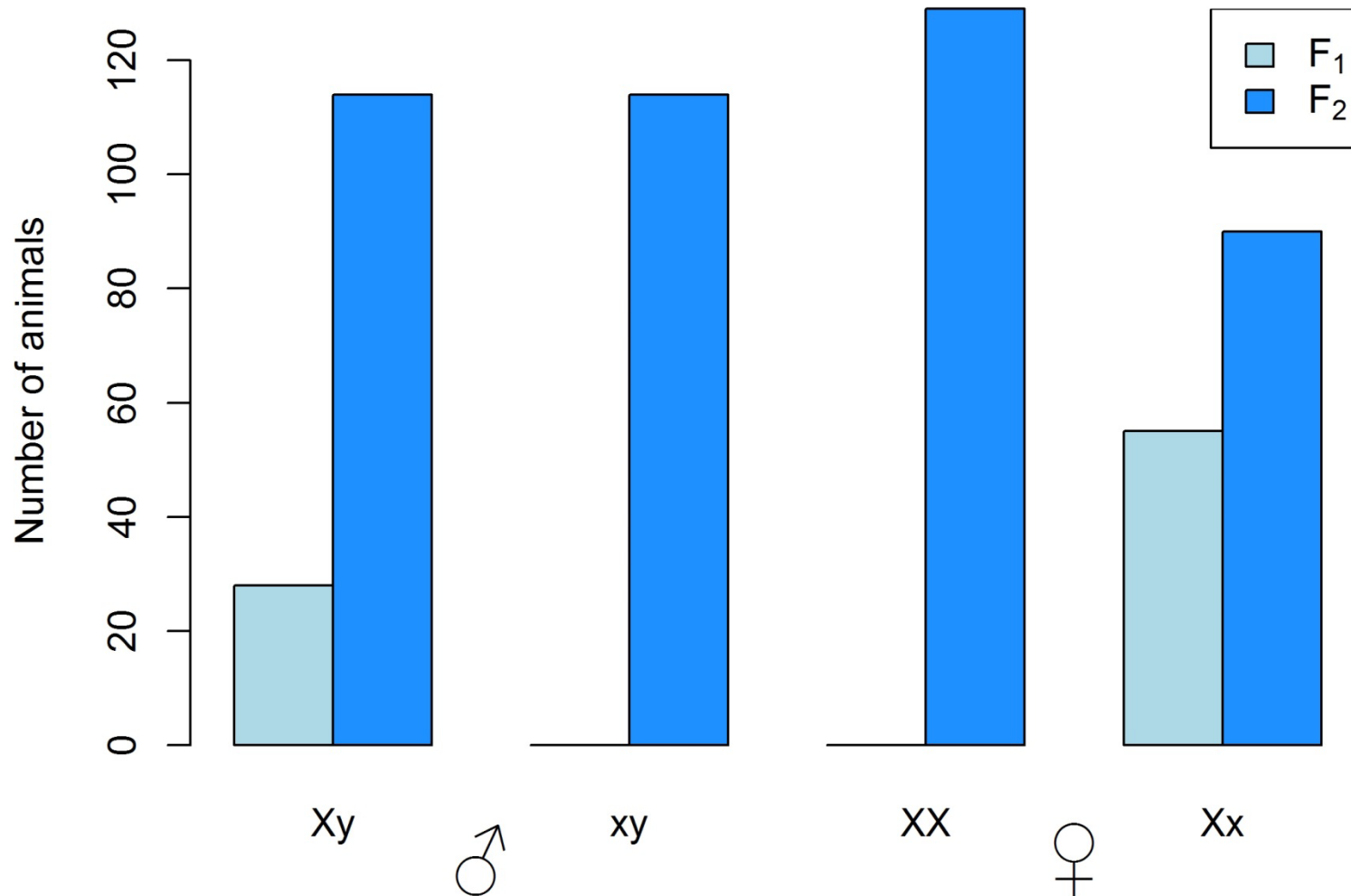
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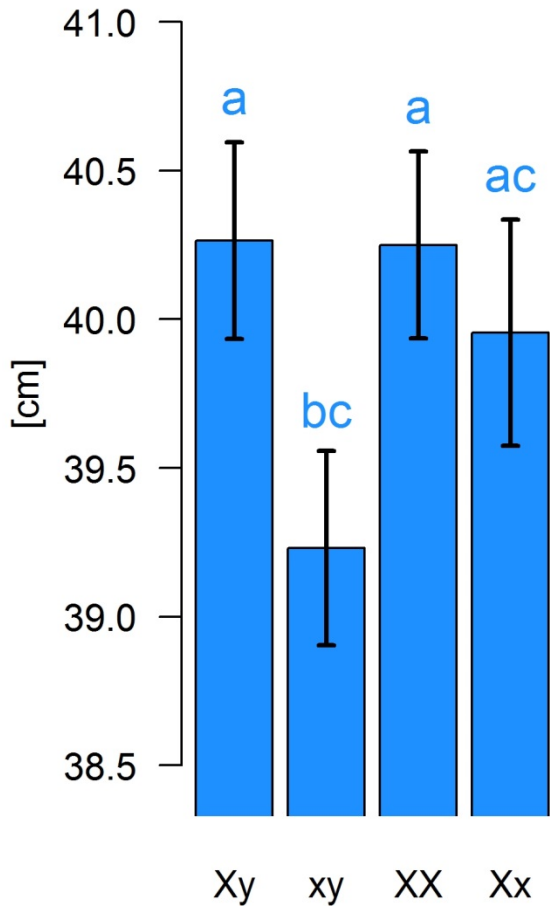
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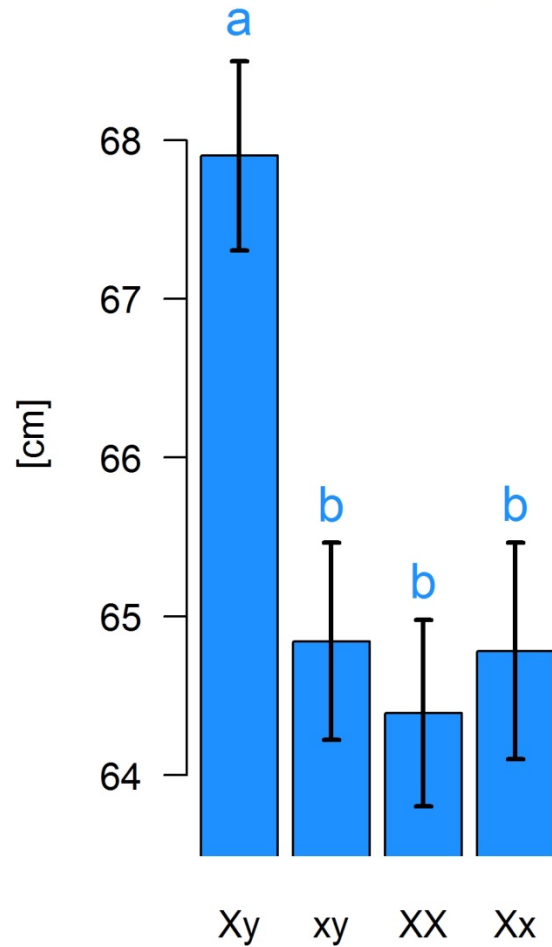
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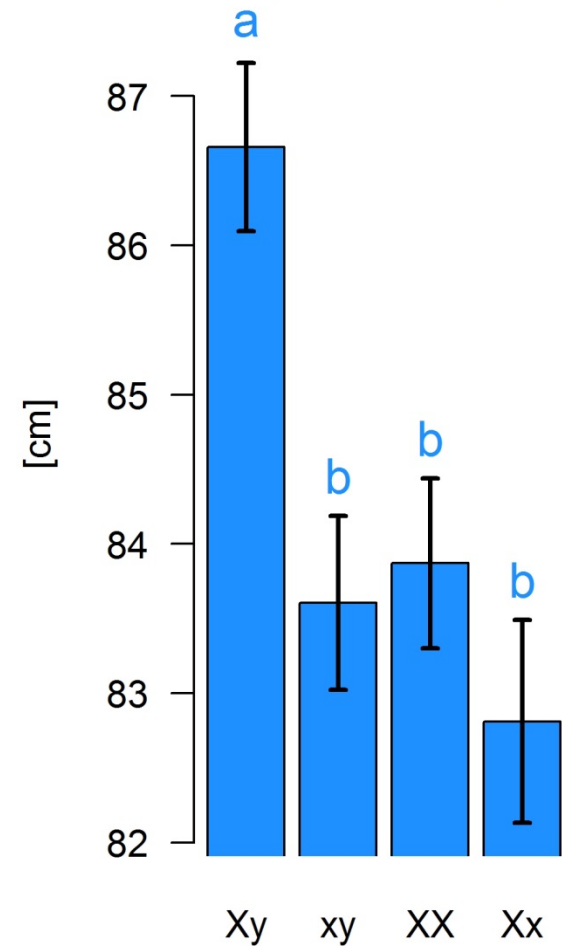
Height at scanning



Height at slaughter



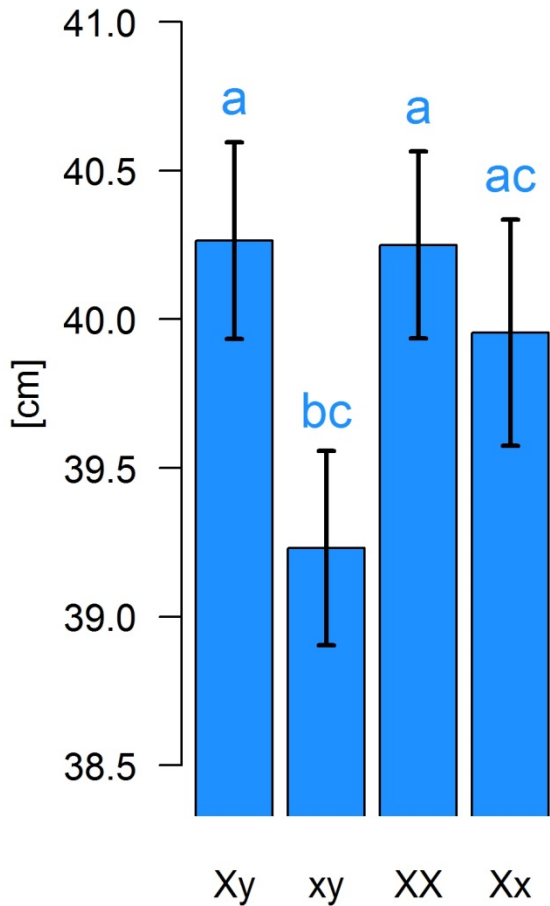
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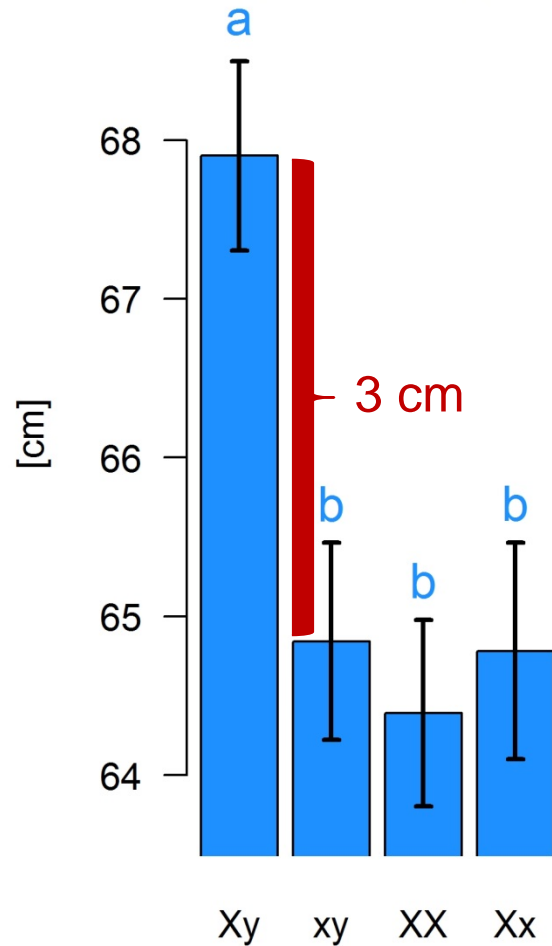
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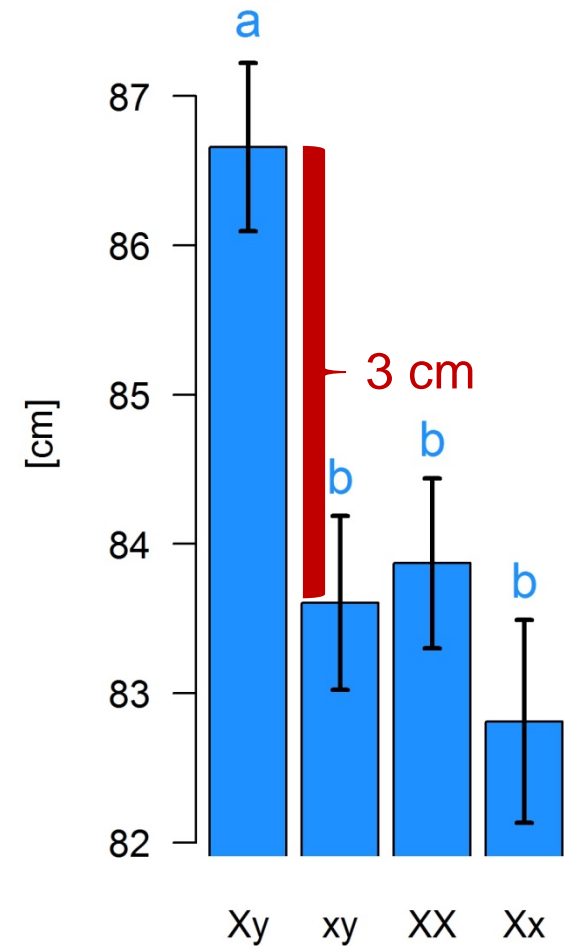
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Acknowledgement



We gratefully acknowledge the travel funding by the European Science Foundation (ESF) in the cluster „Advances in Farm Animal Genomic Resources“ and the DAAD U4 Network for the research stays in Uppsala

Calculations were carried out on the Servercluster at the Multidisciplinary Center for Advanced Computational Science (UPPMAX) provided by SNIC under project accession p2010044

We thank Ellegaard Göttingen Minipigs A/S for funding

We especially thank the EAAP for granting a scholarship for the EAAP Meeting 2015 in Warsaw

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 - Female cross-breds can carry both haplotypes
 - Boars carrying the minipig haplotype are significantly smaller than boars carrying the large pig haplotype (3% shorter and 3% less high)
- The X-chromosomal sweep region explains a considerable part of the total variability of body size**