ETH zürich

Current projects at ETH

SABRE TP Meeting
19 August 2020

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www.ag.ethz.ch

Embrace genetic diversity: development of non-linear reference sequences (1)

Crysnanto and Pausch *Genome Biology* (2020) 21:184
https://doi.org/10.1186/s13059-020-02105-0

Genome Biology

RESEARCH Open Access

Bovine breed-specific augmented reference graphs facilitate accurate sequence read mapping and unbiased variant discovery

Danang Crysnanto* and Hubert Pausch

Check for updates

Crysnanto, Danang

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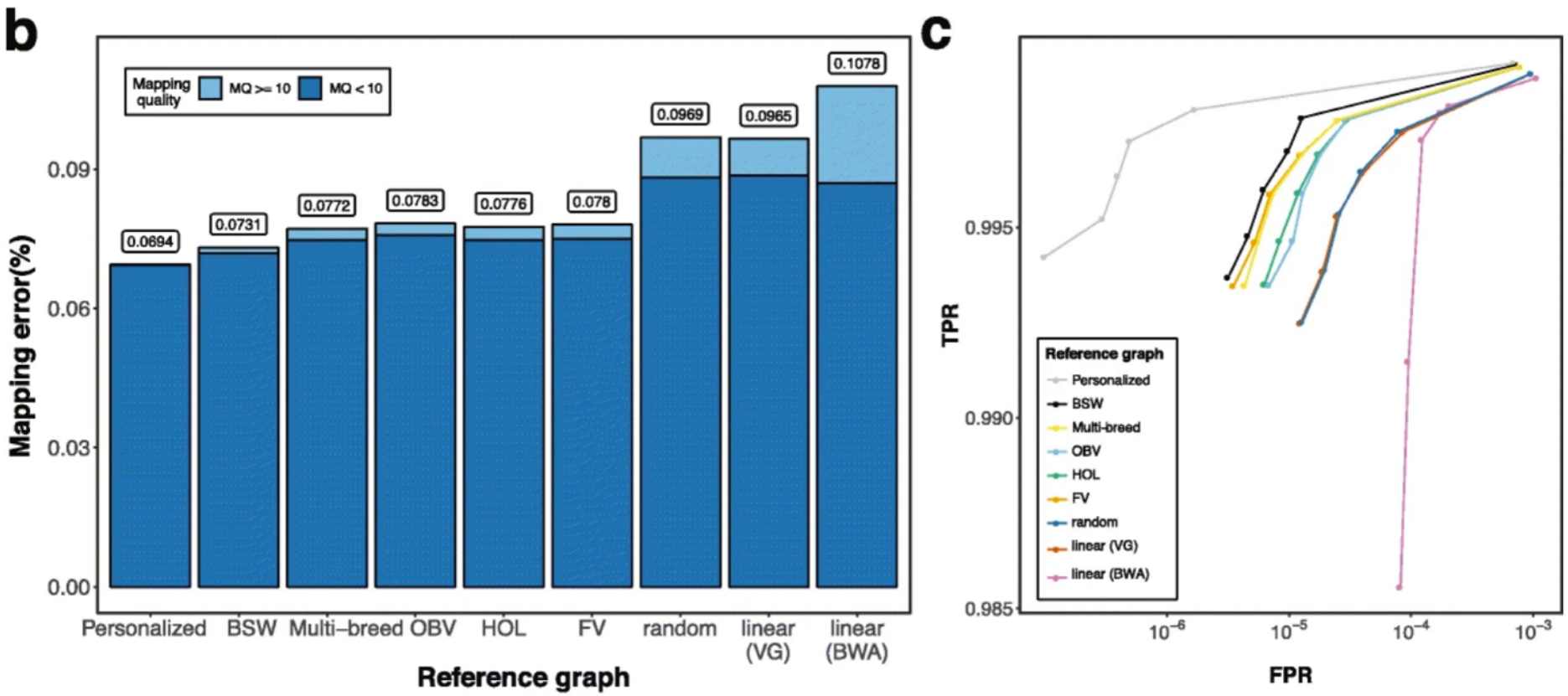
V-Card (vcf, 1kb) ↓

Embrace genetic diversity: development of non-linear reference sequences (2)



Embrace genetic diversity: development of non-linear reference sequences – future directions

- Current work
  - Integration of five haplotype-resolved genome assemblies (Hereford, Angus, Highland, Brahman, Yak) into a unified reference graph to
    - detect non-reference (ARS-UCD1.2) variants and transcripts
    - genotype non-reference variants
    - analyse the expresison pattern of non-reference transcripts

- Future directions (Danang Crysnanto, Audald Lloret-Villas, Alexander Leonard)
  - Integration of breed-specific resolved genome assemblies
  - BSW, OBV and SIM (see later)

The genetics of male fertility in cattle

PLOS GENETICS

RESEARCH ARTICLE

Activation of cryptic splicing in bovine *WDR19* is associated with reduced semen quality and male fertility

Maya Hiltpold[1], Guanglin Niu[2], Naveen Kumar Kadri[1], Danang Crysnanto[1], Zih-Hua Fang[1], Mirjam Spengeler[3], Fritz Schmitz-Hsu[4], Christian Fuerst[5], Hermann Schwarzenbacher[5], Franz R. Seefried[3], Frauke Seehusen[6], Ulrich Witschi[4], Angelika Schnieke[2], Ruedi Fries[7], Heinrich Bollwein[8], Krzysztof Flisikowski[2], Hubert Pausch[1]*

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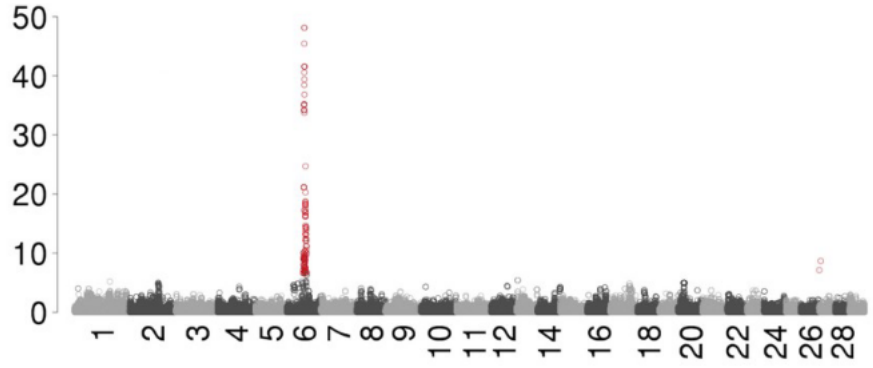
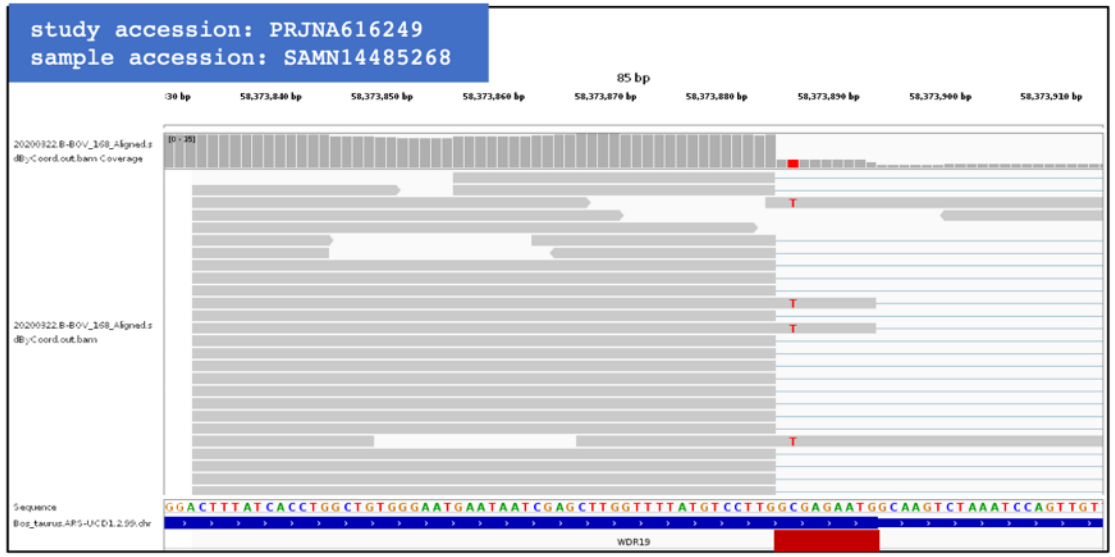
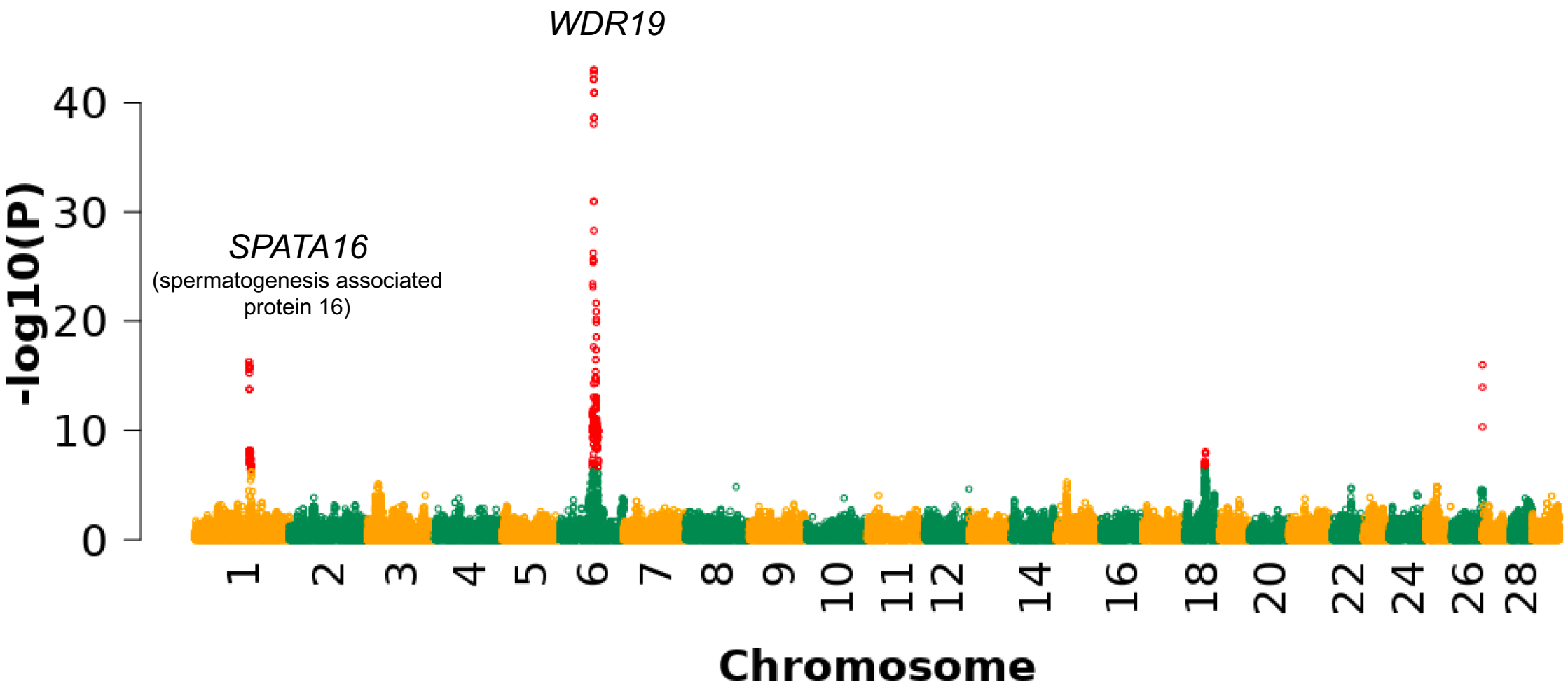




The genetics of male fertility in cattle – future directions: bull fertility



A frameshift variant in *QRICH2* might be associated with poor semen quality in BSW bulls

19 55436705 TC T 25 AR2=0.99;DR2=0.99;AF=0.029;CSQ=-|**frameshift_variant**|HIGH|**QRICH2**|ENSBTAG00000030173|Transcript|ENSBTAT00000018337|protein_coding|16/20||ENSBTAT00000018337.1:c.4929del|….

Summary for INDEL:(Chr 19:55436705 bp)
Reference allele = TC
Alternative allele = T

breed	N	ref/ref	ref/alt	alt/alt	fq(alt)
HER	14	14	0	0	0.000
Nelore	1	1	0	0	0.000
TGV	19	19	0	0	0.000
RGV	14	14	0	0	0.000
FV	50	50	0	0	0.000
NRC	2	2	0	0	0.000
HOL	47	47	0	0	0.000
BSW	244	218	25	1	0.055
OBV_USA	4	4	0	0	0.000
Wagyu	3	3	0	0	0.000
OBV	124	121	3	0	0.012
	522	493	28	1	0.029

nature COMMUNICATIONS

Corrected: Author Correction

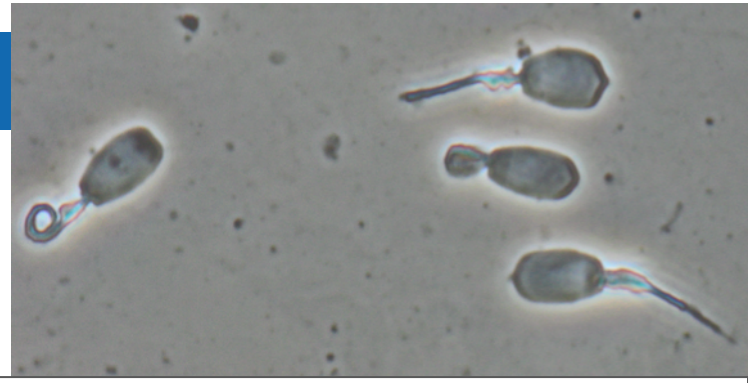
ARTICLE

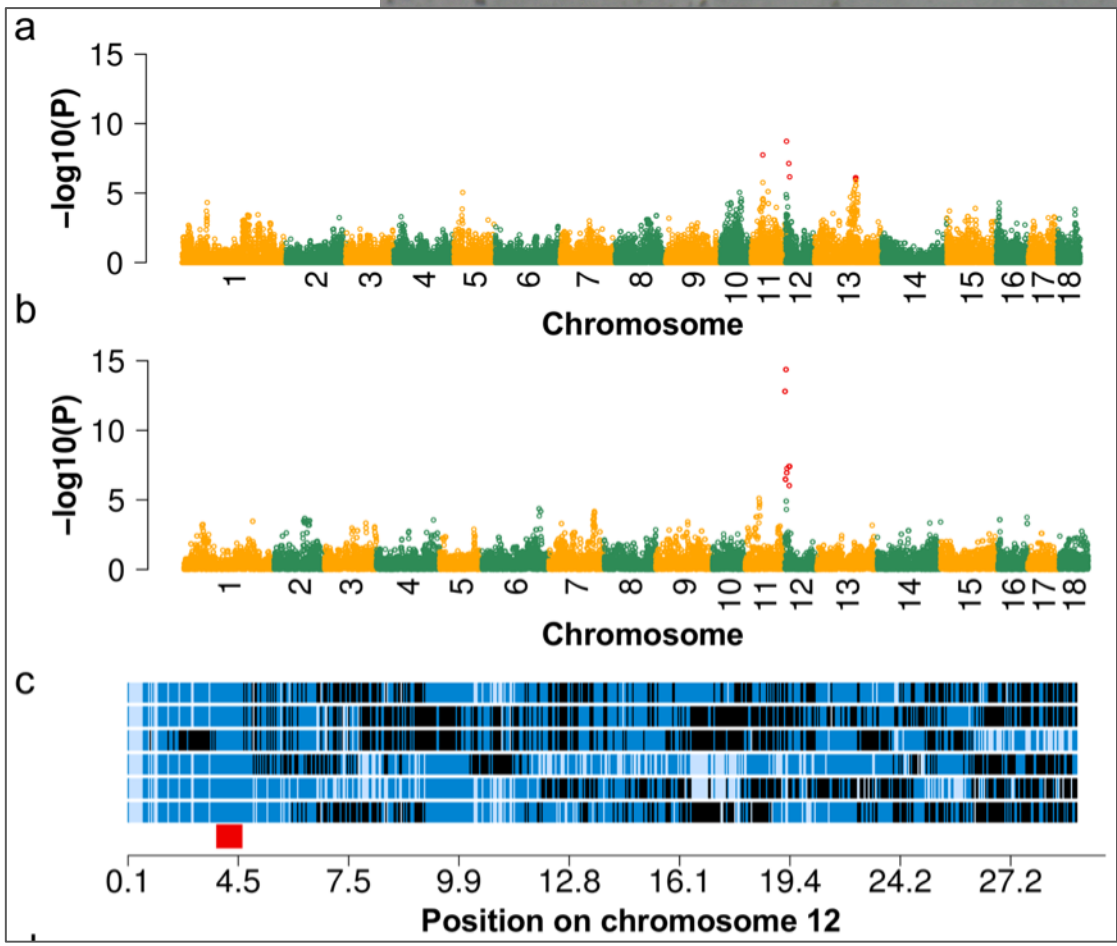
https://doi.org/10.1038/s41467-018-08182-x OPEN

Loss-of-function mutations in *QRICH2* cause male infertility with multiple morphological abnormalities of the sperm flagella

Ying Shen[1], Feng Zhang[2,3,4], Fuping Li[5,6], Xiaohui Jiang[5,6], Yihong Yang[7], Xiaoliang Li[1], Weiyu Li[2], Xiang Wang[1], Juan Cheng[8], Mohan Liu[9], Xueguang Zhang[1], Guiping Yuan[10], Xue Pei[9], Kailai Cai[11], Fengyun Hu[12], Jianfeng Sun[13], Lanzhen Yan[14], Li Tang[1], Chuan Jiang[1], Wenling Tu[9], Jinyan Xu[5,6], Haojuan Wu[8], Weiqi Kong[1], Shuying Li[1], Ke Wang[1], Kai Sheng[1], Xudong Zhao[14,15], Huanxun Yue[5,6], Xiaoyu Yang[16] & Wenming Xu[1]

The genetics of male fertility in pigs (Adéla Nosková)





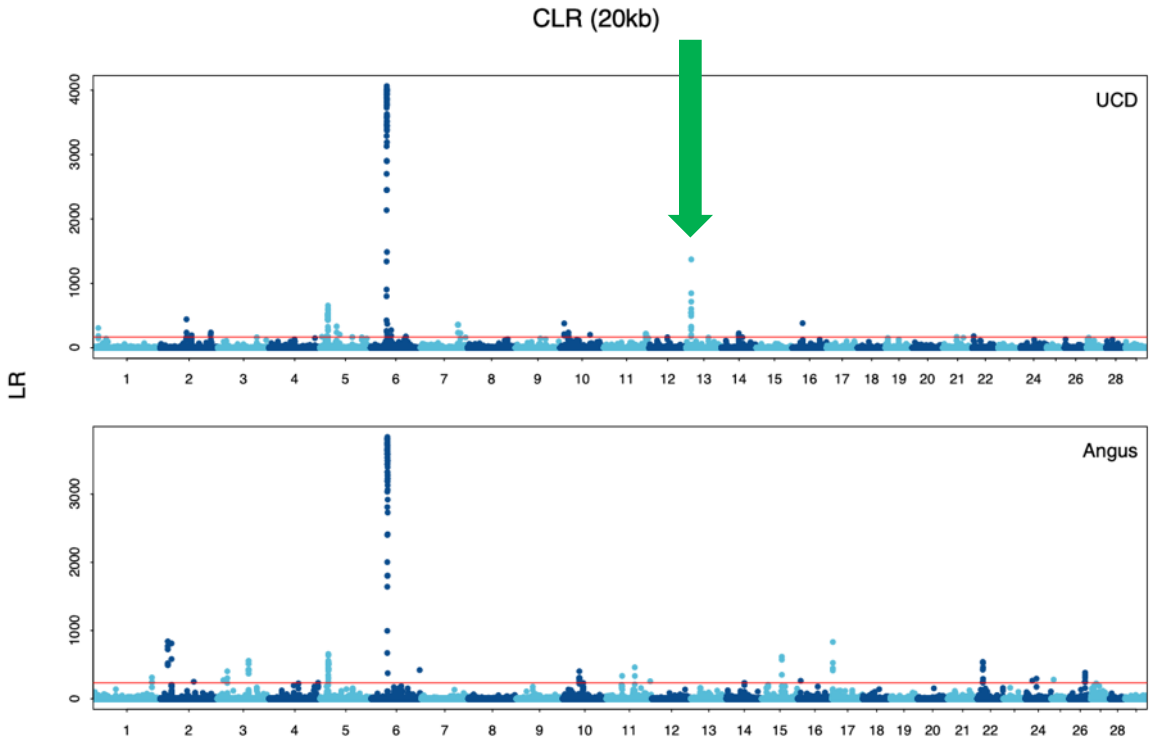
SUISAG

Mutation pattern in conserved intronic elements (Naveen Kadri, Xena Mapel)

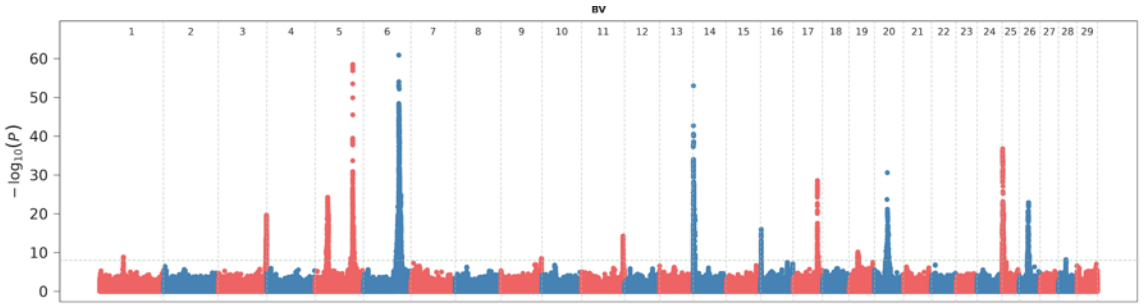
- Establish an eQTL cohort: Collect DNA and RNA sequencing data from 150 BSW bulls (testis tissue)
- Perform eQTL analysis
- Investigate if branch point mutations are eQTL (splicing QTL)
- Assess the effect of branch point mutations on splice site selection and splicing efficiency using PacBio IsoSeq data

De-novo assembly of livestock genomes - Which assembly is the best for a given breed? (Audald Lloret-Villas, Meenu Bhati, Naveen Kadri)

- 161 BSW samples were aligned to Hereford- and Angus-based references

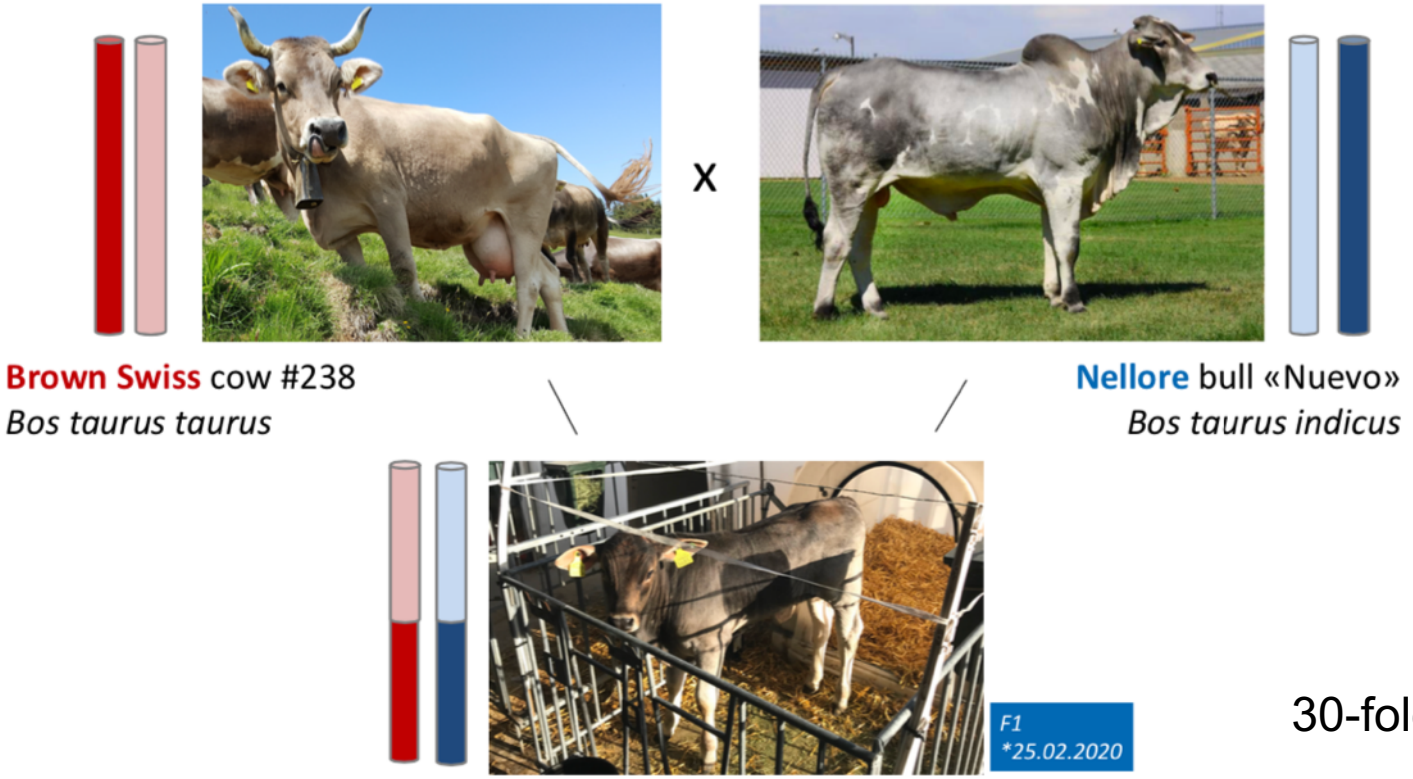


Multi-trait meta analysis with 27 million imputed sequence variants



De-novo assembly of livestock genomes – future directions (Audald Lloret-Villas, Alexander Leonard, Zih-Hua Fang, Niklas Terhoeven)

- The assembly of breed-specific reference genomes using trio-binning



30-fold HiFi coverage

De-novo assembly of livestock genomes – future directions (Audald Lloret-Villas, Alexander Leonard, Zih-Hua Fang, Niklas Terhoeven)

- Sequencing of a BSW x NEL trio has been completed (PacBio HiFi, Illumina paired-end)
- Sequencing of a OBV x OBV trio is underway (PacBio HiFi, ONT, Illumina paired-end)
- 40-fold sequencing of a FV and BSW bull using PacBio has been completed
- These data will facilitate the assembly of breed-specific reference genomes that will be integrated with existing reference-quality assemblies

Many thanks to

- Animal Genomics group members for their great work
- Funding sources for providing resources that facilitate the research I presented (SNSF, H2020, FOAG, Swissgenetics, SUISAG, Micarna SA, ETHZ Foundation, FBF)
- Industry partners for fruitful collaborations, providing data, critical feedback, and implementing results