


Design and Results from an Axiom custom SNP-array for Swiss cattle (SWISScow)

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Swiss Animal Breeding Technology Platform (SABRE-TP) Workshop 2020
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Background

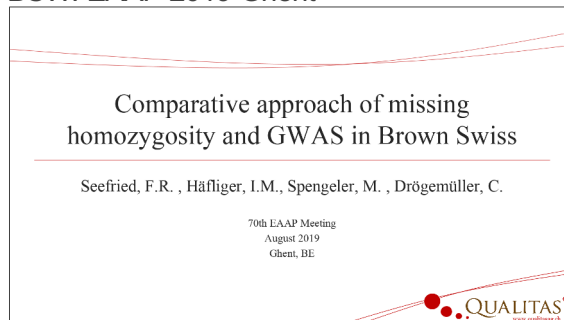
- Routine genotyping of Swiss cattle since 2011
- SNP-arrays: commercial Chips (Illumina 50K, GeneSeek Chips)
- Genotyping labs:
 - CH (Univ. Geneva) - 2012
 - DE (IFN Schönow) 2012 – 2014
 - USA (GeneSeek) since 2014
 - DE (IFN Schönow) since 2020
- Increasing no. of known causal variants since 2011
- Collaboration with GeneSeek
 - Inefficient in terms of individual customer needs
 - Significant additional costs for supplementary tests (Polled, A2, CDH)
 - Several bugs since 2014

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Background – SNF project @ UniBE

- Population specific screening of haplotypes with missing homozygosity (PhD project I.M. Häfliger)
- 4 Swiss cattle populations (BS, OB, SI, HO)
- Results BSW: EAAP 2019 Ghent



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Aims and requirements for the SWISScow chip

- No. of candidate SNPs for population wide screening
 - published recessive causal variants ($n \sim 100$)
 - additional new variants (UniBE project + genome-wide “coding” variants)
- Genotyping under the umbrella of routine genomics
- Highly efficient (workflow and cost)
 - No. of new markers!
- The ultimate goal: A **single** array for all needs
 - Routine checks (Sex Check, ISAG parentage markers)
 - Genomic selection (Imputation accuracy)
 - Recessive traits
 - New variants

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Milestones towards the SWISScow chip

- *Winter 2018/19*: International call at different labs and technologies and internal discussions
- *July 2019*: finish of the SWISScow array
 - 314K chip with 111K Illumina markers included
 - ~100 known recessive disorders from different populations
 - Sex-chromosomal markers that allow gender validation
 - ISAG parentage markers
- *October 2019 – January 2020*: Chip validation
 - Concordance towards Illumina
 - Repeatability
 - International validation (CDCB, Interbull)
- *January 2020*: Go live @IFN

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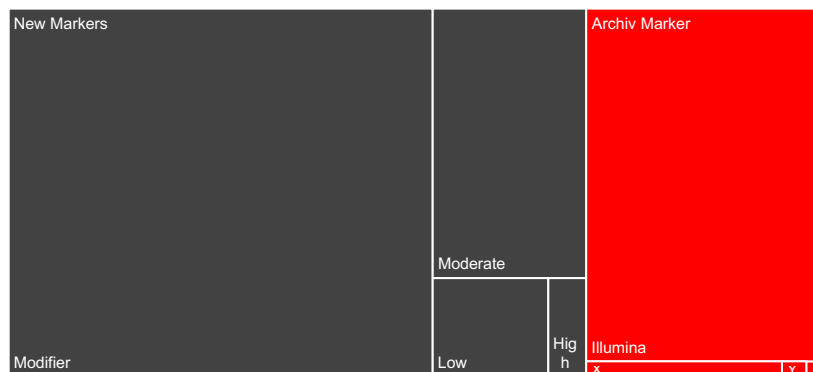
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Chip Design

SWISSCOW Axiom Chip

■ Archiv Marker ■ New Markers

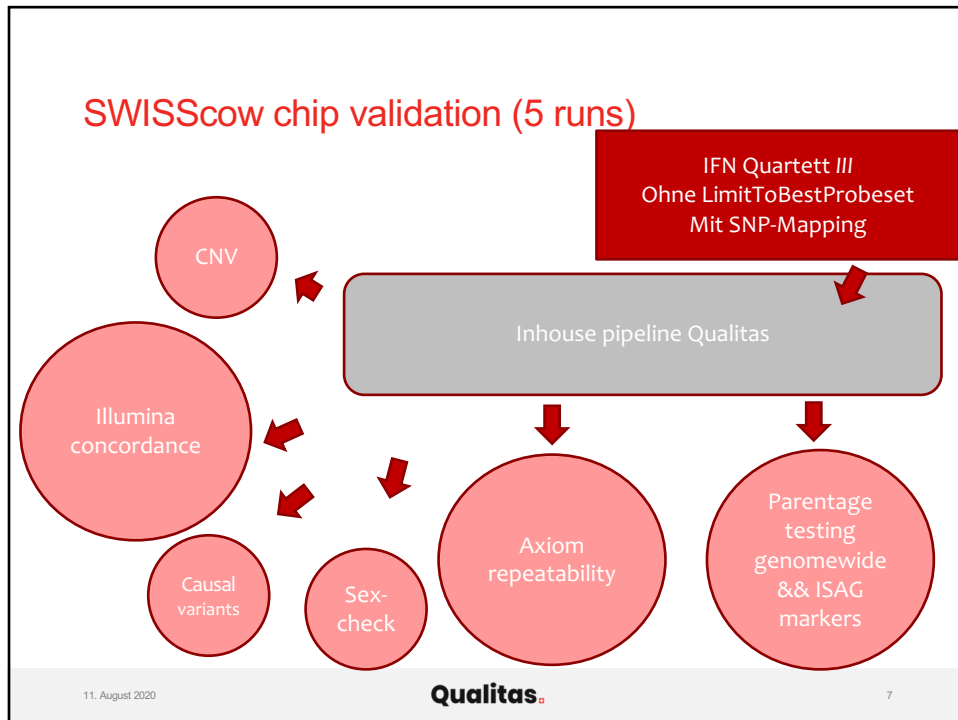


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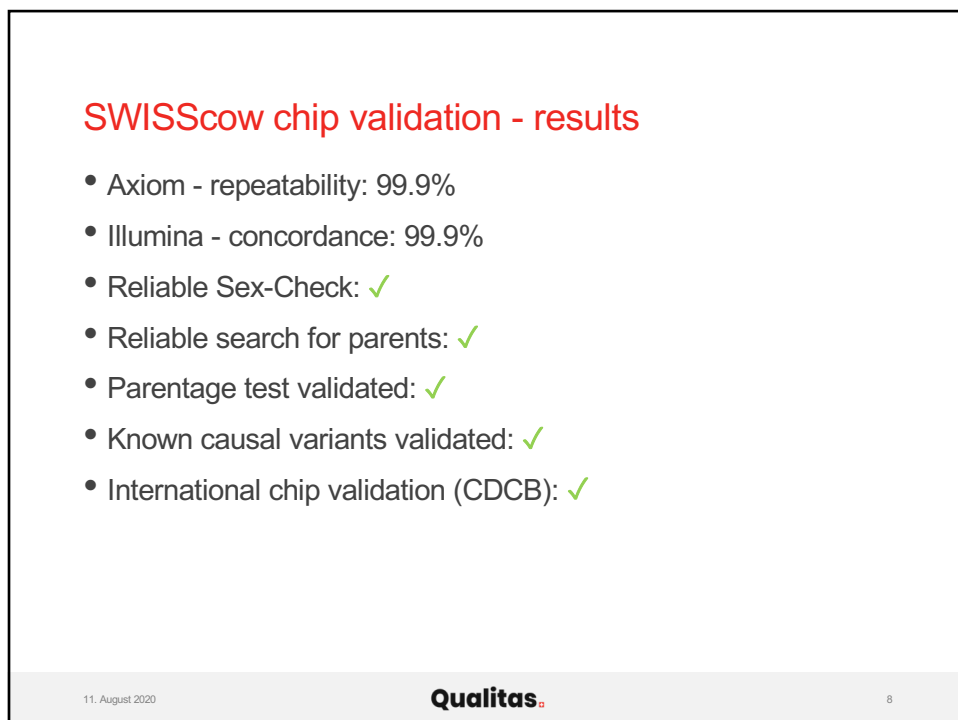
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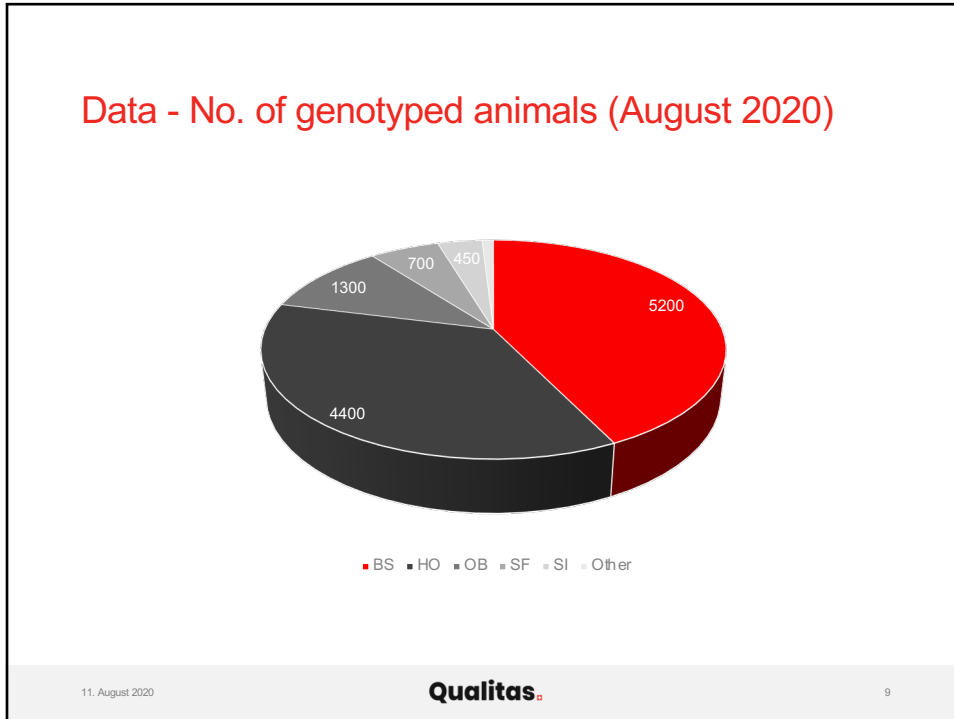
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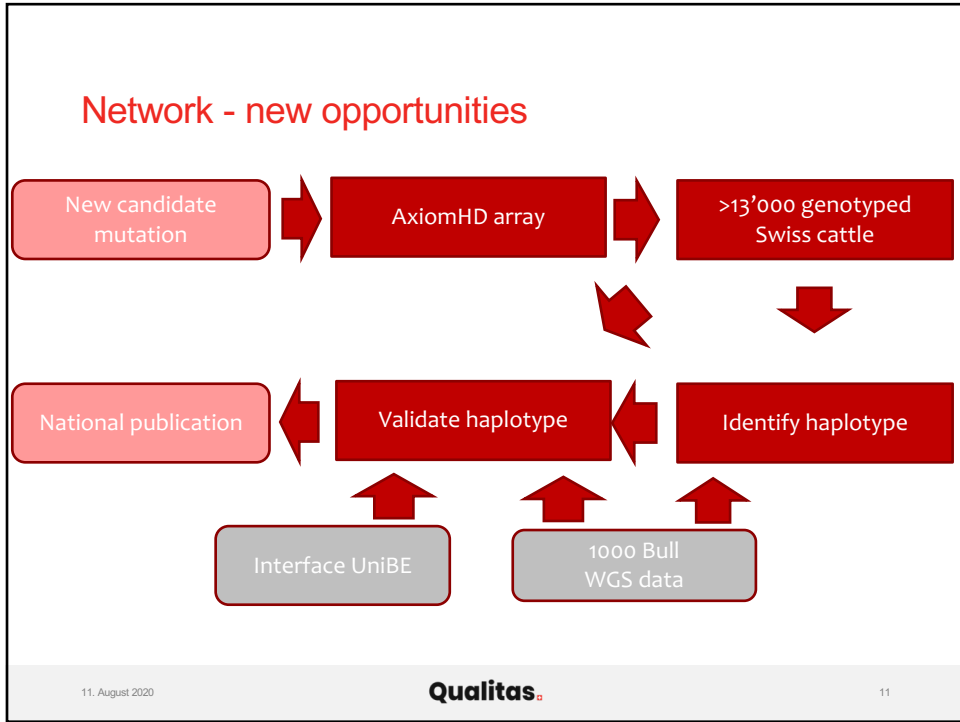
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Results for selected recessive traits

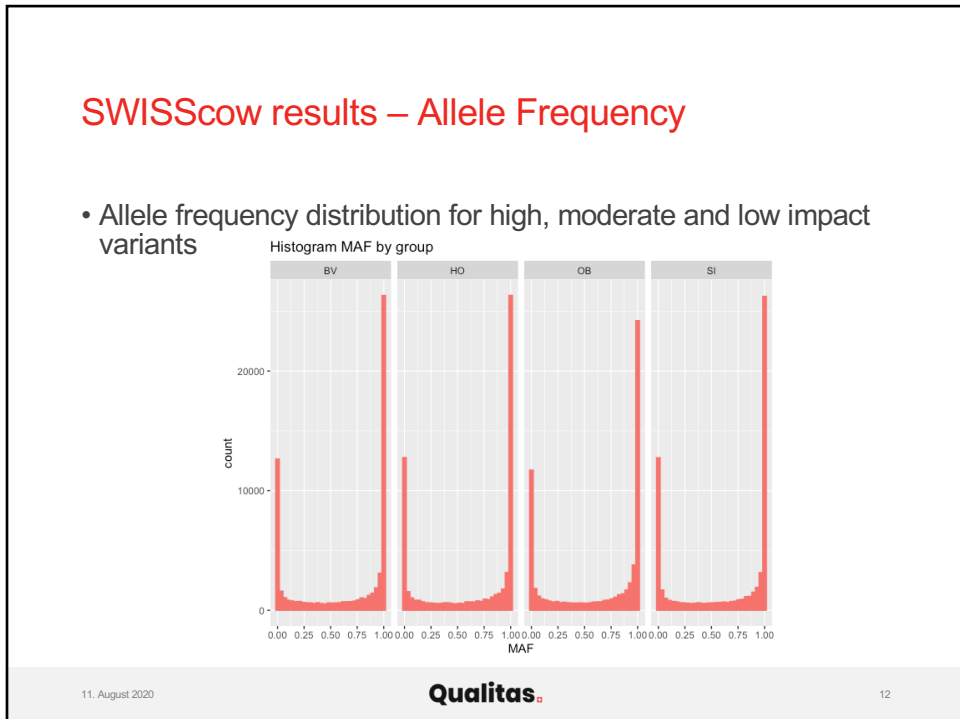
Shortcut (Gene)	Trait	Source	Timescale	SWISScow Array	Previous Genotypes	MAF (%)
RDEG (1bp Insertion <i>RP1</i>)	late onset retina degeneration (later in life)	Literature	Published 2016	✓	-	1% in HOL, (>>SF)
OH1 (G>A SNP <i>CNGB3</i>)	congenital vision impairment due to a retina defect	Own research	work in progress (UniBE)	✓	-	~10% in OB
HH6 (A>G SNP, <i>SDE2</i>)	embryonic lethal (Holstein fertility haplotype 6)	Literature	Published 2020	✓	-	< 1% in HO
WDR19 (C>T SNP, <i>WDR19</i>)	male fertility	ETH, personal comm.	Published 2020	✓	-	~26% in BSW

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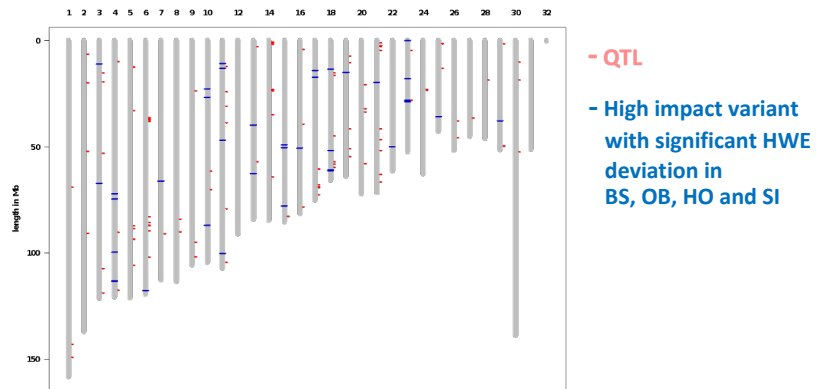


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SWISScow results – HWE

- High impact variants with significant HWE deviation

	BS	HO	OB	SI	Common across populations
No. of markers	203	171	111	73	44



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Forecast – accuracy of genomic prediction based on SWISScow data

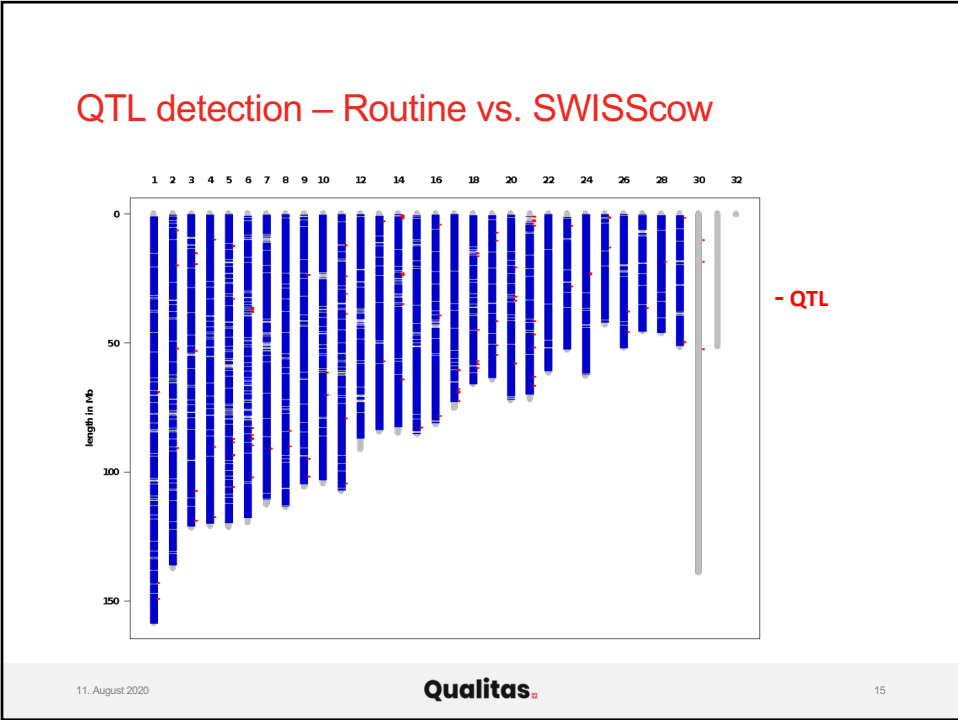
- Assembly ARS-UCD1.2
- GWAS on imputed SWISScow genotypes:
 - Single SNP regression model
 - Stratification: G
 - SNP-Density: 110K / SWISScow
- Trait blocks related to missing homozygosity
 - Fertility
 - Birth
 - Carcass
 - Milk production traits
 - Some conformation traits (bcs, stature, teat length)
 - Traits «under development»
- Comparison with GWAS on routine GEBV system

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QTL detection – Routine vs. SWISScow

Population	Routine == SWISScow (@BTA#bp) No. of QTL	Routine != SWISScow (@BTA#bp) No. of QTL	Additionally observed using SWISScow
Brown Swiss (BS)	21	12	6
Original Braunvieh (OB)	7	9	6
Holstein (HO)	40	32	6

Max. gap: Routine vs. SWISScow position: 1.5Mb (trait ous, pop BS)
Min gap: Routine vs. SWISScow position: 2.4kb (trait dce, pop OB)

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QTL Routine vs. SWISScow - examples

Trait	Pop	Routine	SWISScow	VEP (Gene)
Milk yield	BS	4:63927465 (n.s.)	4:63806731	Moderate (<i>NT5C3A</i>)
Non return rate heifer	BS	17:68518098	17:68575124	Modifier (<i>EWSR1</i>) + HWE dev.
Fat yield	BS	14:1159861	14:1158060	Moderate (<i>ZC3H3</i>)
Teat diameter	BS	6:88697771	6:88960072	Low (<i>LOC100847175</i>)
Carcass conformation score	OB	11:104325525	11:104318491	Moderate (<i>ADAMTS13</i>)
<u>Fat yield</u>	<u>HO</u>	<u>14:609870</u>	<u>14:611019</u>	<u>Moderate (<i>DGAT1 K232A</i>)</u>
Non return rate cows	HO	18:57057494	18:57077568	Moderate (<i>CEACAM18</i>)
Calving ease direct	HO	29:49657267	29:49646800	Moderate (<i>DEAF1</i>)
Birth weight direct	HO	6:36857907	6:37403795	Moderate (<i>LCORL</i>)
Temperament	HO	6:116350271	6:116250399	Moderate (<i>CFAP99</i>)
<u>Rearing success heifer period 2</u>	<u>HO</u>	<u>11:80529287</u>	<u>11:77958994</u>	<u>LoF (<i>APOB</i>) CDH</u>

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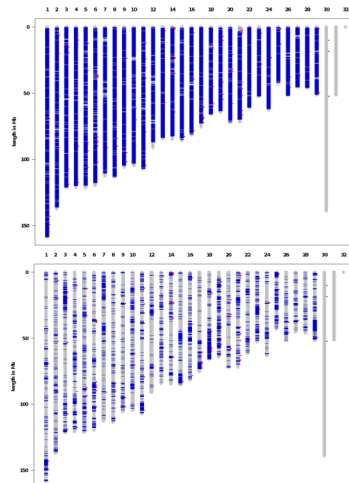
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Outlook – design of a cost efficient Axiom LD array submitted

- Archive Markers:
- New Markers (SWISScow):




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ASR
Arbeitsgemeinschaft Schweizerischer Rinderzüchter
Communauté de travail des éleveurs bovins suisses

- **Project team:** *I.M. Häfliger, M. Spengeler,
C. Drögemüller, F. Seefried*


- **Qualitas:** M. Kraus


- **ThermoFisher:** F. Grandke

- **IFN Schönow:** A. Wagener & team


- **CDCB:** G. Wiggans

- **Collaborator:** H. Pausch






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- Thank you for your attention!

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