

# Livestock genetics - examples of current projects

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Swiss Animal Breeding Technology Platform, Zurich, 5<sup>th</sup> June 2019

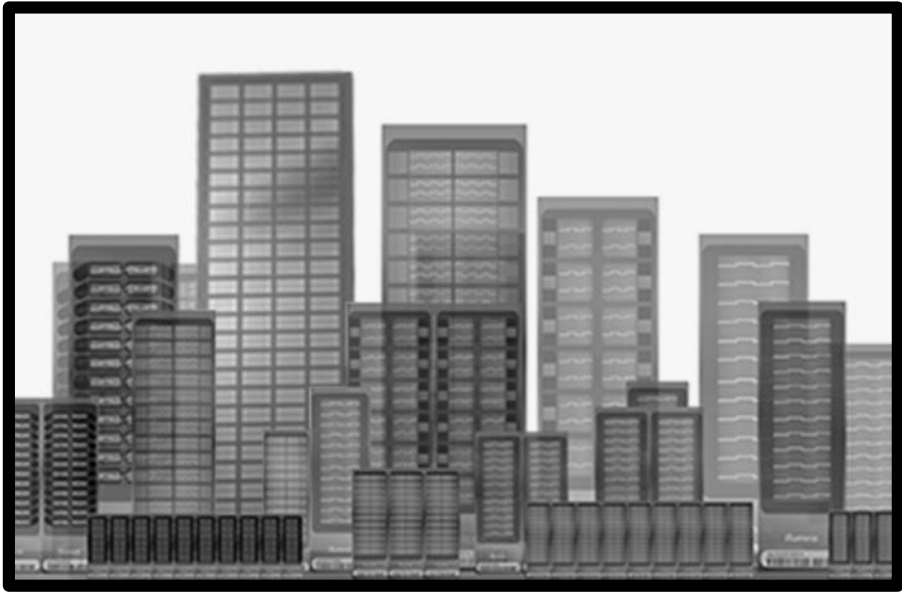
*u*<sup>b</sup>

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b  
UNIVERSITÄT  
BERN

## DNA focused research

(rare) genetic diseases – heritable (morphological/color) traits



SNP data




WGS data

# 2019: WGS of hundreds

goat – cattle – sheep

## 2017: ARS1

Goat Genome About



Ongoing projects Meetings

## 2018: ARS-UCD1.2

**ANNUAL REVIEWS**

*Annual Review of Animal Biosciences*

### 1000 Bull Genomes Project to Map Simple and Complex Genetic Traits in Cattle: Applications and Outcomes

Ben J. Hayes<sup>1,2</sup> and Hans D. Daetwyler<sup>2,3</sup>

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<sup>3</sup>School of Applied Systems Biology, La Trobe University, Bundoora, Victoria 3083, Australia

**Keywords**  
cattle, whole-genome sequences, deleterious, mutations, complex traits

Annu. Rev. Anim. Biosci. 2019. 7:89–102  
First published as a Review in Advance on December 3, 2018

## 2019: Oar\_rambouillet\_v1.0

**SheepGenomesDB**  
Resources for the Sheep Genomics Community

HOME PROJECT OUTLINE DATA SUBMISSION SNP CHIPS



Welcome to the Sheep Genomes Database

The Sheep Genomes Database is funded by the [USDA AFR](#) to provide the sheep genomics research community with a genomics hub. It is an initiative of the [International Sheep Genomics Consortium](#) and extends the consortium's recent achievement to build and release the [sheep reference genome assembly v3.1](#).

## SNF project 2017 - 2021

A comprehensive genetic screen for recessive mutations impairing fertility and rearing success of Swiss cattle

- massive SNP genotyping data of 4 local cattle populations




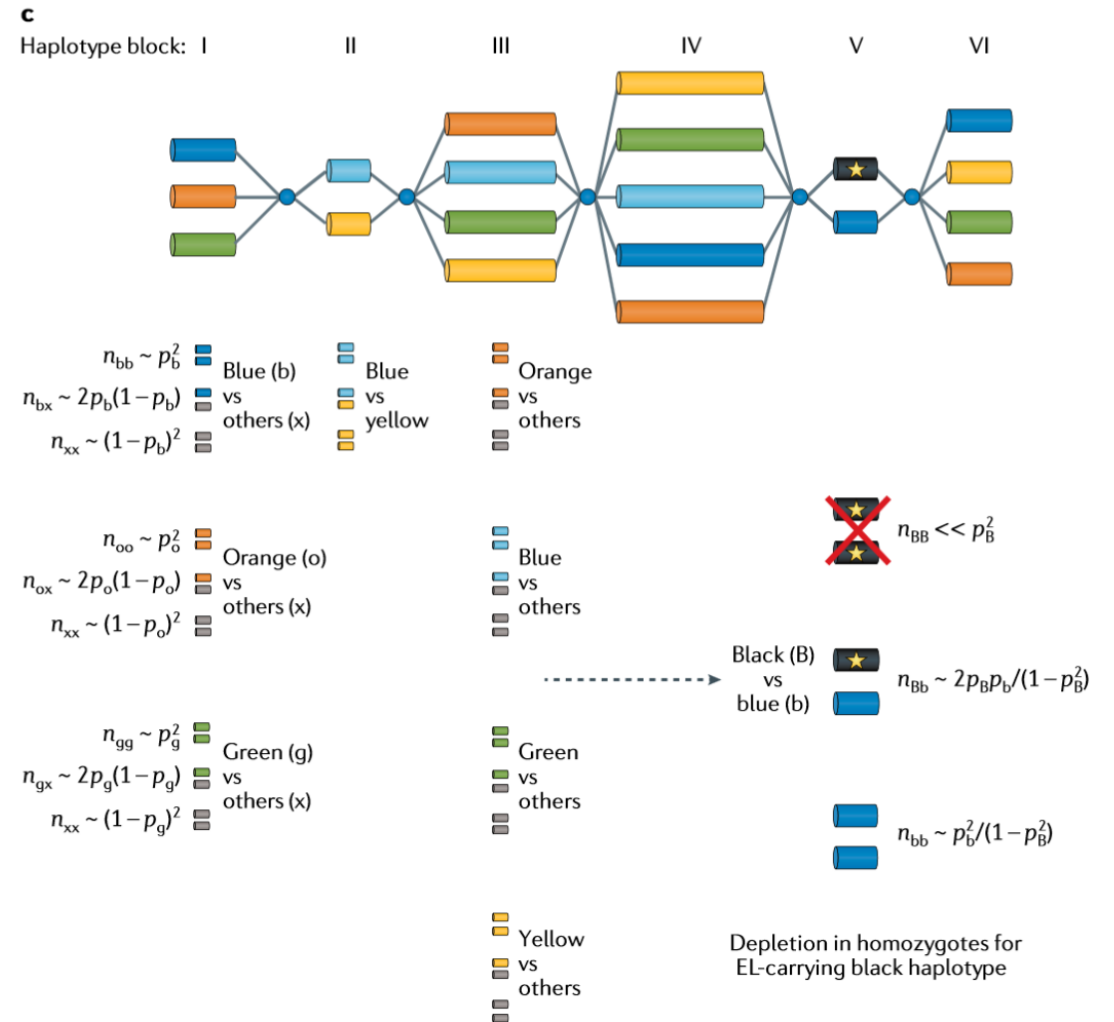
- collaboration with Qualitas AG (Franz Seefried)

→ Identification of genetic variants causing embryonic lethality and congenital disorders

# Harnessing genomic information for livestock improvement

Michel Georges , Carole Charlier & Ben Hayes

Nature Reviews Genetics **20**, 135–156 (2019) | [Download Citation](#) 



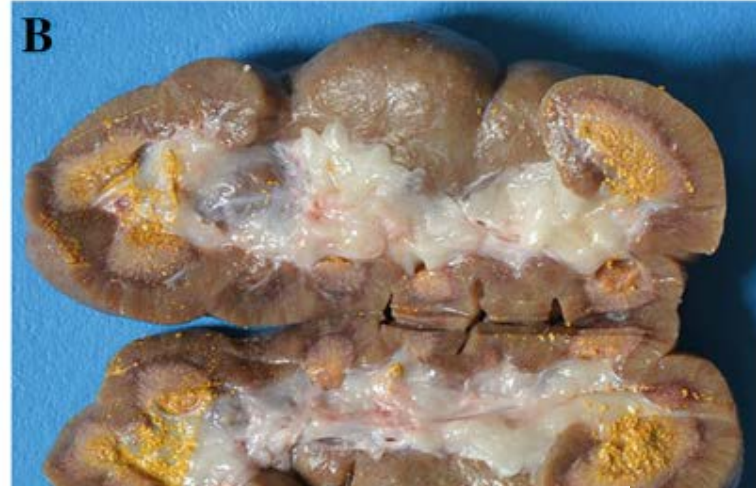
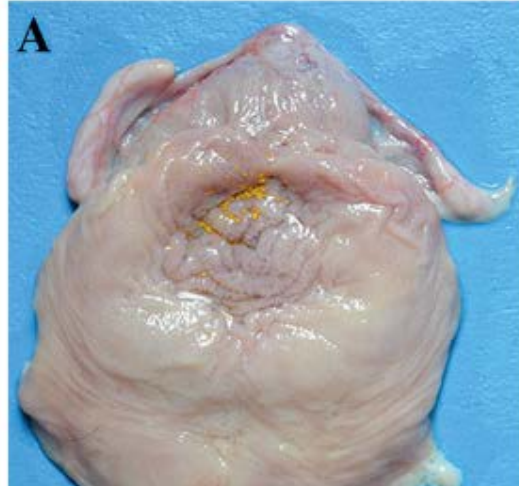
## Recessive mutations compromises fertility

Brachyspina in Holstein: **rarely** the homozygous mutant animals survive to term because this genotype is a relatively common cause of fertility failure





# Recessive mutations compromises rearing success



RESEARCH ARTICLE

Open Access



## A frameshift mutation in MOCOS is associated with familial renal syndrome (xanthinuria) in Tyrolean Grey cattle

Leonardo Murgiano<sup>1</sup>, Vidhya Jagannathan<sup>1</sup>, Christian Piffer<sup>2</sup>, Inmaculada Diez-Prieto<sup>3</sup>, Marilena Bolcato<sup>4</sup>, Arcangelo Gentile<sup>4</sup> and Cord Drögemüller<sup>1\*</sup> 

### Abstract

**Background:** Renal syndromes are occasionally reported in domestic animals. Two identical twin Tyrolean Grey calves exhibited weight loss, skeletal abnormalities and delayed development associated with kidney abnormalities and formation of uroliths. These signs resembled inherited renal tubular dysplasia found in Japanese Black cattle which is associated with mutations in the *claudin 16* gene. Despite demonstrating striking phenotypic similarities, no obvious presence of pathogenic variants of this candidate gene were found. Therefore further analysis was

rarely present in  
Original Braunvieh



# Cholesterol deficiency (CD) in Holstein also occur in *APOB* heterozygotes

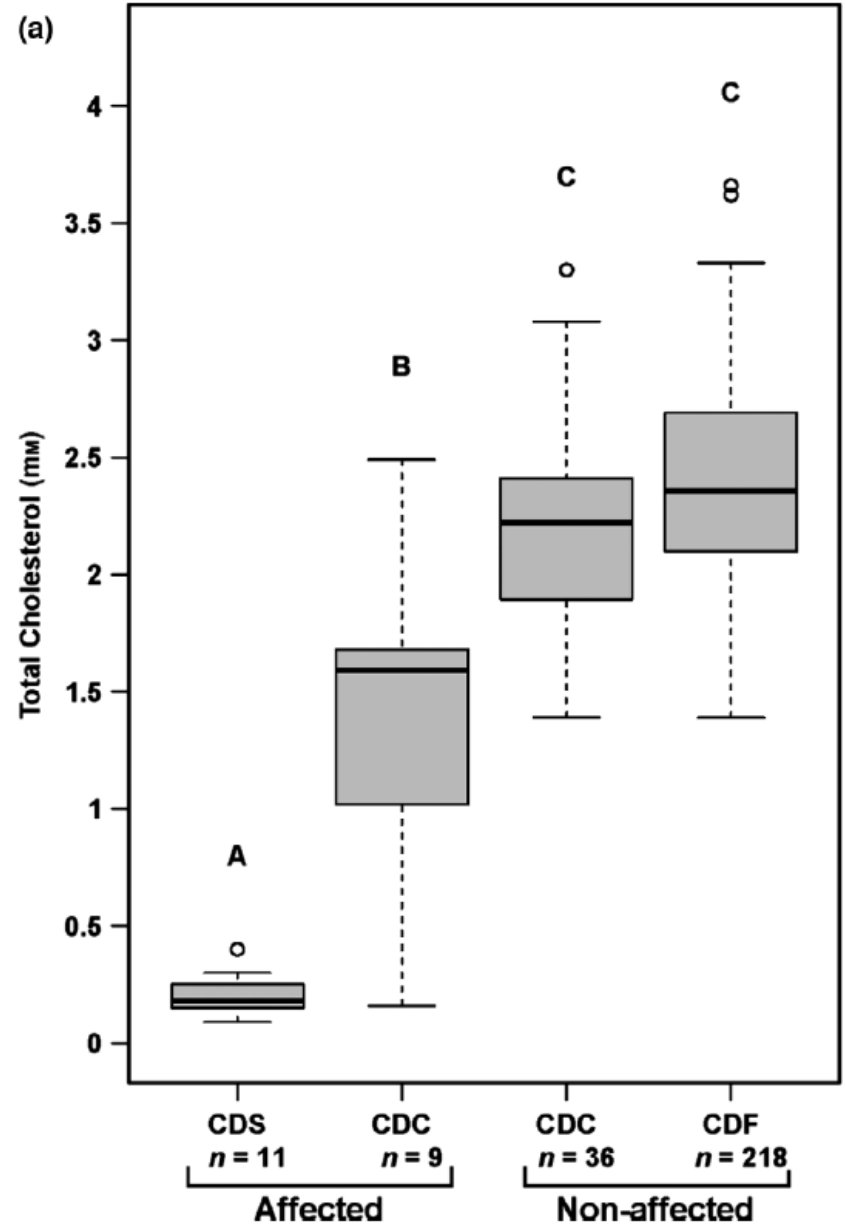
SHORT COMMUNICATION

doi: 10.1111/age.12801

## *APOB*-associated cholesterol deficiency in Holstein cattle is not a simple recessive disease

Irene Monika Häfliger\*, Sonja Hofstetter\*, Thomas Mock†, Manuela Hanna Stettler†, Mireille Meylan†, Kemal Mehinagic‡, Nadine Stokar-Regenscheit‡ and Cord Drögemüller\* 

\*Institute of Genetics, Vetsuisse Faculty, University of Bern, Bern, 3001, Switzerland. †Clinic for Ruminants, Vetsuisse Faculty, University of Bern, Bern 3001, Switzerland. ‡Institute of Animal Pathology, Vetsuisse Faculty, University of Bern, Bern, 3001, Switzerland.





# Screening for missing homozygosity in Original Braunvieh



4'892 animals

density: 135K SNPs

window size: 150 SNPs

# Workflow focus on SNVs and short indels

Population-based  
resequencing

In silico identification  
of segregating coding  
variants in essential genes,  
which are predicted to  
have severe effects on  
protein function

Design of custom SNP  
array to interrogate  
candidate EL

Genotyping of large  
( $n > 10,000$ ) cohorts

Searching for depletion  
in homozygotes:

- In entire population  
(Hardy-Weinberg  
disequilibrium)
- In carrier  $\times$  carrier  
matings ( $<0.25$ )

focussing on high and moderate impact variants in

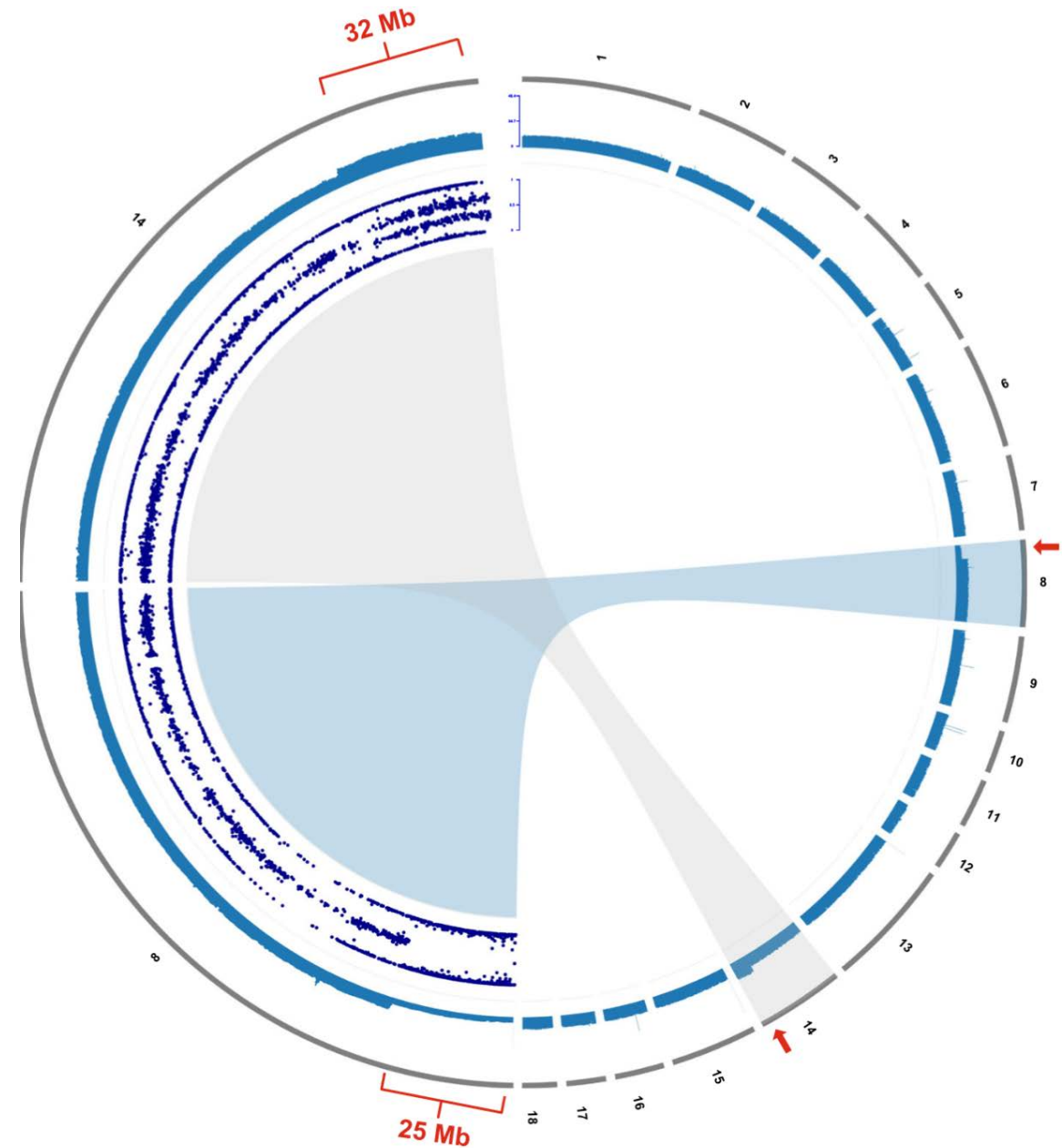
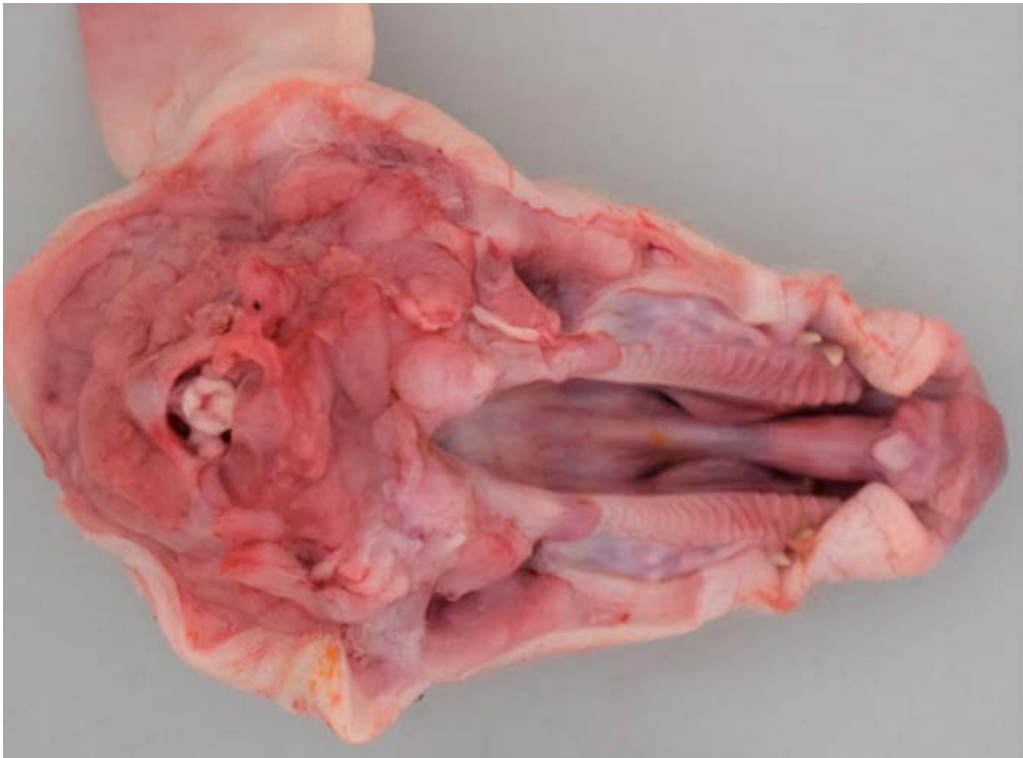
- candidate genes for **embryonic lethality**
- genes with high **pLI scores** ( $pLI \geq 0.9$ ) are extremely loss-of-function (LoF) intolerant
- developmental disorder genes included in the **DDG2P panel**

RESEARCH ARTICLE

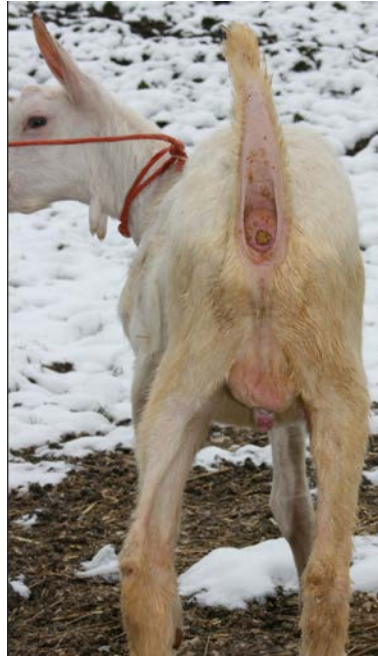
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# Chromosomal imbalance in pigs showing a syndromic form of cleft palate

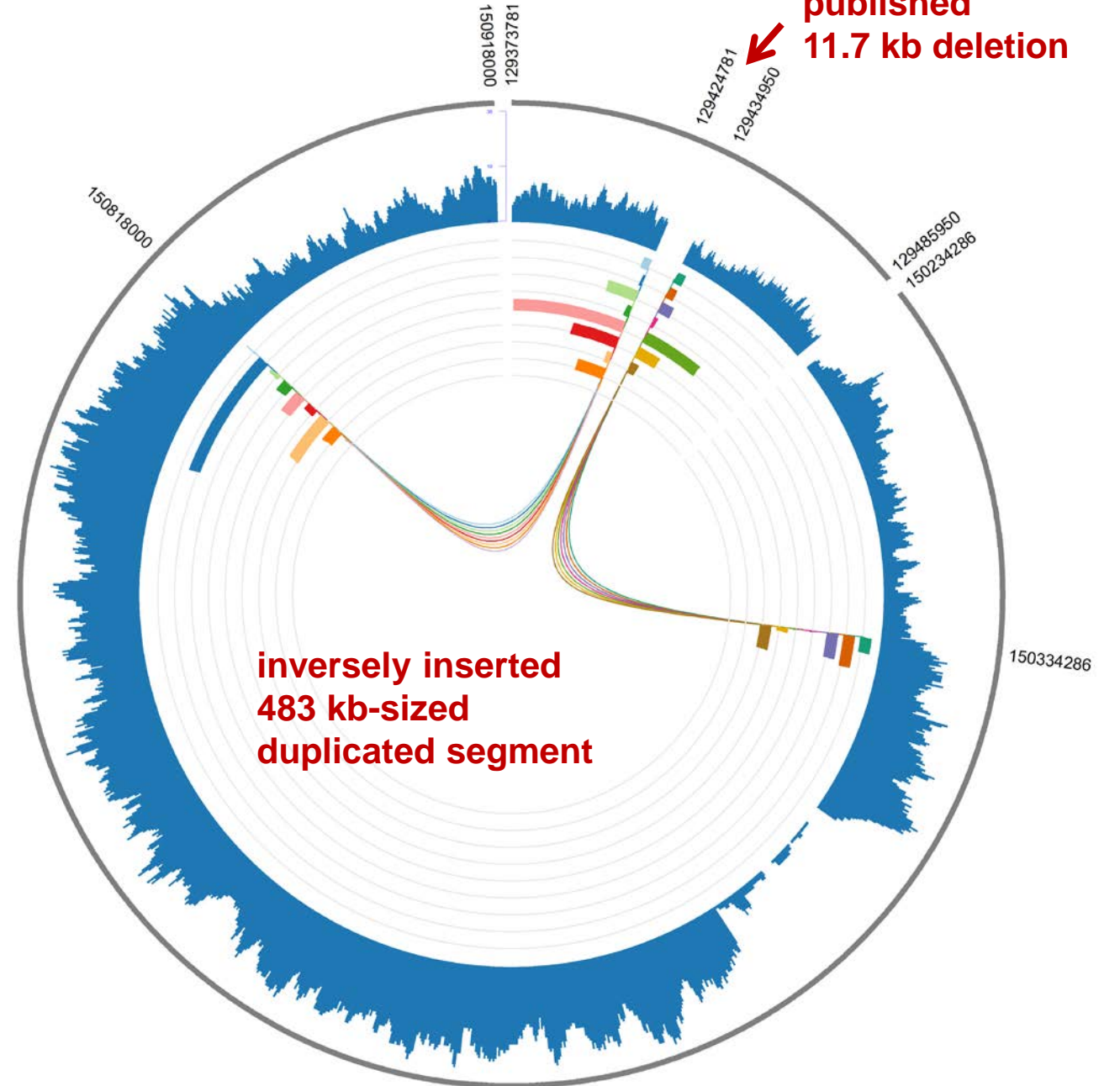
Alexander Grahofer<sup>1</sup>, Anna Letko<sup>2</sup>, Irene Monika Häfliger<sup>2</sup>, Vidhya Jagannathan<sup>2</sup>, Alain Ducos<sup>3</sup>, Olivia Richard<sup>4</sup>, Vanessa Peter<sup>5</sup>, Heiko Nathues<sup>1</sup> and Cord Drögemüller<sup>2\*</sup>



# The caprine polled variant: more complex than known before



published  
11.7 kb deletion





## Take home message

SNV / short indel = only ~half of the variation

CNV / SV = still difficult (and expensive) to detect