

Exploring tissue-specificity in the regulatory landscape of bovine genome



Gabriel Costa Monteiro Moreira, Can Yuan, Sébastien Dupont, Lijing Tang, Young-Lim Lee, Doreen Becker, Mazdak Salavati, Richard Clark, Emily L. Clark, Graham Plastow, Christa Kühn and Carole Charlier on behalf of the BovReg consortium



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 815668

Disclaimer: the sole responsibility of this presentation lies with the authors. The Research Executive Agency is not responsible for any use that may be made of the information contained therein.

ISAG 2023
39th International Society
for Animal Genetics
CONFERENCE

2 – 7 July 2023
CAPE TOWN, SOUTH AFRICA

www.isag.us/2023

BovReg Exploring tissue-specificity in the regulatory landscape of bovine genome

- BovReg consortium brings together scientists from twenty leading laboratories from different countries (EU, Switzerland, international organizations, Canada and Australia)
- Aims to improve our understanding of the cattle genome; also provide a comprehensive map of functionally active genomic features in cattle
- Critical for biological discovery and in linking genotype to phenotype; key knowledge for biology-driven genomic prediction needed by scientific and industry livestock communities.



www.bovreg.eu



@BovReg.H2020



@BovReg



BovReg



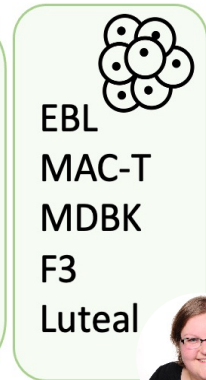
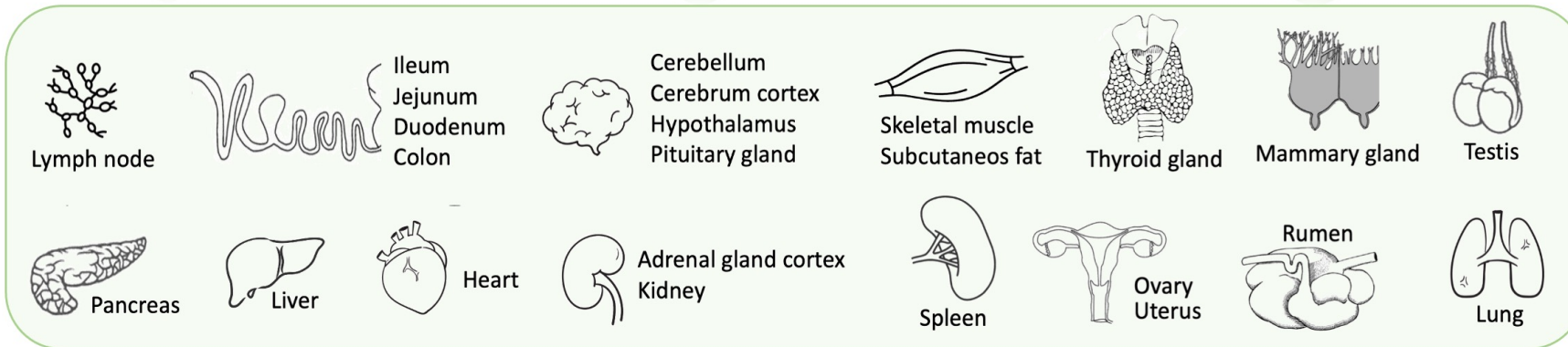
BovReg project

BovReg Exploring tissue-specificity in the regulatory landscape of bovine genome

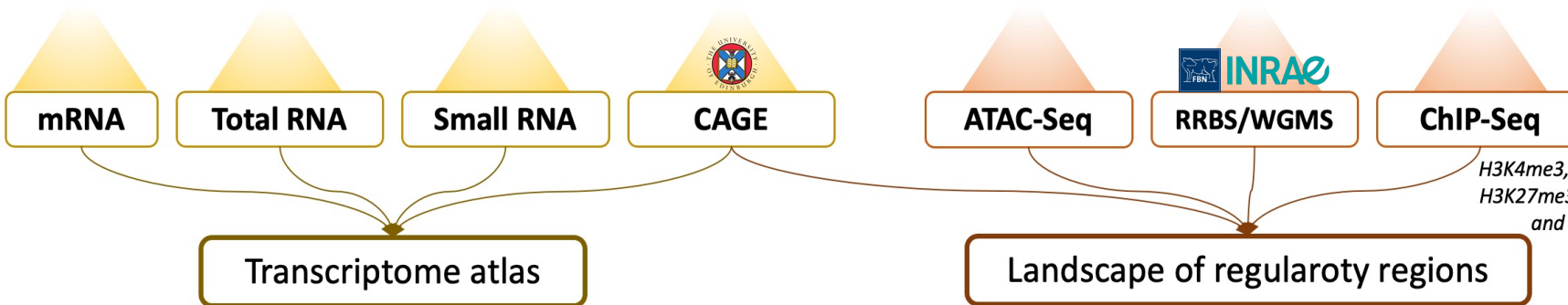
➤ BovReg utilizes a diverse catalogue of tissues for functional annotation.



WGS (30X)



OP14
P103



H3K4me3, H3K4me1,
H3K27me3, H3K27ac
and CTCF

nextflow
nf-core <https://github.com/BovReg>

BovReg Exploring tissue-specificity in the regulatory landscape of bovine genome

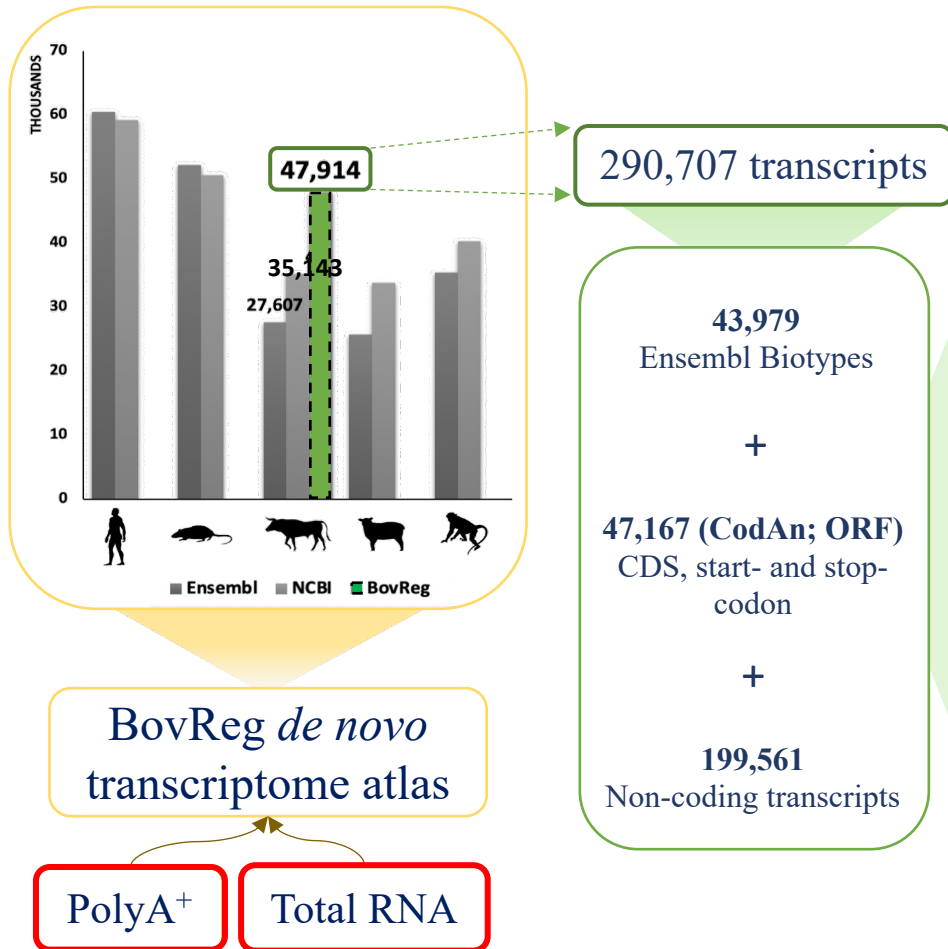


Transcriptome atlas



BovReg Exploring tissue-specificity in the regulatory landscape of bovine genome

- BovReg expanded the catalog of bovine non-coding RNAs by including non-polyadenylated transcripts.
- BovReg improved the transcriptome annotation based on gene models.



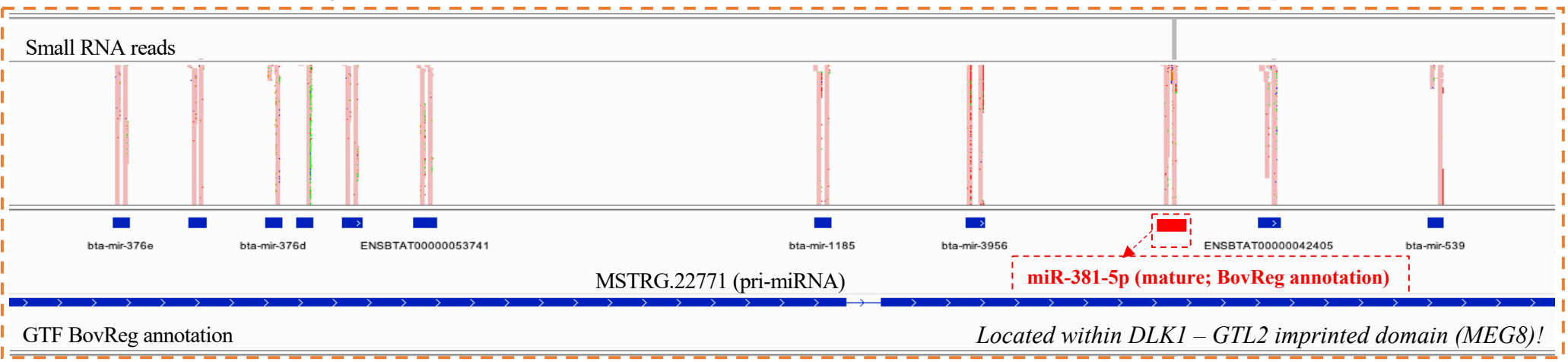
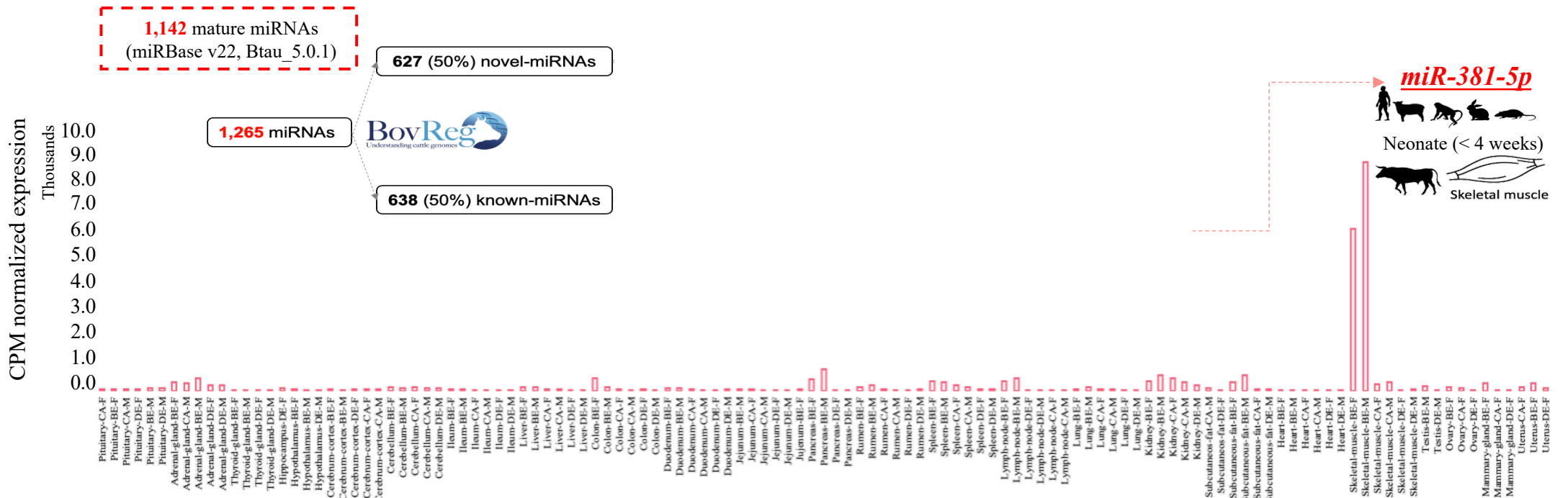
Class code ¹	Features ¹	Compared with bovine annotation	
		Ensembl r.105	NCBI r.106
=	complete transcripts with exact match of intron chain	42873 (14.75%)	36660 (12.61%)
c	transcripts contained in the reference (intron compatible)	4 (0.00%)	3082 (1.06%)
k	containment of reference (reverse containment)	25403 (8.74%)	24814 (8.54%)
m	transcripts with retained introns (all introns matched or retained)	4555 (1.57%)	6321 (2.17%)
n	transcripts with retained introns (not all introns matched or retained)	13812 (4.75%)	14760 (5.08%)
j	multi-exon transcripts with at least one junction match	142987 (49.19%)	150476 (51.76%)
e	single exon transcript partially covering an intron (possible pre-mRNA fragment)	0 (0.00%)	170 (0.06%)
o	other same strand transcripts overlap with reference exons	6422 (2.21%)	9458 (3.25%)
s	transcripts with intron match on the opposite strand (likely a mapping error)	63 (0.02%)	81 (0.03%)
x	exonic transcripts overlap on the opposite strand (like o or e but on the opposite strand)	10569 (3.64%)	8817 (3.03%)
i	transcripts fully contained within a reference intron	10961 (3.77%)	12419 (4.27%)
y	transcripts with a reference transcript within its intron	1871 (0.64%)	999 (0.34%)
p	possible polymerase run-on (no actual overlap)	357 (0.12%)	342 (0.12%)
r	repeat (at least 50% bases soft-masked)	0 (0.00%)	0 (0.00%)
u	none of the above (unknown, intergenic)	30830 (10.61%)	22308 (7.67%)
Total number of transcripts		290,707	

¹ Transcript classification code from gffcompare v.0.12.2¹⁰.

BovReg Exploring tissue-specificity in the regulatory landscape of bovine genome

➤ BovReg expanded the repertoire of mature miRNAs annotated in bovine.

Tissue-specific miRNA



BovReg Exploring tissue-specificity in the regulatory landscape of bovine genome

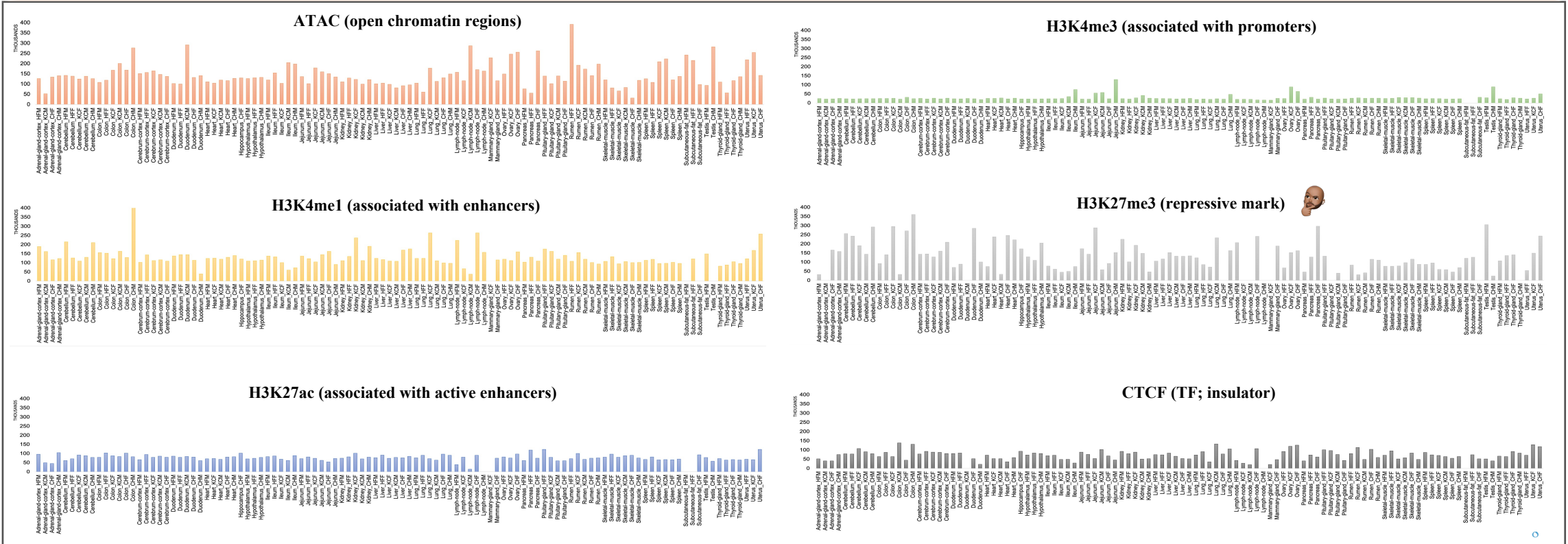
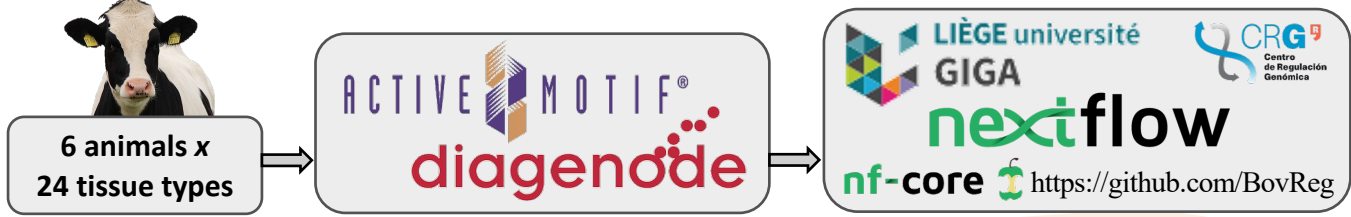


Regulatory regions



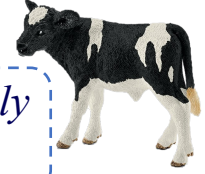
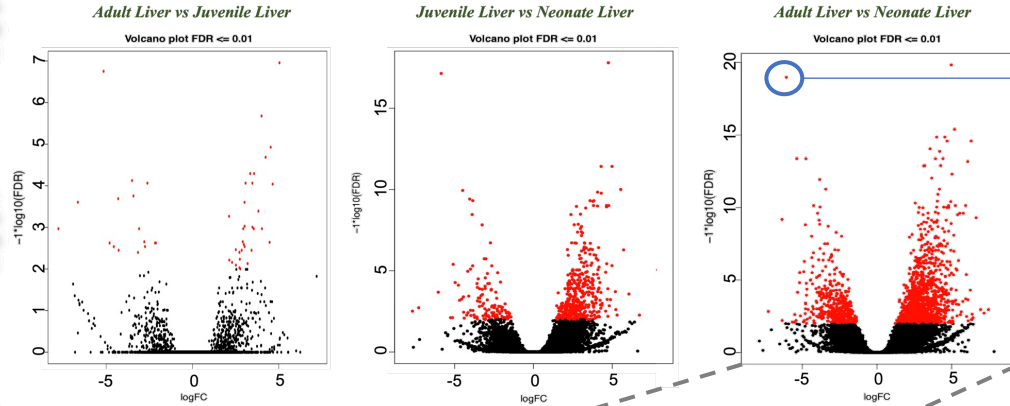
BovReg Exploring tissue-specificity in the regulatory landscape of bovine genome

➤ We identified thousands of peaks for the different marks in our catalogue of tissues!

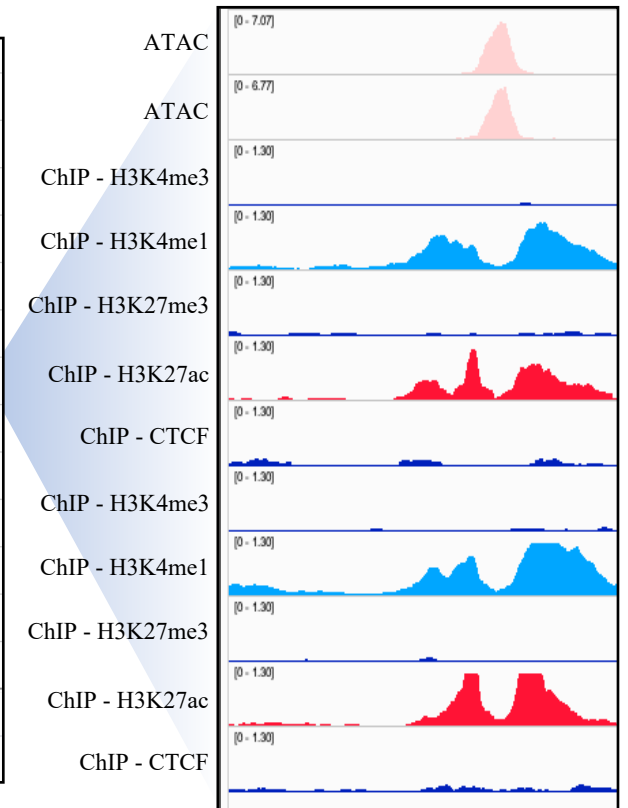
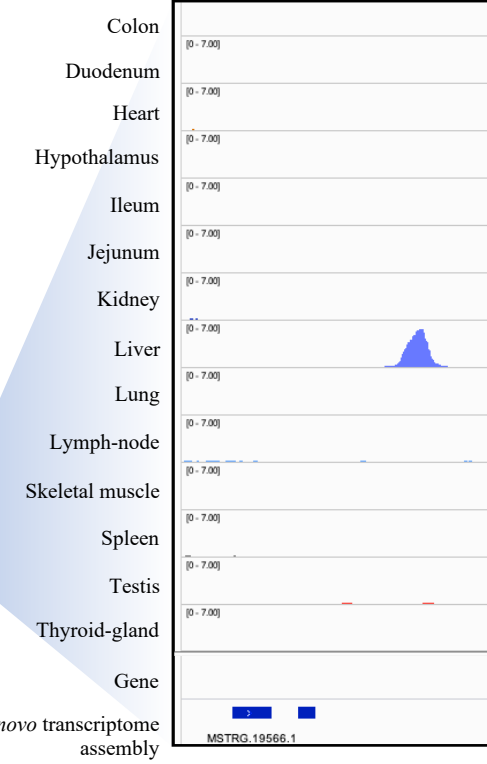
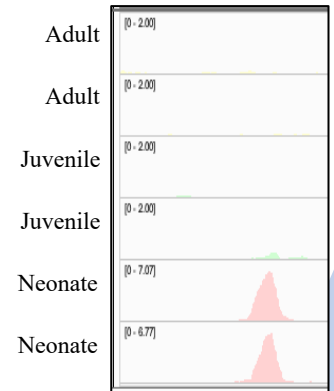
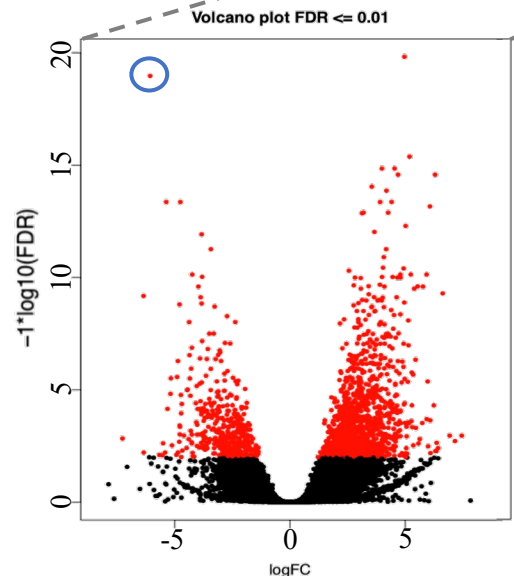


BovReg Exploring tissue-specificity in the regulatory landscape of bovine genome

➤ Expanding the repertoire of regulatory regions in the different stages/ages. Diversity is key!



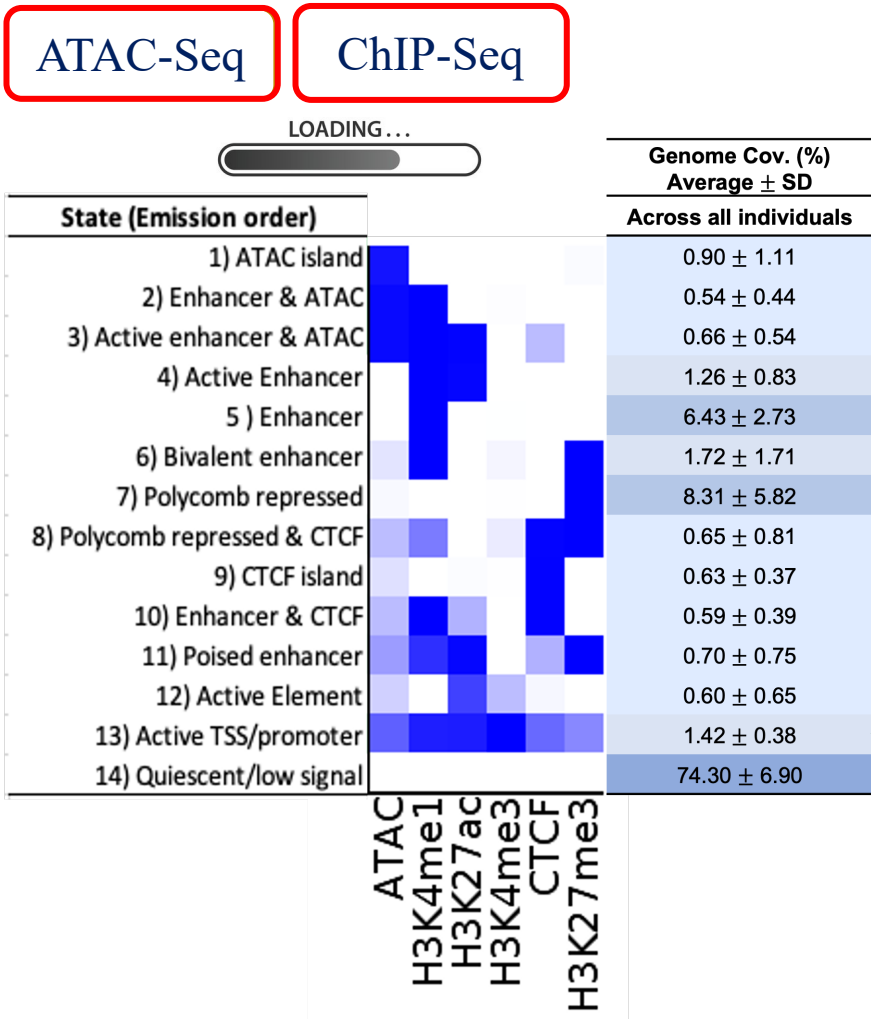
Active enhancer (liver specific) only detected in neonate animals!!



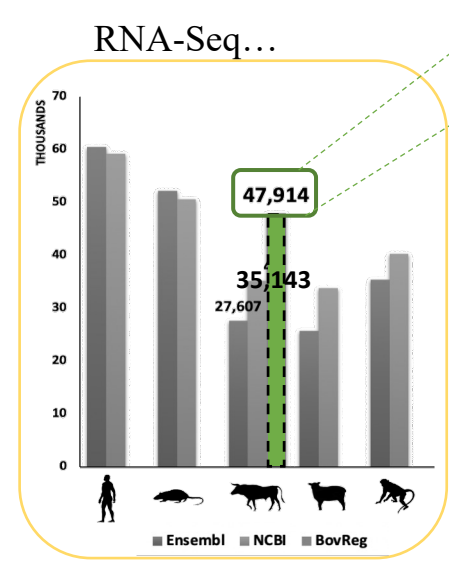
- 1.642 differentially accessible regions
- 423 down (up in Neonate Liver)
- 1.219 up in Adult Liver

BovReg Exploring tissue-specificity in the regulatory landscape of bovine genome

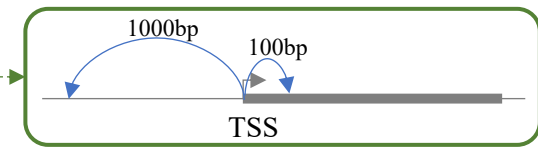
- Around 25% of the genome was covered by different chromatin states (except quiescent).
- The vast majority of TSS annotated on RNA-Seq were validated by chromatin states.



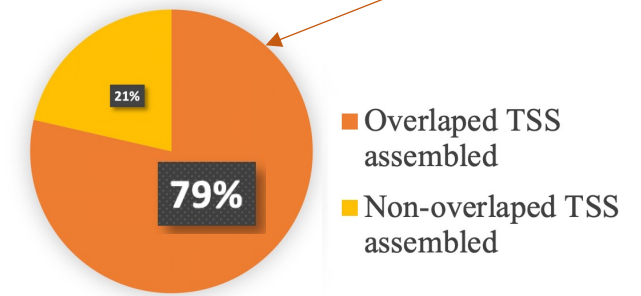
Are these regions in agreement with transcripts assembly?



290,707 transcripts

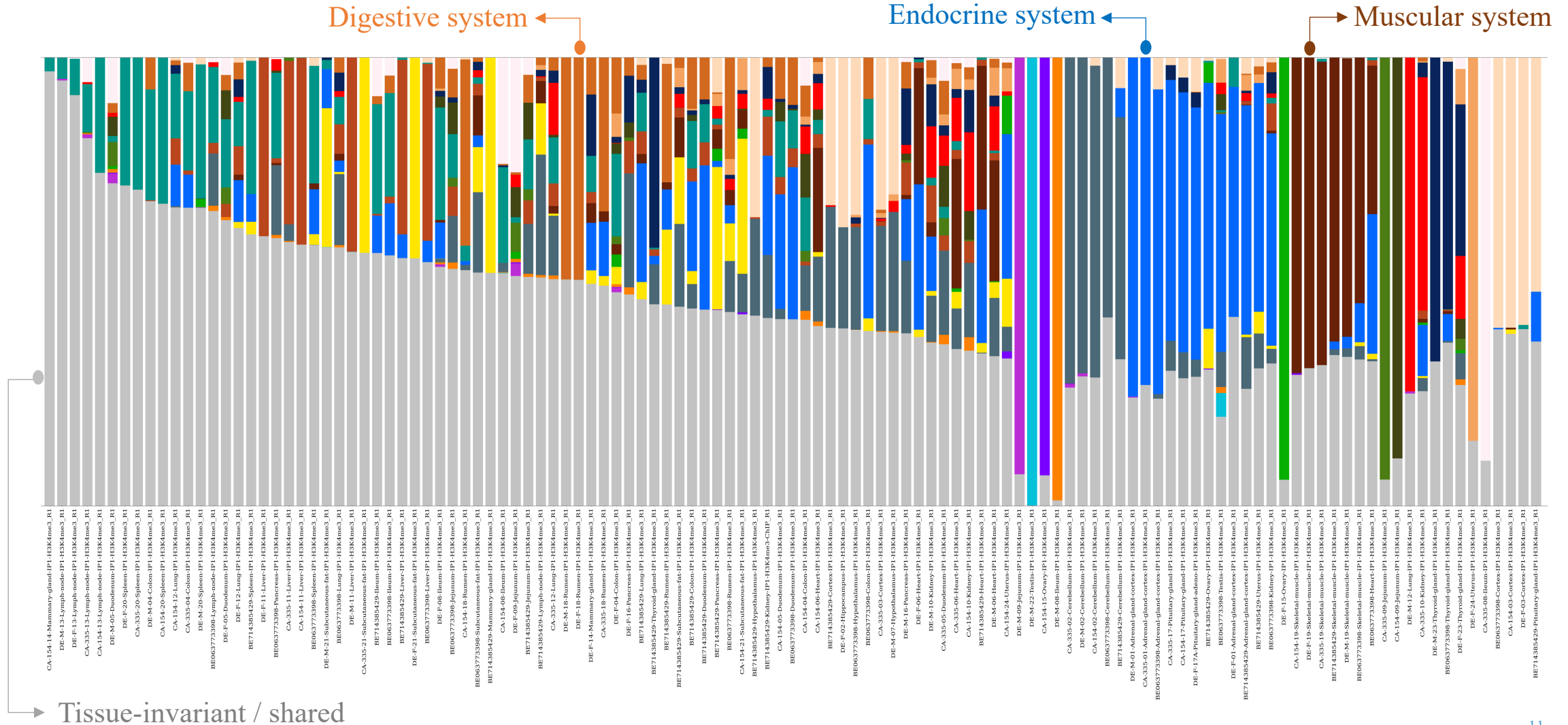


State 13
Active TSS/promoter



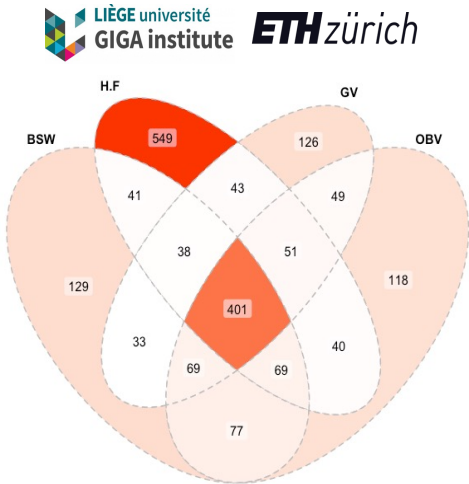


➤ Active TSS/promoter: Tissue-specific and tissue-shared components by non-negative matrix factorization.



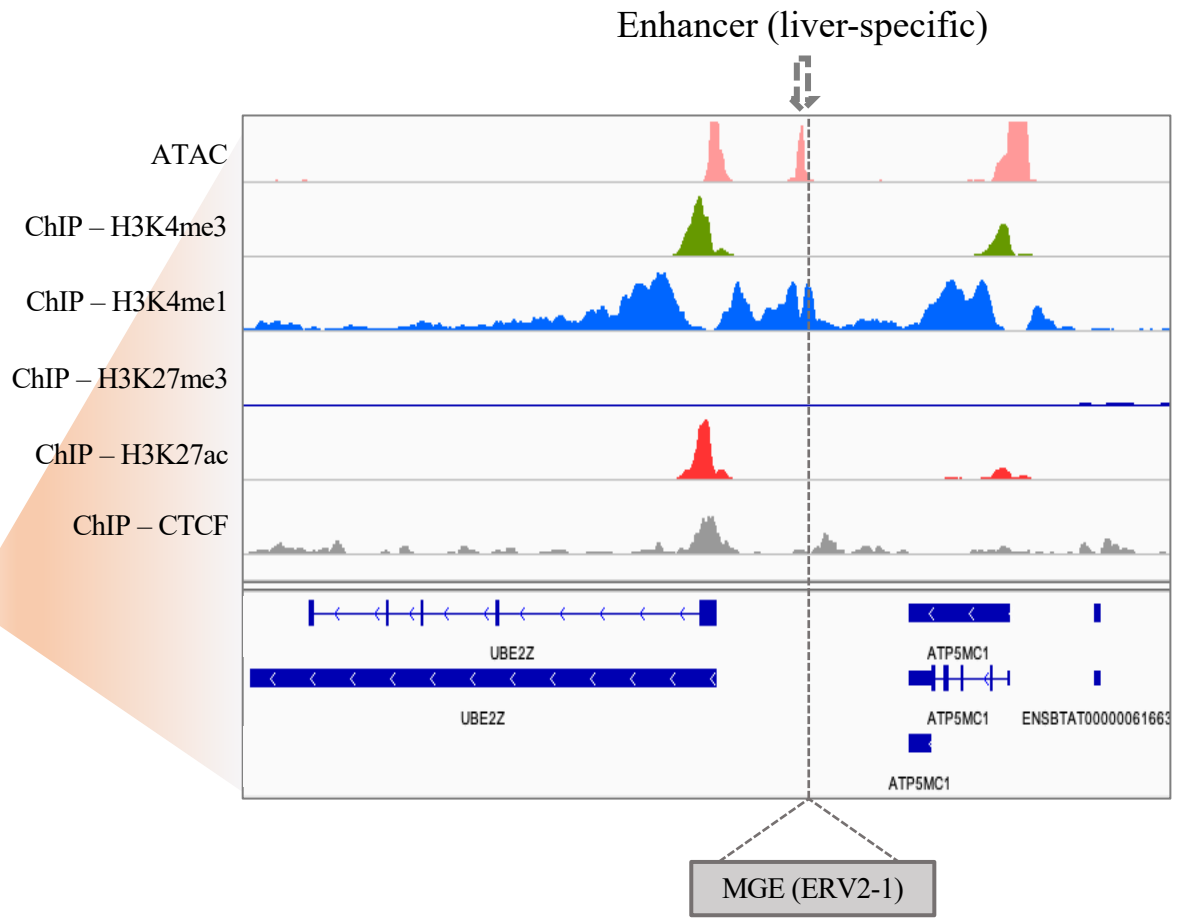
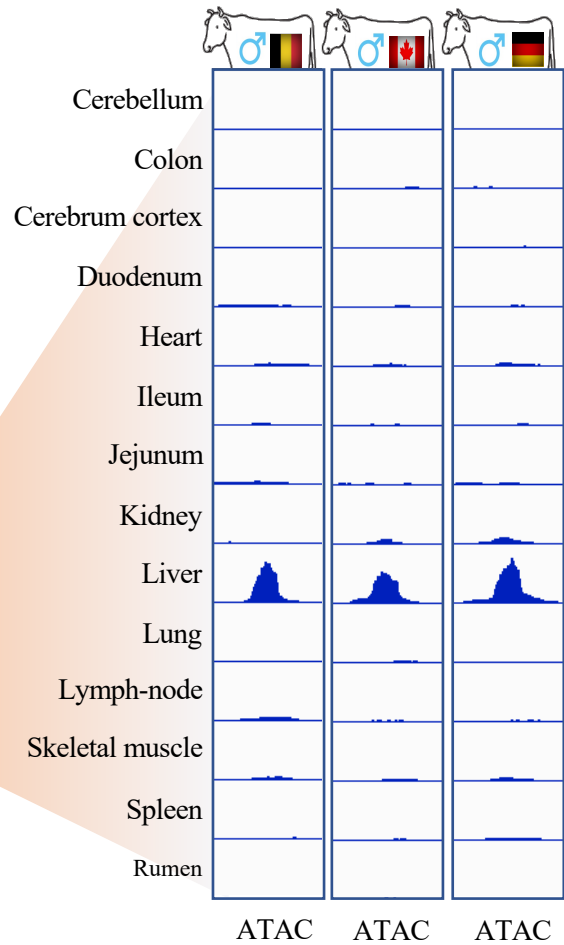


➤ Mobile genetic element co-localized with liver-specific regulatory elements!



Holstein-Friesian (H.F), Brown Swiss (BSW), Grauvieh (GV) and Original Braunvieh (OBV).

> 700 probes in genotyping array (public)



“Given the SV size distribution spike around the size of LTR elements, it is likely such transposable elements will increasingly be identified as a driving force behind bovine phenotypic diversity” - *Pangenome genotyped structural variation improves molecular phenotype mapping in cattle*; Leonard, Mapel & Pausch, bioRxiv 2023.



Perspectives & take-home message

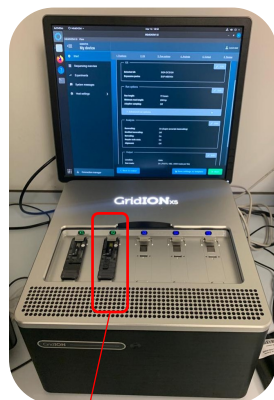
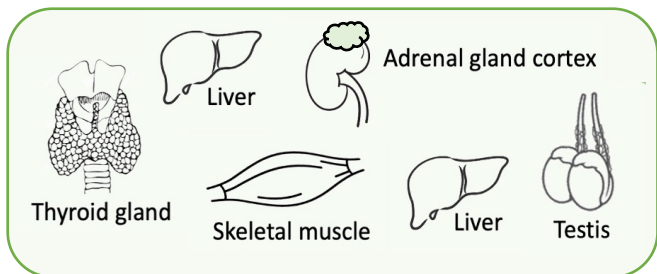


BovReg Exploring tissue-specificity in the regulatory landscape of bovine genome



Perspectives!

- Long-read cDNA sequencing (ONT-Seq)
- First trial: one flow cell - 6 samples



96,623 transcripts assembled

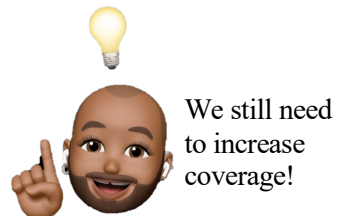


vs

91,445 transcripts assembled Illumina (same samples)

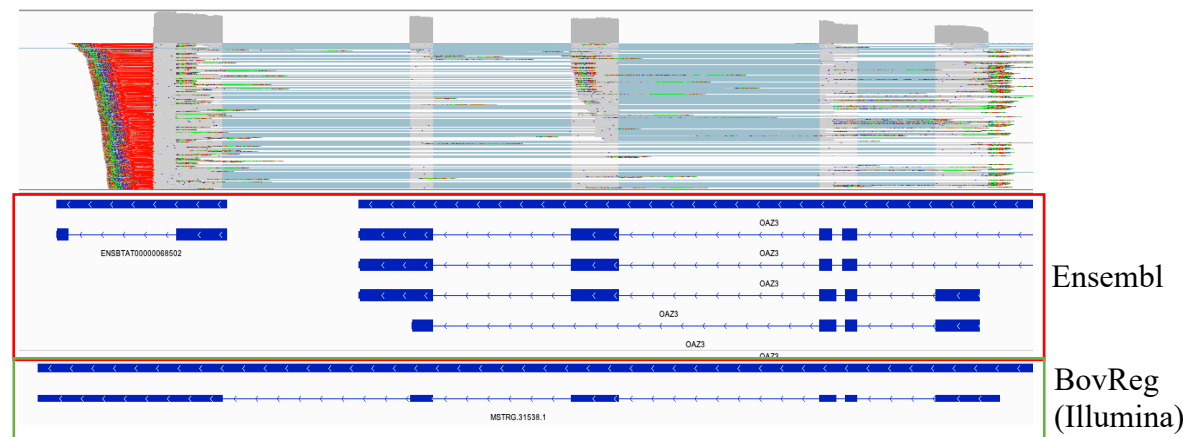
gff-compare

58.68% of the transcripts assembled by Illumina exhibits a perfect match with ONT transcripts!

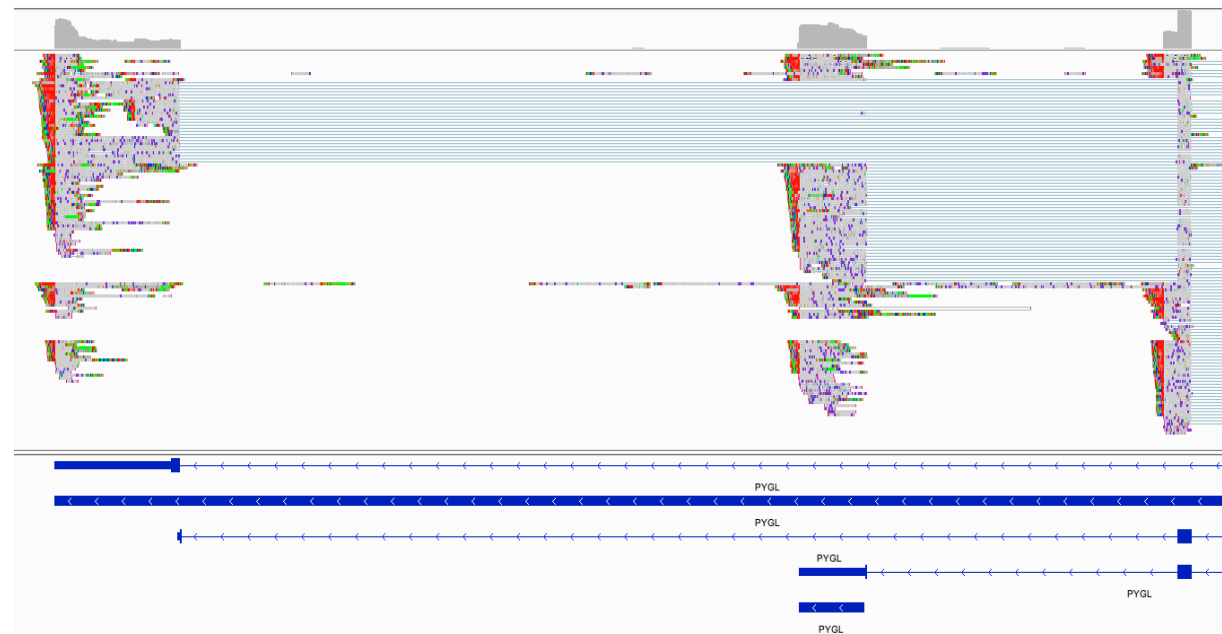


We still need to increase coverage!

- Preliminary data: new isoforms validated.



- Preliminary data: alternative exon usage.



BovReg Exploring tissue-specificity in the regulatory landscape of bovine genome



Perspectives & take-home message!

- BovReg expanded the repertoire of regulatory elements annotated in cattle.
- BovReg identified (unannotated) tissues-specific regulatory elements across different developmental stages.
- Mobile genetic element co-localized with tissue-specific regulatory elements.
- Panel of tests for unfixed MGE insertions in cattle: a legacy of BovReg!

Improving the annotation of the cattle genome by annotating transcription start sites in a diverse set of tissues and populations using Cap Analysis Gene Expression sequencing

Mazdak Salavati ¹,* Richard Clark,² Doreen Becker,³ Christa Kühn,^{3,4} Graham Plastow,⁵ Sébastien Dupont,⁶ Gabriel Costa Monteiro Moreira,⁶ Carole Charlier,^{6,7} Emily Louise Clark,¹ on behalf of the BovReg consortium

¹The Roslin Institute, University of Edinburgh, Edinburgh EH25 9RG, UK
²Edinburgh Clinical Research Facility, Genetics Core, University of Edinburgh, Edinburgh EH4 2XU, UK
³Institute of Genome Biology, Research Institute for Farm Animal Biology (FBN), Dummerstorf 18196, Germany
⁴Faculty of Agricultural and Environmental Sciences, University Rostock, Rostock 18059, Germany
⁵Department of Agricultural, Food and Nutritional Science, Livestock Gentec, University of Alberta, Edmonton T6G 2H1, Canada
⁶Unit of Animal Genomics, GIGA Institute, University of Liège, Liège 4000, Belgium
⁷Faculty of Veterinary Medicine, University of Liège, Liège 4000, Belgium

*Corresponding author: The Roslin Institute, Royal (Dick) School of Veterinary Studies, University of Edinburgh, Edinburgh EH25 9RG, UK.
Email: Mazdak.Salavati@roslin.ed.ac.uk
¹Present address: Dairy Research and Innovation Centre, Scotland's Rural College (SRUC), The Barony Campus, Dumfries DG1 3NE, UK.

BovReg Final Conference

University Foundation
Room "Felicien Cattier"
Bruxelles
(virtual participation available)

14th (afternoon)
15th (full day)
February 2024

Watch out our website www.bovreg.eu for further details to be announced soon!

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 815668.

Thank you for your attention!



www.bovreg.eu

@BovReg BovReg project

@BovReg.H2020 BovReg



WUR, the Netherlands. BovReg General Assembly, October 2022.



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 815668

Disclaimer: the sole responsibility of this presentation lies with the authors. The Research Executive Agency is not responsible for any use that may be made of the information contained therein.

