

GENE-SWitCH: improving the functional annotation of pig and chicken genomes for precision breeding

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Session 84, 31st Aug., EAAP-WAAP-Interbull Congress 2023, Lyon



The regulatory GENomE of SWine and CHicken: functional annotation during development

- Started in July 2019 (4 years) - Extended to: December 2023



www.gene-switch.eu <https://eurofaang.eu> <https://data.faang.org/projects/GENE-SWitCH>



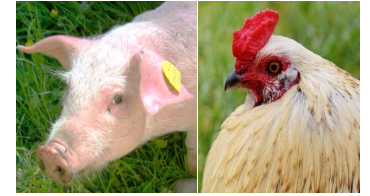
*This project has received funding from the European Union's **Horizon 2020 Research and Innovation** Programme under the grant agreement n° **817998***

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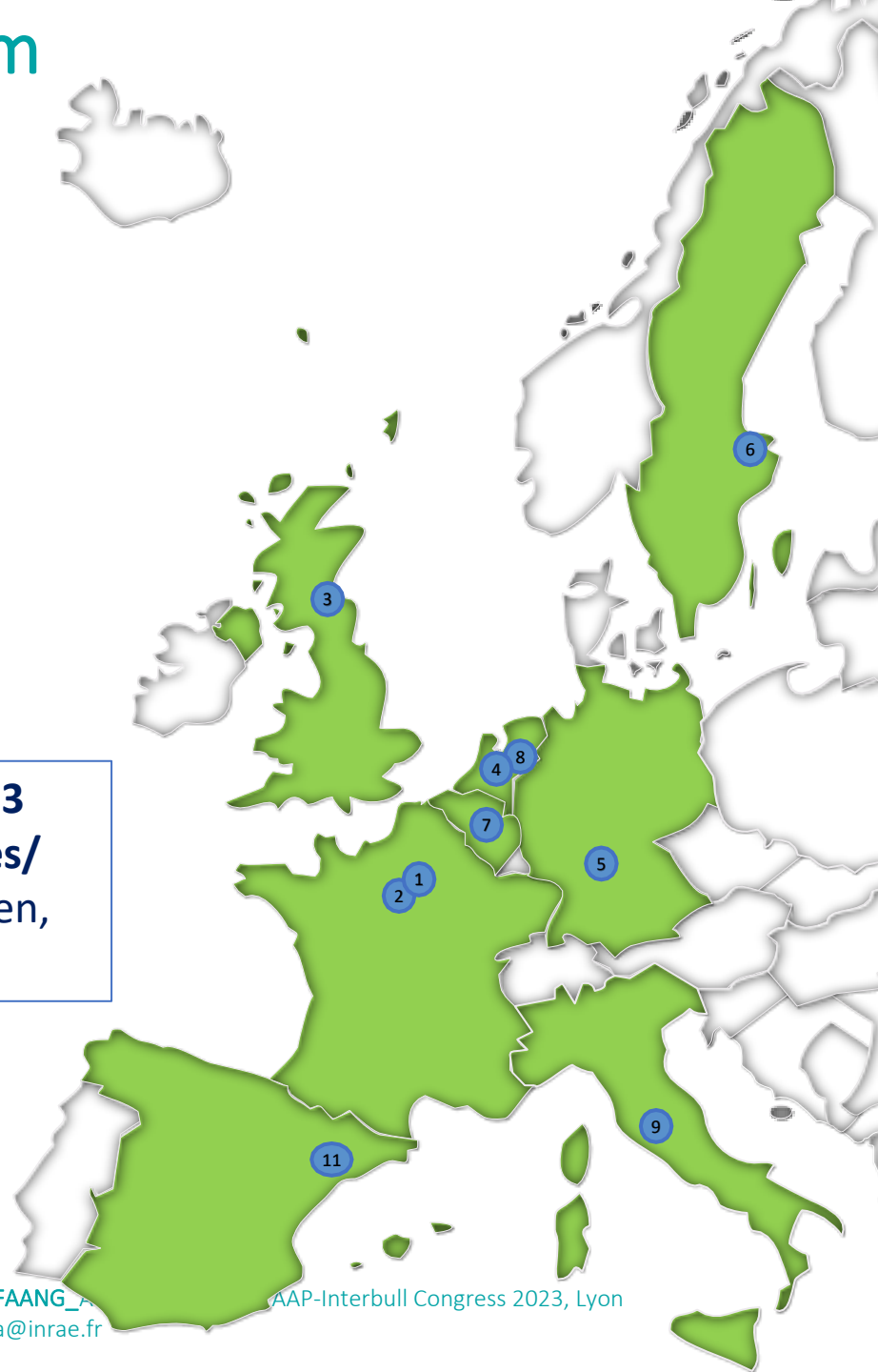


➤ Overall aim



- To deliver underpinning knowledge on the pig and chicken genomes
and
- To enable its translation to the pig and poultry sectors

> Consortium



Collaboration with 3 breeding companies/associations (Aviagen, Hypor B.V. and IFIP)

1.  
2. 
3.  THE UNIVERSITY of EDINBURGH
4.  WAGENINGEN UNIVERSITY & RESEARCH
5.  EMBL-EBI
6.  UPPSALA UNIVERSITET
7.  diagenode
Innovating Epigenetic Solutions
8.  EFFAB
European Forum of Farm Animal Breeders
9.  EAAP
European Federation of Animal Science
10.  HENDRIX GENETICS
11.  IRTA



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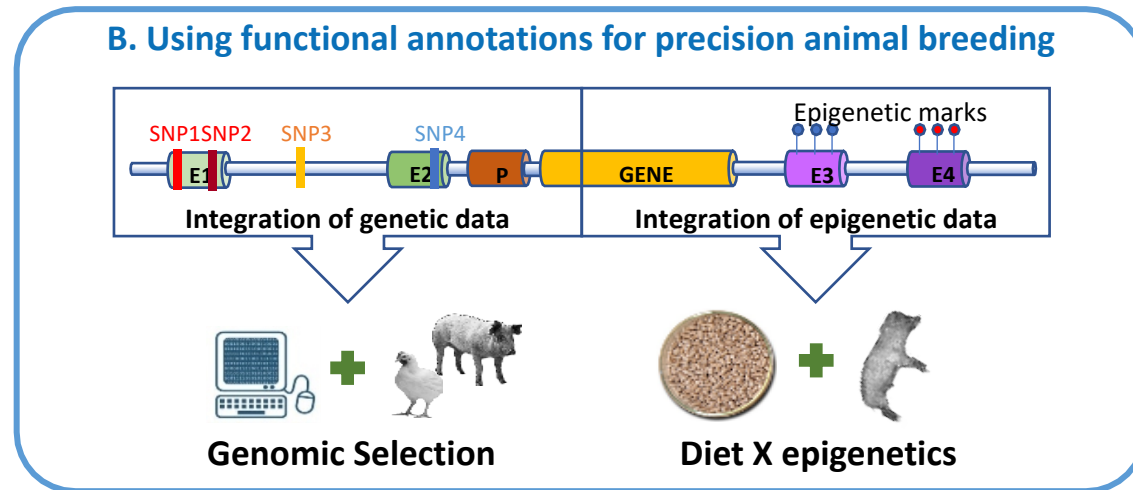
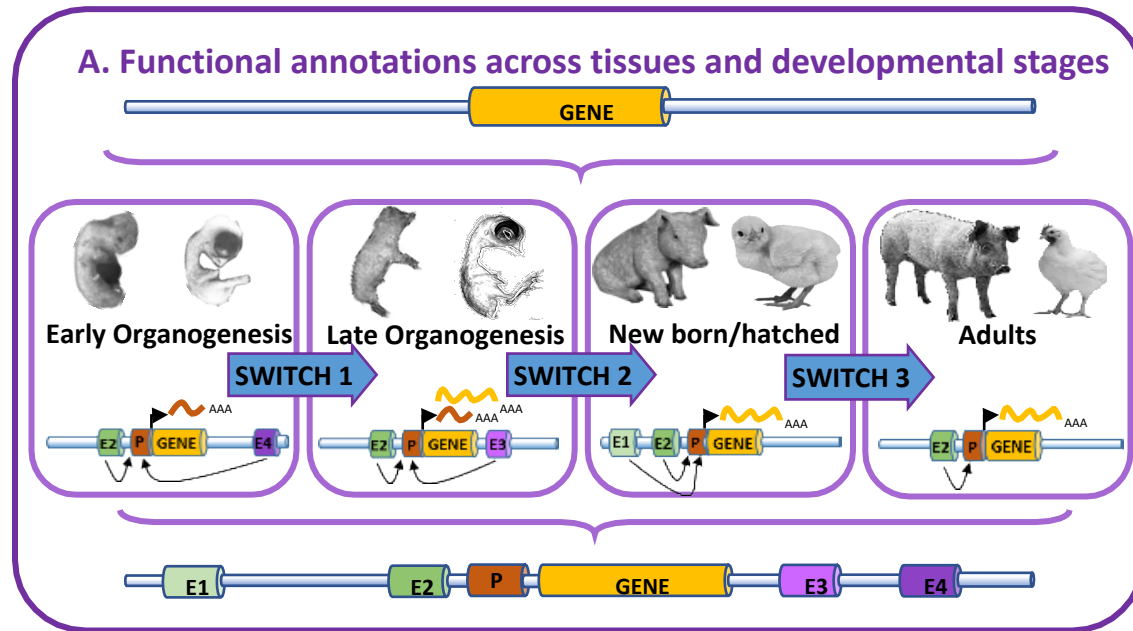
EAAP-Interbull Congress 2023, Lyon



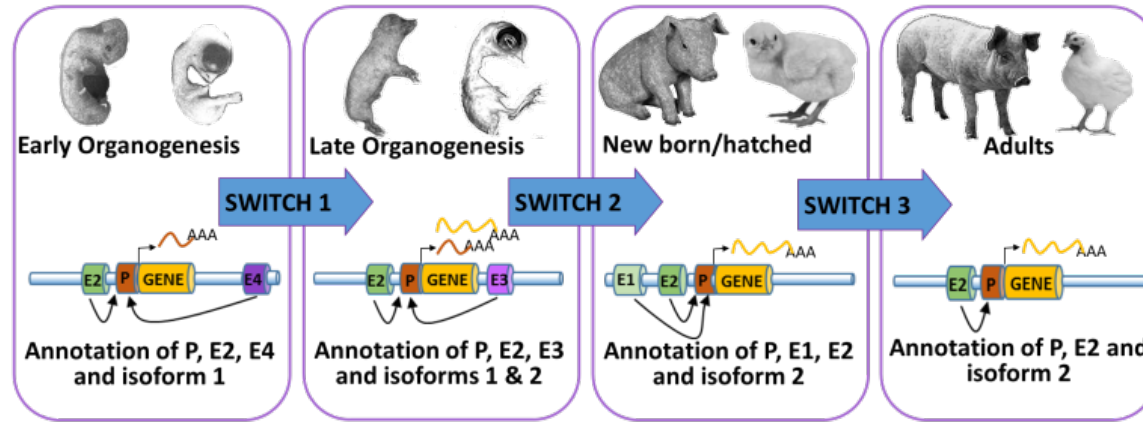
➤ Three specific & interconnected aims



WP7 (Project management and consortium coordination)
WP8 (Ethics requirements)



➤ Aim A: Functional annotations across tissues and developmental stages



Aims:

- Identify the functional elements of chicken and pig genomes across three developmental stages.
 - Characterize their tissue specificity and temporal dynamics (“switches”)
 - Characterize their patterns of conservation and variation (mammals vs. birds).
- Deliver high-quality, richly annotated genome annotation maps open to the community.



EMBL-EBI

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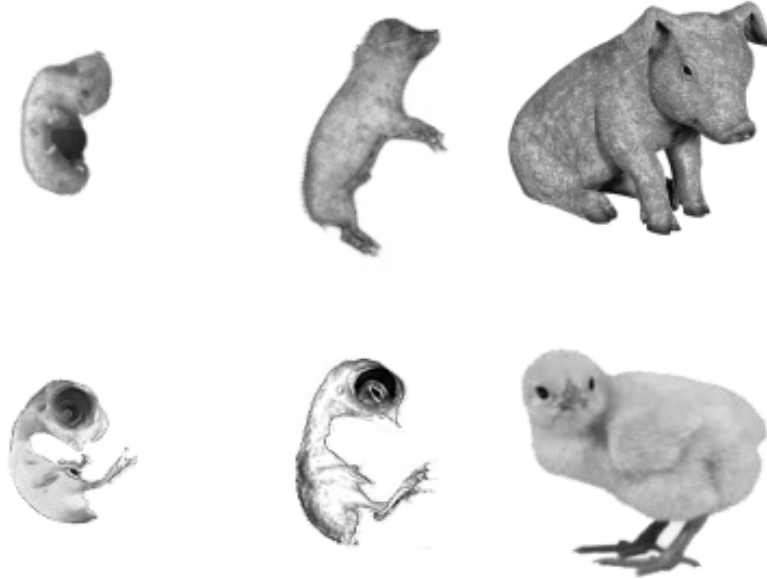
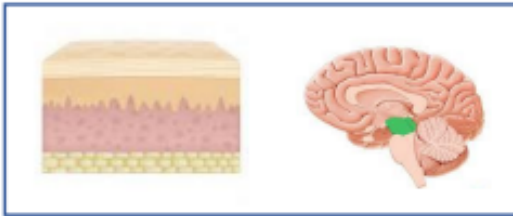
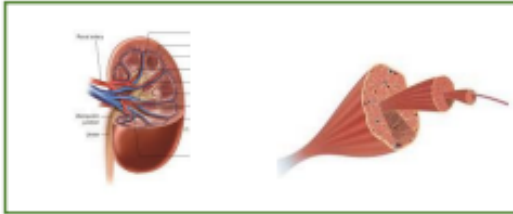
Inserm

WAGENINGEN
UNIVERSITY & RESEARCH

diagenode

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- Aim A-Results_Pig and chicken samples and metadata from seven targeted tissues at three developmental stages (WP1)



+ 6 additional tissues

(brain cortex, heart, stomach, spleen, large intestine, gonads)

New and improved standardised sampling and analysis protocols
(<https://data.faang.org>)

➤ Aim A-Results_omics datasets (WP1)

Assay		Number of libraries		Raw reads number per library (mean)		Accession Number	
		SSC	GGA	SSC	GGA	SSC	GGA
	ATAC-seq	84	84	100M	105M	PRJEB44468	PRJEB45945
	IgG	78	77	48M	58M	local server	
ChIP-seq	CTCF	82	78	51M	52M	local server	
	H3K4me1	80	76	95M	115M	local server	
	H3K4me3	83	76	50M	57M	local server	
	H3K27me3	83	81	103M	126M	local server	
	H3K27Ac	84	77	53M	61M	local server	
RNA-seq	mRNA-seq	84	84	150M		PRJEB41970	PRJEB42025
	smallRNA-seq	84	84	65M		PRJEB42001	PRJEB42041
	Iso-seq	21	21	3.5M		PRJEB50963	PRJEB48060
DNA methylation	RRBS	63	63	59M	55M	PRJEB41822	PRJEB41829
	WGBS	21	21	36X*	31X*	PRJEB42772	PRJEB42775
Capture Hi-C		12	12	180M	200M	PRJEB44486	local server

Raw data on <https://data.faang.org/GENE-SWitCH>

and ENA under the terms of the Fort Lauderdale agreement and Toronto Statement.

➤ Aim A-Results_ Analysis pipelines for primary analyses (WP2)

- Extensions and refinement of other nf-core community pipelines and new developments

JOURNAL ARTICLE

nf-core/iseq: simple gene and isoform annotation with PacBio Iso-Seq long-read sequencing

Sébastien Guizard , Katarzyna Miedzinska, Jacqueline Smith, Jonathan Smith, Richard I Kuo, Megan Davey, Alan Archibald, Mick Watson

Bioinformatics, Volume 39, Issue 5, May 2023, btad150,

<https://doi.org/10.1093/bioinformatics/btad150>



PAPER

TAGADA: a scalable pipeline to improve genome annotations with RNA-seq data

Cyril Kurylo,^{1,†} Cervin Guyomar,^{1,†} Sylvain Foissac^{1,*} and Sarah Djebali²

¹GenPhySE, Université de Toulouse, INRAE, INPT, ENVT, Toulouse, France and ²IRSD, Université de Toulouse, INSERM, INRAE, ENVT, Univ Toulouse III - Paul Sabatier (UPS), Toulouse, France

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FOR PUBLISHER ONLY Received on Date Month Year; revised on Date Month Year; accepted on Date Month Year

NAR Genomics and Bioinformatics, 2023, pp. 1–11

doi: [DOI HERE](#)

Advance Access Publication Date: Day Month Year
Paper

Submitted

GSM pipeline (bisulfite sequencing data) from extension of nf-core methyl-seq pipeline (De Vos et al. in prep.)

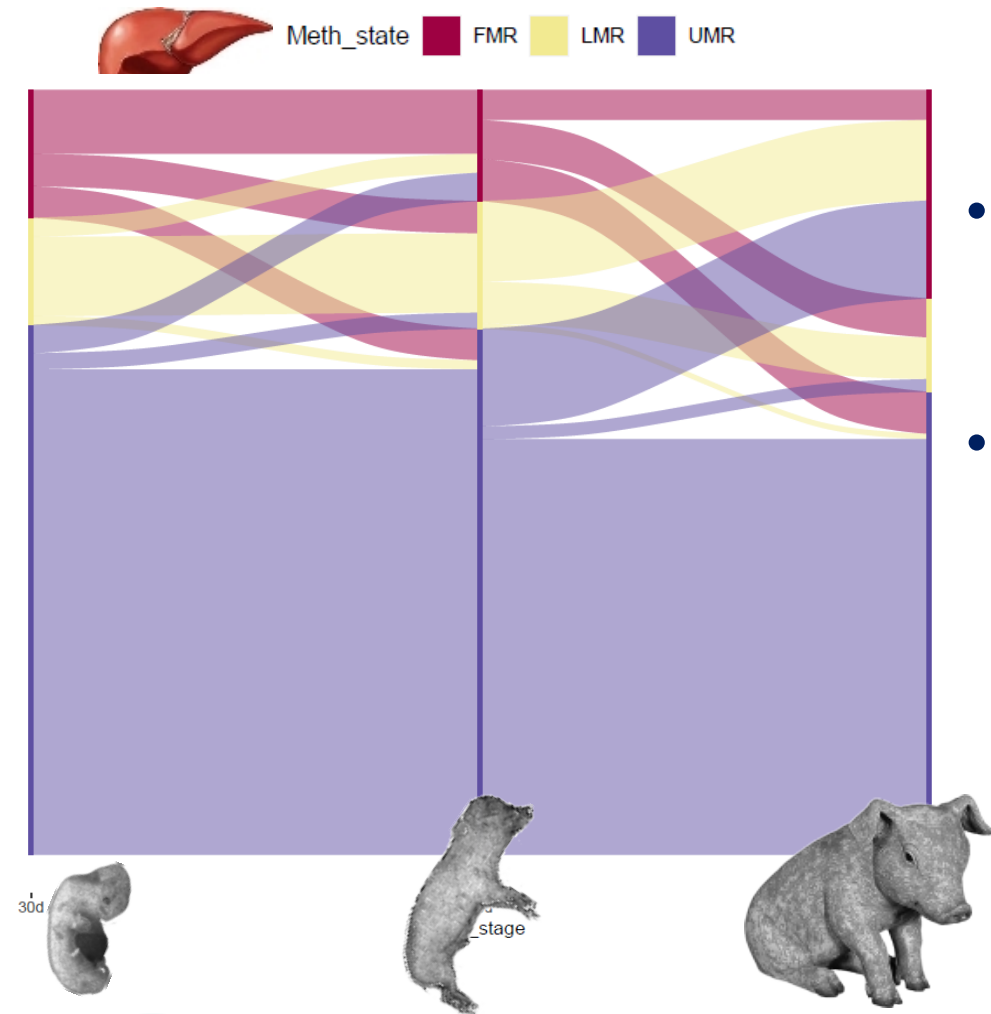
Github links for all assays' pipelines available on
<https://data.faang.org/GENE-SWitCH>

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➤ Aim A-Results_ Dynamics of functional sequences and comparative analyses (WP2)



- Several 'new' genes and transcripts identified by RNA-seq, sRNA-seq and Iso-seq data.
- Expected enrichment of open chromatin around promoters and TSS by ATAC-seq.
- Methylation 'switches' by WGBS and RRBS (De Vos et al. – left picture as example in porcine liver)

➤ Ongoing:

- Analyses of ChIP-seq and capture Hi-C data
- Integrative analyses to characterize switches and comparative analyses
- Various papers in prep.

➤ Aim A-Results_ Genome annotations (WP2)



JOURNAL ARTICLE

Ensembl 2023

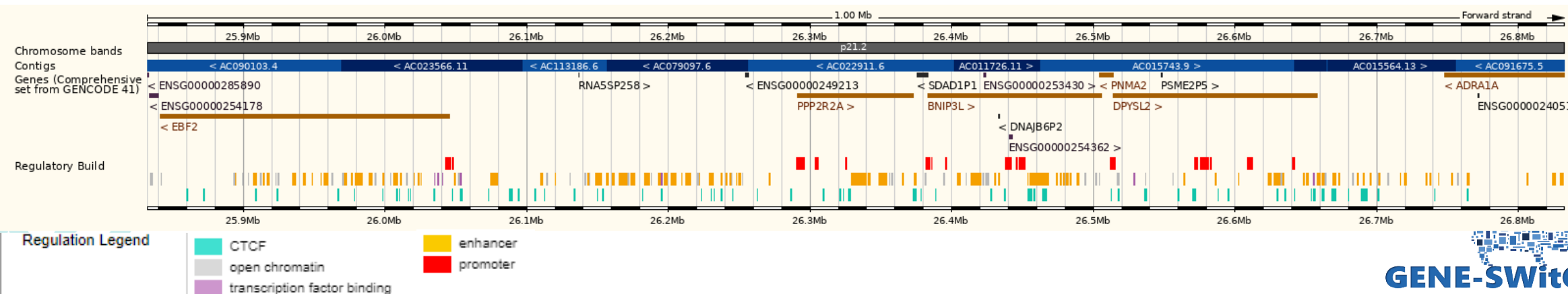
Fergal J Martin ✉, M Ridwan Amode, Alisha Aneja, Olanrewaju Austine-Orimoloye, Andrey G Azov, If Barnes, Arne Becker, Ruth Bennett, Andrew Berry, Jyothish Bhai ...
Show more

Nucleic Acids Research, Volume 51, Issue D1, 6 January 2023, Pages D933–D941,
<https://doi.org/10.1093/nar/gkac958>

A first Ensembl Regulatory Build being constructed for pig and chicken (jungle fowl, a broiler and a white leghorn) genomes.

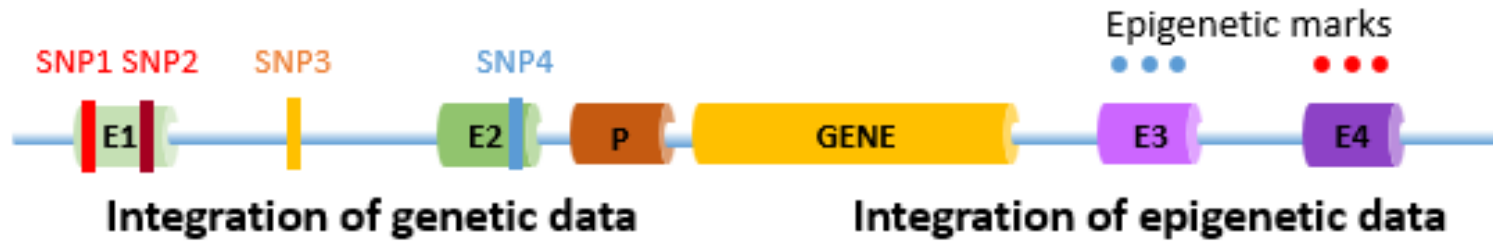
- Ensembl Release 110 went live in July 2023 (addition of new regulation data)
- Ensembl Release 111 is adding enhancer annotation for Release.

➤ **Freely publicly available and accessible via the Ensembl Genome Browser.**



➤ Aim B: Using functional annotation for precision animal breeding

Two different approaches:



Can functional annotations enhance the prediction accuracy of breeding values in commercial populations?



Provide a basis for future studies focused on better farm management (e.g. using lower-quality, more sustainable feed)



Genomic Selection

➤ WP4: Improving predictive models for genomic selection

Aim:

- Extend genomic prediction models to exploit new annotation maps of pig and chicken generated in GENE-SWitCH.

This is achieved by:

- Developing new genomic prediction models.
- Generating fine-mapped QTL and eQTL.
- Validating the models in large scale commercial data.



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➤ Aim B-Results (WP4)

OXFORD **G3** Genes | Genomes | Genetics
G3, 2021, 11(11), jkab225
DOI: 10.1093/g3journal/jkab225
Advance Access Publication Date: 7 July 2021
Investigation

An evaluation of the predictive performance and mapping power of the BayesR model for genomic prediction

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²BioEcoAgro Joint Research Unit, INRAE, Université de Liège, Université de Lille, Université de Picardie Jules Verne, Peronne 80203, France
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¹Author contributed equally to this work.

OXFORD **G3** Genes | Genomes | Genetics
G3, 2022, 12(4), jkac039
https://doi.org/10.1093/g3journal/jkac039
Advance Access Publication Date: 15 February 2022
Genomic Prediction

Prediction performance of linear models and gradient boosting machine on complex phenotypes in outbred mice

Bruno C. Perez¹, Marco C. A. M. Bink², Karen L. Svenson³, Gary A. Churchill² and Mario P. L. Calus^{3,*}

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²The Jackson Laboratory, Bar Harbor, ME 04609, USA, and
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BayesRCO
GitHub
<https://github.com/FAANG/BayesRCO>

(GIGA)ⁿDB
Revolutionizing data dissemination, organization, and use

Supporting data for "Identification of transcriptional regulatory variants in pig duodenum, liver and muscle tissues"

Dataset type: Phenotyping, Genomic, Transcriptomic
Data released on May 11, 2023

Crespo-Piazuelo D, Aclouque H, González-Rodríguez G, Mengellaz M, Mercat M, Bink MCAM, Huisman AE, Ramayo-Caldas Y, Sánchez J, Ballester M (2023) Supporting data for "Identification of transcriptional regulatory variants in pig duodenum, liver and muscle tissues" GigaScience Database. <http://dx.doi.org/10.5524/102388>
DOI: 10.5524/102388

Mollandin et al. BMC Bioinformatics (2022) 23:365
<https://doi.org/10.1186/s12859-022-04914-5>

BMC Bioinformatics

RESEARCH Open Access

Accounting for overlapping annotations in genomic prediction models of complex traits

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OXFORD **G3** Genes | Genomes | Genetics
G3, 2022, 12(11), jkac258
https://doi.org/10.1093/g3journal/jkac258
Advance Access Publication Date: 26 September 2022
Investigation

Adding gene transcripts into genomic prediction improves accuracy and reveals sampling time dependence

Bruno C. Perez¹, Marco C.A.M. Bink², Karen L. Svenson³, Gary A. Churchill² and Mario P.L. Calus^{3,*}

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²The Jackson Laboratory, Bar Harbor, ME 04609, USA,
³Animal Breeding and Genomics, Wageningen University & Research, 6700 AH Wageningen, The Netherlands
^{*}Corresponding author: Animal Breeding and Genomics, Wageningen University & Research, P.O. Box 338, 6700 AH Wageningen, The Netherlands. Email: mario.calus@wur.nl

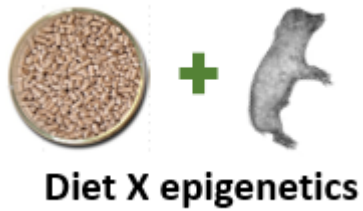
Model development:

- BayesRCO software is freely available & applicable to large-scale data (~60k individuals and ~50K SNPs)
- Machine learning is especially useful for traits with epistatic gene action

Potential of using functional annotation in genomic prediction:

- Can be used to optimize (50k) SNP panel

**Next talks by
E. Tarsani and
B. Perez!**



Diet X epigenetics

➤ Aim B. Influence of maternal diet on epigenetic programming of offspring (WP5)

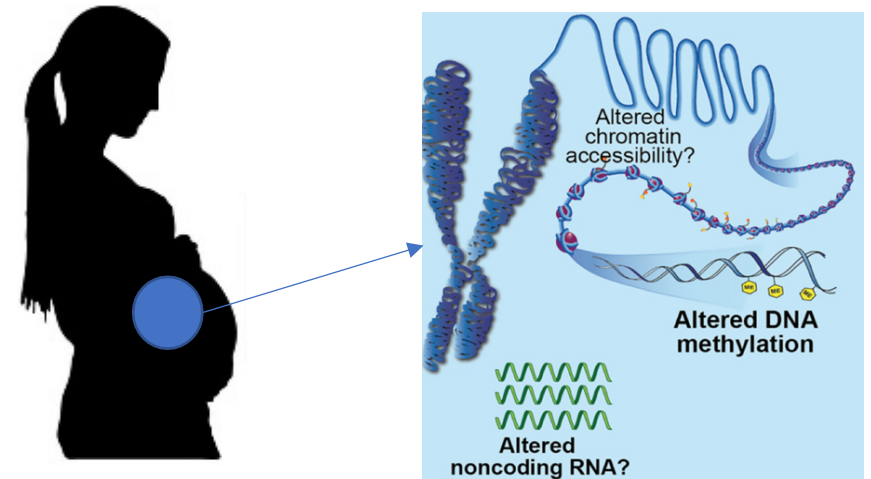
Diet is a major environmental factor in animal breeding

Fermentation of non-digestible carbohydrates by colon microbiota:

- SCFAs (Short Chain Fatty Acids) metabolites: several documented functional and epigenetic effects
- Gut microbiota alter host histone acetylation and methylation in multiple (adult) tissues mainly via SCFAs (*Krautkramer et al., 2016, Molecular Cell*)

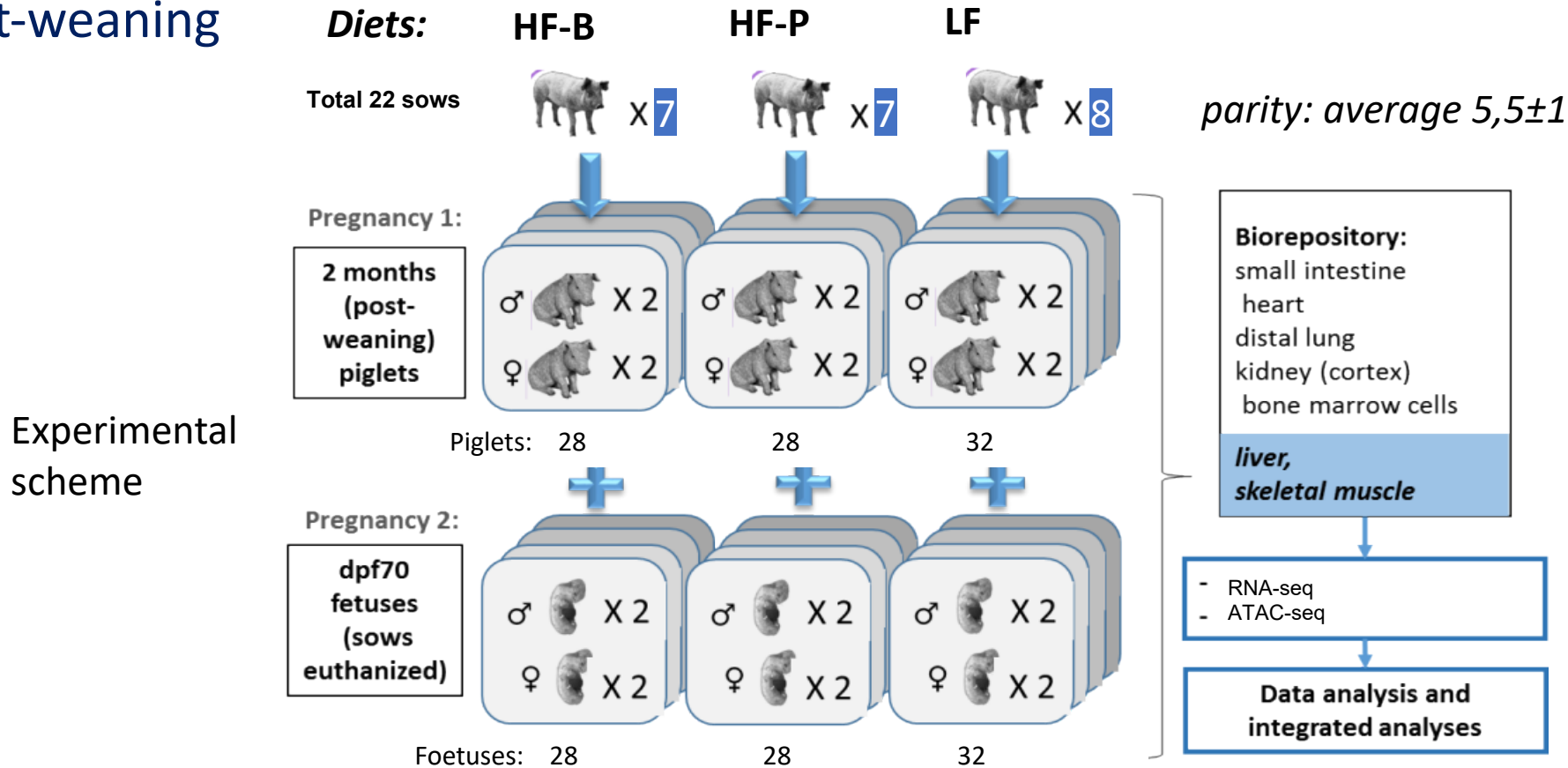
Maternal nutrition:

- Contributes to the establishment of the epigenetic profiles in the foetus.
- Evidence of impact on individual susceptibility to certain diseases or disorders in the offspring later in life.



➤ Aim B. Influence of maternal diet on epigenetic programming of offspring (WP5)

- To detect the epigenetic effects of maternal diets varying for fibre contents on the foetus *in utero* (muscle and liver)
- To evaluate the potential “persistence” of epigenetic marks in piglets post-weaning



Paper in preparation: “Long-term effects of high fiber maternal diets on the functional genome of pig offspring”. S. Chalabi, L. Loonen et al.



➤ Aim C: Standardization of data and processes, dissemination and outreach

- Coordination, standardisation, validation, curation and archiving of GENE-SWitCH data (WP3)
- Establishing the European node of FAANG DCC (WP3)
- Data dissemination and novel presentation, through FAANG Data Portal (<https://data.faang.org>) (WP3)
- Enabling use of produced knowledge to further improve the effectiveness of genomic selection in the pig and poultry sectors (WP3 and WP6)
- Implement conventional and innovative training and capacity building activities for both academics and industry stakeholders (WP6)



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➤ Aim C. Some testimonials from stakeholders (WP6)

(from: Stakeholder panel at GENE-SWitCH 4th AM, Rome, June 2023)

"The GENE-SWitCH project represents a critical milestone in advancing animal breeding through functional annotation and genomics" (FAO)

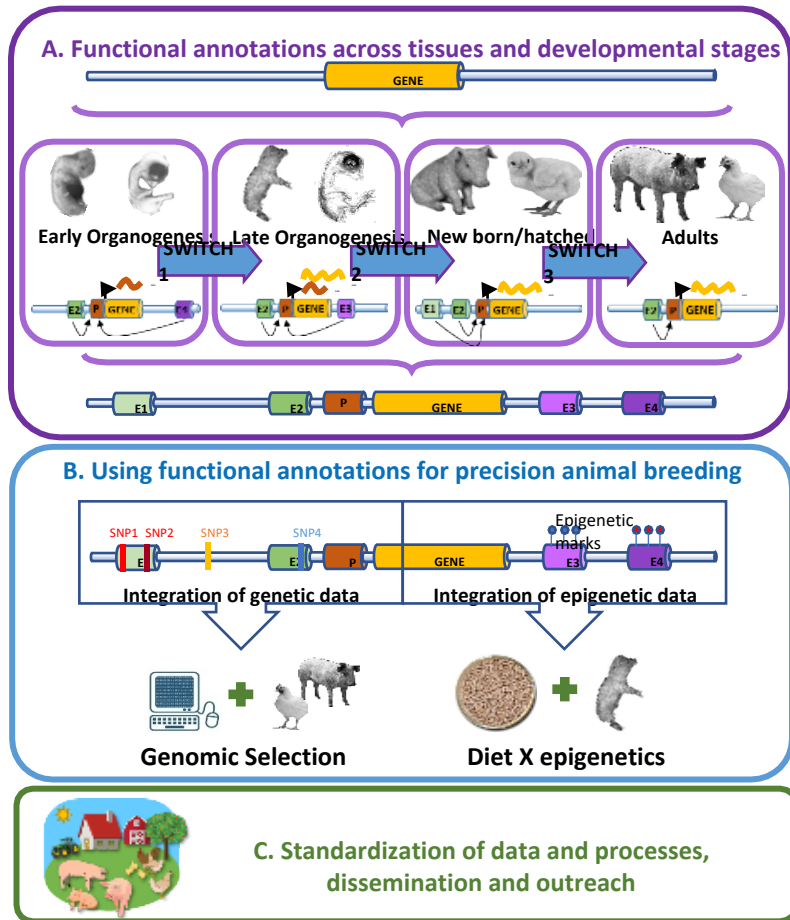
"The outcomes of this project have the potential to impact food security significantly." (FAO)

"We can use the functional annotation data from GENE-SWitCH to reduce environmental load and mortality as well as increase animal health and welfare." (attending breeding companies)

"The task of establishing a connection between genotype and phenotype poses a significant challenge. Fortunately, functional annotation is a valuable tool in guiding breeding companies towards addressing this issue." (attending breeding companies)



➤ The impacts of GENE-SWitCH



- High-quality reference annotation maps for the whole research community.
- Cutting-edge research results: paving the way to further studies and strategies.
- European stakeholders benefits: an increased understanding of the value of functional genome annotation to face current and future challenges to achieve sustainable productions.

The EuroFAANG Research Infrastructure provides a great opportunity to increase these impacts in Europe and beyond.

➤ With big thanks to all participants in GENE-SWitCH



Annual meeting 2023 hosted by EAAP in Rome (June 2023)



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**Thank you for your
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