GENE-SWitCH

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

Aims, results and impacts of H2020 GENE-SWitCH*

(*) June 2019 - Dec. 2023

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BovReg Final conference, Brussels, 14-15 February 2024

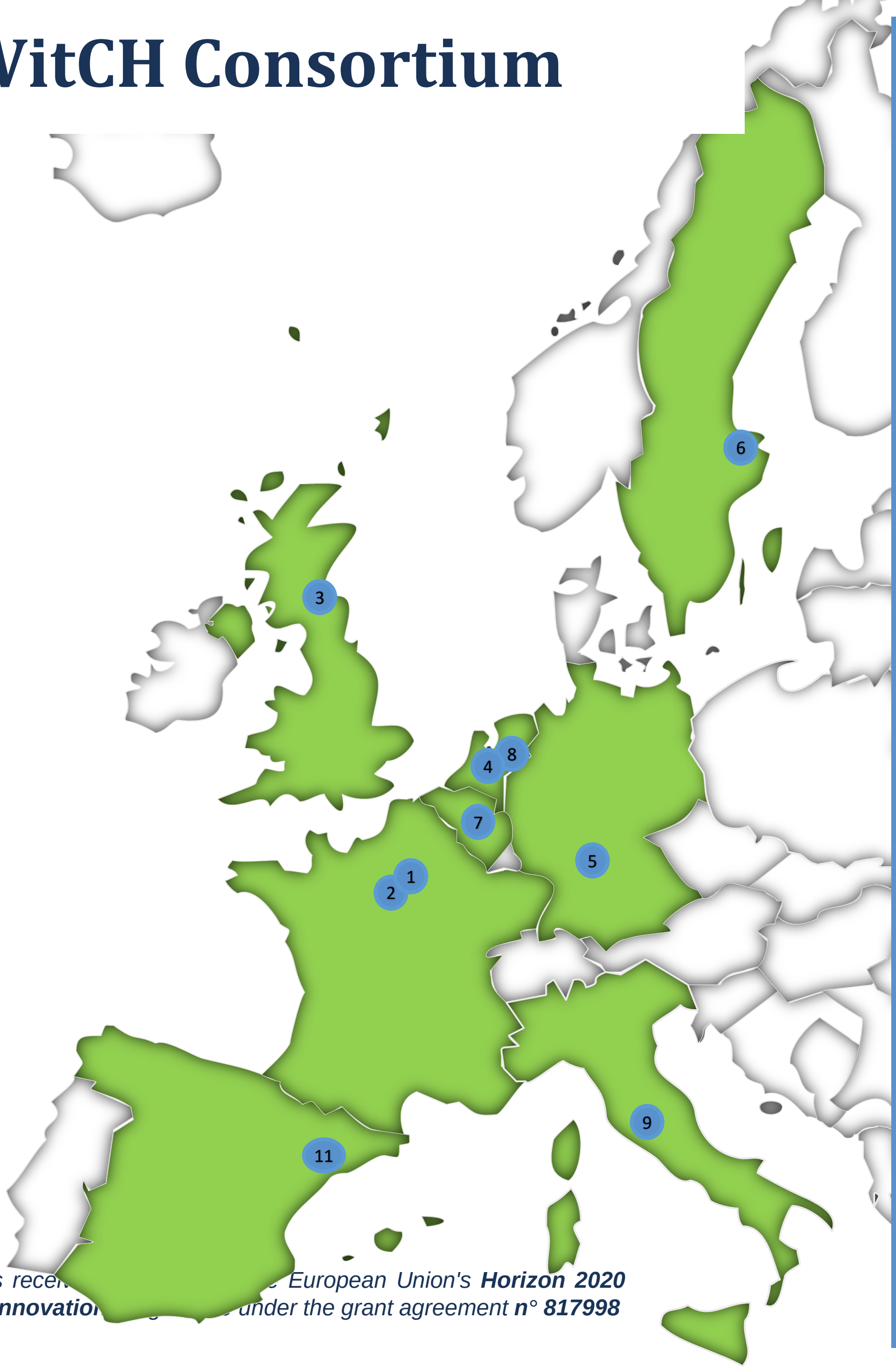
GENE-SWitCH

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

BovReg
Understanding cattle genomes

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

GENE-SWitCH Consortium



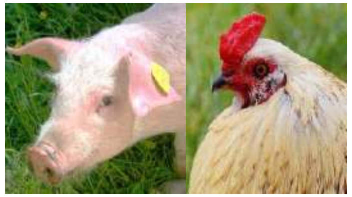
1. INRAE Inserm
2. INRAE transfert
3. THE UNIVERSITY of EDINBURGH
4. WAGENINGEN UNIVERSITY & RESEARCH
5. EMBL-EBI
6. UPPSALA UNIVERSITET
7. diagenode Innovating Epigenetic Solutions
8. EFFAB European Forum of Farm Animal Breeders
9. EAAP
10. HENDRIX GENETICS
11. IRTA

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

*This project has rece… European Union's **Horizon 2020***
Research and Innovatio…** under the grant agreement **n° 817998

GENE-SWitCH

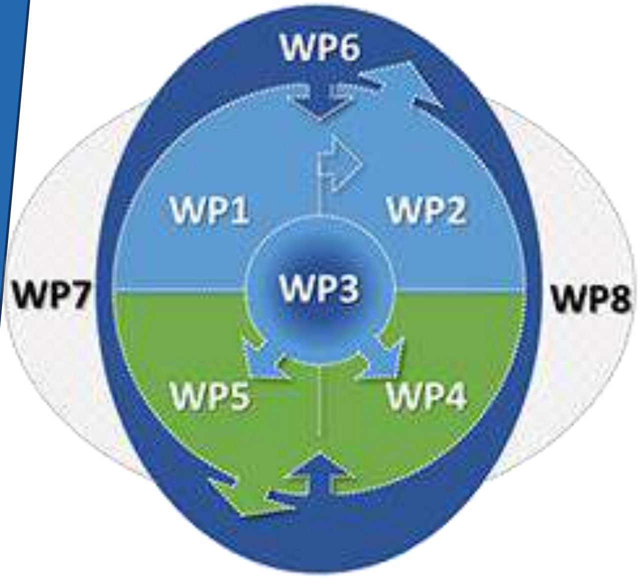
The global aim



- To deliver underpinning knowledge on the pig and chicken genomes

and,

- to enable its translation to the pig and poultry sectors

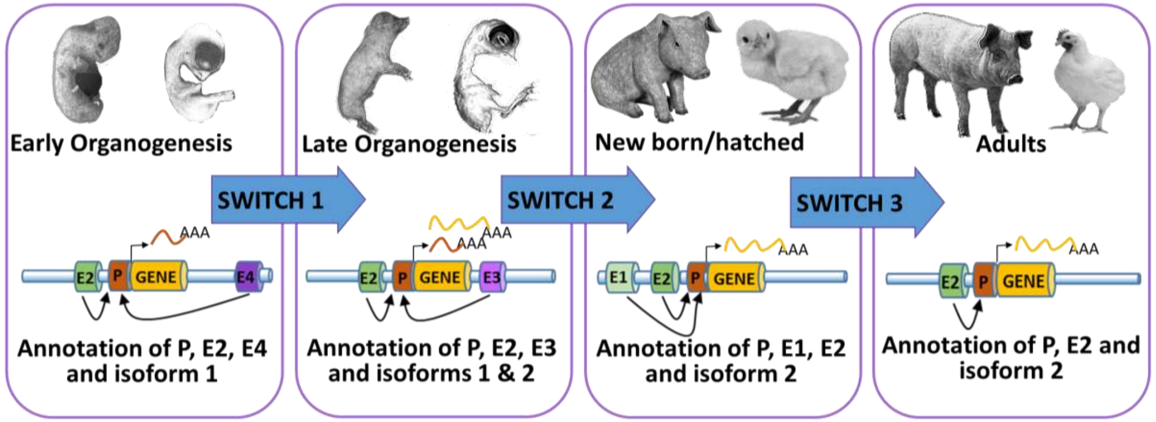


WP7 (Project management and consortium coordination)
WP8 (Ethics requirements)

Three specific interconnected aims:

A. Functional annotations across tissues and developmental stages (WP1, WP2, WP3)
B. Using functional annotation for precision animal breeding (WP4, WP5)
C - Standardization of data and processes (WP3), **dissemination and outreach** (WP6)

Aim A - Functional annotations across tissues and developmental stages



Early Organogenesis

Annotation of P, E2, E4 and isoform 1

SWITCH 1

Late Organogenesis

Annotation of P, E2, E3 and isoforms 1 & 2

SWITCH 2

New born/hatched

Annotation of P, E1, E2 and isoform 2

SWITCH 3

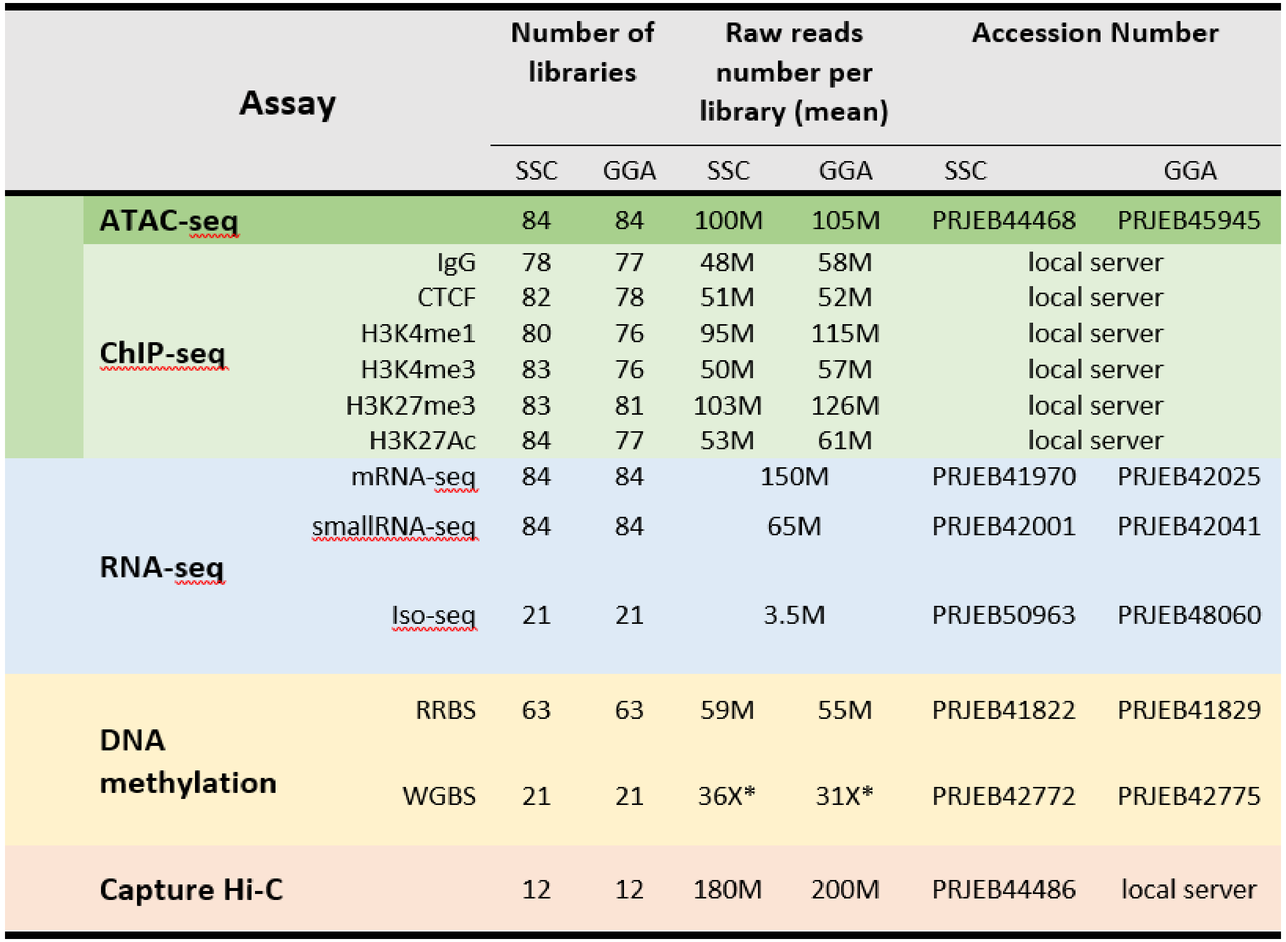
Adults

Annotation of P, E2 and isoform 2

- **Identify the functional elements of chicken and pig genomes in 7 tissues across 3 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.**

Aim A - Identify the functional elements of chicken and pig genomes across developmental stages

Raw QC data



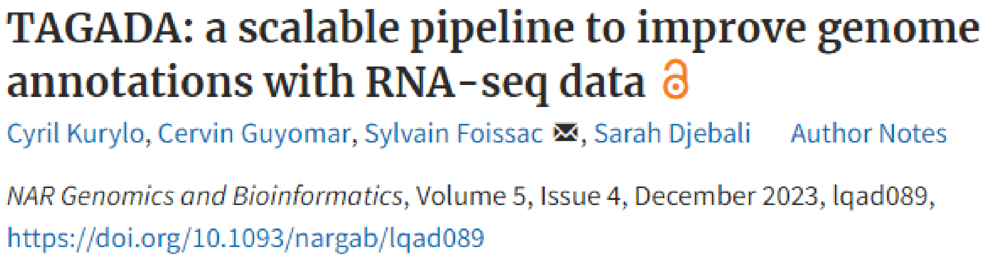
Assay		Number of libraries		Raw reads number per library (mean)		Accession Number	
		SSC	GGA	SSC	GGA	SSC	GGA
ATAC-seq		84	84	100M	105M	PRJEB44468	PRJEB45945
ChIP-seq	IgG	78	77	48M	58M	local server	
	CTCF	82	78	51M	52M	local server	
	H3K4me1	80	76	95M	115M	local server	
	H3K4me3	83	76	50M	57M	local server	
	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

Pipelines

nf-core/isoseq: 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



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

Cyril Kurylo, Cervin Guyomar, Sylvain Foissac ✉, Sarah Djebali Author Notes

NAR Genomics and Bioinformatics, Volume 5, Issue 4, December 2023, lqad089, https://doi.org/10.1093/nargab/lqad089

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

On https://data.faang.org/GENE-SWitCH under the terms of the Fort Lauderdale agreement and Toronto Statement.

GENE-SWitCH

Aim A- A first Ensembl Regulatory Build for pig (7 breeds) and chicken (jungle fowl, a broiler and a white leghorn)

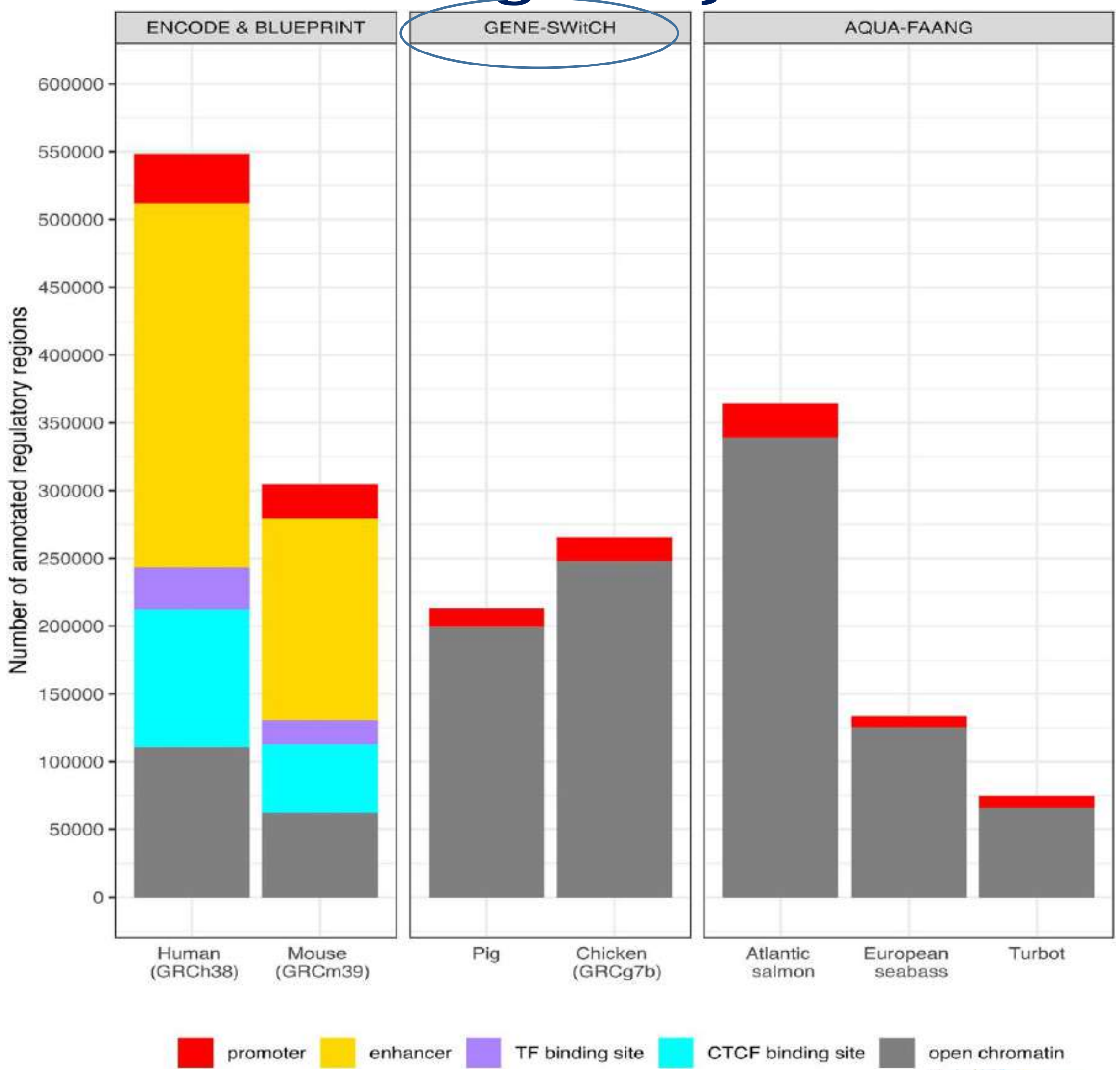
Amongst the first Ensembl regulatory annotations for the genomes of vertebrate species other than human and mouse

Ensembl 2024

Peter W Harrison, M Ridwan Amode, Olanrewaju Austine-Orimoloye, Andrey G Azov
Matthieu Barba, If Barnes, Arne Becker, Ruth Bennett, Andrew Berry, Jyothish Bhai ...
Show more

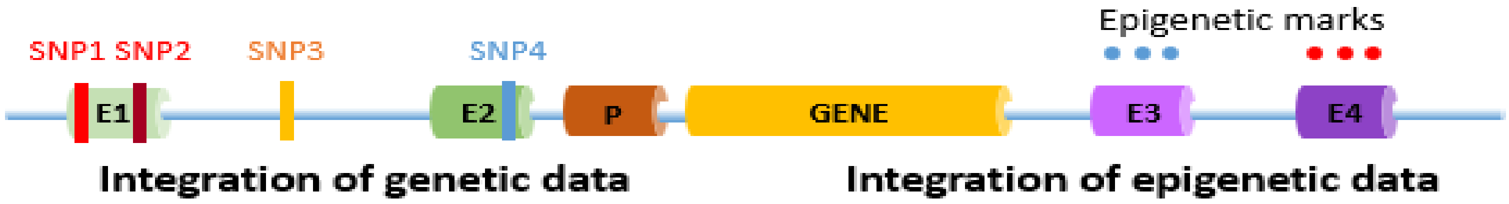
Nucleic Acids Research, Volume 52, Issue D1, 5 January 2024, Pages D891–D899,
https://doi.org/10.1093/nar/gkad1049

Ensembl Release 111 (Jan 2024) relabeled some annotated regions as enhancers based on their overlap with relevant histone ChIP-seq peaks

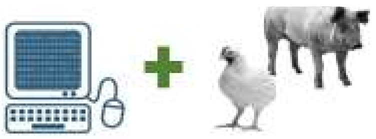


Aim B. Using functional annotation for precision animal breeding

Two different approaches:

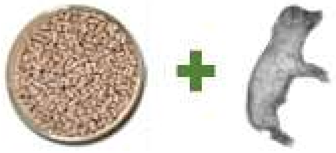


WP4



Genomic Selection

WP5



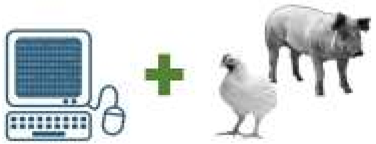
Diet X epigenetics

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)

WP4: Improving predictive models for genomic selection

Leader: HENDRIX GENETICS



Genomic Selection

WAGENINGEN
UNIVERSITY & RESEARCH

INRAE

THE UNIVERSITY of EDINBURGH

IRTA

UPPSALA
UNIVERSITET

GENE-SWitCH

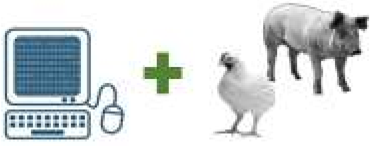
Aim:

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

Achieved by:

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

WP4 Main outputs



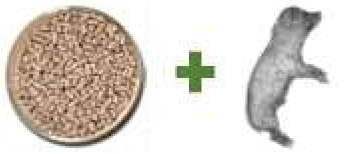
Genomic Selection

- Important focus on model development:
  - BayesRCO software is freely available
  - Machine learning models better explain phenotypes for epistatic traits
- Gene expression explains considerable variance, depending on moment of sampling
- QTL-mapping:
  - eQTL in pigs
  - Fine-mapped QTL in chickens
- Validation genomic prediction in commercial populations:
  - Combining annotations (using FAETH scores) improves accuracy in pigs

Mollandin F. et al. (2021) https://doi.org/10.1093/g3journal/jkab225
Mollandin F. et al. (2022) https://doi.org/10.1186/s12859-022-04914-5
Perez B.C. et al. (2022) https://doi.org/10.1093/g3journal/jkac039
Perez B.C. et al. (2022) https://doi.org/10.1093/g3journal/jkac258
More papers in progress

https://github.com/FAANG/BayesRCO

WP5: Epigenetic effects of maternal high fibre diets in utero and the offspring


Diet X epigenetics

Leader: WAGENINGEN UNIVERSITY & RESEARCH

INRAE

Inserm

diagenode

EMBL-EBI

SFR SCHOTHORST FEED RESEARCH

AARHUS UNIVERSITY

GENE-SWitCH

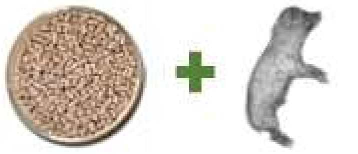
Aim:

➢ To assess the epigenetic effects of maternal diets varying in fibre content on pig fetuses and weaned piglets

Achieved by:

- a dedicated *in vivo* experiment (maternal diets differing in fiber contents, 2 progenies, focus on liver and muscle)
- Analysis of differentially transcribed genes and chromatin accessibility regions from offspring and fetuses
- Integrative analyses (including microbiota composition, short chain fatty acid measures, weight phenotypes)

WP5 Main outputs



Diet X epigenetics

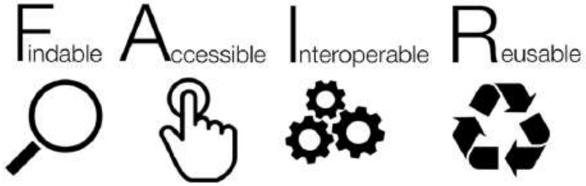
High fiber contents in maternal diets determine a pervasive alteration of the functional genome of the liver and muscle tissues of the pig offspring

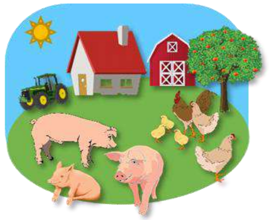
- Transcriptomic and epigenetic effects are better detectable in piglets (*10-weeks old, all on the same diet after weaning*) than in fetuses
- Effects on piglet phenotypes (weight, SCFAs, microbiota) not statistically significant.
- Evidence for an anti-inflammatory phenotype in both liver and muscle triggered by high fibers

Chalabi S., Loonen L. et al. Paper in preparation

A basis for further studies into the impact of maternal diets on progeny phenotypes (e.g. infectious disease responses)

Aim C - Standardization of data and processes (WP3), dissemination and outreach (WP6)





EMBL-EBI

EFFAB
European Forum of Farm Animal Breeders

EAAP
European Federation of Animal Science

Several activities implemented throughout the project:

- Coordination, standardisation, validation, curation and archiving of GENE-SWitCH data
- Clustering activities with the other H2020 projects = start of EuroFAANG
- Enabling use of produced knowledge to improve the effectiveness of genomic selection in the pig and poultry sectors
- Implement training and capacity building activities (for both academia and industry)

Did GENE-SWitCH match the expected impacts?

- ➢ **Delivered high-quality reference annotation maps**, with impact on several areas of fundamental and applied science (e.g. for animal industry specialists)

- ➢ **Delivered and tested new genomic prediction models** that include genome annotations to improve precision breeding–efficiently disseminated to industry

- ➢ **Paved the way for follows-up investigations**:
  - By other ongoing European projects, notably GERONIMO
  - For nutritional studies focused on using lower-quality, more sustainable feed

- ➢ **Has co-founded EuroFAANG**, that provides a great opportunity for large scope G2P research in Europe in the next decade.

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All about GENE-SWitCH is here: https://www.gene-switch.eu/

DELIVERABLES

DATA PORTAL

SCIENTIFIC PUBLICATIONS

KEY ACHIEVEMENTS

BOOK OF ABSTRACTS

Hybrid event,
6-8 Nov. 2023

GO TO THE FINAL CONFERENCE PAGE

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→ FAANG
Functional Annotation of Animal Genomes
10 Years

GENE-SWitCH

A “final” big thanks to all participants and FAANG/EuroFAANG collaborators

Final (hybrid) conference, Brussels 6-8 Nov. 2023

…and to the BovReg consortium for hosting us today

BovReg Final conference, Brussels, 14-15 February 2024

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Understanding cattle genomes

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