



GENE-SWITCH

Newsletter - Issue 7

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Editorial by E. Giuffra and H. Acloque

GENE-SWitCH is now in its home stretch. All the datasets have been produced and deposited on public databases so that they can be accessed by all stakeholders, in particular on [the FAANG initiative's dedicated portal](#). The various tools used to analyze and facilitate the exploitation of these data are being published or finalized. Very soon, the scientific community and the companies working on these two species will be able to view and re-use these data and exploit

them for their own development. The project has also paved the way to optimize the use of functional annotations to predict traits of interest from genotypes better. It has also provided insights into how in utero nutritional programming can modulate the epigenome of tissues of interest and their biology.

The project's final conference, to be held on 6, 7 and 8 November in Brussels, will provide a broad overview of GENE-SWitCH results and their impacts on the poultry and pig sector. You are all welcome to meet us there.

News

GENE-SWitCH Project Holds Successful Annual Meeting in Rome; discussing Innovations in Genomic Research for Poultry and Pig Breeding

Funded by the European Union, the collaborative research project GENE-SWitCH aims to advance functional genomics and its practical implementation in monogastric breeding. With a focus on identifying and characterising functional genomic elements, implementing FAANG innovation, and standardising data and processes, GENE-SWitCH strives to enhance genetic improvement, animal welfare, and environmental sustainability in the poultry and pig sectors.



On the 14th and 15th of June in Rome, the GENE-SWitCH project convened its fourth and last annual meeting. The event brought together leading experts, stakeholders, and project partners to discuss the latest advancements and results of GENE-SWitCH and to explore new ways to address societal



challenges regarding livestock breeding through wide-ranging technologies.

The meeting began with a warm welcome to all attendees, marking the start of a two-day event. An introduction and program presentation followed, outlining the schedule ahead. The agenda comprised a series of presentations and workshops focused on the project's three main pillars:

- Pillar 1: Identification and characterisation of functional genomic elements.
- Pillar 2: Implementing FAANG (Functional Annotation of Animal Genomes) innovation for animal breeding.
- Pillar 3: Standardisation of data and processes, dissemination, and outreach.

Prominent highlights from the meeting included in-depth presentations on the project's pillars, as well as a fascinating talk by Pr. Huaijun Zhou from UC Davis (USA), giving an overview of the research made on functional annotations of pig and chicken genomes and their use to characterise traits of interest on the American side.

The meeting also facilitated dedicated time for Work Package (WP) meetings, allowing participants to engage in focused discussions and collaborations within their respective areas of expertise. The vibrant atmosphere continued during the social dinner, providing an opportunity for informal networking and strengthening professional relationships.

Some key messages from the annual meeting are:

- the release of improved annotations based on the GENE-SWitCH datasets that are publicly available and are included in the Ensembl107 release;
- the importance of the regulatory switches observed during organogenesis to control gene expression in pig and chicken;
- the added value of functional information to improve the prediction of some traits but also the methodological challenges to

associate functional information with genetic variants;

- the importance of the maternal diet in modulating the phenotype of piglets in target tissues, in particular regarding immunity;
- a survey to improve ontogeny terms for livestock species and to take into account the specificity of their associated phenotypes.

On the second day, the focus shifted towards presenting GENE-SWitCH's main results for gathering stakeholders' feedback. The stakeholder workshop explored pressing questions regarding regulatory approaches, policy implications, and measures necessary to ensure the responsible and widespread adoption of these ground-breaking technologies. Topics such as food security, environmental impact, sustainability, and the need for improved phenotyping technologies garnered significant attention from participants.

"The GENE-SWitCH project represents a critical milestone in advancing animal breeding through functional annotation and genomics" stated Paul Boettcher, representing the Food and Agriculture Organization (FAO). **"The outcomes of this project have the potential to impact food security significantly, but we must address the challenges faced by developing countries, such as infrastructure limitations."**

In particular, stakeholders insisted on the need to go further to evaluate functional annotations to improve prediction accuracy, particularly for traits with small reference populations or complex traits (health, behaviour, resilience, welfare). Functional annotations will also help identify genetic variants associated with pleiotropic or harmful effects but also those with strong biological/phenotypical effects but low frequency in populations. Finally, a global effort is needed to sensitise policymakers and citizens to the importance of such molecular and computing tools to improve the sustainability and resilience of livestock production systems.



Indeed, industry representatives emphasized the importance of policymakers' support for developing the poultry and pig sectors. The meeting highlighted the need for policymakers to align with breeders and farmers, and to consider regional variations and sustainability aspects while addressing the costs associated with implementing genetic improvements.

"Improving animal welfare, enhancing genetic improvement tools, and ensuring sustainable practices are critical for the poultry and pig industries," affirmed Ana Granados, Director of the European Forum of Farm Animal Breeders (EFFAB). **"Policymakers play a crucial role in facilitating the adoption of new knowledge and supporting breeding companies and farmers in practical applications."**



The annual meeting concluded with the presentation of an action plan for the upcoming months, emphasizing the commitment to continue research, effective communication, and the translation of scientific advancements into policy-relevant outcomes.

GENE-SWitCH and EMABG: A Thriving Collaboration Bringing Genetics to Life

In an exciting partnership, the GENE-SWitCH project has teamed up with the European Master of Animal Breeding and Genetics (EMABG) program, led by BOKU and other prestigious institutions. Together, we embarked on a journey to bridge the gap between cutting-edge research and passionate learners. The response has been overwhelming,

with master's and early career students enthusiastically participating in a series of enlightening webinars. The sessions explored three captivating themes:

- Annotation and its Practical Applications: We delved into the world of genome annotation, with Hervé Acloque (INRAE) sharing GENE-SWitCH's ground-breaking work in "The Regulatory Genome of Swine and Chicken." Sebastien Guizard (UEDIN) then guided us through "What is annotation and its use?" and revealed the secrets of "How to annotate a genome."
- Genomic Prediction Unveiled: In this session, Mario Calus (WUR) explained the "Use of functional annotation and other omics in genomic prediction." Bruno Perez (Hendrix Genetics) illuminated the path of "Validating the prospects of functional annotations in genomic prediction in pigs." Andrea Rau (INRAE) rounded off the session with insights into "Accounting for predicted variant effects in genomic prediction in poultry."
- The Role of Epigenetics in Monogastric Breeding: Linda Loonen (WUR) provided a fascinating look into the "Influence of Maternal Diet on SCFA levels and microbiota," while Smahane Chalabi (INRAE) uncovered the effects of maternal diet on pig epigenome and transcriptome, from mother to fetus to piglet.

The response from EMABG students and researchers has been incredible, reflecting a thirst for knowledge in animal breeding and genetics. The GENE-SWitCH project is committed to fostering collaboration and acting as a platform for discovery and learning.

For those who couldn't make it to these webinars could watch them from [our YouTube channel](#).



EUROFAANG's Genotype-to-Phenotype Research to Transform Animal Breeding: Showcased at EAAP 2023 Conference

The EAAP 2023 Conference in Lyon, France, hosted a well-attended session on August 31st, titled "EUROFAANG: Genotype-to-phenotype research across Europe & beyond." The session commenced with an enlightening introduction by Emily Clark of the University of Edinburgh and Christa Kühn from FBN, shedding light on "EuroFAANG - An infrastructure for farmed animal genotype to phenotype research in Europe and beyond." Amongst the notable presentations, Elisabetta Giuffra (INRAE) unveiled the GENE-SWitCH project, dedicated to enhancing the functional annotation of pig



and chicken genomes for precision breeding. Eirini Tarsani (UEDIN) delved into genome-wide association studies for broilers' body weight using sequencing and SNP chip data. Bruno Perez (Hendrix Genetics) presented groundbreaking work on using methylation annotation to improve genomic predictions of gene expression in pigs.

Notably, the panel discussion, chaired by Emily Clark and Christa Kühn, brought together industry stalwarts, including Abe Huisman, Romain Morvezen, Olivier Demeure, and Clotilde Patry, to deliberate on how the European animal breeding sector can harness the EuroFAANG Research Infrastructure and its evolving knowledge. The session encapsulated

cutting-edge research to reshape animal breeding practices across Europe and beyond.

The EuroFAANG panel discussion emphasized the significance of genetic diversity, the integration of new information, and the need for basic research and cost-efficient tools to advance genotype-to-phenotype research in farmed animals. Collaboration between industry and research was recognized as a vital component in addressing the challenges and seizing the opportunities within the field of animal breeding.

GENE-SWitCH training on utilization of GENE-SWitCH data in Ensembl and beyond

An advanced bioinformatics training workshop titled "EuroFAANG GENE-SWitCH workshop: utilisation of GENE-SWitCH data in Ensembl and beyond" was held virtually.

The course provided detailed training on the optimal utilization of the wealth of data generated by the GENE-SWitCH project. The course focused on the [Ensembl Genome Browsers](#) new comprehensive and integrated annotation of the chicken and pig genomes, including a deeper dive into the analysis performed on gene annotation and regulation. The course also included presentations on the research and results conducted as part of the GENE-SWitCH project that is delivering new underpinning knowledge for pig and chicken aquaculture. Video recordings from a number of the training presentations are planned to be released through the [GENE-SWitCH YouTube channel](#) so watch this space.



News from EuroFAANG

The [EuroFAANG cluster](#), consisting of six Horizon 2020 projects associated with the FAANG initiative, focuses on understanding the functional aspects of animal genomes and their impact on physical traits in farmed animals. The cluster aims to address challenges in animal production, such as resource efficiency, animal welfare, and environmental impact. In 2022, the cluster submitted a proposal to establish the European Research Infrastructure (RI) project, which the EU approved. The project aims to develop a formalised infrastructure for genotype-to-phenotype (G2P) research in European farmed animals. The kick-off meeting in Berlin in February emphasised collaboration and milestones, focusing on creating a web portal for centralised access to resources and data. Surveys will be conducted to build a network of experts and gather insights on technological advancements for genotype-to-phenotype prediction. The EuroFAANG RI project will establish a common infrastructure and service access policy in collaboration with other research infrastructures. It will engage breeding companies, scientific experts, and the FAANG initiative to drive G2P research in European-farmed animals. For more information, feel free to contact the project team.

EuroFAANG RI Project Coordination:
EuroFAANG-RI@fbn-dummerstorf.de

Project progress

The GENE-SWitCH project made significant progress in the past year, with key highlights including:

- Release of improved annotations for pig and chicken in the Ensembl107 release. These annotations are based on the comprehensive GENE-SWitCH datasets and are now publicly accessible on the Ensembl website.
- Identifying regulatory switches during organogenesis is crucial in controlling gene expression in pig and chicken tissues,

providing valuable insights into genetic regulation.

- Demonstrating the enhanced predictive power of functional information in improving the accuracy of trait prediction, showcasing the value of integrating functional genomics into breeding practices.
- Challenges encountered in effectively linking functional and genetic information, highlighting these two aspects' complexity and methodological hurdles.
- Characterization of the impact of maternal diet on modulating the immune-related phenotypes of piglets in target tissues, shedding light on the role of maternal factors in shaping offspring traits.
- Conducting a survey to refine ontogeny terms for livestock species, ensuring the consideration of specific phenotypic characteristics associated with different developmental stages.

These advancements represent important milestones in the GENE-SWitCH project and contribute to the broader goal of enhancing functional genomics applications in monogastric breeding for improved genetic improvement, animal welfare, and environmental sustainability.

In the spotlight

Mario Calus (WUR) WP4 Leader



I was born in 1978 and grew up in the most southwestern corner of the Netherlands, on a small farm with dairy cattle and crops that evolved into a 200-head Belgian Blue beef cattle

farm currently owned by my sister and brother-in-law. I obtained my MSc (2001) and PhD (2006) in Animal Breeding and Genetics at Wageningen University. I then worked for eleven years at the Animal Breeding and Genetics Department of Wageningen Livestock Research. Since 2017 I have been an associate



professor at the Animal Breeding and Genomics Chair Group of Wageningen University & Research, and my main area of expertise is on genomic prediction and genomic selection of a variety of livestock species. Since obtaining my PhD in 2006, I have been working for seventeen years in the scientific development of genomic selection and its implementation in collaboration with the breeding industry. I have been involved as one of the PIs in the Dutch public-private partnership Breed4Food (www.breed4food.com) since 2012, and I am currently the program leader of Breed4Food. I have supervised 11 PhD students, with an additional 5 ongoing, and have trained 7 postdocs. I have (co)authored >150 peer-reviewed articles. Currently, I am Senior Editor for the section Complex Traits of GENETICS, and I am one of the co-Editors-in-Chief of Genetics Selection Evolution.

In the EU-funded GENE-SWitCH, I am co-leading Work Package 4 and leading Task 4.2. I am currently also a Work Package leader in the EU-funded project GeroNIMO.

Marco Bink (Hendrix Genetics), WP4 Co-leader



I was born in 1968 and grew up on a mixed dairy-crop farm in The Netherlands. In 1993 I obtained my MSc degree in Animal Breeding at Wageningen University. A research visit of six

months at the Department of Animal Breeding of Cornell University, Ithaca (NY) USA, was part of preparing my PhD thesis that I successfully defended at Wageningen University in 1998.

That same year, I started a postdoctoral animal and plant breeding project, evolving into a permanent research position at the Department of Biometrics of Wageningen University and Research in 2001. Over 15 years, I took multiple positions, including group leader and senior scientist, with responsibilities for the acquisition, management, execution, and

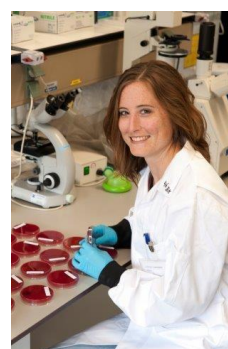
communication of collaborative research projects. The funding was from national and international plant breeding companies, science agencies and governments. Meanwhile, I have been on research leaves at the University of Helsinki, Pioneer Hybrid International, and the University of Washington. My research covered the assessment, application, and development of statistical methods and software to estimate genetic parameters and to predict breeding values from large amounts of pedigree, DNA-marker and phenotypic data on plants and animals.

In March 2016, I started as a senior quantitative geneticist at Hendrix Genetics Research Technology and Services B.V. In 2022 my role evolved into team lead genetics and genomics. In this role, I contribute to strengthening the research and product development activities in the different species in line with our vision of “Better breeding today. Brighter life tomorrow”.

In the EU-funded GENE-SWitCH, I am co-leading the Work Package 4 and leading Task 4.5.

Young scientists

Linda Loonen (WUR)



Linda Loonen is a molecular cell biologist who obtained her PhD in the Host-microbe interactomics (HMI) group at Wageningen University, The Netherlands, while focusing on antimicrobial peptides and their role in host immunity and microbiota.

After that she did 2 post-doc projects in which she investigated novel food and microbial sources that could serve as aryl hydrocarbon receptor (AhR) ligands, and their effect on host immunity. She is currently hired as a permanent researcher in the HMI group where she works on the GENE-SWitCH WP5, under supervision of Prof. Jerry Wells.

Within work package 5 of the GENE-SWitCH project we focus on the effect of the maternal



diet on the epigenome of their offspring. This work package examines the impact of the diet, specifically varying levels and types of fibers, on the epigenome and associated gene expression in two key tissues, the liver and skeletal muscle. The different levels of fibers in the sow's diet lead to different amounts of short chain fatty acids (SCFA) in the mother due to microbial fermentation in the gut. The microbiota produces the SCFA's acetate, propionate and butyrate, and their production can be influenced by the host's diet (in this case the sow). SCFA play a role in intestinal homeostasis, helping to explain why changes in the microbiota (due to amongst others diet) can contribute to the pathophysiology of human diseases. SCFA also have effects on tissues and organs beyond the gut, through their circulation in the blood: they can induce epigenetic changes in the genome through effects on the activity of histone acetylase and histone deacetylase enzymes. Furthermore, epigenetic imprinting, the process in which DNA and/or chromatin structure is modified or altered according to the parent's epigenetic marks, likely occurs in utero, highlighting the importance of the maternal diet in early life. Therefore, the effect of the maternal diet will be assessed in this work package on both epigenetic and transcriptional differences in both fetuses and piglets.

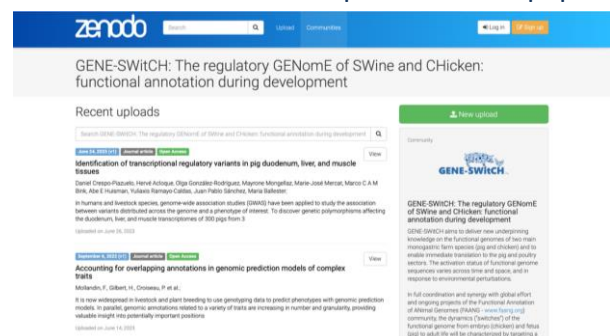
In this work package, an animal experiment was performed where sows were impregnated twice. Of the first pregnancy organs were harvested of piglets of 10 weeks of age, of the second pregnancy the same organs but then of fetuses at day 70 post-fertilization were harvested. The sows received 3 different diets, which would lead to different levels of SCFA in the sow serum, possibly leading to epigenetic changes in the offspring. During both pregnancies serum and feces was collected of the sows at different time points. At sacrifice of piglets and fetuses, multiple tissues were taken, of which the skeletal muscle and liver were the main target tissues for further analysis. A biorepository of the other collected tissues is

currently stored at WUR. Liver and muscle were used for both RNA-seq and ATAC-seq, to evaluate changes in gene expression and look at possible epigenetic effects.

At our side (WUR) we performed amongst others the wet lab experiments: the animal experiment (in collaboration with Schothorst feed research), harvesting all samples and making the biorepository, and we did the SCFA analysis in serum and feces of the sows and piglets. Furthermore, we looked at the microbiota composition in both sow and piglet. SCFA were measured using LC-MS for serum and GC for feces. 16s profiling for the microbiota was done on microbial DNA isolated from feces. Analysis of the results showed that no big differences could be found in the levels of acetate, butyrate and propionate in the serum of the sows. This is most likely due to clearance of these SCFA's in the liver. Further analysis regarding the microbiota, and combining the different data sets is currently still being fine-tuned while we are preparing a manuscript with the whole WP5 team.

GENE-SWitCH on Zenodo Platform

GENE-SWITCH opened a [Zenodo account](#), which hosts the 13 open access papers



published by partners since the start of the project.

Upcoming events

GENE-SWitCH final Conference will take place in Brussels on the 6, 7 and 8 of November 2023. The first two days will be focused on the project's results and include a panel session dedicated to the 10th anniversary of FAANG. The third day of the event will be joint with the



GERONIMO project and focused on stakeholders and policy. To register [click here](#).

GENE-SWitCH
FINAL CONFERENCE

6 - 7 - 8
NOVEMBER
2023

Brussels, Belgium

- GENE-SWitCH RESULTS
- DEDICATED PANEL 
- JOINT STAKEHOLDERS & POLICY EVENT
WITH 

This project has received funding from the European Union's Horizon 2020 Research and Innovation Programme under the grant agreement of 867986 @GeneSwitch - www.gene-switch.eu

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