Rumigen

TOWARDS IMPROVEMENT OF **RUMI**NANT BREEDING
THROUGH **GEN**OMIC AND EPIGENOMIC APPROACHES

Newsletter - Issue 2

August 2023

The RUMIGEN project has received funding from the European Union's Horizon 2020 Research and Innovation Programme under Grant Agreement N°101000226.

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Editorial by Eric Pailhoux, project coordinator, INRAE

Dear RUMIGEN Partners,

We are already at the end of the second year of this project. The writing of the first periodic report (scientific and financial reports) for the Commission marked the end of 2022. Once again, I would like to thank all those involved in RUMIGEN for preparing these reports, which went so smoothly. Our work over the first 18 months was presented and discussed in Brussels on February 14th by all the members of the Executive Committee. At this meeting, our project officer of the EC Colombe Warin, assisted by the external expert Pekka Uimari (professor in animal breeding at the University of Helsinki), gave us their recommendations and suggestions for the project's future. This first project-review meeting went very well, and the discussions were very constructive. The second highlight of RUMIGEN took place in Toledo, Spain, where we held our second annual meeting on 22 and 23 May 2023.

Fifty-six RUMIGEN participants attended, representing virtually all the organizations involved in the project. Despite a busy schedule, the meeting was held in a relaxed atmosphere, reflecting the increasingly close-knit network of partners. The interdisciplinary of the project sometimes led to more sustained exchanges and was reinforced by the presentation of the ERC project "The BoS" by Roxane Gabet and François Thoreau from SPIRAL, which aims to describe and analyze how societal values are translated into the bodies of cattle. Alice Barrier from UEDIN (Innovation Management Group) also led an interesting session dedicated to putting some of the project's future results into perspective. To be complete, I must also acknowledge the perfect organization by our Spanish colleagues from INIA, particularly Clara Diaz Martin and Oscar Gonzalez Recio and Anne Jarousse from INRAE Transfert, helped by the ICAR conference organizers.

From a scientific point of view, the project is progressing practically as planned. The quantitative genetics studies, based on a large amount of data already available at the start of the project, are beginning to produce interesting results, some of which have already been published. The genome editing work is progressing as planned, with many lambs carrying the SLICK mutation being born at the Roslin Institute. Construction of the epigenotype Chip is about to begin at Illumina. One of its representatives, André Eggen, came to present the tool and its various constraints at the epigenetics workshop. Many discussions took place during the various workshops, notably around genome editing with the participation of our external ethical expert Andy Greenfield, whom I would like to thank very much, and also around the construction of the four scenarios that will serve as a basis for the opinion surveys aimed at redefining the areas of societal acceptability around the future of livestock farming in Europe.

In conclusion, the RUMIGEN project has reached cruising speed, the various aspects are progressing well, and the results should arrive in numbers during this third year that we are embarking on together. The participants are starting to get to know each other better, and the group work and discussion sessions are fruitful and constructive. Let's keep up this excellent momentum.

News

Annual Meeting of RUMIGEN Project Explores Breakthroughs in Livestock Breeding and Epigenetics

Toledo, Spain - The 2nd Annual Meeting of the RUMIGEN project, funded by the European Union's Horizon 2020 program, commenced on May 22nd at the Palacio de Congresos de Toledo "El Greco". The two-day event brought together breeding company representatives, policymakers, and renowned poultry and pig breeding researchers to discuss the latest advancements in functional annotation of monogastric genomes and epigenetics.

The agenda for the first day featured a series of presentations and workshops focusing on various work packages (WP) of the RUMIGEN project. The discussions covered project management, the impact of trade-offs on productive lifespan, selection and genetic diversity, epigenetic biomarkers, prenatal farming practices, sustainable breeding programs, and more.

Attendees had the opportunity to learn about the main results achieved in each work package and engage in insightful discussions during the question and answer sessions. The meeting also featured a presentation on "The BoS" project, an ERC project coordinated by François Thoreau from Liège University. This groundbreaking project aims to further advance research in livestock breeding by exploring innovative approaches and leveraging cutting-edge technologies. Integrating the BoS

project into the discussions added valuable insights and perspectives to the Annual Meeting of the RUMIGEN project, contributing to the overall goal of enhancing livestock breeding practices.

Throughout the day, participants took breaks to network and exchange ideas during coffee and lunch sessions. The collaborative atmosphere fostered valuable connections and knowledge sharing among experts in the field.

On the second day, the focus shifted to specific workshops on social acceptance of breeding approaches, dissemination and communication, genome editing potential assessment, and epigenetics. Parallel sessions provided a platform for in-depth discussions and exploration of key research areas.

The meeting concluded with a joint session involving the European Rare Breeds Federation (ERFP) workshop. Attendees had the opportunity to learn about the strategy for animal genetic resources (AnGR) in Europe and the establishment of a new European reference centre for endangered animal breeds. The session was followed by a delightful cocktail featuring products from autochthonous breeds.

The Annual Meeting of RUMIGEN Project was a significant platform for stakeholders to discuss the uptake and implementation of research findings in poultry and pig breeding. The collaborative efforts showcased the project's commitment to sustainable and innovative breeding practices, aligning with the goals of the EU Green Deal and the Farm to Fork Strategy.

Participation in events from partners

RUMIGEN Partners Engage in Key Events to Showcase Project Progress

In the past year, RUMIGEN, a collaborative research project focused on advancing animal breeding through epigenetics, has made significant strides. Partners of the project actively participated in various international events, highlighting their groundbreaking research and sharing insights with the scientific community. Here are some notable events where RUMIGEN partners made their mark:

1. Illumina's 'Epigenetics - the full picture' 2022 Virtual Event: From April 25th to 28th, 2022, the esteemed virtual event, hosted by Illumina, provided a platform for experts to delve into the world of epigenetics. At this event, INRAE introduced the RUMIGEN epichip, an innovative tool that enables comprehensive epigenetic analysis in animal breeding research. The presentation garnered attention and demonstrated the project's commitment to pushing the boundaries of epigenetic understanding.
2. ICAR Interbull Meeting in Montreal: The ICAR Interbull Meeting, held from May 30th to June 3rd, 2022, in Montreal, brought together professionals involved in animal evaluation and genetics. IDELE, IRIAF, CSIC-INIA, WUR, and INRAE, key partners of RUMIGEN, presented a poster on the project's initial findings related to new phenotypes for heat tolerance traits. Their research shed light on the development of new breeding tools in the context of climate change, showcasing the project's relevance and potential impact.
3. World Congress on Genetics Applied to Livestock Production (WCGALP): At the WCGALP held in Rotterdam from July 3rd to 8th, 2022, INRAE and IDELE showcased their ongoing research on genotype by temperature-humidity index interactions. Their poster presentation focused on studying the effects of environmental factors on milk production and udder health traits in Montbeliarde cows. This research contributes to understanding the relationship between genetics and environmental conditions, crucial for sustainable and efficient livestock production.
4. Assemblée Générale Eleveurs de Savoie: On August 12th, 2022, during the Assemblée Générale Eleveurs de Savoie, ELIANCE captivated attendees with a thought-provoking presentation titled "Pourras-t-on d'ici 10 ans prédire les performances des animaux grâce à l'épigénétique?" (Will we be able to predict animal performance through epigenetics within 10 years?). ELIANCE emphasized the potential of epigenetics to revolutionize breeding practices and pave the way for future advancements.
5. Comité Scientifique et Technique Elevage CNIEL: The Comité Scientifique et Technique Elevage CNIEL, held on October 19th, 2022, in Paris, provided a platform for INRAE, IDELE, and ELIANCE to present their ongoing research on heat tolerance in dairy cows. Titled "Tolérance des vaches laitières à la chaleur: projets de recherche en cours et à construire" (Heat tolerance in dairy cows: ongoing and future research projects), the presentation highlighted the significance of current and future studies in this area.

RUMIGEN partners' active engagement in these events emphasizes the project's commitment to advancing animal breeding through innovative research and collaboration. Their valuable contributions not only enhance scientific knowledge but also pave the way for improved breeding tools and practices in the face of changing climates.

FABRE TP Annual Meeting Showcases RUMIGEN Project and Future Research Priorities

On Wednesday, May 31st, the FABRE TP (Farm Animal Breeding and Reproduction Technology Platform) held its Annual Meeting, bringing together members of the FABRE TP and EFFAB (European Forum of Farm Animal Breeders) to discuss the latest developments in animal genetics and reproduction.

During the meeting, the RUMIGEN project was also presented to the representatives of the breeding sector. Recognising the need for breeding scenarios that align with stakeholder and citizen acceptance, RUMIGEN seeks to address the trade-offs associated with current genomic selection

practices. Genomic selection, while delivering short-term genetic improvement, has led to a decline in long-term genetic diversity utilisation and limited consideration of environmental impacts on animal genetic potential.

The participants also engaged in a workshop to define the research and innovation needs in animal genetics and reproduction. Esteemed guest speaker Nikos Zampoukas from DG RTD, European Commission, shed light on the Horizon EU 2025-27 and the next EU Research Framework, outlining the strategic direction for future endeavours. The FABRE TP Research Agenda 2025-2030 was also presented, highlighting the focus areas and key objectives for advancing animal genetics and reproduction research. Furthermore, the EuroFAANG project took the stage, showcasing the benefits of research infrastructure for research institutions and breeding companies. The day concluded with a dynamic World Café session, allowing participants to engage in lively discussions and exchange ideas on pertinent topics. The insights gathered from this interactive session will contribute to shaping the future direction of animal genetics and reproduction research.

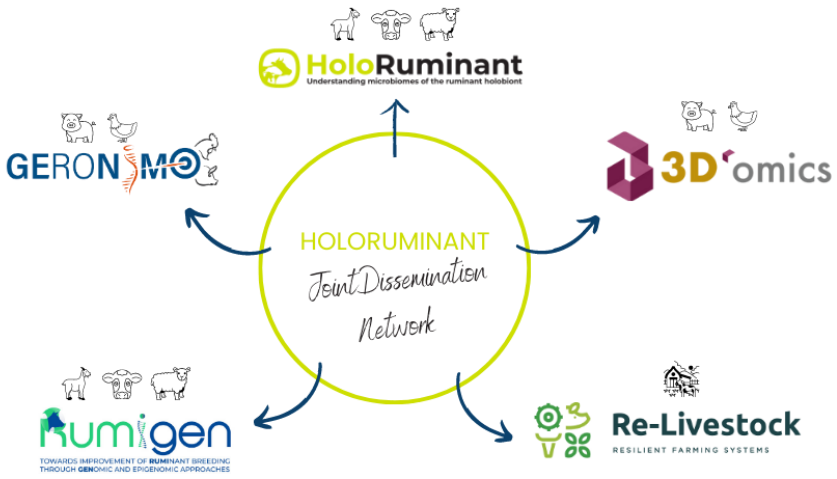
In the closing remarks, the conclusions drawn from the day's discussions were highlighted, emphasising the collective commitment to advancing knowledge and innovation in the field.

The FABRE TP Annual Meeting proved to be an essential platform for fostering collaboration, sharing expertise, and charting a course for future animal genetics and reproduction advancements. The event successfully showcased the remarkable progress of the RUMIGEN project and established a strong foundation for future collaborations within the scientific community and industry stakeholders.

Joint Dissemination Clustering: HoloRuminant

RUMIGEN joins the HoloRuminant Joint Dissemination Network

RUMIGEN is pleased to announce its participation in the HoloRuminant Joint Dissemination Network (JDN), a collective effort launched by the HoloRuminant project. The JDN embraces five projects (HoloRuminant, 3D'omics, RUMIGEN, GEroNIMO and Re-Livestock) representing a complementary effort to reduce the environmental and climate footprint of livestock production - while guaranteeing genetic diversity and efficient production in a more constrained environment - by focusing on the mitigation of GHG emissions, improving the health and welfare of farmed animals and increasing the sustainability of animal production systems.



Through the Joint Dissemination Network, these projects collaborate to optimize and share resources and communication materials to serve international initiatives better. This autumn, the JDN will launch a series of webinars as a starting point for upcoming collective activities. More details will be forthcoming soon. Keep an eye out for updates!

EuroFAANG Project

The EuroFAANG cluster, consisting of six Horizon 2020 projects associated with the global FAANG initiative, focuses on understanding the functional aspects of animal genomes and their impact on physiological traits in farmed animals.

The cluster aims to generate data that can be used to address challenges in animal production, such as resource efficiency, animal health & welfare, and environmental impact. A new Horizon Europe project proposal was submitted in 2022 under the call "Research Infrastructure Concept Development", which was built on the framework provided by the six EuroFAANG cluster projects. Successfully approved by the EU, the new EuroFAANG Research Infrastructure (RI) project will now develop a concept for a formalized infrastructure for farmed animal genotype-to-phenotype (G2P) research in Europe (EuroFAANG).

The kick-off meeting for the EuroFAANG RI in Berlin in February emphasized collaboration and milestones, focusing on creating a concept for a web portal for centralized access to resources and data. Surveys will be conducted to build a network of experts and gather insights on several aspects of G2P research, including biobanks, genome editing and other technological advances.

The EuroFAANG RI project aims to work with other research infrastructures, including those for data and farmed animal phenotyping, to fill the gap in the ESFRI RoadMap for farmed animal science. 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

Code EFABAR and RUMIGEN

The collaboration between the code EFABAR and the RUMIGEN project can bring together a shared commitment to responsible and sustainable cattle breeding practices. Code EFABAR provides the guiding principles and guidelines for balanced breeding. At the same time, RUMIGEN focuses on scientific research, technological advancements, and stakeholder engagement to address the challenges and goals outlined in Code EFABAR.

Code EFABAR's principles showcase that genetic diversity is managed effectively within and across cattle populations to preserve endangered and non-endangered genetic resources. RUMIGEN also addresses animal welfare, engages stakeholders through a multi-actor approach to assess the social acceptability of breeding technologies and incorporates societal perspectives in defining breeding goals and selecting appropriate technologies.

Through their collaboration, Code EFABAR and RUMIGEN can work towards developing guidelines for future breeding programs, ensuring that responsible breeding practices are implemented. These guidelines consider genetic diversity management, animal welfare, environmental sustainability, and stakeholder engagement, creating a roadmap for breeders and stakeholders.

The collaboration between Code EFABAR and RUMIGEN could reflect a shared vision for responsible cattle breeding, where ethical considerations, scientific advancements, and stakeholder engagement come together to shape the sector's future. By combining their efforts, Code EFABAR and RUMIGEN can contribute to advancing responsible and sustainable breeding practices, promoting the well-being of animals, preserving genetic diversity, and meeting societal expectations.

Publications

- Estimation of genotype by temperature-humidity index interactions on milk production and udder health traits in Montbeliarde cows - A. Vinet, S. Mattalia, R. Vallée, C. Bertrand, B. C. D. Cuyabano, D. Boichard - Genetics Selection Evololution 55, 4 (2023) - https://doi.org/10.1186/s12711-023-00779-1

Meet the consortium

Didier BOICHARD (INRAE) - WP1

Didier Boichard graduated from AgroParisTech (Agricultural University of Paris) and did his PhD in dairy cattle fertility. He joined INRA (now INRAE) in 1982 and made his main research contributions in dairy cattle genetics and breeding. He has been deeply involved in the French national genetic evaluation for dairy cattle. In 2002, in close collaboration with the French breeding industry, he implemented a large-scale marker-assisted selection program, which evolved in 2008 towards genomic selection. From 2002 to 2009, he led the Animal Genetics Division of INRAE (200 researchers, 500 total staff). He is presently leading the Bovine Genetics and Genomics research group at INRAE in Jouy-en-Josas (close to Paris), involved in research on the genetic variability of phenotypes and genetic and genomic evaluation. He is the author or co-author of more than 180 peer-reviewed papers and co-editor-in-chief of Genetics Selection Evolution. In Rumigen, he is involved in heat tolerance (WP3), use of epigenetic information (WP6), and practical implementation of solutions (WP8); he also contributes to the general management of the project.

Sophie Mattalia (IDELE) – WP3

Sophie Mattalia is the leader of WP3 in RUMIGEN; a team focused on studying tradeoffs in the context of climate change. Within the animal genetics department of IDELE, the French Livestock Institute, she holds the position of head of the team dedicated to the genetic evaluation of ruminants, including bovines, sheep, and goats. Their activities encompass both research and development, as well as providing services to the industry. Throughout her career, Sophie has delved into various R&D topics, particularly focusing on genetic and genomic evaluations of bovines. She has also been a member of the steering committee of Interbull for 16 years. Furthermore, she has contributed to the genetic improvement of novel traits, such as health and robustness. Presently, Sophie's R&D activities revolve around constructing and managing R&D programs in animal breeding. In collaboration with Didier Boichard (INRAE) and Sébastien Fritz (Eliance), she coordinates the Mixed Unit of Technology (UMT) eBIS. This partnership, recognized by

the Ministry of Agriculture, unites their three teams in pursuit of common R&D programs focused on the genetic improvement of bovines.

Upcoming events

SAVE THE DATE : EuroFAANG EAAP 2023

EUROFAANG is thrilled to announce that it will be organising a stakeholder session at the EAAP 2023 conference in Lyon on the 31st of August. The "EuroFAANG: genotype-to-phenotype research across Europe and beyond" session will delve into the organisation's pioneering research initiatives. Chaired by Emily Clark from UEDIN, the session will kick off with a warm welcome and an introduction to EuroFAANG's mission by Emily Clark and Klaus Wimmers from UEDIN and FBN, respectively. The session will feature three key projects: GENE-SWItCH, BovReg, and AQUA-FAANG, each with 45 minutes dedicated to their presentations. GENE-SWItCH will focus on enhancing the functional annotation of pig and chicken genomes and genome-wide association studies for body weight in broilers. BovReg will explore improved genomic and biology-driven predictions for dry matter intake in cattle using whole-genome sequencing. AQUA-FAANG aims to decode genome function in farmed finfish and integrate functional annotation data for genomic prediction in European sea bass. Following these presentations, the session will cover GEroNIMO, RUMIGEN, and the HoloRuminant project, highlighting the importance of genomics and breeding tools in monogastric, climate change, and the genetic basis of ruminant microbiomes, respectively. The session will conclude with a panel discussion featuring esteemed industry experts who will explore the opportunities and barriers to implementing EuroFAANG's research findings in the European animal breeding sector. The session promises to be an insightful and engaging gathering of stakeholders, driving innovation and collaboration in genotype-to-phenotype research.

Progress

WP2 Room of acceptance

Exploring the "Room of Acceptance" for Ruminants Rasmus Mikkelsen, Danish Board of Technology

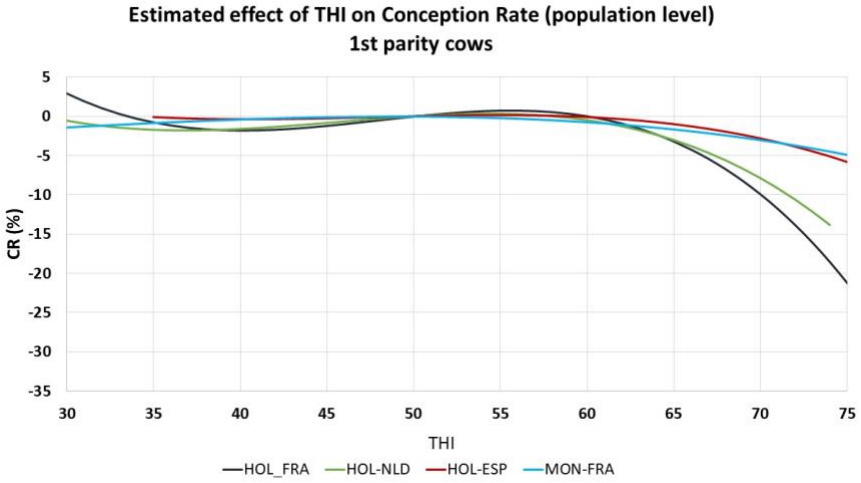
In agriculture, societal acceptance plays a crucial role in determining the success or failure of adopting gene-based adaptations to ruminants. However, previous applications of new technologies in agriculture have faced significant protests, particularly in Europe, leading to a polarized debate between supporters and opponents of new technologies. This entrenchment has hindered progress in creating socially acceptable gene technology applications. The RUMIGEN project aims to develop a multidimensional framework called the "Room of Acceptance" to address this issue. This framework defines the boundaries within which new breeding technologies applied to ruminants are acceptable to society. By considering multiple dimensions, the Room of Acceptance offers a more nuanced perspective on the acceptability of these applications. The initial version of the Room of Acceptance consists of 16 dimensions, with 27 subdimensions, which collectively shape the boundaries of societal acceptance. It is important to note that the boundaries may not be fixed but can vary over time and context. Developers of new breeding technologies can utilize the Room of Acceptance to prioritize their efforts based on societally and environmentally relevant criteria. Additionally, the Room of Acceptance can be useful for societal organizations considering under what conditions certain types of new breeding technology could be acceptable. The development of the Room of Acceptance is an ongoing process within the RUMIGEN project, starting with initial insights and gradually incorporating additional information, workshops, scenario studies, and discussions.

Ultimately, the goal is to create an ex-post Room of Acceptance incorporating validated dimensions and refined contextual considerations. This will be achieved through a thorough citizen engagement process. For this purpose, various scenarios have been created based on the dimension identified in the Room of Acceptance. These scenarios are designed to form the basis of citizen engagement, where the preliminary boundaries of the room will be tested. Through thorough and meaningful engagement with a range of citizens across the EU, the citizen engagement will validate and adapt the findings in the Room of Acceptance. In conclusion, the Room of Acceptance offers a multidimensional framework for evaluating the acceptability of new breeding technologies in ruminants. By combining this new approach with thorough citizen engagement, the ongoing development of this framework within the RUMIGEN project aims to provide a valuable tool for fostering dialogue and understanding between stakeholders, which will not only provide insight into this specific topic but which might also provide a guide for how to carry out this type of social acceptability study in the future. As we progress, we anticipate further insights and refinements to ensure the Room of Acceptance becomes a robust and useful resource.

WP3 Results on reproduction

Impact of heat load on the Fertility of European dairy cattle populations Sophie Mattalia, IDELE

Dairy farmers are increasingly conscious of the negative effects of high temperatures on farm productivity. Characterizing the response in productive and reproductive performance and health to increasing heat loads is important to establish management practices and develop selection tools to enhance the adaptation of European dairy production to climate change. This has been one of the objectives of WP3 of RUMIGEN, which contributes to generating sustainable and socially acceptable breeding programs. French national data basis (BDNZ) and National databases provided by breeder associations (CRV for the Netherlands and CONAFE for Spain) together with weather information from national meteorological agencies (Météo-France, KNMI and AEMET), were used to estimate the curve of response fertility to changes in heat load suffered by the cows. More specifically, the fertility trait analyzed was conception rate (CR), defined as the success or failure to conceive with first insemination from first lactation Holstein cows in France, Spain and The Netherlands and first lactation Montbéliarde cows in France. The heat load was measured from the average daily Temperature-Humidity Index (THI: index combining both temperature and relative humidity) on the day of the record and the seven days post AI. Estimated responses to increase in THI for each dairy breed are shown in the following graph.



The graph shows how CR remains stable within a thermo-neutral range of THI values to decline after reaching a heat stress threshold. Mild heat stress thresholds for each breed were similar, around 65 units of THI, which is equivalent to average daily temperatures of 21ºC with a relative humidity of around 30%, and more severe heat stress was observed beyond values of 70 units of THI (around 26ºC of daily average temperature and 30% of relative humidity).

Slopes of decay in CR showed substantial differences across countries, ranging from 0.79 points per degree of THI beyond the mild heat stress threshold in Holstein cows in Spain to 2.25 points per degree of THI in Holstein cows in France. Smaller response to heat stress was thought to be associated with the acclimation of animals in regions with continuous high temperatures in summer and heat abatement (in Spanish farms) in contrast with a succession of heat waves followed by comfortable temperatures, as well as perhaps less structural heat mitigation on farms in the case of Dutch and French Holsteins. The decrease in fertility was more limited in the Montbéliarde breed, showing clear differences between breeds.

The studies continue to propose new breeding tools that can better account for the impact of temperature and relative humidity on fertility traits. The first results suggest that the selection on fertility using the present tools (current genetic evaluations provided in each country) is still relevant with increasing temperatures and that the selection on fertility today is essential to prepare future generations to be adapted to climate change.

EuroFAANG movie

Animals possess remarkable phenotypic variation in different climates, which allows them to adapt to diverse environmental challenges. This variation is influenced by both coding and non-coding regions of their DNA. While coding regions consist of genes and constitute only a small portion of the genome, the non-coding regions, comprising 95% of the genome, play a crucial role in regulating essential traits such as milk production and disease resistance. Understanding these non-coding regions and their regulatory elements through functional genome annotation is vital for effectively selecting and breeding animals with desired traits, enhancing productivity and resilience in agriculture.

The EuroFAANG initiative, part of the FAANG consortium, focuses on three H2020-funded projects: AQUA-FAANG, BovReg, and GENE-SWitCH. These projects are dedicated to unravelling the functional aspects of fish, cattle, chicken, and pig genomes. By advancing our functional genomics knowledge, EuroFAANG aims to drive innovation in animal breeding, sustainable farming systems, and agricultural practices to meet economic and societal demands. To stay updated on the groundbreaking advancements in functional genomics and contribute to a more efficient and sustainable future for animal agriculture, visit the project websites or follow EuroFAANG on social media.

Functional annotation of farmed animal genomes is crucial to fully comprehending these regulatory elements and their interactions. Functional annotation creates a comprehensive map of genome features, acting as a navigational reference for geneticists.

Coordinator: Eric Pailhoux (INRAE)

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For more information visit our website:

www.rumigen.eu

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