



A European infrastructure for farmed animal genotype to phenotype research

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1. Introduction

This document describes key aspects of Transnational access (TNA) to EuroFAANG services and how this will be organised and managed. As we are in the concept development and design phase of the research infrastructure (RI), this is a living document that will be updated regularly throughout the lifecycle of the RI. E.g. we anticipate that many new partners will join during the construction phase and this is briefly being touched upon in section 2.3.

The EuroFAANG research infrastructure's main aim is enabling Genome to Phenome (G2P) research in farmed animals by the wider European research community by providing:

1. Access to data, including genomic and phenotype data, and sample metadata.
2. Access to in vitro cellular models to link in vitro and in vivo phenotypes.
3. Access to biobanks of reference samples, including organoids and genome edited cell lines.
4. Access to world leading expertise, in G2P research for farmed animals.
5. Access to training, to establish the next generation of researchers in farmed animal science.

TNA to EuroFAANG services (section 2.2) will enable users within Europe to use technologies that otherwise would be unavailable or difficult to be used within their research projects. TNA thus strengthens the impact of the RI and supports the scientific community. TNA is also key to further strengthen the infrastructure itself by extending its knowledge base and increasing the biological resources and data connected to these resources. This will lead to higher quality research outputs and better sharing and exploitation of results. This will further strengthen collaboration between research groups, stakeholders and other research infrastructures in a way that will help to optimise research programmes and priorities and strengthen the institutions.

2. The EuroFAANG Research Infrastructure

The EuroFAANG research infrastructure builds on the goal of the global Functional Annotation of Animal Genomes initiative (FAANG) (<https://www.faang.org>) to discover fundamental knowledge of genome function to decipher the Genome to Phenome (G2P) link in farmed animals (terrestrial and aquatic). By bridging the gap between cell, tissue, and whole animal scale knowledge, the FAANG initiative aims to provide genomic information to sustainably improve farmed animal production in the face of challenges to the agri-food sector including a growing human population, changing climates, and increased public concern about the welfare of production animals. The overarching aim of the EuroFAANG research infrastructure is to facilitate research and innovation regarding genotype to phenotype (G2P) prediction in farmed animals (terrestrial and aquatic) to achieve sustainable, efficient, and socially accepted farmed animal production in Europe. The research priorities of FAANG for the coming decade to reach these aims are shown in figure 1. The

EuroFAANG infrastructure continues to improve established as well as develop new technologies “beyond the state of the art” for G2P research.

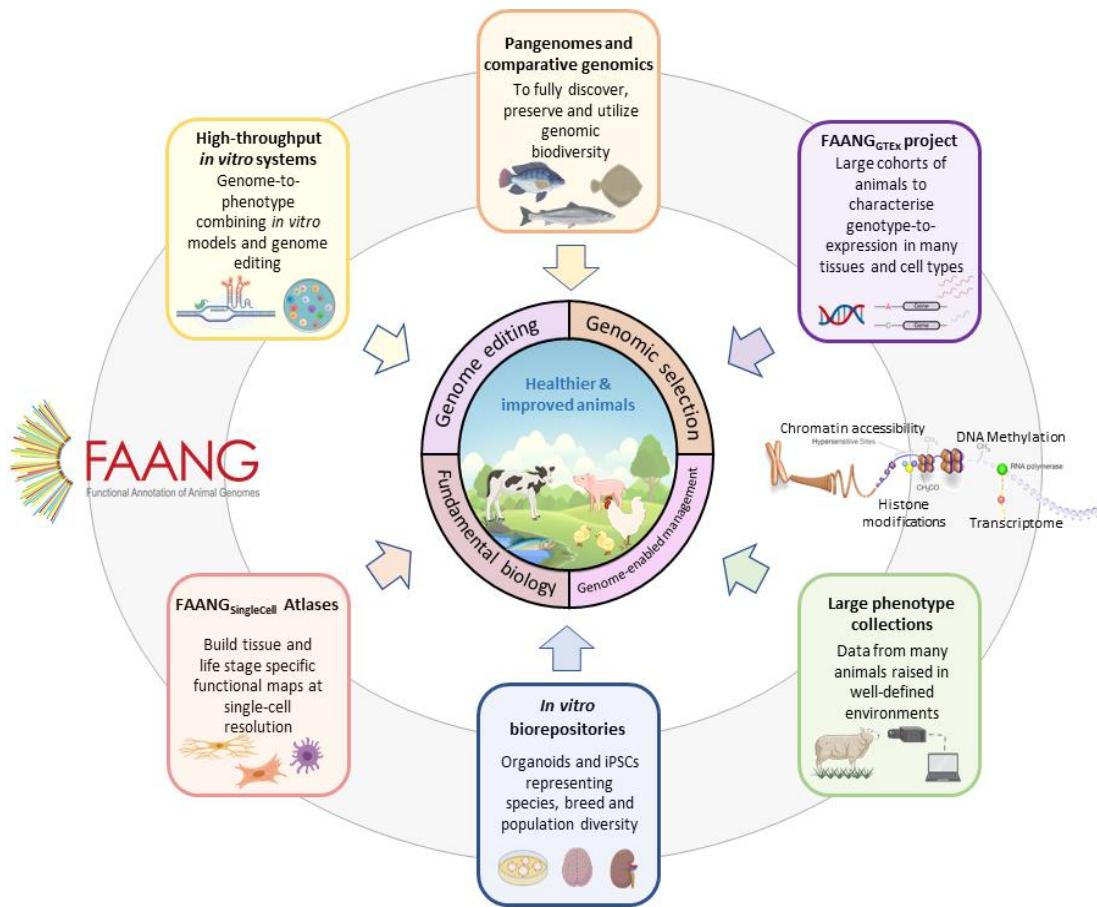


Figure 1: Research priorities for the FAANG consortium for the coming decade. From Clark et al. 2020 From FAANG to fork: application of highly annotated genomes to improve farmed animal production. *Genome Biology*, 21, 285.

2.1 The EuroFAANG Research Infrastructure Consortium Partners

The EuroFAANG research infrastructure (RI) community is an open research community that strives to continue to expand its membership and coordination (see section 1.3). Currently, the EuroFAANG RI consists of 7 partners from 6 EU member states, and the UK (Figure 2, Table 1). The EuroFAANG RI is coordinated by FBN.

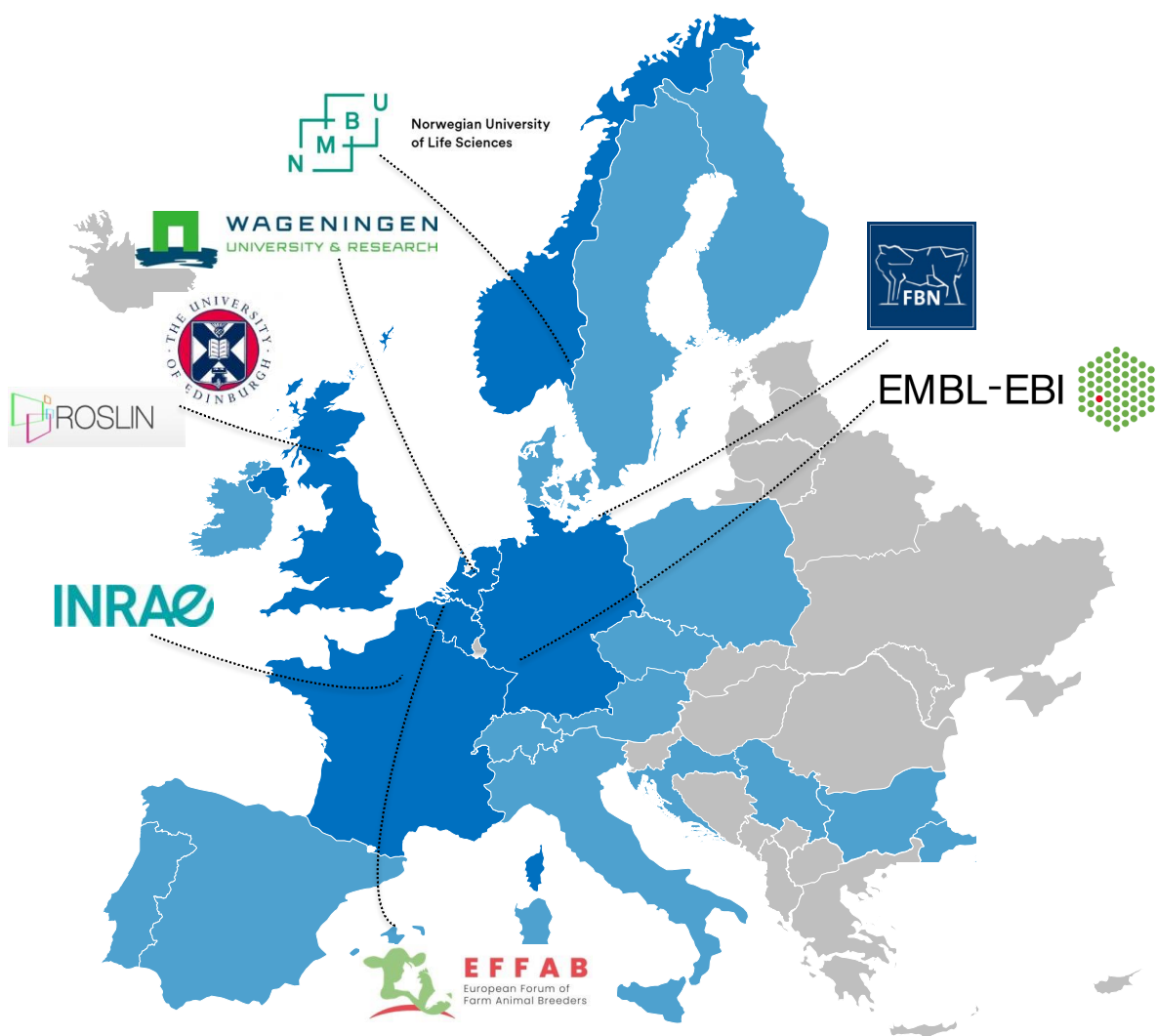


Figure 2: EuroFAANG geographical coverage. Countries with partners contributing to FAANG are shown in blue with the current participants of the EuroFAANG RI consortium highlighted in dark blue.

Table 1. EuroFAANG research infrastructure consortium partners

Participant organisation name	Country
FBN – Forschungsinstitut für Nutztierbiologie	Germany
UEDIN – University of Edinburgh	UK
INRAE – Institut National de Recherche pour l’Agriculture, l’Alimentation et l’Environnement	France
WU – Wageningen University	Netherlands
EMBL – The European Molecular Biology Laboratory	Germany
EFFAB – European Forum of Farm Animal Breeders	Belgium
NMBU – Norges miljø- og biovitenskapelige universitet	Norway

2.2 EuroFAANG Resources

In vitro models are a key element of EuroFAANG due to ethical considerations, cost effectiveness and time efficiency. They accelerate scientific progress and improve the understanding of complex biological processes by providing the opportunity to perform high-throughput screenings, manipulate variables and observe cellular and molecular mechanisms in a controlled environment and increasingly mimic conditions in vivo.

The EuroFAANG infrastructure offers access and use of a wide range of tissues, cryobanked organoids and genome edited cell lines (in vitro models) from different species, breeds and populations. The EuroFAANG infrastructure has expertise in a wide variety of techniques to use these resources to further our knowledge regarding G2P (Table 2). The use of the in vitro cellular models allows in depth precision phenotyping and will contribute to a reduction of the use of experimental animals (3Rs).

A barrier to a more widespread use of in vitro cell models for G2P research is that they often require strong efforts for adapting the existing lab methodologies across different species (e.g. calibration of culture media components for organoid culture and differentiation) and for improving their reproducibility. Moreover, it is difficult to keep pace with the evolution of methodologies, e.g. towards more complex models physiologically closer to the organ/biological functions they model, and towards high throughput solutions for phenotyping and genetic manipulation. Dealing with these challenges requires the joining of resources and expertise in EuroFAANG and a growing number of contributors and TNA accents to better link in vitro and in vivo phenotypes for more accurate G2P.

Table 2: Capabilities of consortium partners in relevant areas for linking genotype to phenotype in farmed animals.

	Data Management	Elixir Node	High Performance Computing	Bio-repositories	In vitro Models	Genome Editing	In vitro Phenotyping	In vivo Phenotyping	Contribution to EU infrastructure projects (SmartCow/PigWeb/AquaEx cel) on in vivo phenotyping	Next Gen Sequencing Platforms	Single cell Sequencing	Dedicated Communication Teams	Partnerships with animal breeders
INRAE	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓
UEDIN	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓		✓
WU	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓		✓
EMBL	✓	✓	✓	✓ data					✓	✓ data	✓ data	✓	
FBN	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓		✓
EFFAB						a			✓			✓	✓
NMBU	✓	✓	✓			✓		✓		✓	✓		✓

2.3 Expanding the EuroFAANG infrastructure

2.3.1 New Partners

The EuroFAANG research community encompasses a larger set of partner countries than the present INFRADEV project. Thus, identifying additional partners and initiatives will be necessary to ensure the EuroFAANG infrastructure to be dynamic and flexible incorporating access to new and developing research facilities and capabilities that are beyond the state of the art. The consortium formation, identification of new partners and development of a business plan are the main objectives of work package 1 of the EuroFAANG concept development project. New partners, that will expand available resources for G2P and/or that provide new techniques or facilities for G2P research will be invited to join the consortium in the next phase of EuroFAANG RI development. Criteria to be invited as new partners are based on to what extent they will improve the activities as described in section 2.3.2 below. In addition to becoming future RI partners, institutions from across Europe will make significant contributions to the EuroFAANG concept development phase through involvement in think tanks, workshops, surveys, and active G2P research contributing data to EuroFAANG.

2.3.2 Services offered by EuroFAANG RI to its users

The EuroFAANG research infrastructure underpins G2P research in farmed animals by providing training and access to data, resources and research technologies. In addition to expanding the infrastructure by integrating new partners that will provide new services to users, further increasing the available biological resources (biobanking) and data connected to these biological resources are key to strengthen and improving the infrastructure. The use of the resources available within the infrastructure by different users (TNA) will have an exponential effect on the usefulness and attractiveness of the infrastructure for both academic researchers and industry. The availability of relevant biological material that reflects the genetic variation of the study species and populations is of particular importance to the relevance and sustainability of the infrastructure. The EuroFAANG RI in principle strives to be open, but the inclusion of industrial resources and data with IP rights also offers clear advantages and increases the relevance of the infrastructure. We realize that this might generate potential friction with the aim of FAANG for open science and open public access to the biological material. TNA by industrial users will be evaluated considering the balance of added value to the infrastructure versus protection of IP rights of these industrial users (Described in sections 2 below).

3 Arrangements for Transnational Access

TNA will provide the academic and industry communities with an efficient and easy way to access a wide range of first-class genomics research facilities across Europe as well as online access to data essential for G2P research. The facilities cover a range of state-of-the-art facilities for high throughput genomics, tissue culture / organoid research, CRISPR-Cas genome editing and high-

performance compute infrastructure and data sources (table 2) for research on all major livestock and aquaculture species. The aim of this Procedural Manual is to set out the potential rules governing financial support for TNA, as well as the procedures to be adopted in selecting projects to be funded by the EuroFAANG research infrastructure during the implementation phase of the infrastructure.

3.1 Support offered for TNA and access fees for commercial users.

The TNA programme offers external users, access to the research infrastructures of EuroFAANG RI partners. The starting point of TNA is open science with open access to all data. However, as outlined in 2.3.2 exceptions are possible for resources with connected IP rights, but only if this results in a clear added benefit to the infrastructure. EuroFAANG is engaged to provide as much as open and free access as financially possible, especially for member and observer countries. For sustainability reasons, free-open access will not always be implemented, in which case user fees may apply, especially for users from countries that are not contributing members or for those following a market-driven mode of access. At this moment, it is impossible to define the actual fees required for obtaining access to the RI. However, we can identify the basic principles that will be used to define these fees:

1. Use by academia with full open access of the results and data
2. Use by industry with full open access of the results and data
3. Use by industry partly open but with restrictions (IP)
4. Degree of funding and support of the RI by EU and national funding agencies
5. Definition of access units according to the type of access : on site versus remote access, either to models or to data

The guiding principle to be used is that the fees for TNA cover the operating costs of facilities, but that the RI will cover costs for supervision of experiments and operation of specialised technical equipment. EuroFAANG will seek funding mechanisms to reduce the cost of access for users, for example through research collaborations or TNA supported by EU-funded projects. Therefore, unless the RI has secured specific funding to assist TNA, travel and subsistence costs for a visit to the research infrastructure and costs for consumables and detailed analyses will be covered by the users of the RI. TNA and required fees will be evaluated by the EuroFAANG Orientation committee (see section 3.4).

3.2 Condition of eligibility

Researchers from any country can apply for access to facilities of this Research Infrastructure, although priority (at least 80% of all funded access) will be given to researchers from organisations legally established within an EU Member or Associated State. Access to the infrastructure from non-associated third countries will require a strong justification and will be monitored closely. Applications must be made to use a Research Infrastructure in a different country to that of the lead researcher. Priorities for access, for European or national projects, may need to be set by the

national nodes. The country in which the applicant is working is considered rather than the applicant's nationality. First-time users and users who do not normally have access to specific installations in their home country are particularly encouraged to apply.

3.3 Obligation for open science practices of Transnational Access

As an infrastructure, EuroFAANG will be supporting the community generation of open data and research output for genotype to phenotype research. To this end, a key aspect is the development of a data policy, supported by rich metadata and format standards, to ensure all data generated by the infrastructure is open and FAIR. All the data generated will be collated in the context of existing EuroFAANG, FAANG and community datasets in the FAANG Data Portal. The existing EuroFAANG projects and EMBL Data Coordination Centre pride themselves on ensuring the reusability of generated data and research outputs by providing rich supporting metadata, detailed mandatory protocols of research and analysis methods, links to the open access analysis software and parameters that generated the data, and clear provenance and licensing.

All EuroFAANG data will be submitted through a brokered submission system that will ensure compliance with EuroFAANGs metadata standards and the data format standards that it develops in collaboration with Elixir. The design and establishment of this EuroFAANG data structure is a main goal of work package 3 of the current EuroFAANG concept development project. The EuroFAANG data portal will hold all data within the trusted public archives of EMBL that are part of the Elixir Infrastructure. EuroFAANG data will follow the FAANG data sharing principles (<https://www.faaang.org/data-share-principle>) that promotes open science practices, pre-publication data-sharing, collaboration and data reuse for benefit to the community and acceleration of research. All of the raw data will be released pre-publication under Fort Lauderdale and Toronto principles to provide maximum benefit to the community. The EuroFAANG Data Management Plan further outlines EuroFAANG data management policies, commitments to FAIR (Findable, Accessible, Interoperable, and Reusable) principles, open and ethically managed data deposition and access.

3.4 Data Policy and access principles

In addition to the Data Management Plan, a parallel document that mirrors the EuroFAANG TNA guide is under development that will outline the EuroFAANG RI data policy and access principles. The EuroFAANG common data access policy is an important counterpart to the TNA access policy, that will define the data handling expectations, data access requirements, conformation with data standards and FAIR principles of all users of the EuroFAANG infrastructure. The Data Access policy will conform with existing European policies and will cover the interoperability of the different infrastructure elements, connection to the Data Coordination Centre at EMBL, transfer and curation of data in the public archives and presentation of data through FAANG data portals and related services.

The Data Policy and Access Principles will be published alongside the TNA Access Policy for the RI. Just as with this TNA document, the EuroFAANG Data Policy will also be a living document that will be updated regularly throughout the lifecycle of the RI and in conjunction with updates to this TNA guide. The data access policy will be supported by the development of a common data structure for EuroFAANG. The Data Access Policy and Data Management Plan are being led by EMBL who have managed the Data Coordination Centre for global FAANG since 2015. The first version of this document is due to be published in December 2023.

3.5 Application and selection procedure

Applications for Transnational Access should be made in accordance with the guidance published on the EuroFAANG web portal currently under development (WP2). Applicants should contact the access officer or committee (EuroFAANG WP1) to discuss their research plans in advance of submitting an application. Depending on the research plans, the access officer can decide to transfer the queries to the EuroFAANG Orientation Committee to obtain a more comprehensive mentoring for TNA applicants. The Orientation Committee is composed of representatives from all institutions of the EuroFAANG RI. Applications for Transnational Access will be reviewed by an expert selection panel and an independent ethics adviser. Based on these reviews, taking into account the selection criteria as outlined below (section 3.5), this committee decides on the approval of the application in consultation with the host institution.

All work must comply with the European Union legislation on the protection of animals used for scientific purposes (Directive 2010/63/EU), as well as any national requirements and scientific policies and regulations (e.g. related to genome editing) in the country where the work will be conducted. If participation by the TNA applicant is required during the experiment, it should be ensured that the person participating has the appropriate training and licenses.

3.6 Selection criteria

Projects for TNA will be selected based on the following criteria:

- High scientific quality
- Efficient use of resources
- Address questions relevant for G2P
- Fitness of purpose of the experimental design, including an ethical assessment
- Additional funding (enabling support the direct costs of the experiments by externally funded projects /consumables)
- Open access vs IP rights (industrial users)
- The extent to which the experiments are or will be embedded within ongoing or new research projects
- Experience, training of the visiting scientist
- Strengthening of EuroFAANG network
- Potential to increase the value of the resources of the infrastructure
- Geographical distribution
- Equality, diversity and inclusion metrics

3.7 Reporting Procedure

To monitor and guide the TNA projects, TNA users are expected to deliver a detailed data management plan (DMP) before the start of the TNA and a concise report upon termination of the TNA project. Reports should be submitted using the online TNA tool available on the infrastructure website and are valid only if approved by the TNA provider and the TNA management team. In addition, to further improve the TNA programme, a mandatory follow-up questionnaire will be sent to all TNA users. This questionnaire is expected to be submitted together with the final report.

In each publication and communication resulting from a TNA project, it is mandatory to acknowledge the contribution of EuroFAANG RI in addition to the other funders.

3.8 Reimbursement procedure

For users from academia and research institutes, the EuroFAANG research infrastructure will subsidise the costs of travel and subsistence costs for one planning visit to the research infrastructure, within the funding limits set by EuroFAANG (tables 3 and 4). It is expected that participants will seek out the most cost-effective form(s) of travel with the lowest CO₂ impact. These costs will only be reimbursed once the follow-up questionnaire and the final report have been completed and submitted along with a reimbursement claim form.

Boarding passes, travel agency invoices, original tickets or e-tickets must be submitted with the reimbursement claim form. For reimbursement of travel expenses incurred in a currency other than Euro, conversion will be made using the official ECB exchange rate on the date of the expense. The cost of a journey by private car (user's personal or company car) is calculated at a rate per km in accordance with the internal rules of the TNA provider concerned. Fuel is included in the kilometre rate. Road tolls may be paid extra. When two or more participants travel together by car, travel costs will be reimbursed to only one person. The total cost of travel by car cannot exceed the maximum cost of an equivalent flight. Car rental costs cannot be covered unless it is the more convenient way to travel. Car insurance costs cannot be covered.

3.9 TNA Agreement

A formal agreement between the TNA provider and the TNA user will be signed, describing all the details regarding e.g. the unit of access, the travel budget, the ownership of the results, the publication policies, and the additional costs not covered by EuroFAANG. Depending on the governance model chosen by the EuroFAANG infrastructure (WP1), the agreement will either be between the user and the TNA provider or between the user and the infrastructure itself. EuroFAANG will create a template for TNA agreement to be used by all partners and, a checklist of important items to include in the agreement will be available through the EuroFAANG web portal.