Moving towards Precision Breeding in European aquaculture: AQUA-FAANG results and their impacts

By Professor Dan Macqueen and Professor Sigbjørn Lien

Executive Summary: **The H2020 AQUA-FAANG project has generated extensive new functional genomics datasets in the six main finfish species farmed in European aquaculture. This article introduces these datasets, how they are being shared with the research and innovation community, and how AQUA-FAANG results provide valuable opportunities to develop precision breeding strategies to increase aquaculture sustainability and profitability.**

The issue:

Aquaculture is vital to European and global nutritional security, and this role becomes increasingly important with the continued trend of human population growth, driving greater demand for high-quality dietary protein, healthy fatty acids and micronutrients. Finfish farming faces many challenges to sustainable production and expansion, including the constant threat of infectious diseases and climate change, which is enabling new pathogens to enter aquaculture systems while posing further issues to fish health and welfare. Addressing such challenges requires a multi-pronged approach, with selective breeding providing a keystone strategy to ensure fish with the most desirable characteristics are farmed now and in the future.

Genomics provides a vital toolbox for commercial breeding programmes in farmed animals. Selective breeding using genetic markers linked to traits (genomic selection - GS) is currently widely used to farm fish with favourable characteristics, e.g. disease resistance. While the 'current generation' of selective breeding is effective when the animals are close relatives, it becomes less effective when animals are distantly related – from different populations, or across generations. This is because the selection performed is not directly based on the underlying genetic variants causing the desired traits. In fact, there are millions of genetic variants within any species, but most have zero effect on traits.

If selective breeding involved targeting the much smaller number of genetic variants that truly influence favourable characteristics (causal variants), it would become highly effective in distantly related animals. This type of **precision breeding** would have a range of positive impacts that drive increased sustainability and profitability of the aquaculture sector. However, identifying causal variants is challenging and requires cutting-edge techniques.

AQUA-FAANG contribution to solutions:

AQUA-FAANG has produced extensive new datasets to identify regions of the genetic code (i.e. the genome sequence) that impact biological traits in the main finfish species farmed in European aquaculture. We call these regions 'functional', and they include DNA elements that control how genes are expressed in different conditions, for example during development or following a challenge to the immune system. Genetic variants in such

regions of the genome are much more likely to affect traits of importance to aquaculture than randomly selected variants. The AQUA-FAANG project represents a great advancement because this type of data is extremely limited in farmed animals and its generation was a huge effort spanning several years, requiring collaboration by many partner organizations around Europe.

The AQUA-FAANG approach involves **genome functional annotation**, leveraging advanced high-throughout DNA sequencing technologies to reveal and describe different types of functional regions in genomes. The project generated genome functional annotation data across diverse sample types in the six species, including:

- Different stages of **embryonic development** – these early life stages play a crucial role in determining traits of relevance to aquaculture and adult fish health
- Different tissues of adult fishes of **both sexes** at two stages of **sexual maturation –** these tissues were selected for relevance to a range of aquaculture traits
- After immune stimulation with **viral and bacterial** molecular signals – sampling the primary immune organ of fish

This comprehensive set of samples was used to generate almost 5,000 new sequencing datasets across the six target species. AQUA-FAANG data captures **how genes are expressed** and how **DNA elements in the genome are activated or repressed**, during fish development from embryo to adult, and following challenge to the immune system.

How can this data be used to advance precision breeding? AQUA-FAANG datasets add multiple new layers of information on the genetic architecture of farmed fish characteristics, and allow researchers, for the first time, to prioritize genetic variants with increased probability of impacting traits in the target species (for visualization see figure XX). This information can be used in a range of applications, including building new genetic tools and approaches for breeding that have better accuracy without adding significant financial costs. It can also help reduce the current reliance of industry on measuring important breeding traits (e.g. disease challenge experiments) across different generations, which is expensive and problematic in regards to animal welfare.

AQUA-FAANG data will be vital for future applications of genome editing in the targeted fish species. Genome editing is a powerful tool for inducing precise genetic changes that can improve the long-term sustainability of aquaculture. A major bottleneck for implementing this technology is the need to identify high-priority regions for editing. AQUA-FAANG data provides these target regions and will allow scientists to make more precise changes in the genome, which will be vital not only for research, but also potential future applications in aquaculture practise.

The AQUA-FAANG project **shares** all of its **data openly through the Ensembl Genome Browser**, which enables researchers and industry to scan the genome of each target species to identify functional regions of interest. Furthermore, Ensembl unlocks opportunities for researchers and aquaculture breeding companies to quickly and easily overlap their bespoke datasets with AQUA-FAANG annotations, empowering new opportunities for precision breeding applications in different countries and organizations across the globe.

Applications and potential impact:

In summary, AQUA-FAANG has opened the door for precision aquaculture breeding to play a significant role in addressing the challenges and opportunities outlined above, contributing to the development of a sustainable, resilient, and competitive EU aquaculture sector.

The AQUA-FAANG project's genomics datasets hold significant promise for aquaculture:

1. **Precision Breeding:** AQUA-FAANG identifies genetic variants linked to desirable traits, enabling precise breeding even in distantly related fish. This enhances sustainability by optimizing resource use and reducing costly trait measurement experiments.

2. **Efficiency and Profitability:** The data streamlines commercial breeding, accelerating the development of superior fish lines. This boosts profitability and reduces resource expenditure.

3. **Disease Resistance:** AQUA-FAANG data aids in breeding disease-resistant fish, minimizing the need for antibiotics and promoting healthier populations.

4. **Genome Editing:** The project facilitates precise genome editing for sustainability, targeting regions that enhance resource utilization and environmental friendliness.

5. **Global Collaboration:** AQUA-FAANG's open data sharing fosters global collaboration, driving innovation in precision breeding techniques.
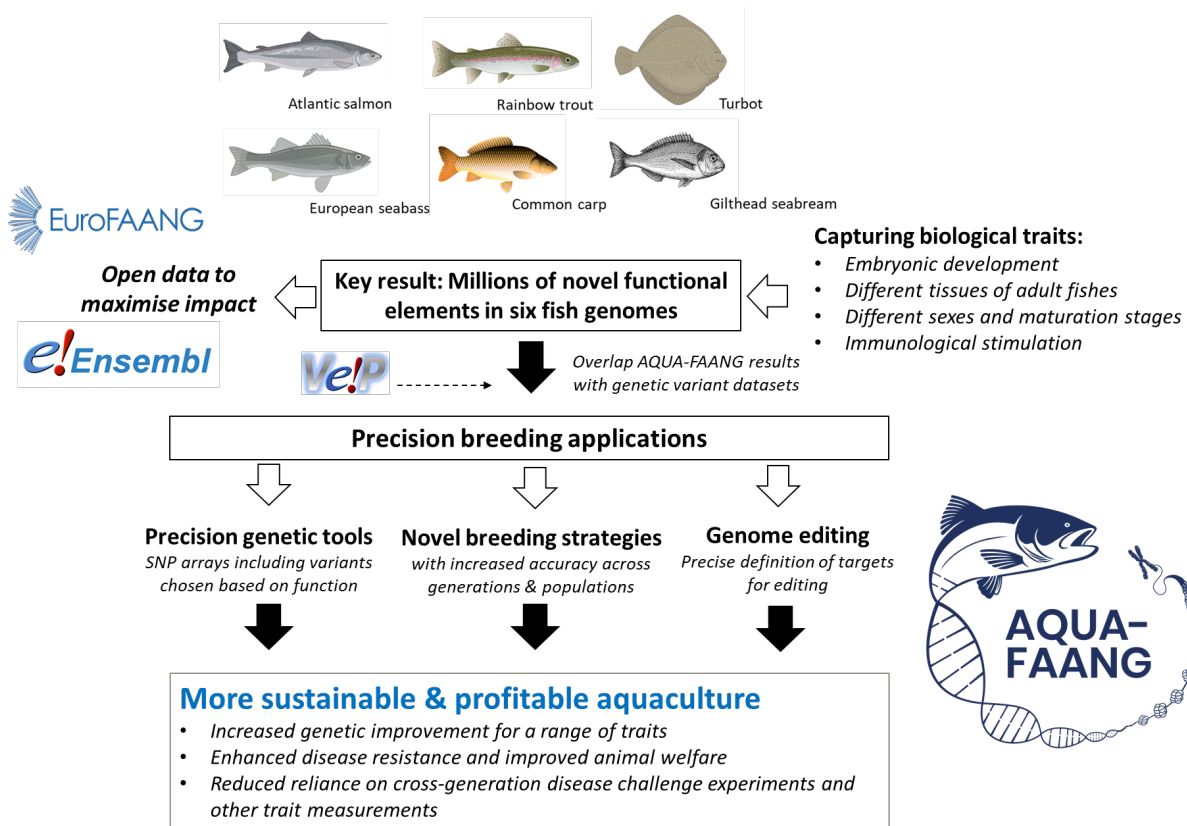
AQUA-FAANG datasets support precision breeding applications in finfish aquaculture
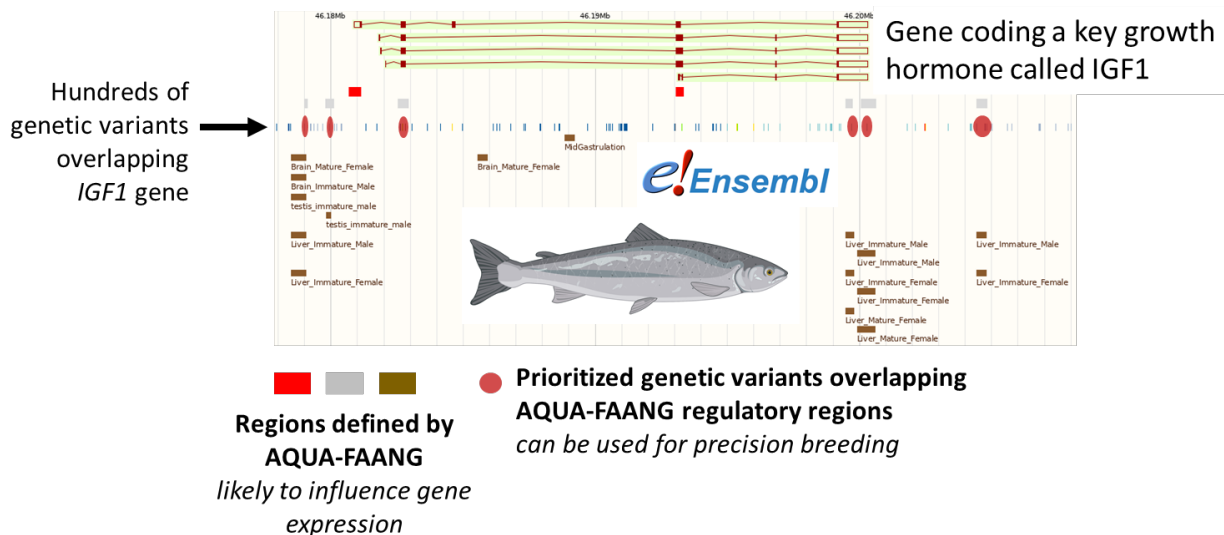
An example of how AQUA-FAANG datasets can be used to prioritize genetic variation that may be influencing how genes are expressed in different biological conditions.