

AQUA-FAANG: Empowering Aquaculture Research and Innovation By Genome Functional Annotation

Dr Peter Harrison. European Bioinformatics Institute, EMBL-EBI

On behalf of AQUA-FAANG consortium



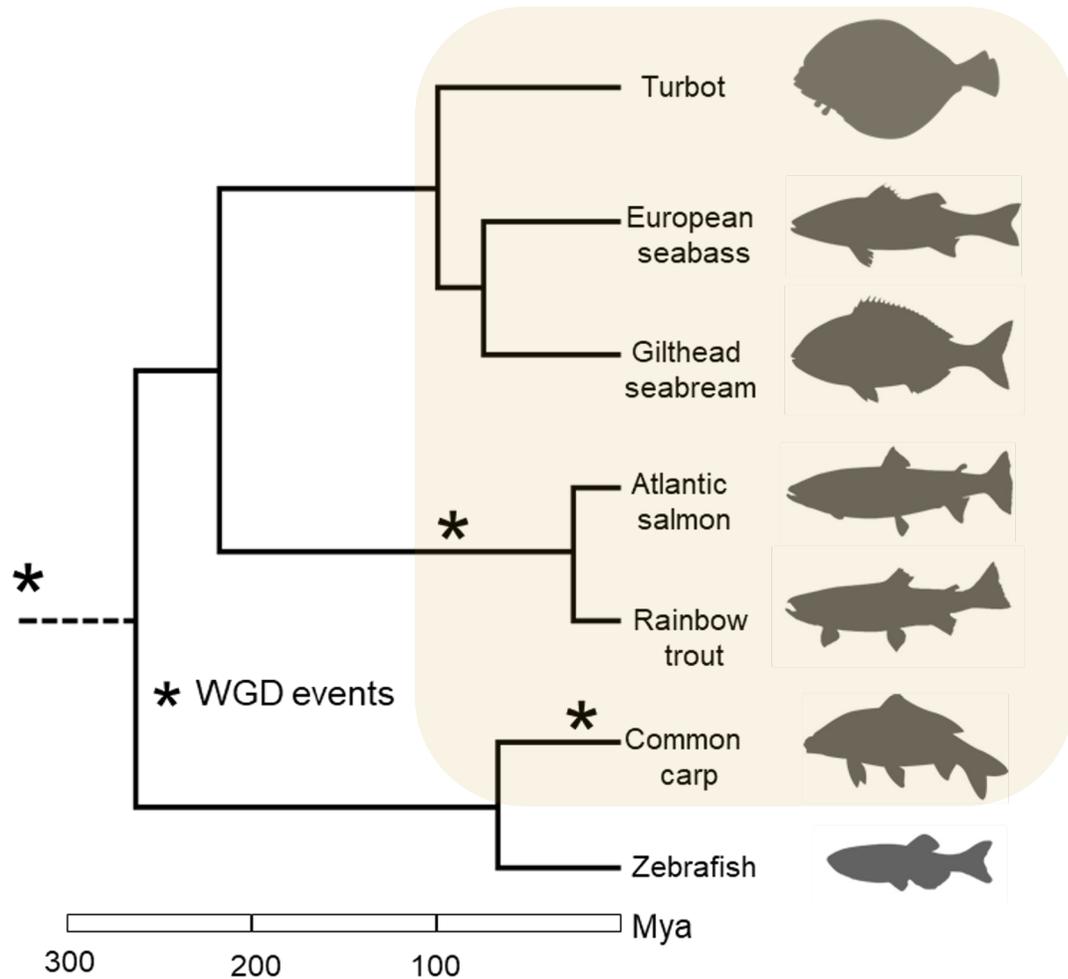
Functional Annotations of Animal Genomes (FAANG) Workshop – PAG31 – San Diego – Jan 16th 2024



AQUA-FAANG has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 817923. www.aqua-faang.eu



AQUA-FAANG



Aim: produce genome-wide functional annotation maps for six commercially important fish species

- Funded at 6 million Euros by H2020
- May 2019 to Oct 2023
- Coordinated by Sigbjørn Lien & Dan Macqueen
- One of the six EuroFAANG projects



AQUA-FAANG Consortium



Universities



research institutes



SME's and International Organisations



14 academic partners & 10 industry partners across 9 countries

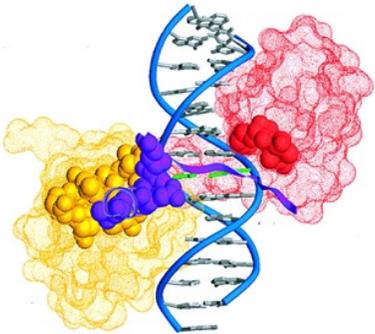


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Specific objectives

AQUA-FAANG:

Step-improvement in functional annotation of genome regulation and expression



Overall objective

Scientific **IMPACT** *Commercial*



1) Standardize protocols - share data and expertise

2) Annotation of healthy and immune active states

3) Predict disease resistance and other traits

4) Enhance functional annotation by a comparative understanding

5) Engage stakeholders and ensure results are converted to practice

Specific objectives

European Aquaculture:

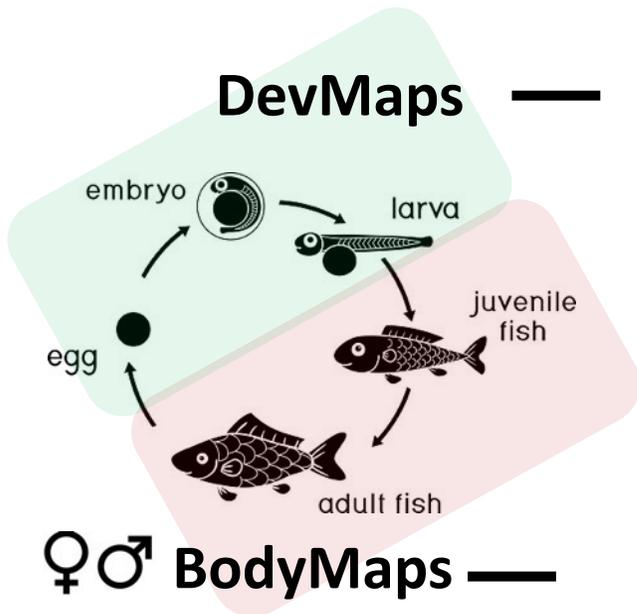
- **SUSTAINABLE**
- **COMPETITIVE**
- **PROFITABLE**



AQUA-FAANG - functional annotation

Regulatory elements, chromatin epigenetic state and gene expression

- Standard samples across species - *different life stages, tissues from both sexes, and responses to immune challenge*



Six standardized stages of embryogenesis (all assays) plus at least six additional stages (RNA-Seq)

Tissue panel in both sexes, sexually immature and mature:

- Liver, brain, gill, intestine, skeletal muscle, head kidney, ovary and testis

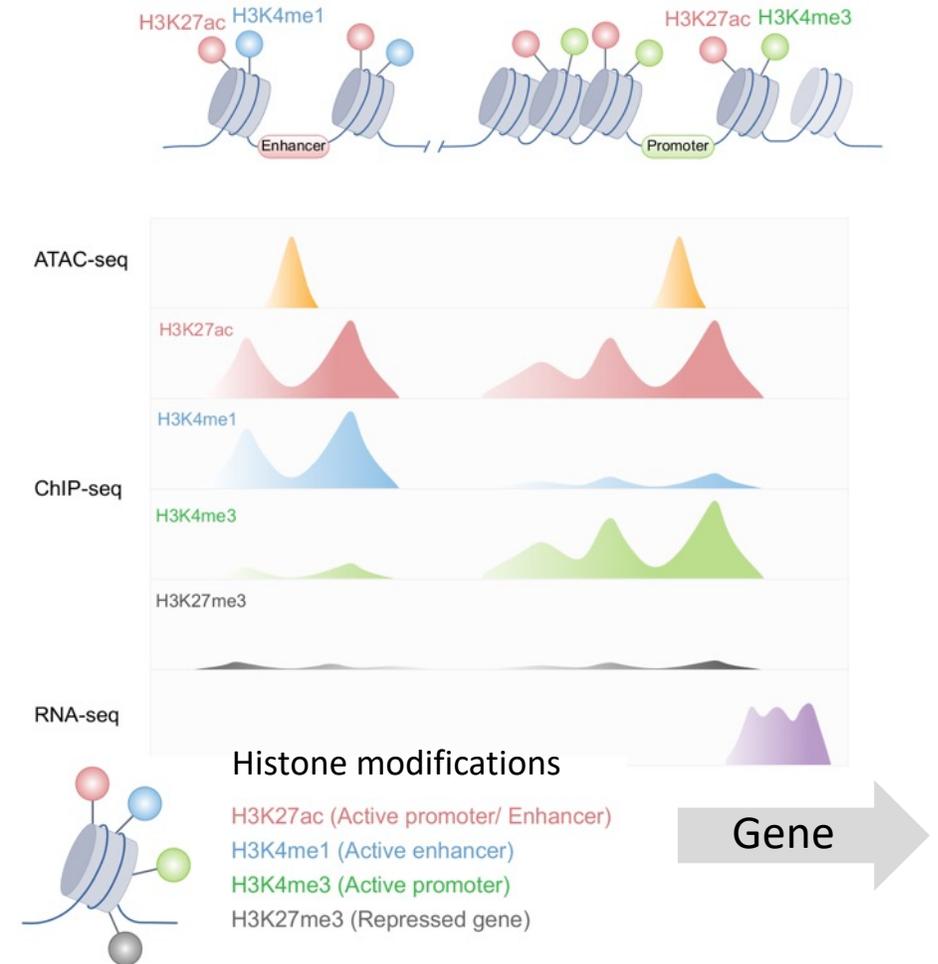
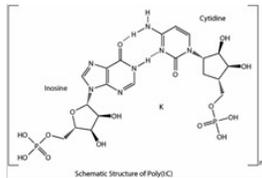


Image credit: Pooran Dewari

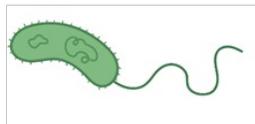
AQUA-FAANG - functional annotation

Regulatory elements, chromatin epigenetic state and gene expression

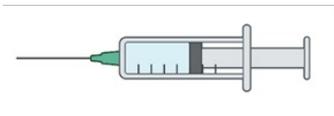
- Standard samples across species - *different life stages, tissues from both sexes, and responses to immune challenge*



Poly I:C



**Inactivated
Vibrio**



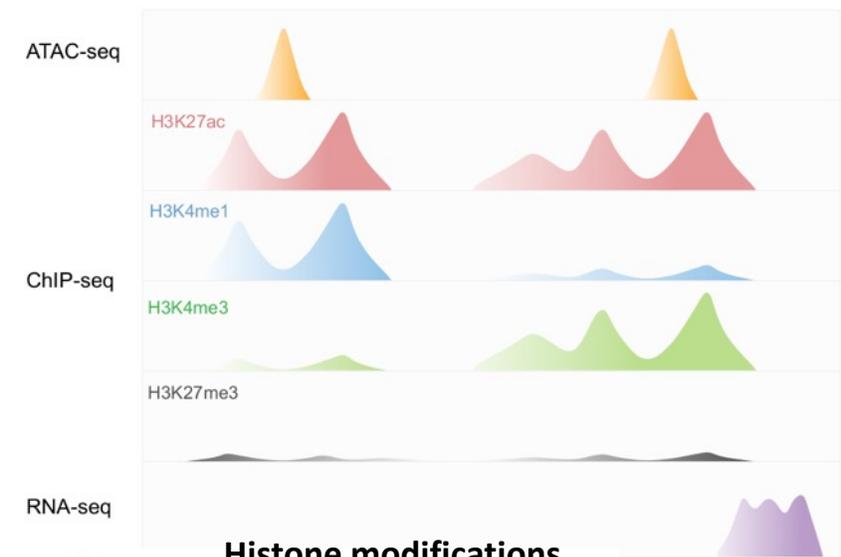
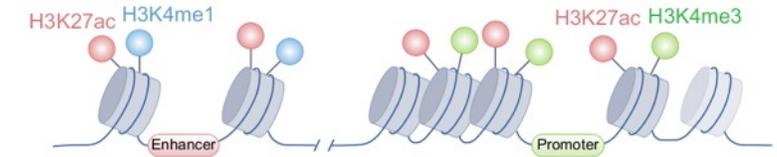
In vivo



In vitro

ImmunoMaps

- Head kidney samples - primary haemopoietic organ
- Poly I:C (viral mimic)
- Inactivated *Vibrio* (pro-inflammatory response)
- PBS controls
- in vivo* I.P. injection and *in vitro* leucocyte cultures



Histone modifications

- H3K27ac (Active promoter/ Enhancer)
- H3K4me1 (Active enhancer)
- H3K4me3 (Active promoter)
- H3K27me3 (Repressed gene)

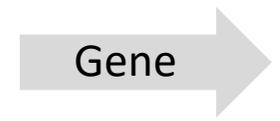
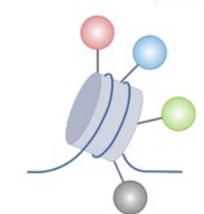
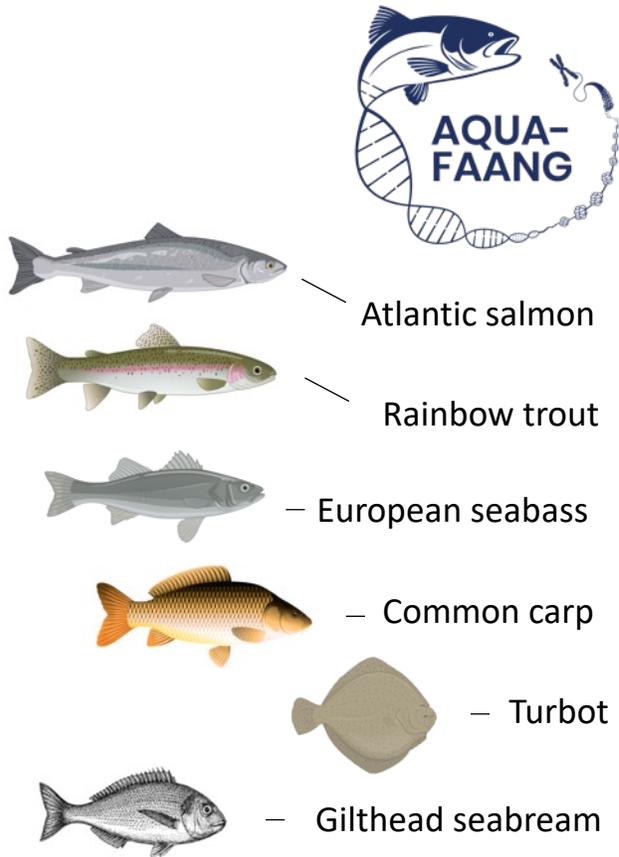


Image credit: Pooran Dewari

Data produced across species



	BodyMaps			DevMaps			ImmunoMaps		
	RNA-Seq <i>mRNA + small</i>	ATAC-Seq	ChIP-Seq	RNA-Seq <i>mRNA + small</i>	ATAC-Seq	ChIP-Seq	RNA-Seq <i>mRNA + small</i>	ATAC-Seq	ChIP-Seq
Atlantic salmon	108	60	299	71	21	106	54	36	78
Rainbow trout	114	60	239	71	15	95	122	68	52
European seabass	116	60	257	75	18	61	54	36	126
Common carp	108	60	240	67	18	68	59	36	123
Turbot	108	60	194	62	18	56	54	36	114
Gilthead seabream	116	60	166	62	18	45	88	36	119

Approx. 4,700 sequencing datasets produced across species as basis for functional annotations

- > 50 trillion DNA base pairs of new information on genome function
- Many partners and individuals involved – **too many to acknowledge individually, amazing team effort**

Data analysis & sharing

Data used to **update gene model predictions** (RNA-Seq) and produce **novel annotations of regulatory features** (ATAC-Seq & ChIP-Seq) in **Ensembl genome browser**

EMBL-EBI



Peter
Harrison

Garth
Ilsley

Fergal
Martin

 e!Ensembl

 Ve!P



Data Portal

FAANG is the **F**unctional **A**nnotation of **A**nimal **G**enomes project. We are working to understand the genotype to phenotype link in domesticated animals.

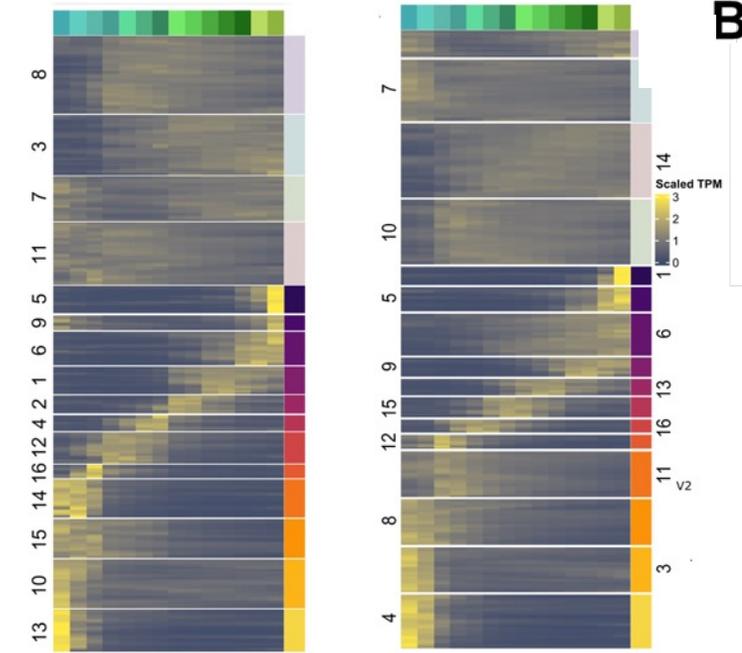
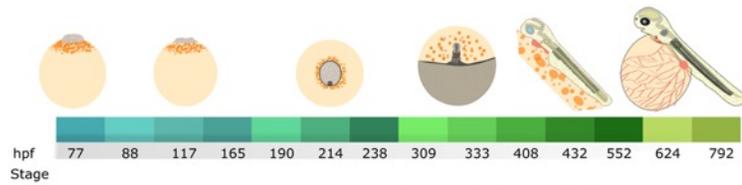
This data portal will help find and browse FAANG's data. Let us know what you think at faang-dcc@ebi.ac.uk.

Data and metadata available on FAANG data portal

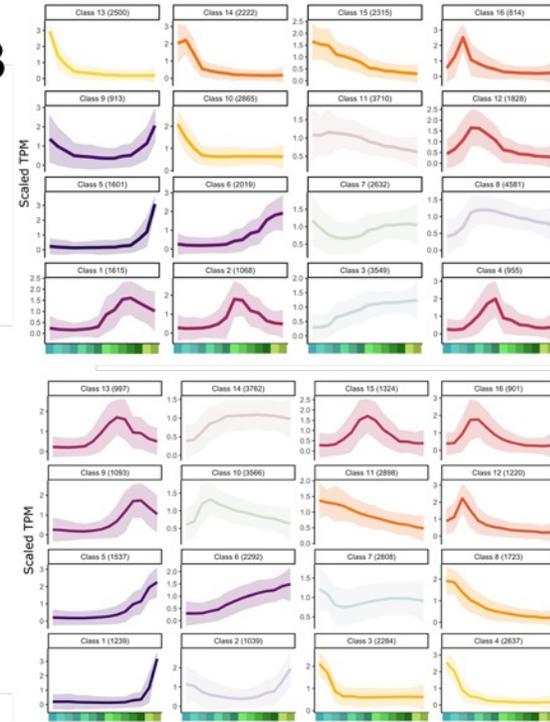
- Partners performed own data analysis and annotations using nf-core pipelines - *for standardization and to harmonise with other EuroFAANG projects*
- Large up-step in competence in bioinformatics for regulatory data

 nf-core 

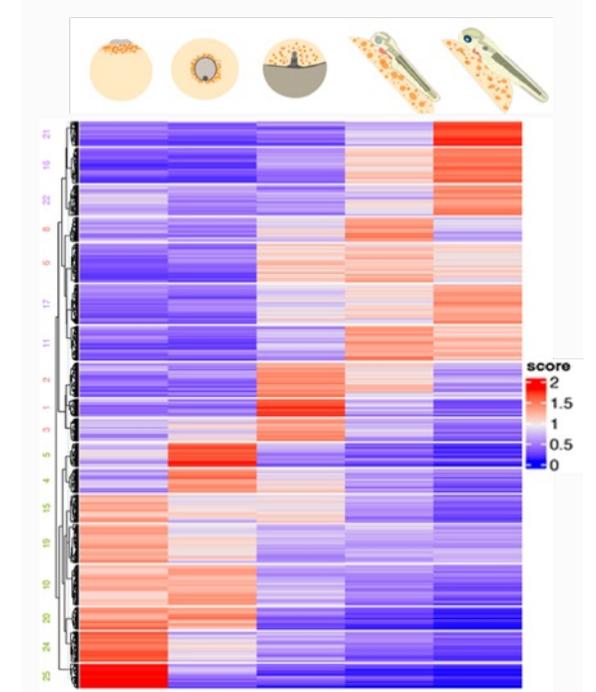
Highlights: revealing functional activity in fish genomes



B



Transcriptome



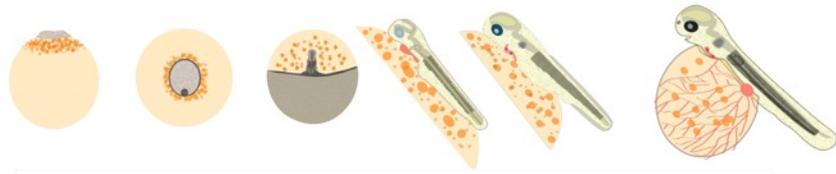
Chromatin accessibility

Self organizing map clustering: expression & chromatin accessibility



Imperial College London

Highlights: revealing functional activity in fish genomes



Embryogenesis stages Image credit: Diego Perojil



Tissue panel from immature & mature fish

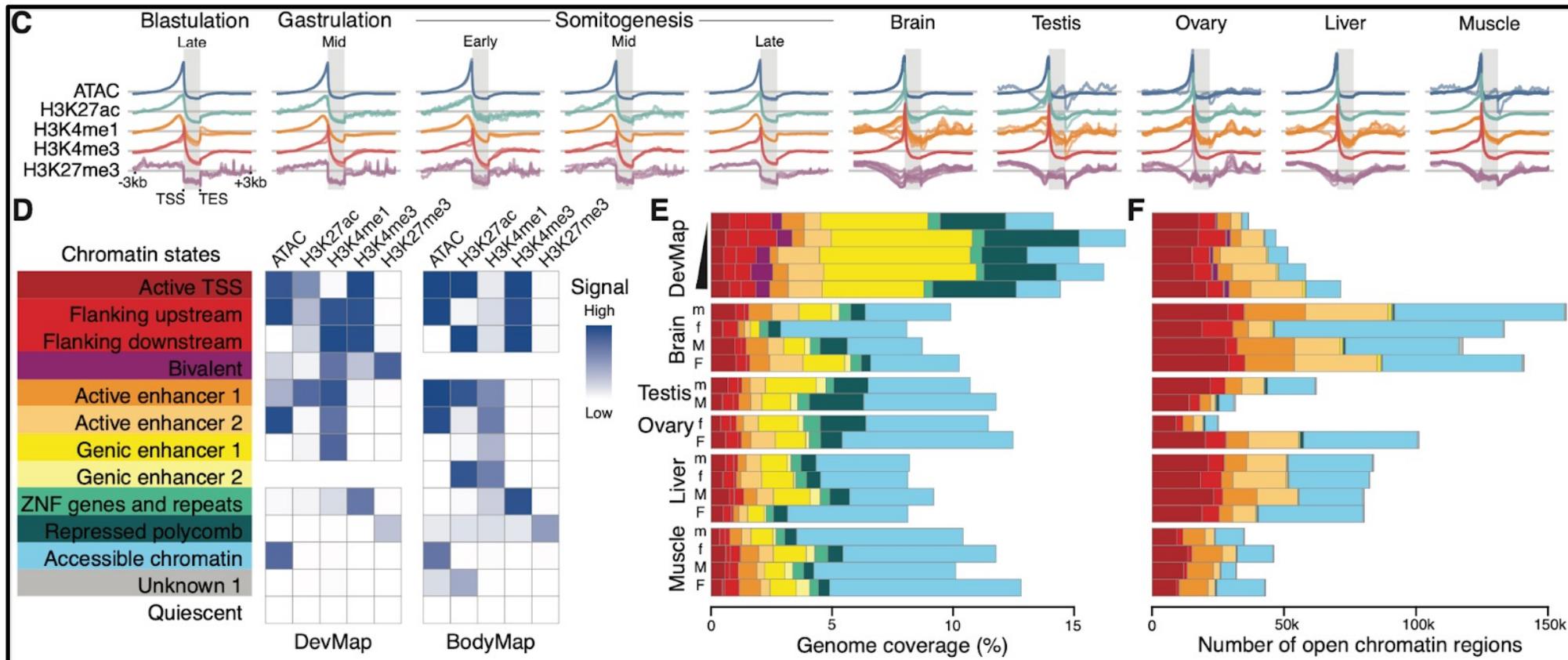
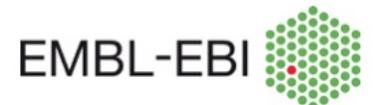
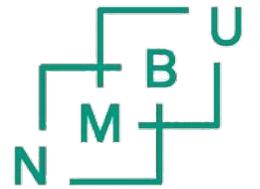
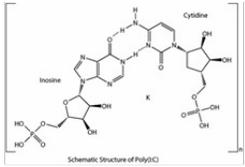


Image credit: Gareth Gillard

Highlights: revealing functional activity in fish genomes

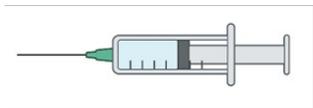


Poly I:C



Inactivated *Vibrio*

Regulatory regions were activated in response to pathogen signals -> variants overlapping such elements are likely to influence disease resistance phenotypes



In vivo



In vitro

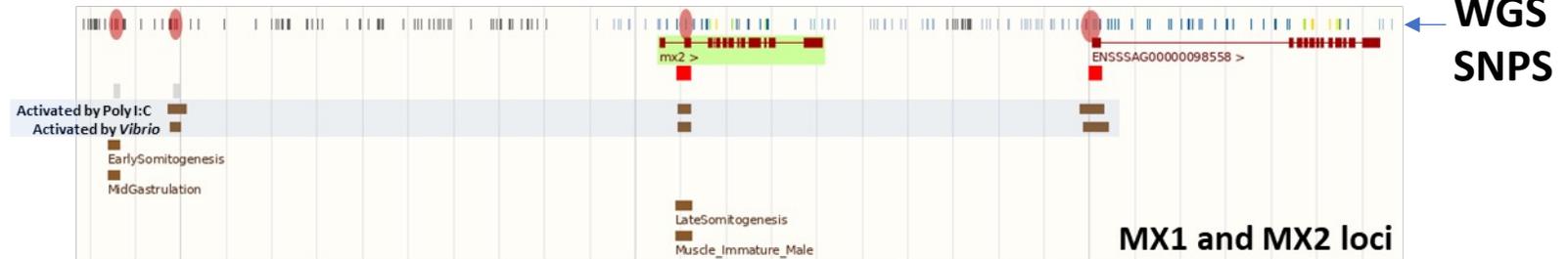
- Strong activation of regulatory elements surrounding interferon pathway genes in response to poly I:C (viral mimic)

Mx Proteins: Antiviral Gatekeepers That Restrain the Uninvited

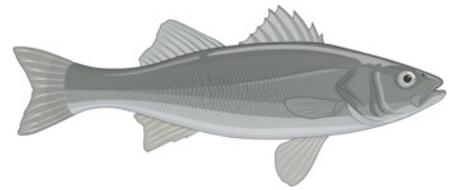
Judith Verhelst, Paco Hulpiau, Xavier Saelens

Inhibition of Infectious Pancreatic Necrosis Virus Replication by Atlantic Salmon Mx1 Protein

Rannveig Larsen, Torunn P. Røkenes, and Børre Robertsen*



Highlights: functional annotation to understand the genetic basis of disease resistance



Parents

WGS

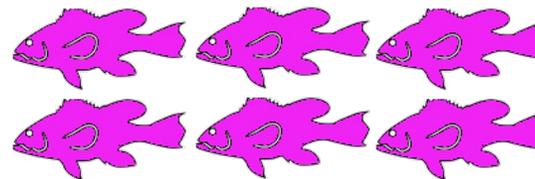
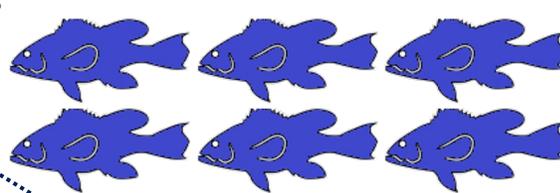
Imputation

8.4M Imputed Variants

35K SNP array

VNN resistance QTL identification and mapping

25 males x
25 females

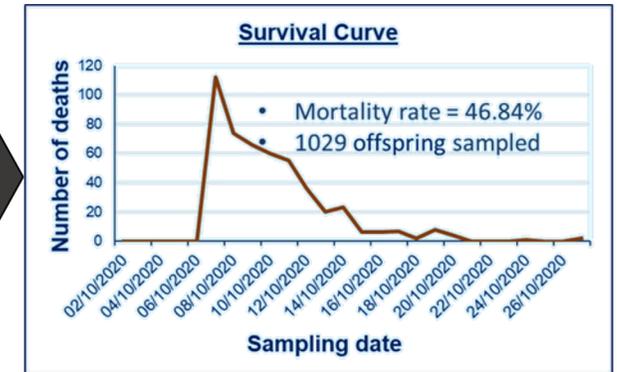


1029 offspring



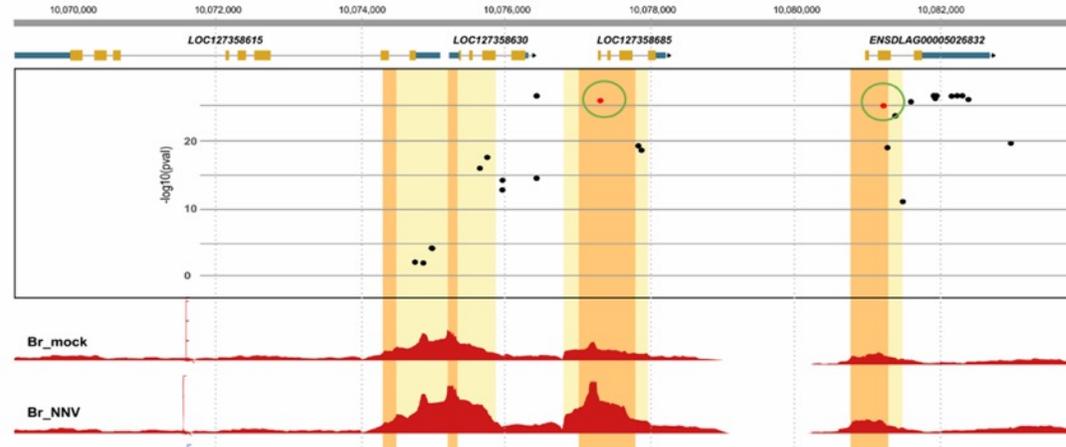
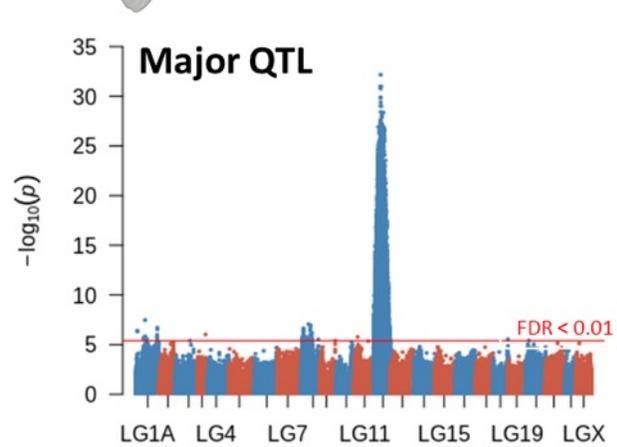
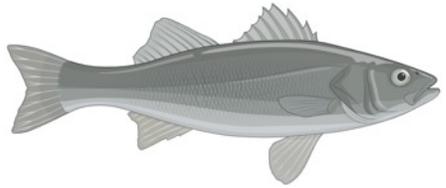
Survival data

RNA-seq & ATAC-seq

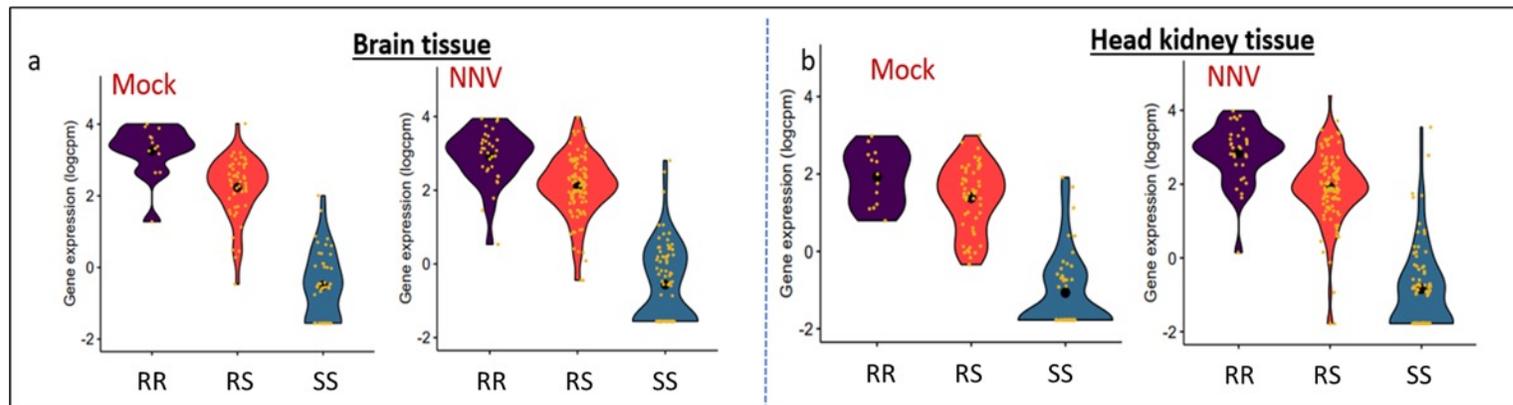


Exemplar study to uncover the functional genetic architecture of viral nervous necrosis resistance

Highlights: functional annotation to understand the genetic basis of disease resistance



Two SNPs in open chromatin of two copies of ifi2712a

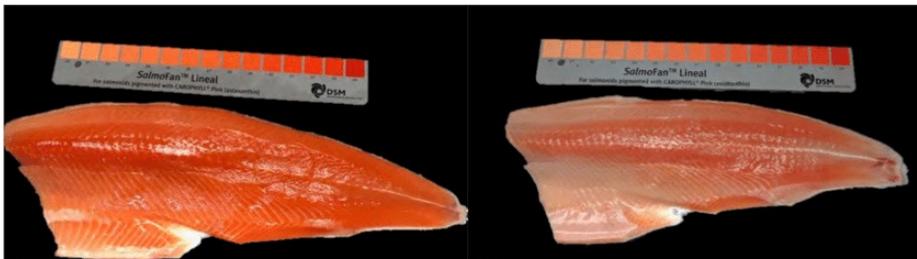
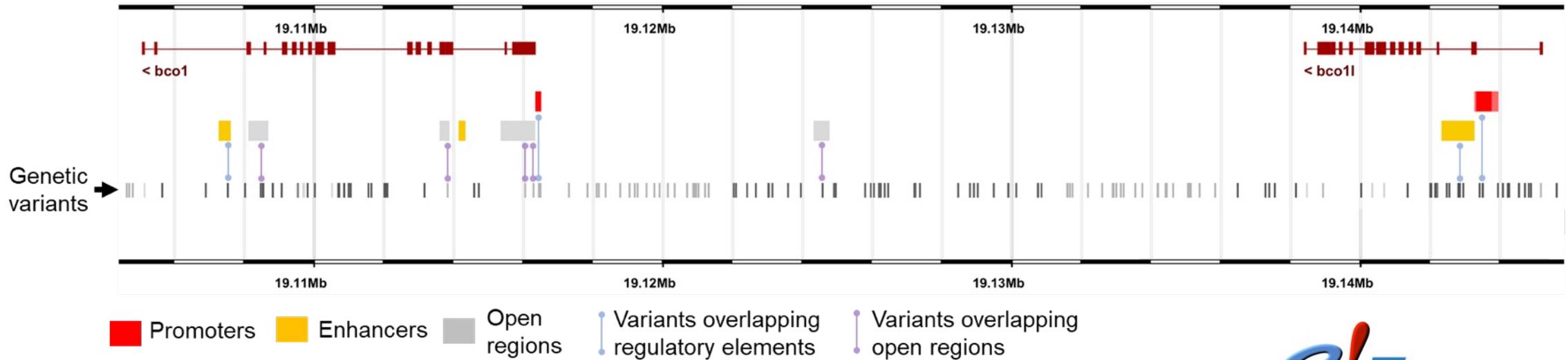
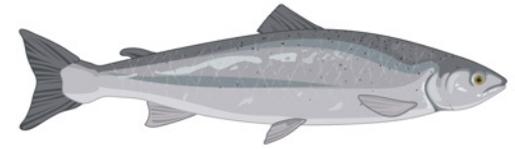


eQTL analysis - ifi2712a RNA levels associated with resistance in virus target tissues

Exemplar study to uncover the functional genetic architecture of viral nervous necrosis resistance

Highlights: prioritizing variants

e.g. 40 kb region impacting flesh colour



Small number of variants overlap regulatory elements and open regions – more likely to be influencing trait



- Biological traits:**
- Embryonic development
 - Different tissues of adult fishes
 - Different sexes and maturation stages
 - Immunological stimulation

Millions of novel functional elements in six fish genomes

Open data to maximise impact



Applications leveraging improved understanding of genotype to phenotype

- Novel genetic tools**
SNP arrays including functional variants
- Novel GS models**
Increased accuracy across generations and populations
- Genome editing**
Improved target regions for editing

More sustainable and profitable aquaculture

- Increased genetic improvement for a range of traits
- Enhanced disease resistance and reduced reliance on multi-generational disease challenge experiments
- Improved animal welfare

Exploiting functional annotation for more precise breeding

Deeper annotation will increase resolution to identify causative variants

Figure adapted from Johnston et al. 2024. AQUA-FAANG whitepaper - In Revision (Aquaculture)

Summary of achievements

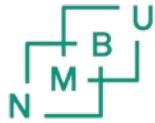


1. Developed standardized functional annotation protocols for six major aquaculture species and shared the resulting data and expertise
2. Generated and interpreted functional annotation maps for both healthy and immune activated states to identify functional regions across tissues, life stages, sexes, and after viral or bacterial challenge
3. Exploited functional annotation to help predict functionality of variants responsible for resistance to aquaculture pathogens and used project results to improve breeding approaches in aquaculture
4. Developed resources and methods for comparative analysis of functional annotation datasets, to reveal genomic elements conserved across species and in relation to WGD events in fish evolution
5. Actively engaged many project stakeholders in aquaculture sector through a comprehensive program of communication, dissemination, and exploitation activities





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INRAE



UNIVERSITY OF ABERDEEN



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POLISH ACADEMY OF SCIENCES

UNIVERSITAT DE BARCELONA



Imperial College London



AquaGen

Valle à Zuliani



OVAPISCIS

Stolt Sea Farm

grupo culmarex



EuroFAANG

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Rumigen
TOWARDS IMPROVEMENT OF RUMINANT BREEDING THROUGH GENOMIC AND EPIGENOMIC APPROACHES

HoloRuminant
Understanding microbiomes of the ruminant holobiont

Thank you for your attention!

FAANG
Functional Annotation of Animal Genomes
10 Years

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