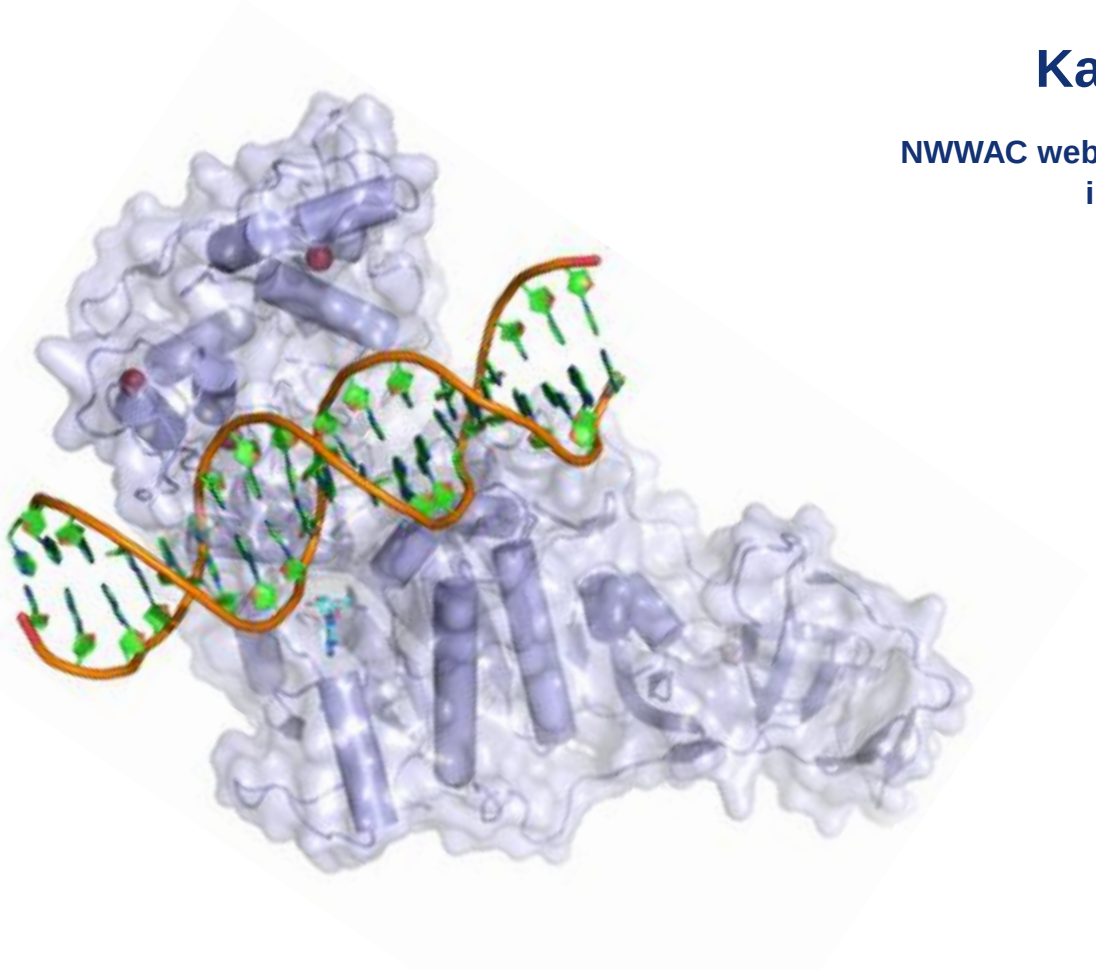
Ocean warming shapes embryonic developmental prospects of the next generation in Atlantic cod?

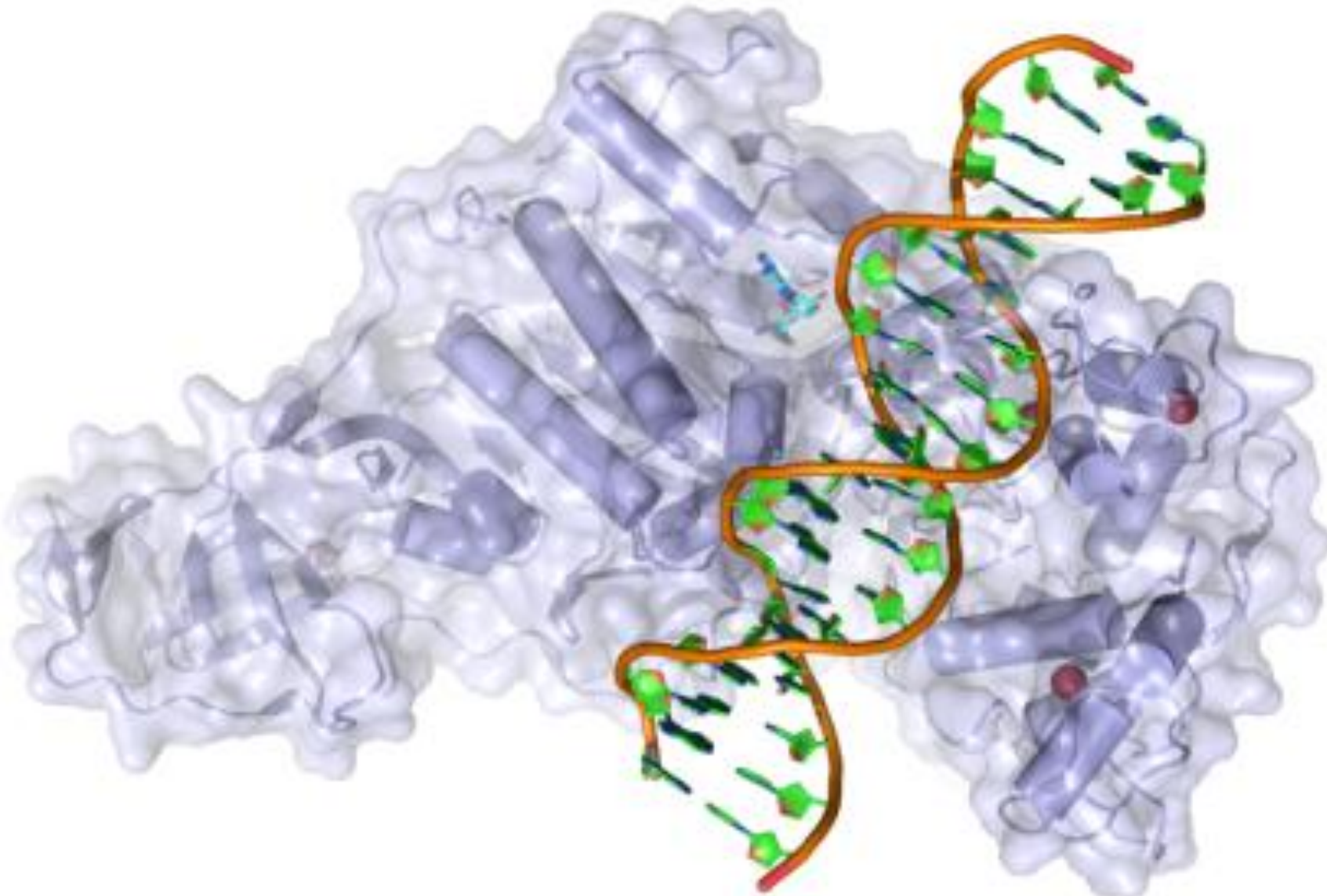
Kaja H. Skjærven

NWWAC webinar on climate change impacts on cod in the Celtic Sea, June 2024

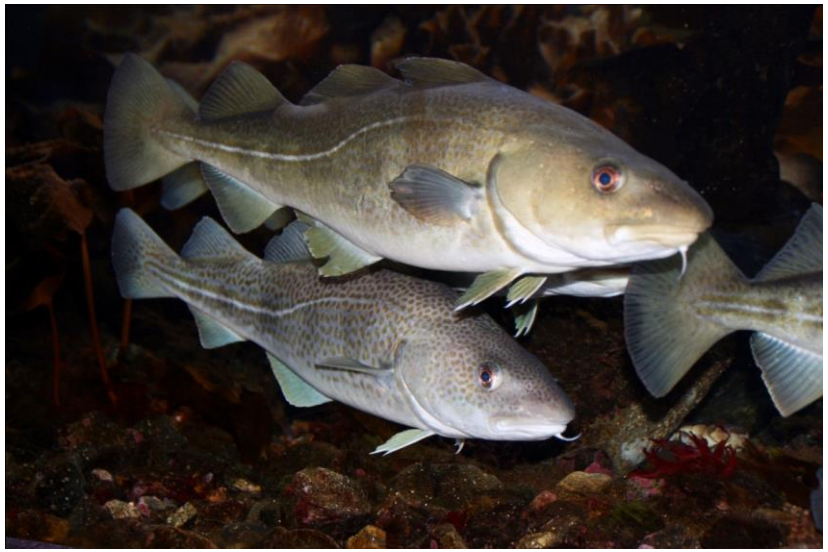


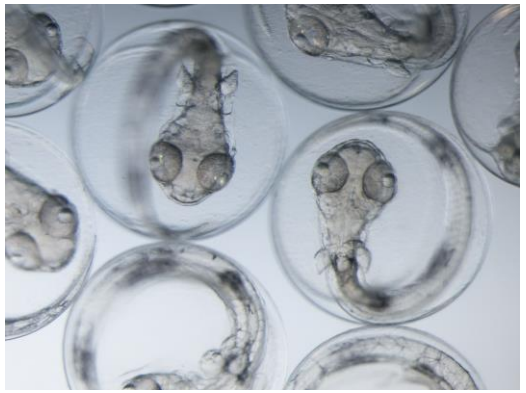
FHF

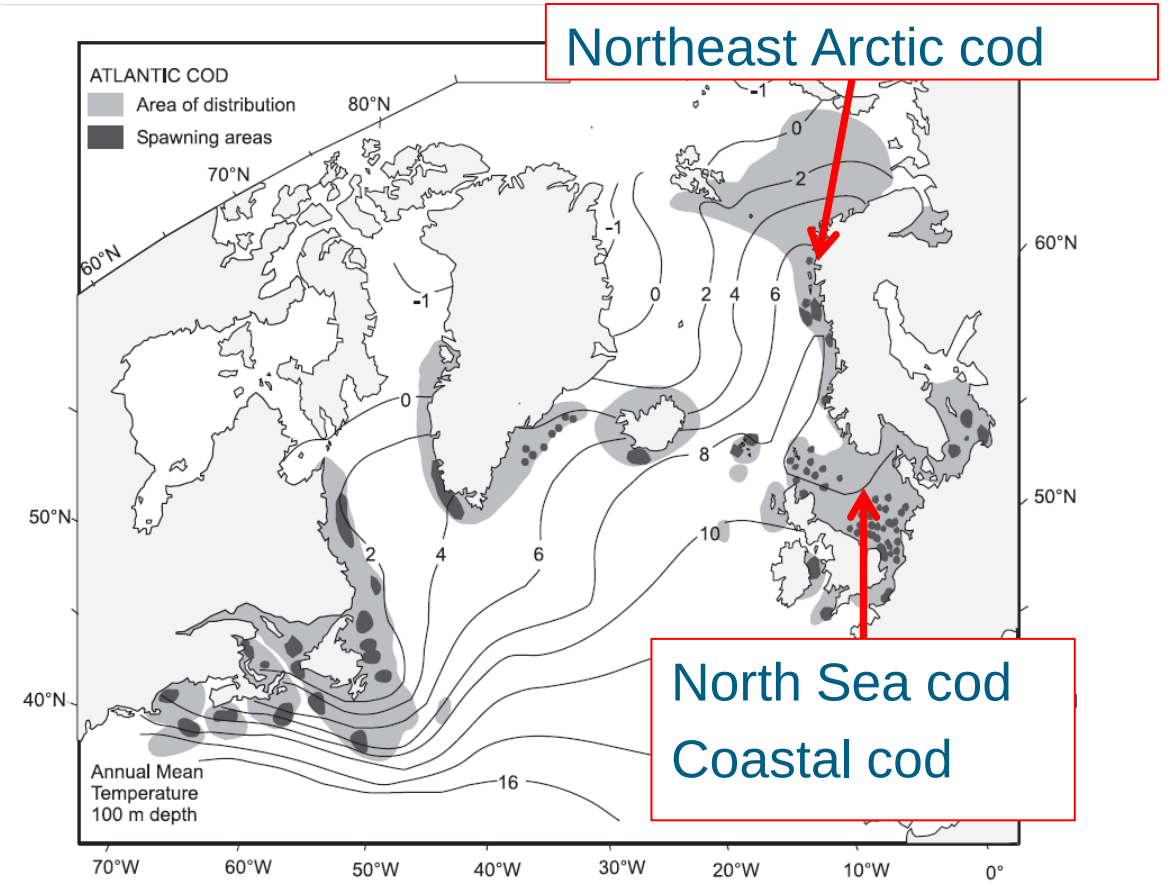
The Research Council of Norway



Atlantic cod (*Gadus morhua*)



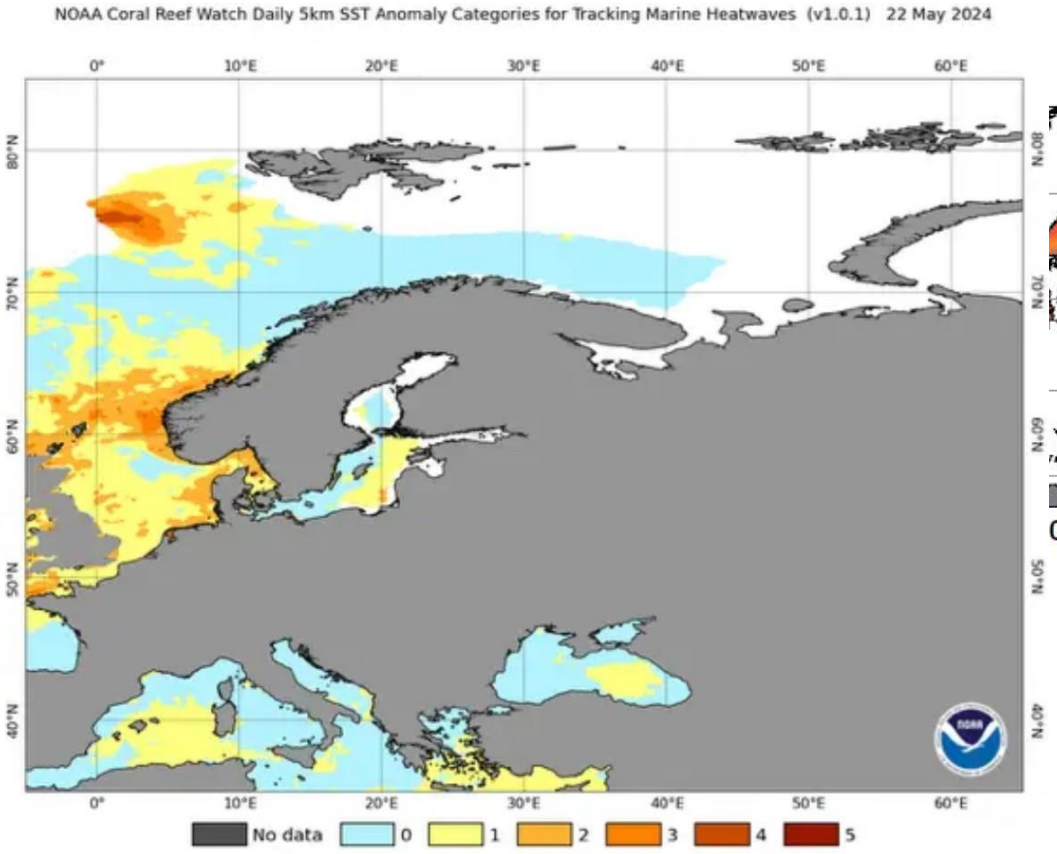


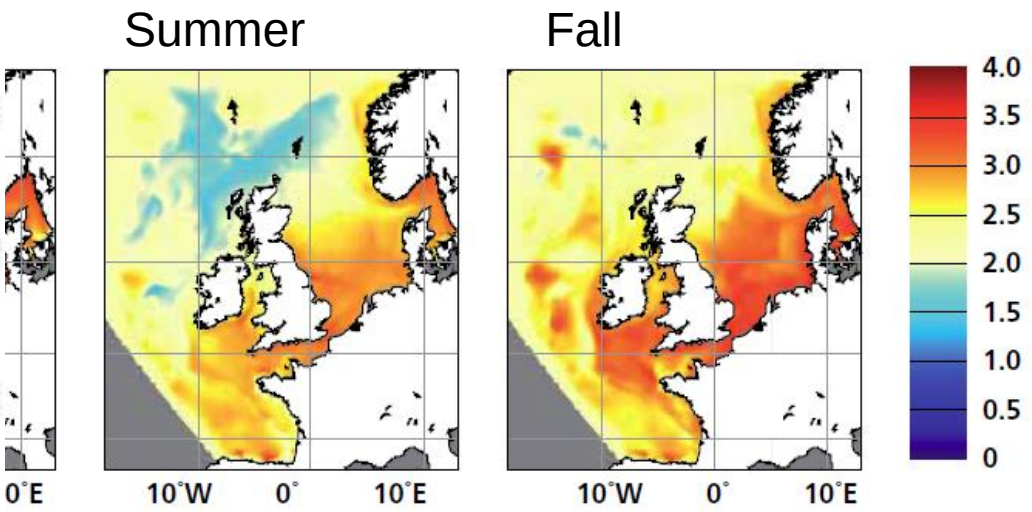


Map: Sundby et. al 2000

- Batch spawner
- Spawning pelagic eggs

Simulated increase in sea surface temperature

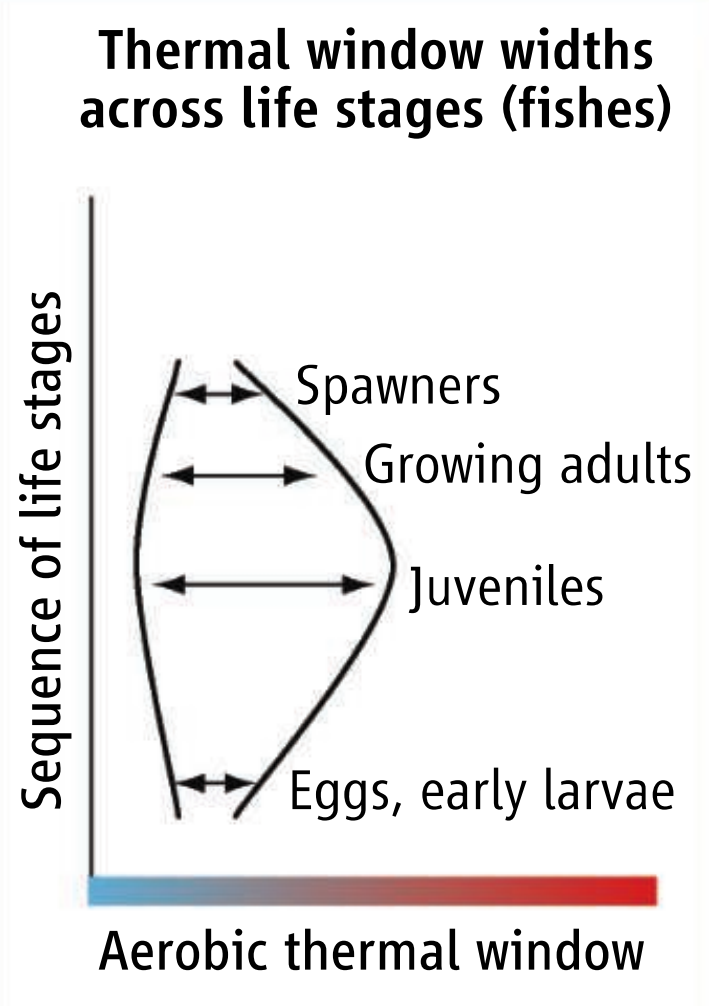




Indicates that the North sea and Norwegian coast is projected to become up to 4 °C warmer over the next century

UK Climate Projections Briefing report — UKCIP09 Jenkins et al. 2010

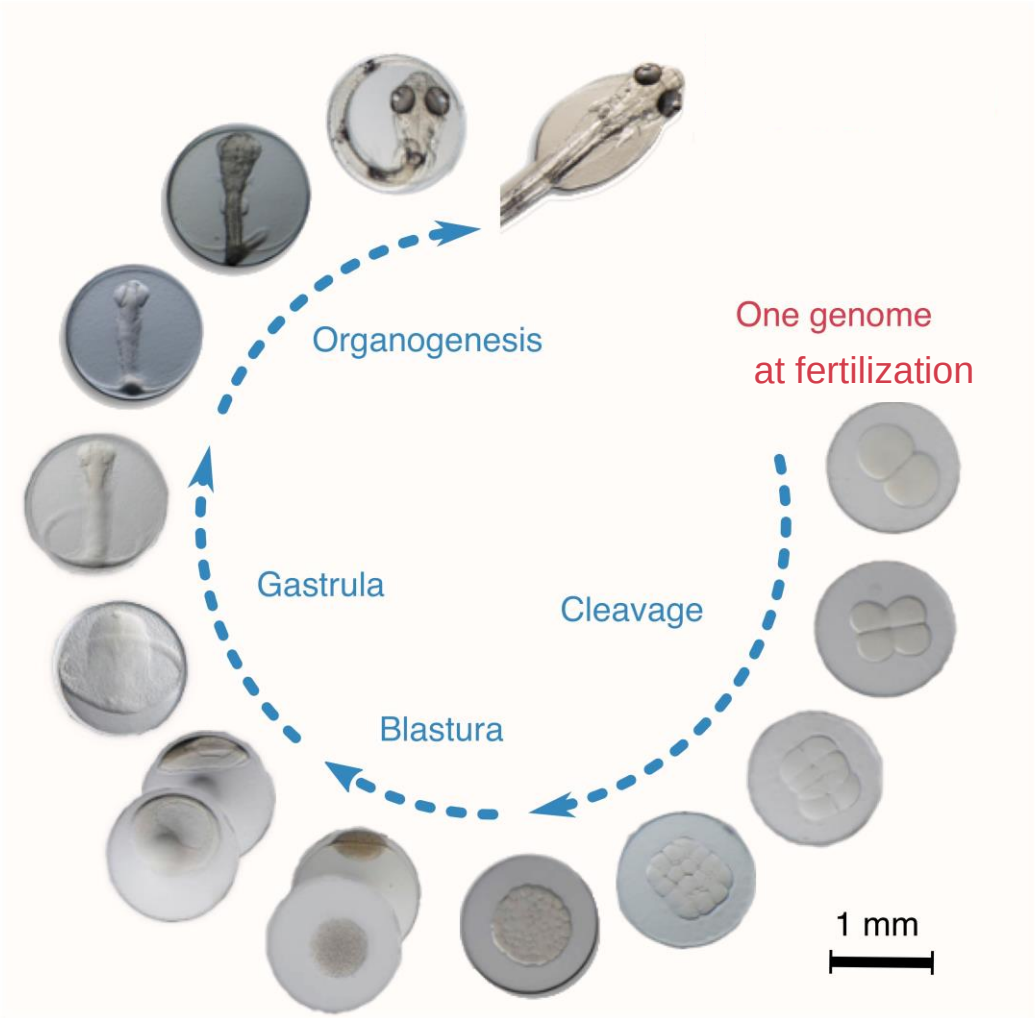
Embryonic egg stage is the thermal bottleneck

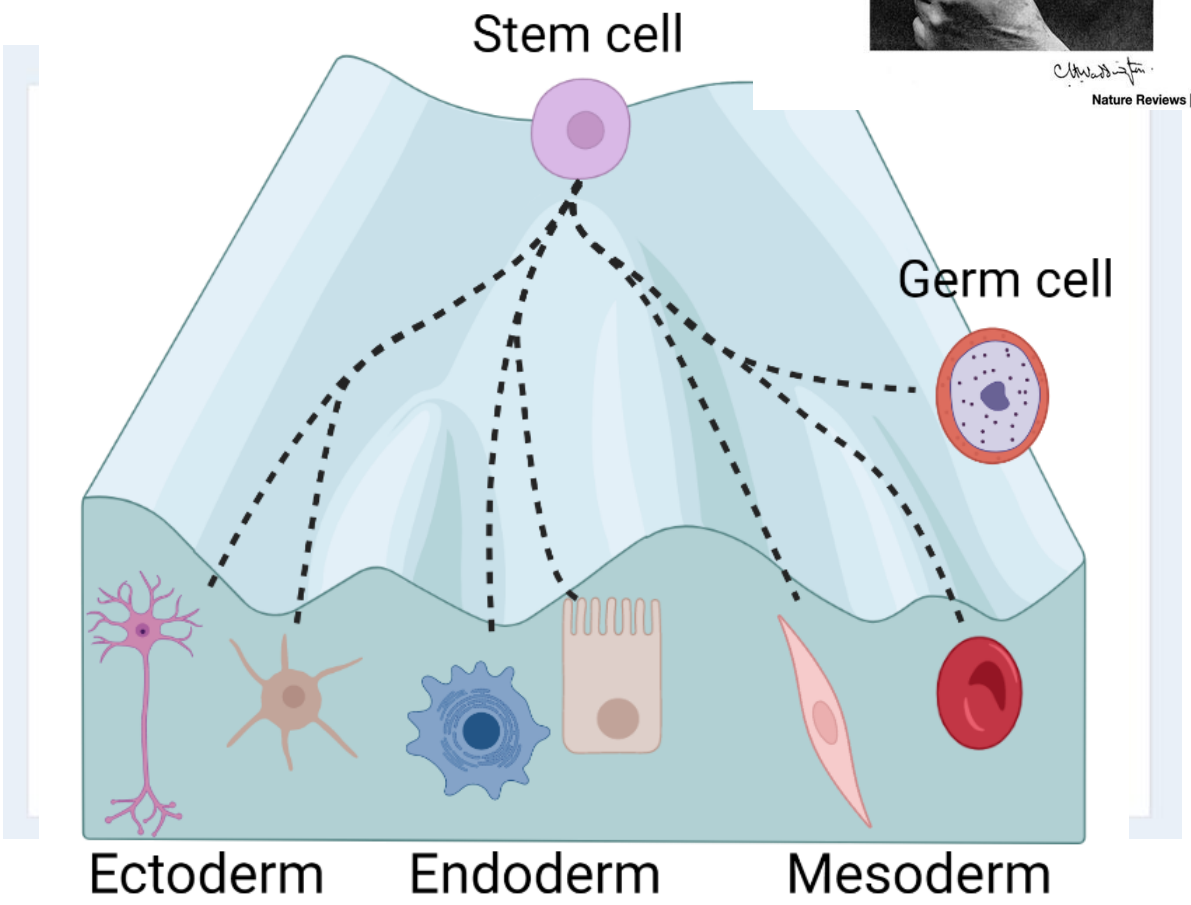


Pörtner & Farrell, 2008. Science

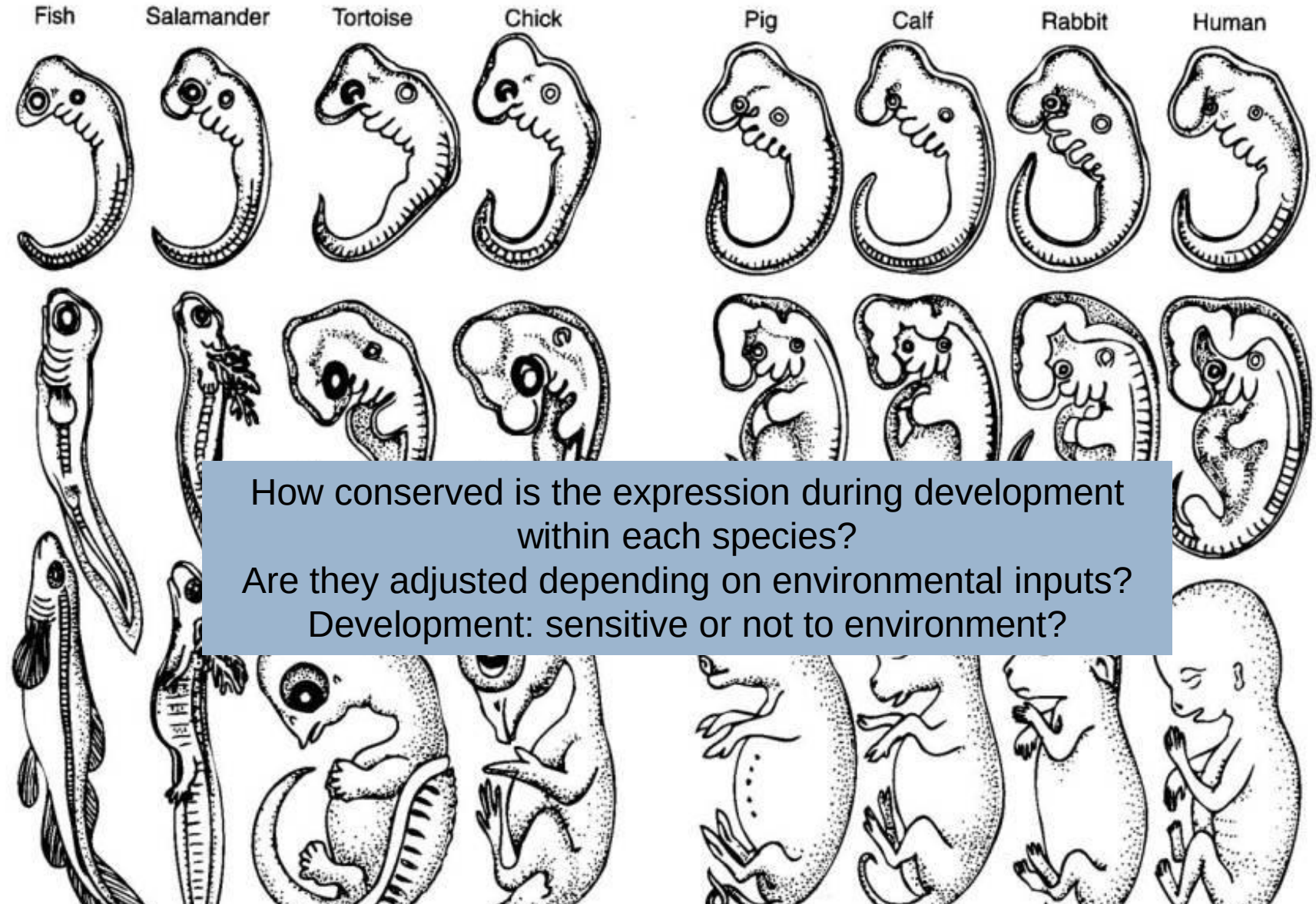
Embryology

Nature Reviews | Genetics



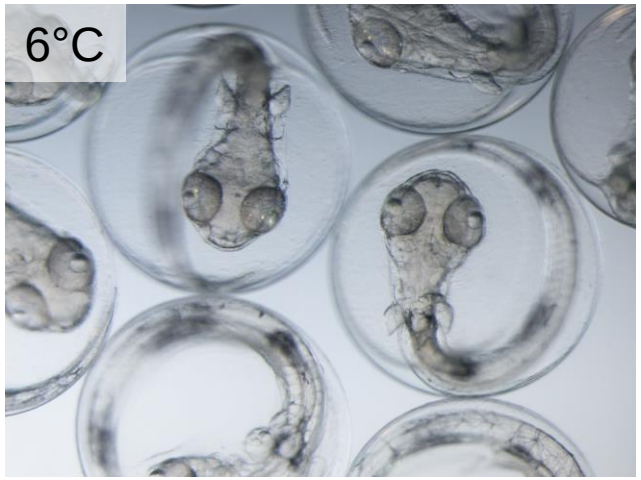


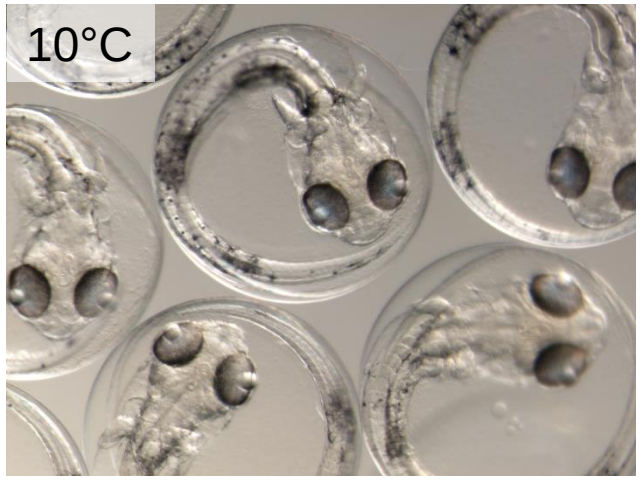
Similarities among vertebrate embryos



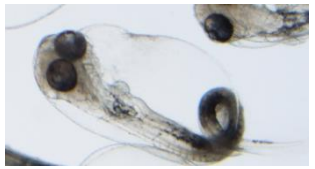
How conserved is the expression during development within each species?
Are they adjusted depending on environmental inputs?
Development: sensitive or not to environment?

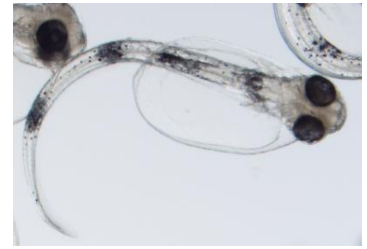
Heckels 1874





→ 10°C incubation:
Higher mortality
Sensitive eggs
Deformities





Nutrition and Epigenetics Broodstock and Offspring

bioRxiv
THE PREPRINT SERVER FOR BIOLOGY

New Results

Altered spawning seasons of Atlantic salmon broodstock genetically and epigenetically influence cell cycle and lipid-mediated regulations in their offspring

Takaya Saito, Marit Espe, Maren Mommens, Christoph Bock, Jorge M.O. Fernandes, Kaja H. Skjaerven

doi: https://doi.org/10.1101/2024.02.03.578741

The Research Council of Norway

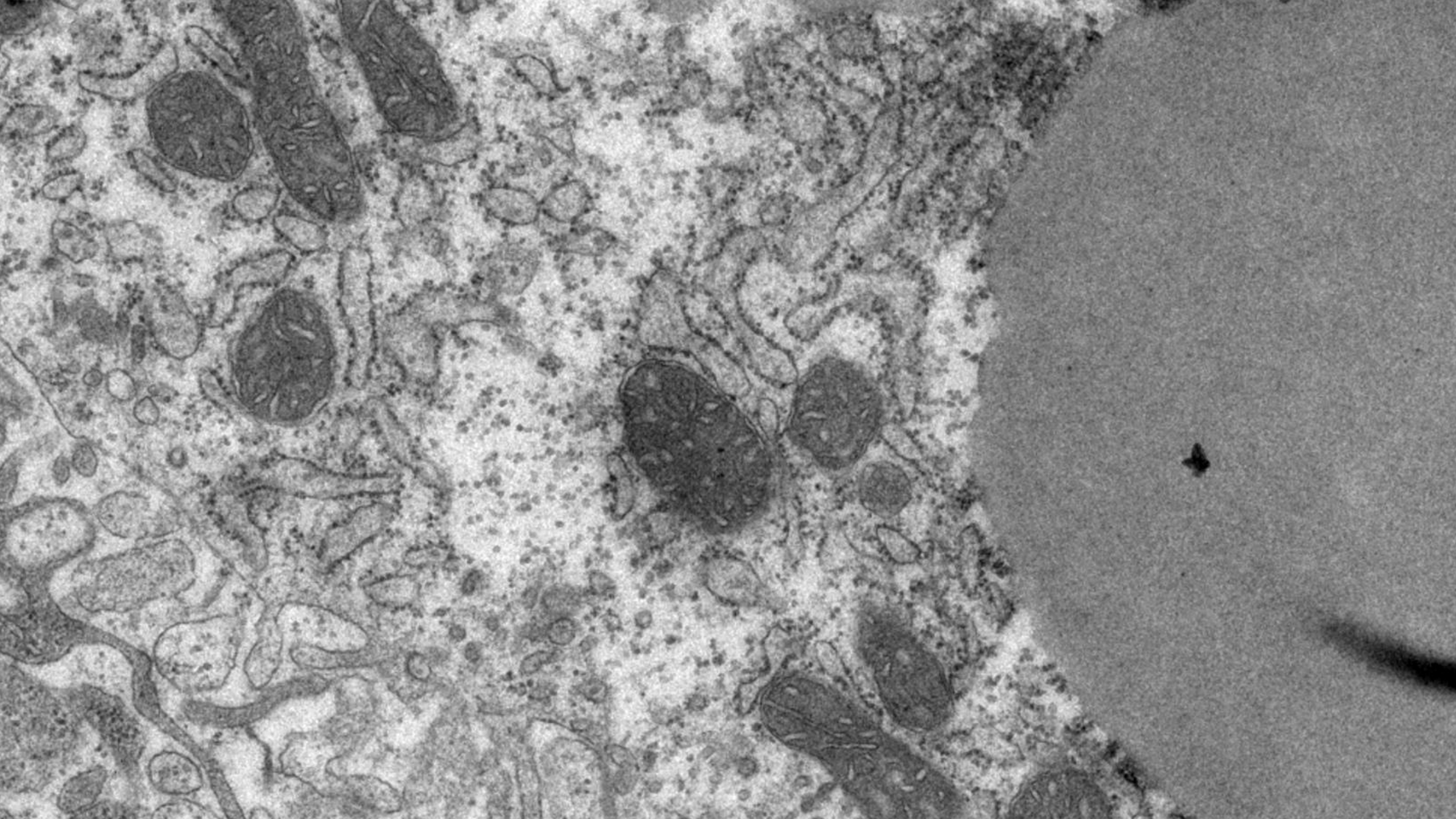
NORD University

metanomics health

BIOCRATES LIFE SCIENCES The Deep Phenotyping Company

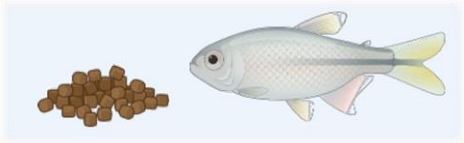
AquaGen

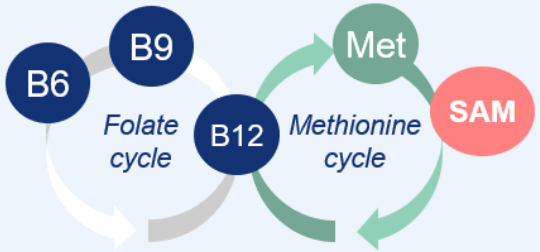
Ce–M–M– Research Center for Molecular Medicine of the Austrian Academy of Sciences



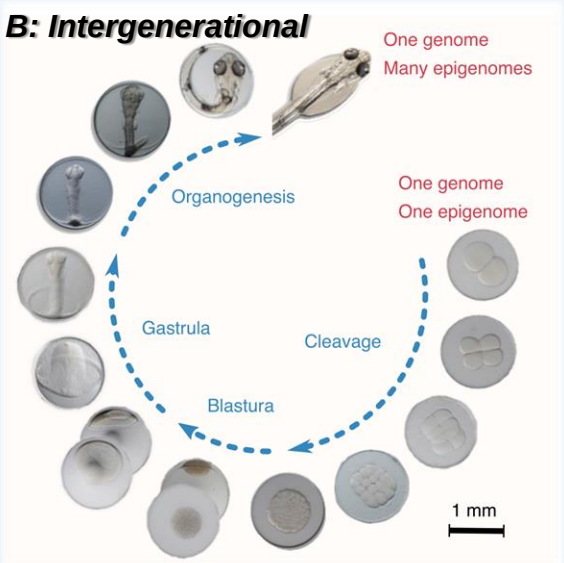
Nutrients

A: Intragenerational

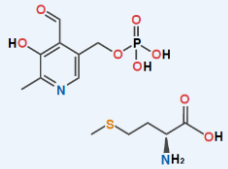




B: Intergenerational



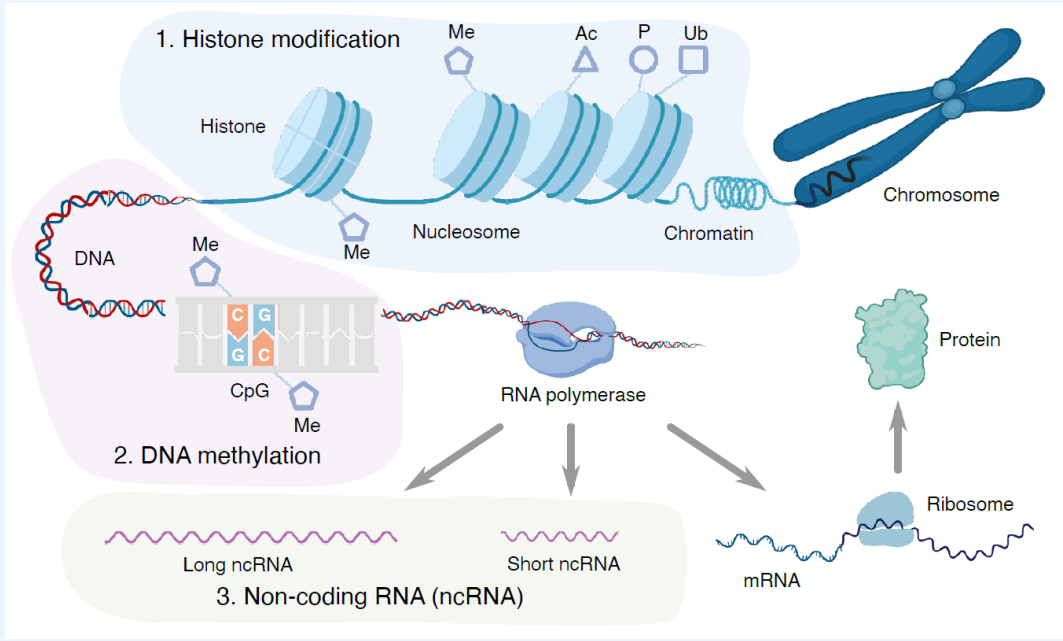
Metabolites

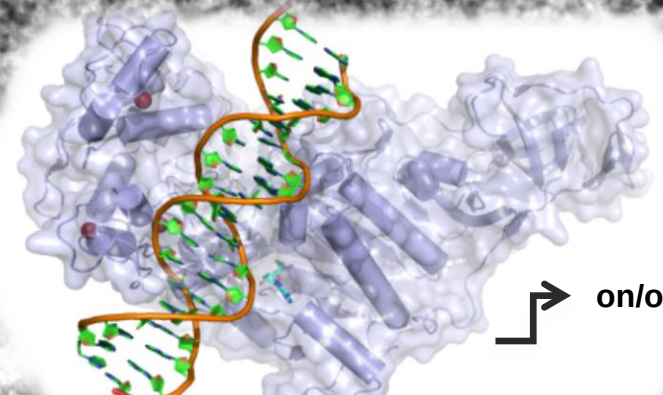


SAM

Acetyl CoA

Epigenetic mechanisms





on/off?

Background

Denne ruggen av en stamfisk er med på å føre de beste genene videre, så den passes godt på av de ansatte i Aqua Gen.

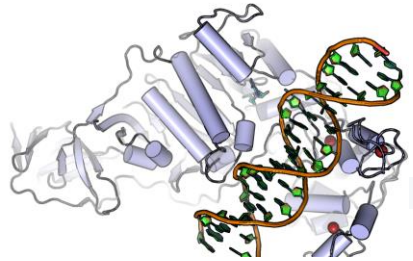
- Broodstock females are manipulated to spawn both earlier and later than the normal spawning season

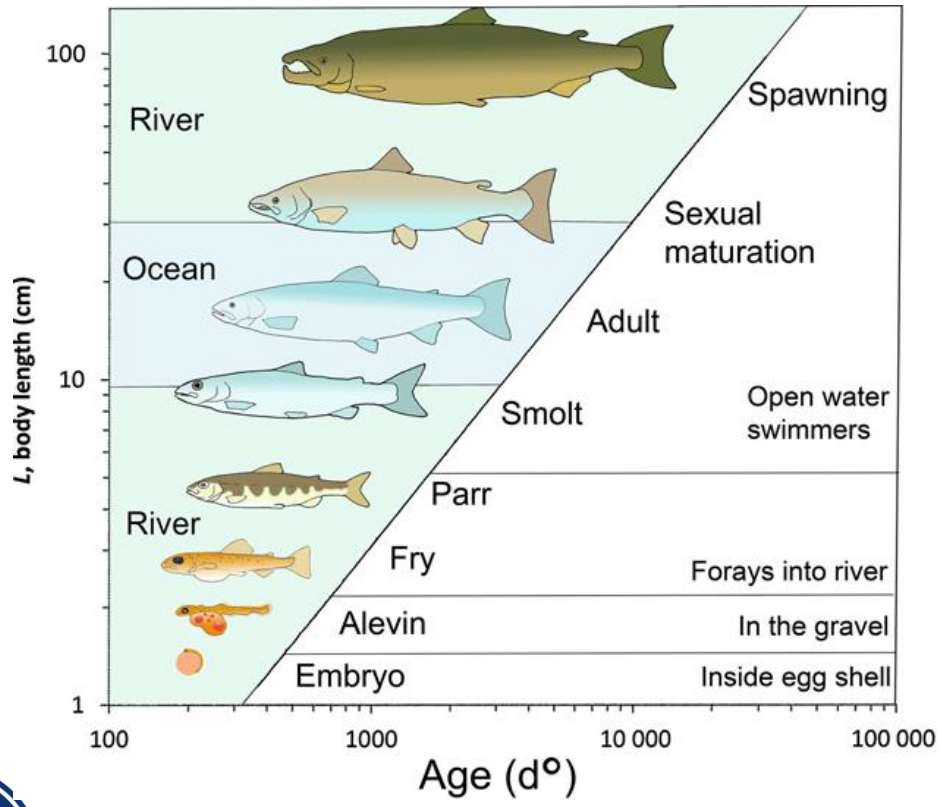
  Why: to produce offspring throughout the year-

  How: can be controlled by regulation of feeding, light and temperature regimes

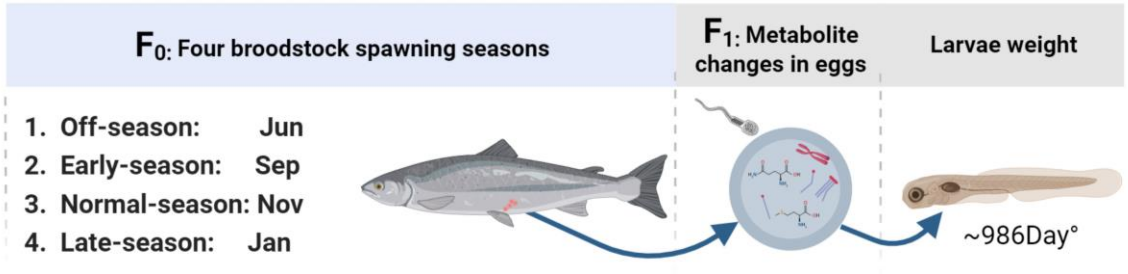
- Aim: to investigate if the spawning season differs in nutritional status, RNA seq and meDNA
- Help from Aqua Gen AS: Kyrksæterøra
- # broodfish <<< # offspring

Light and temperature to adjust time for spawning



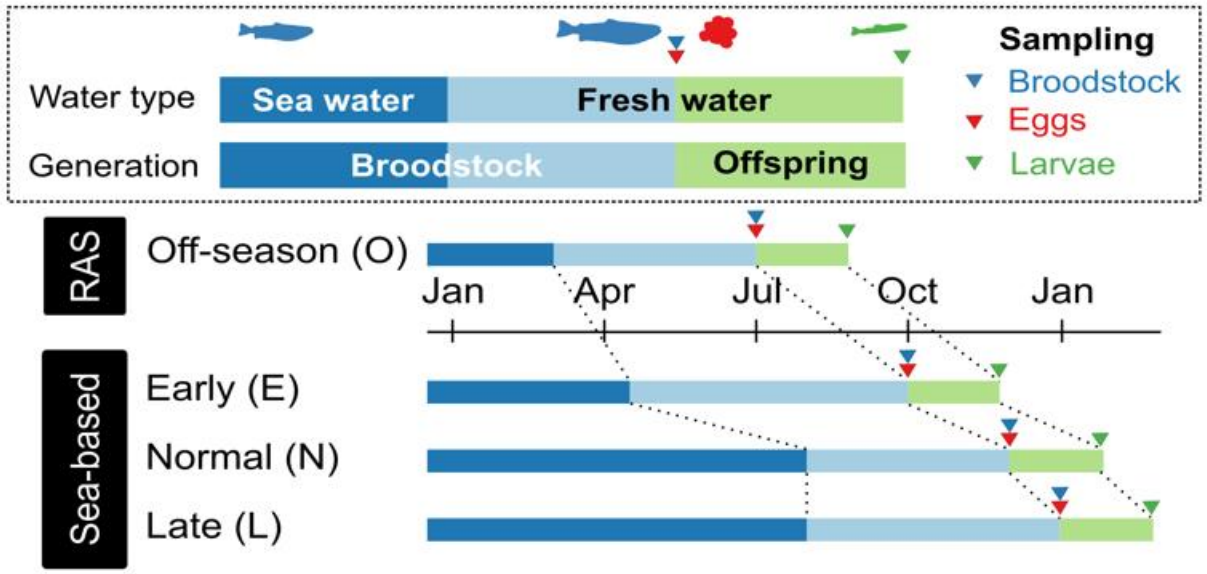


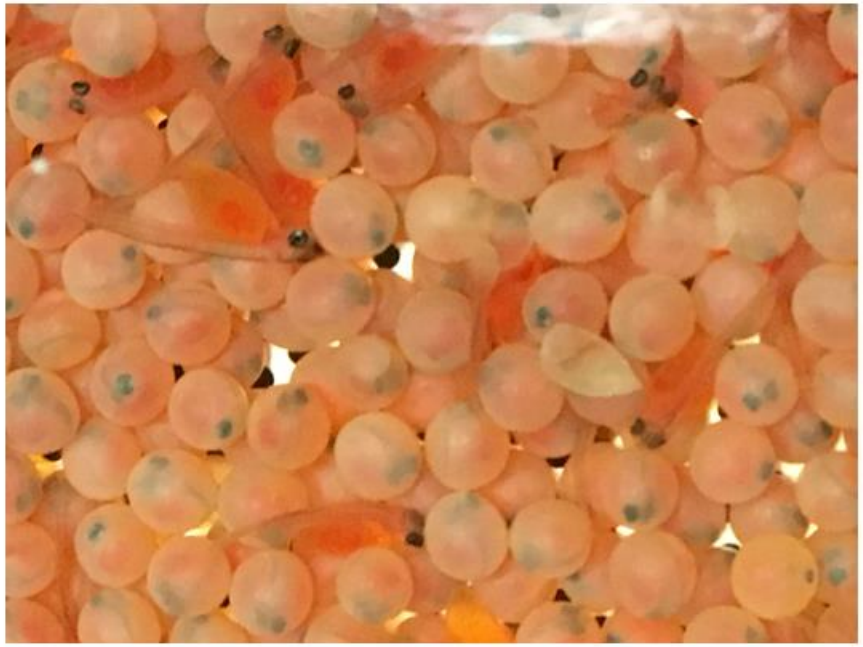
Kryvi et al,. 2017 Journal of anatomy DOI: 10.1111/joa.12679



Season	Spawning	Starvation
Off-season	June	109
Early	Sept	163
Normal	Nov	120
Late	Jan	166

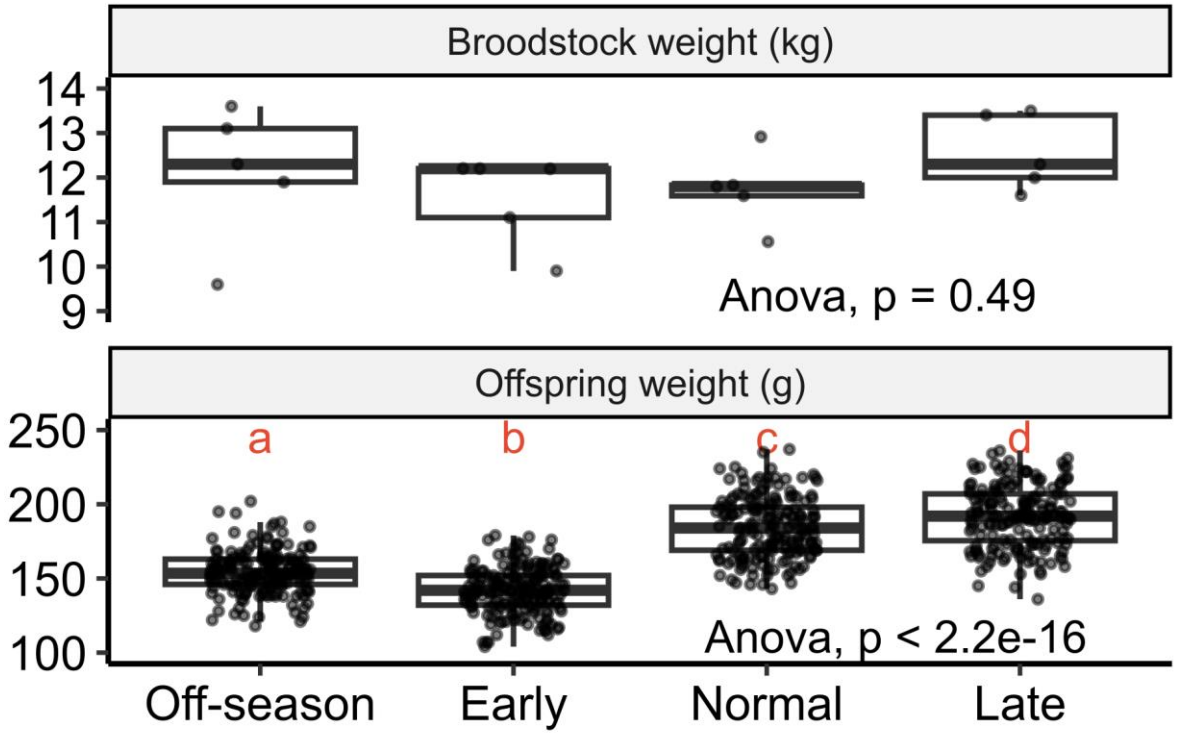
Compared four spawning seasons:





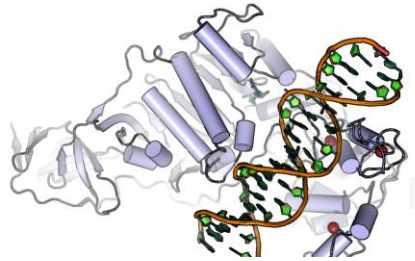
- Off: June (RAS)
- Early: Sept
- Normal: Nov
- Late: Jan

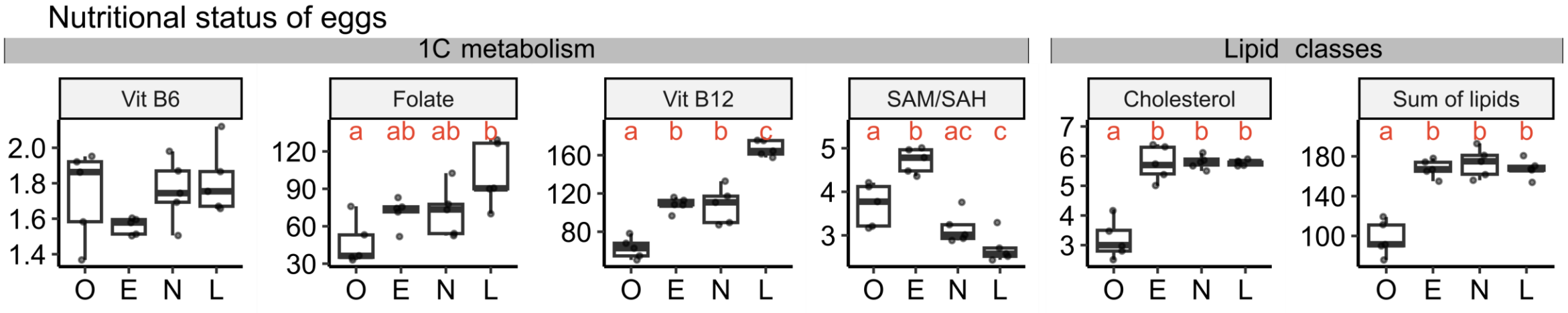
Growth performance



Egg/liter	
Off-season	6155
Early	5835
Normal	5082
Late	4613

Spawning seasons: impact nutritional status of eggs





ELSEVIER

Aquaculture

Volume 554, 30 May 2022, 738187

Earlier or delayed seasonal broodstock spawning changes nutritional status and metabolic programming of growth for next-generation Atlantic salmon

Kaja H. Skjærven [a], Maren Mommens [b], Anne-Catrin Adam [a], Takaya Saito [a], Eystein Oveland [a], Marit Espe [a]

ELSEVIER

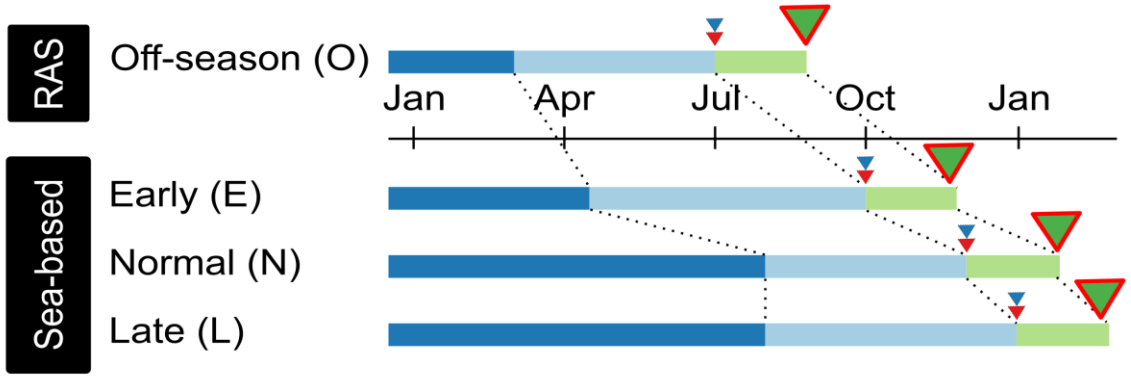
Comparative Biochemistry and Physiology Part A: Molecular & Integrative Physiology

Volume 247, September 2020, 110717

Out-of-season spawning affects the nutritional status and gene expression in both Atlantic salmon female broodstock and their offspring

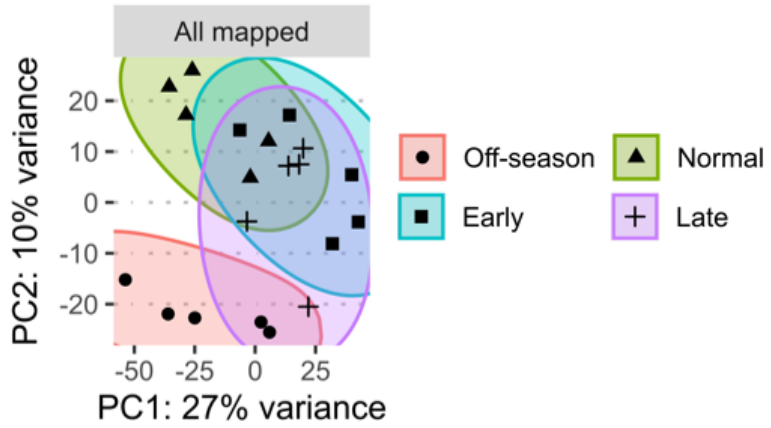
Kaja H. Skjærven [a], Eystein Oveland [a], Maren Mommens [b], Elisa Samori [a], Takaya Saito [a], Anne-Catrin Adam [a], Marit Espe [a]

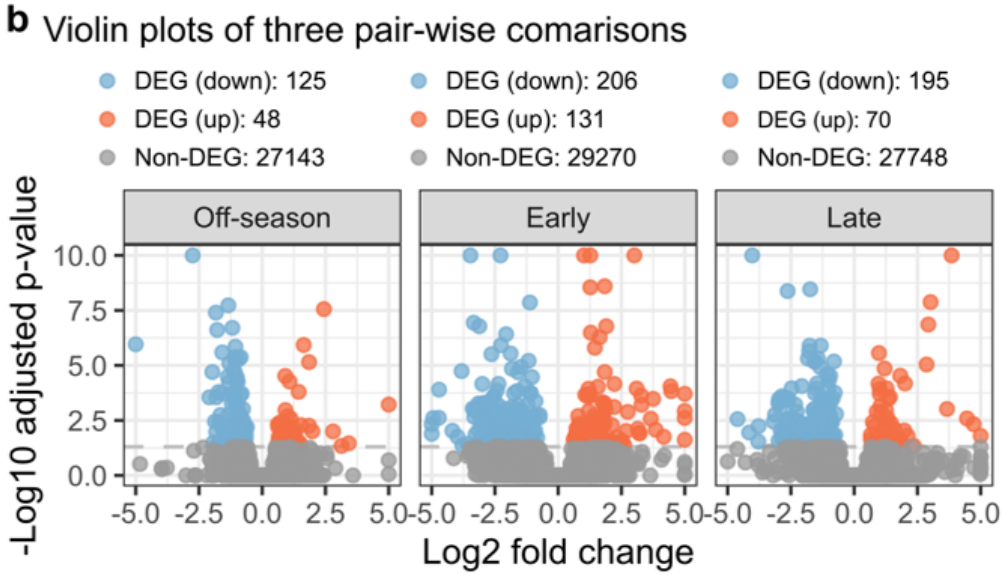
Omics analysis



- Larvae liver samples
- Gene expression with RNA-seq
- DNA methylation with bisulfite sequencing

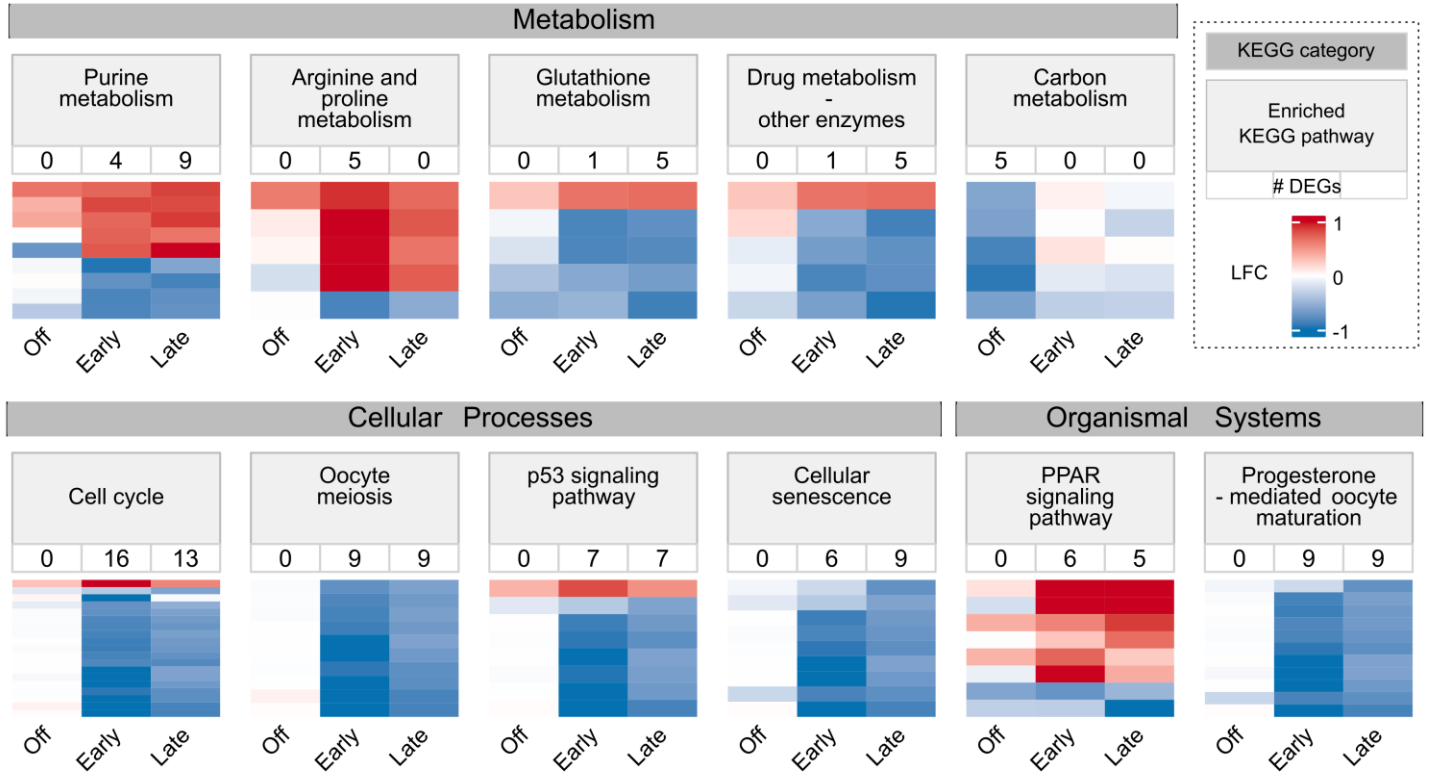
Results of gene expression analysis





- Off-season is different: Broodstock from RAS
- Similarity between early and late seasons
- More downregulation of mRNA expression compared to normal season
- Off: 173 Early: 337 Late: 265 DEGs

11 biological pathways changed in offspring liver



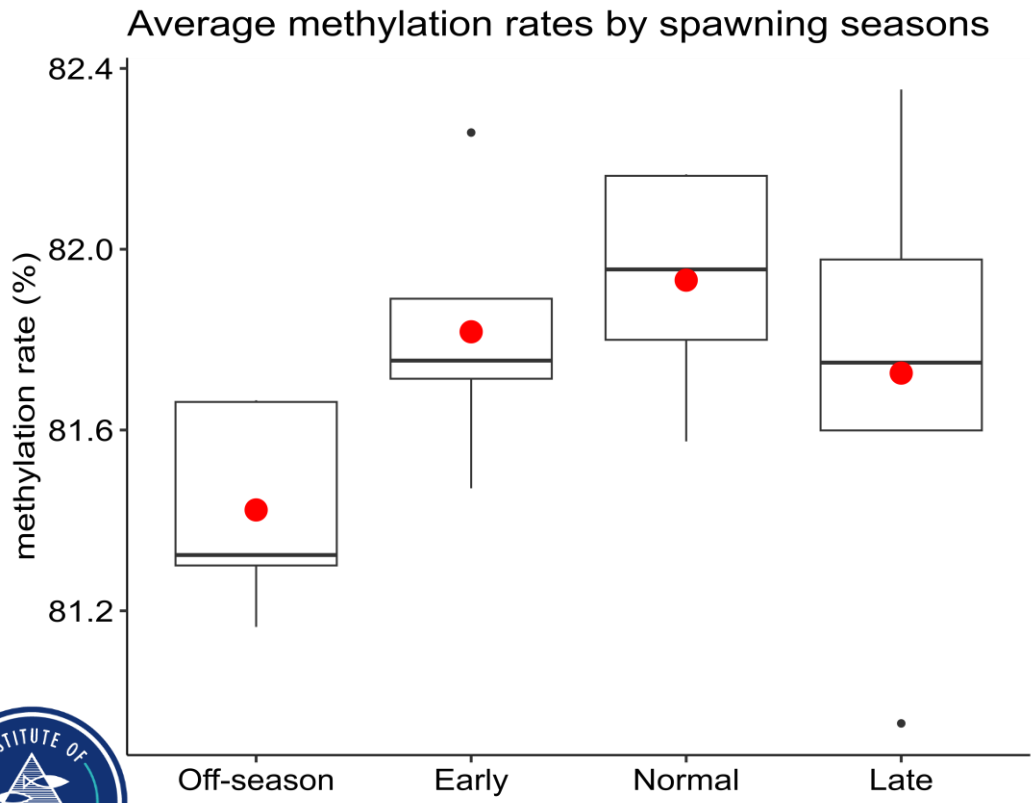
Off: the carbon metabolism.
All five DEGs associated with carbon metabolism showed down-regulation

Early and late:

- consistent expression patterns in terms of up- and down-regulation
- cellular processes: strong down-regulation

These findings may be linked to variations in the nutritional status of the eggs.

DNA methylation analysis

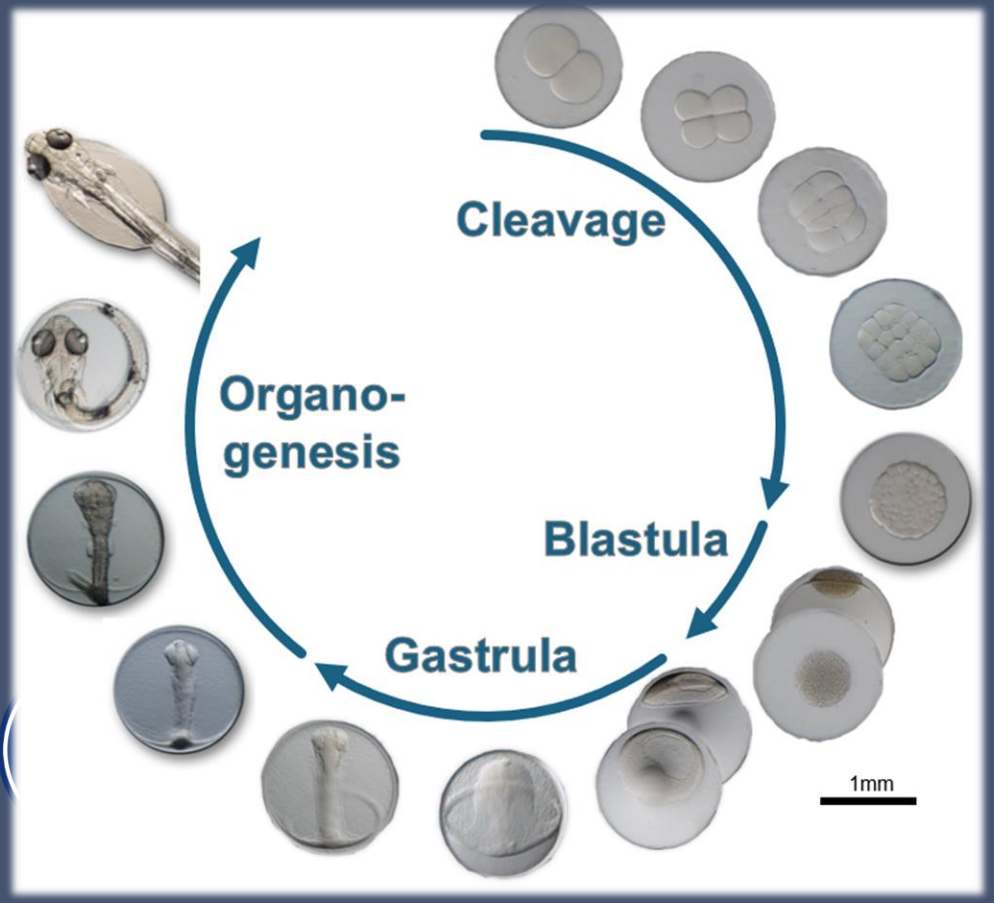


Correlation DMC with DEGs: Cell cycle genes are regulated

Gene ID	Symbol	DMC[1]			DEG[2]			Gene name	Function
		Off-season	Early	Late	Off-season	Early	Late		
106562317	caprin-1	Hypo	(Hypo)	(Hypo)	Down	(Down)	(Down)	caprin-1	Cell cycle
106599887	cyp8b1	Hypo	-	-	Down	-	-	5-beta-cholestane-3-alpha,7-alpha-diol 12-alpha-hydroxylase	Metabolism, cytochrome P450
106588407	kifc1	-	Hypo	Hypo	-	Down	Down	carboxy-terminal kinesin 2	Cell cycle, Meiosis
106582038	adrenodoxin	-	Hypo		-	Down	-	adrenodoxin	Metabolism, cytochrome P450
106604665	slc43a1a	-	Hypo	-	-	Up	(Up)	solute carrier family 43 member 1a	Transporter
106561604	aurkb	(Hyper)	Hyper	Hyper	-	Down	Down	aurora kinase B	Cell cycle
106570052	lpin1	-	Hyper	-	-	Up	-	phosphatidate phosphatase LPIN1	Metabolism

Correlating methylation differences with corresponding LFCs, we found 11 DMCs:
4 DMCs in P250, 7 DMCs in P1K associated with DEGs.
caprin-1 and *kifc1:* hypo-methylated CpG sites, *aurkb:* hyper-methylated CpG sites; all three: Downreg.
CpG methylation differences greater than 30% lacked clear association with DEGs in the liver

Climate change and adaptation via maternal mRNA? Broodstock and Offspring



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Received: 14 November 2023; **revised:** 15 February 2024; **accepted:** 16 February 2024
Original Article

Ocean warming shapes embryonic developmental prospects of the next generation in Atlantic cod

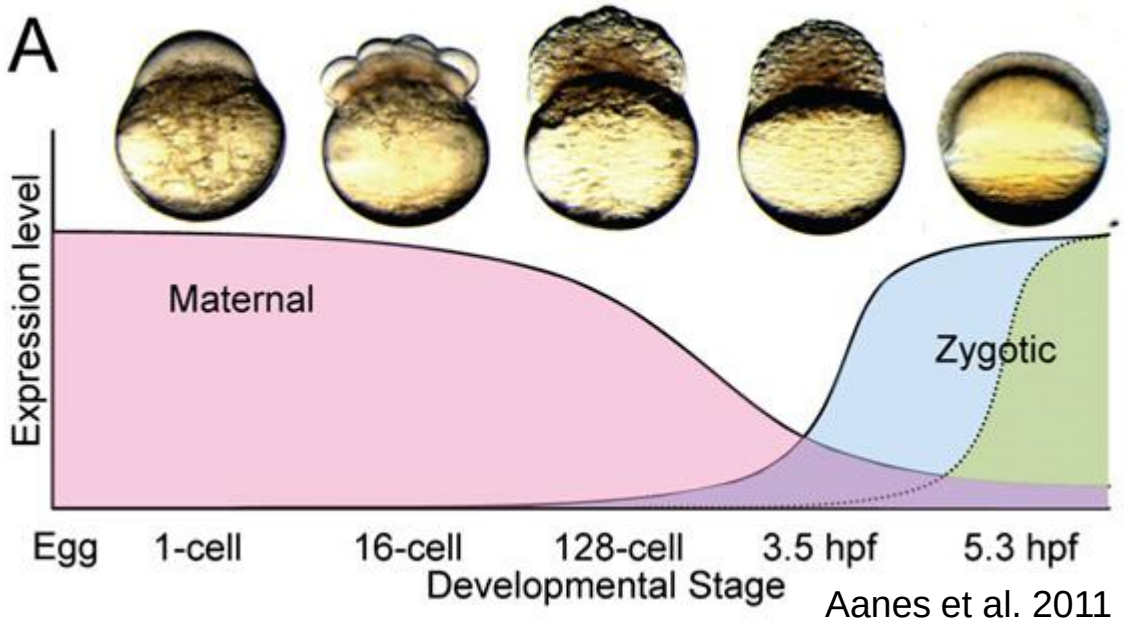
Kaja H. Skjærven [1,†], Maud Alix [2,†], Lene Kleppe [1,†], Jorge M.O. Fernandes [3], Paul Whatmore [1], Artem Nedoluzhko [3], Eva Andersson [1], Olav Sigurd Kjesbu [1,*]

[1]Institute of Marine Research, P.O. Box 1870 Nordnes, 5817 Bergen, Norway
[2]Institute of Marine Research, Austevoll Research Station, 5392 Storebø, Norway
[3]Faculty of Biosciences and Aquaculture, Nord University, 8049 Bodø, Norway

Research questions:

- Changes in broodstock incubation temperature: change the maternal mRNA in the newly fertilized eggs?
- Can the differences be detected in the ovarian tissue several months before spawning?

Mid-Blastula Transition

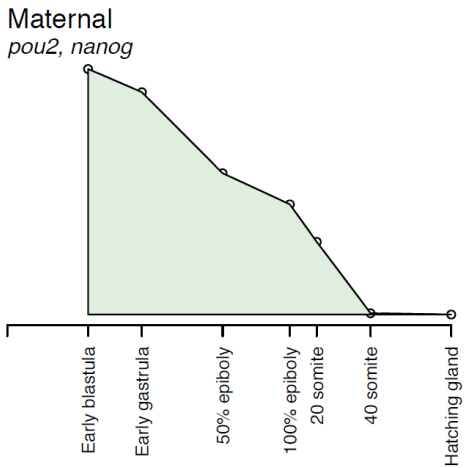


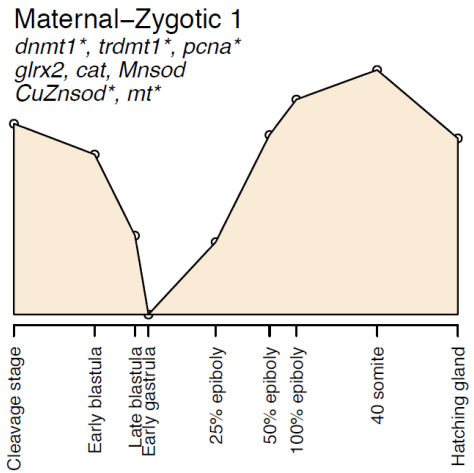
Aanes et al. 2011

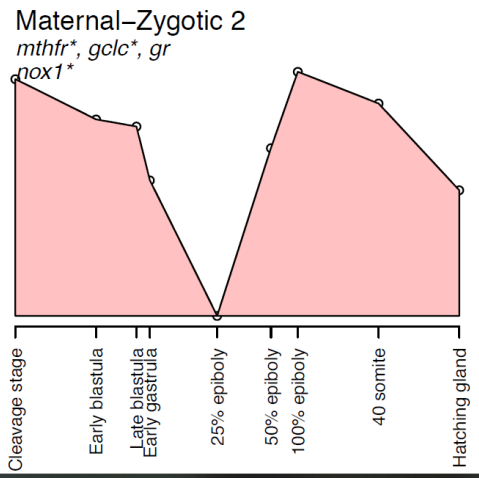
- Early embryonic development is controlled by maternal mRNA
- Zygotic transcription is initiated

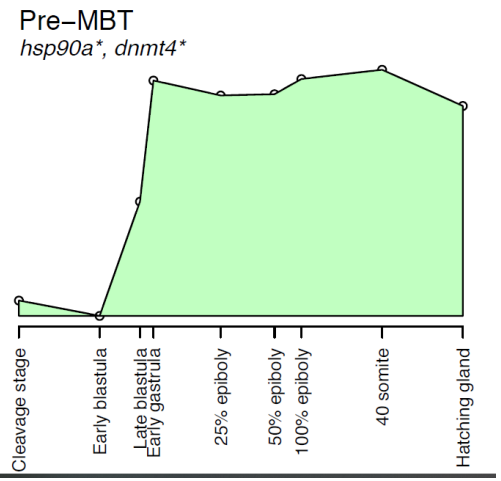
Maternal-to-zygotic transition

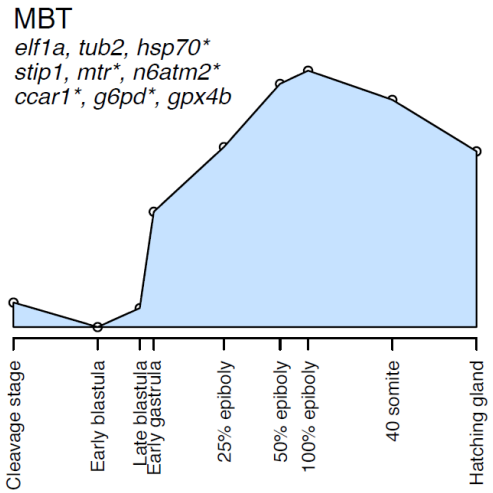
Maternal-to zygotic transition in cod embryos

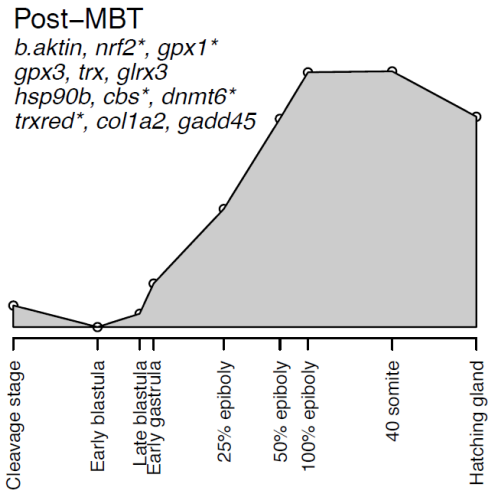






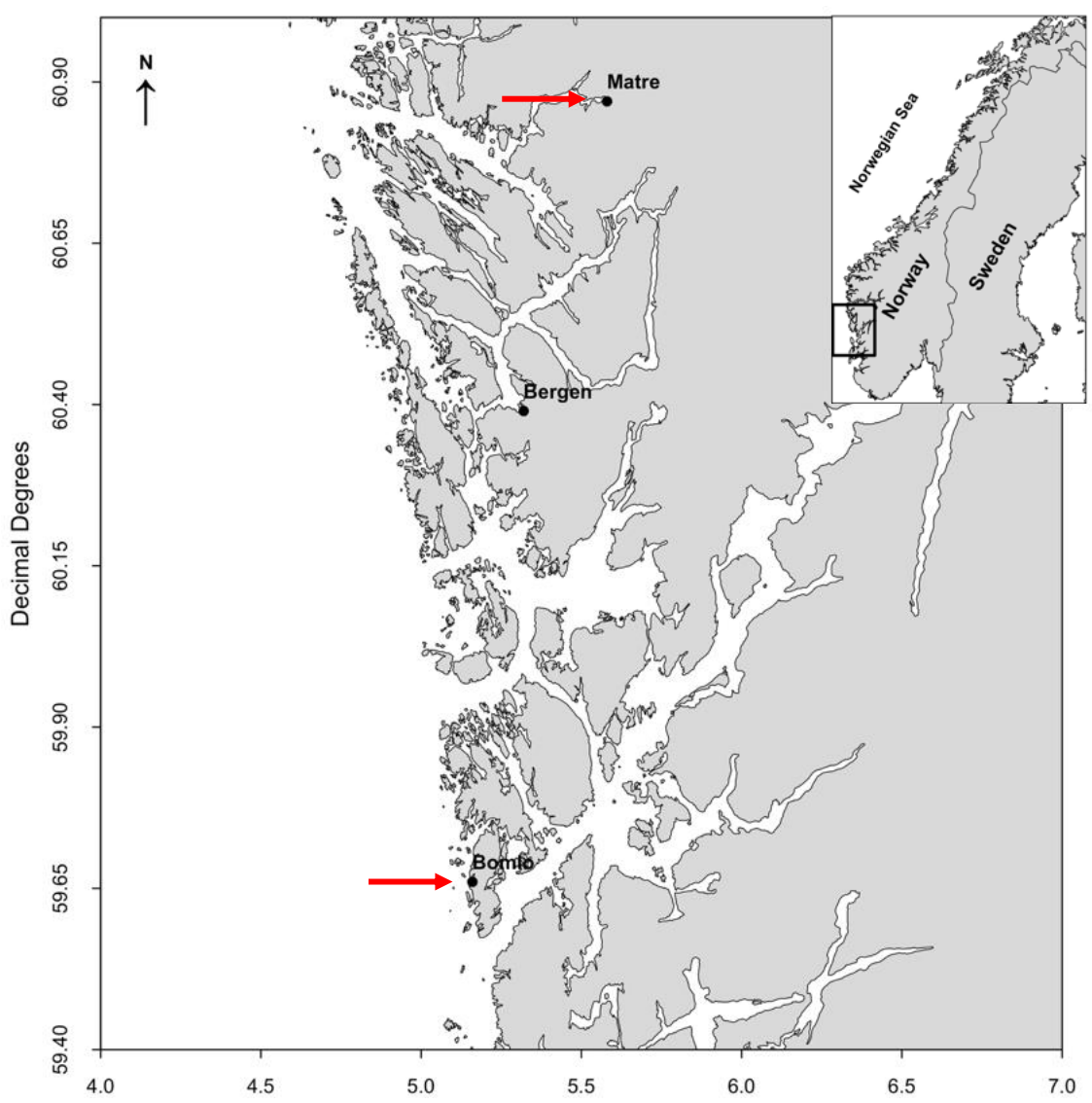






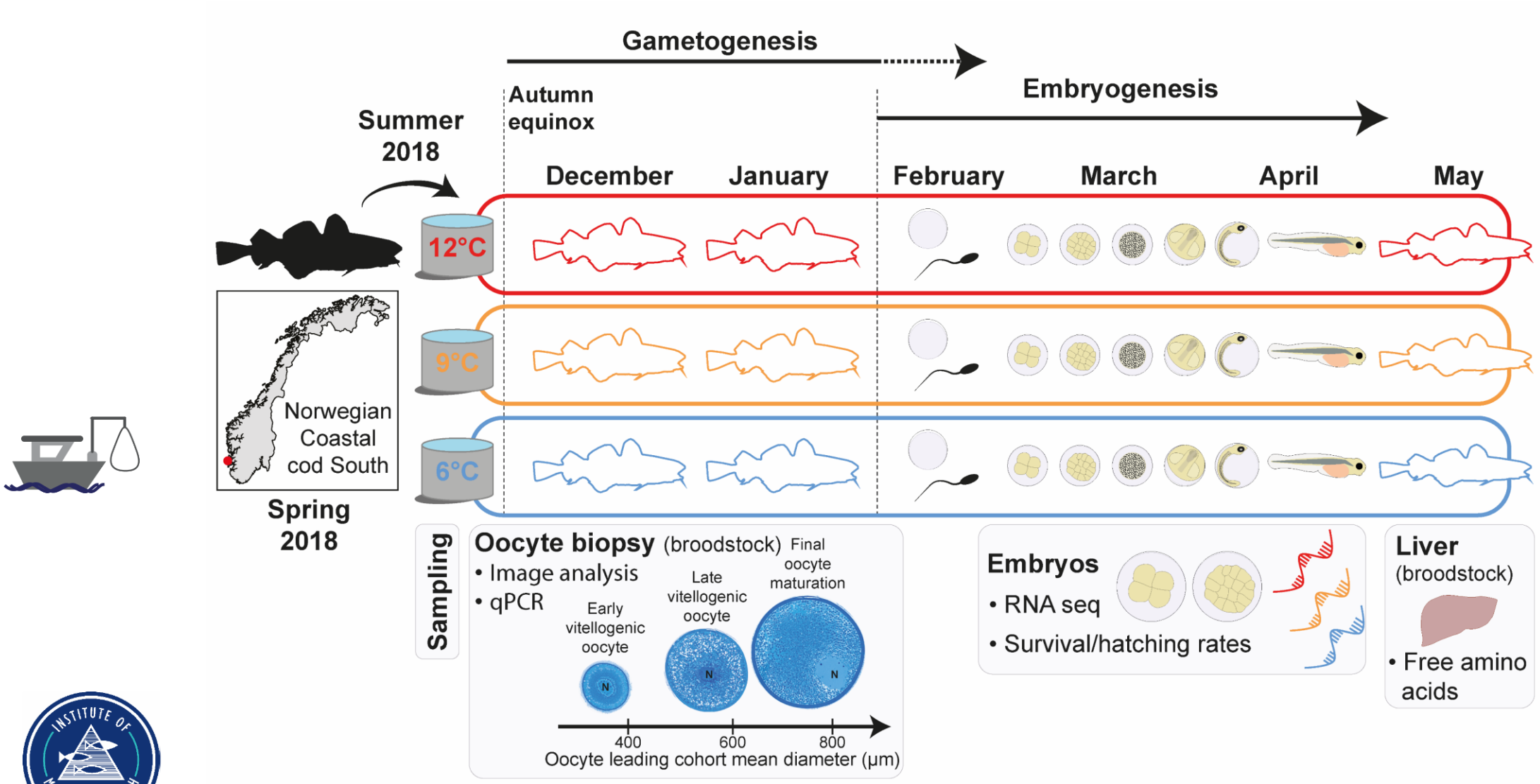
Redrawn from Skjaerven et al., 2010, 2011, 2014

Fish collection



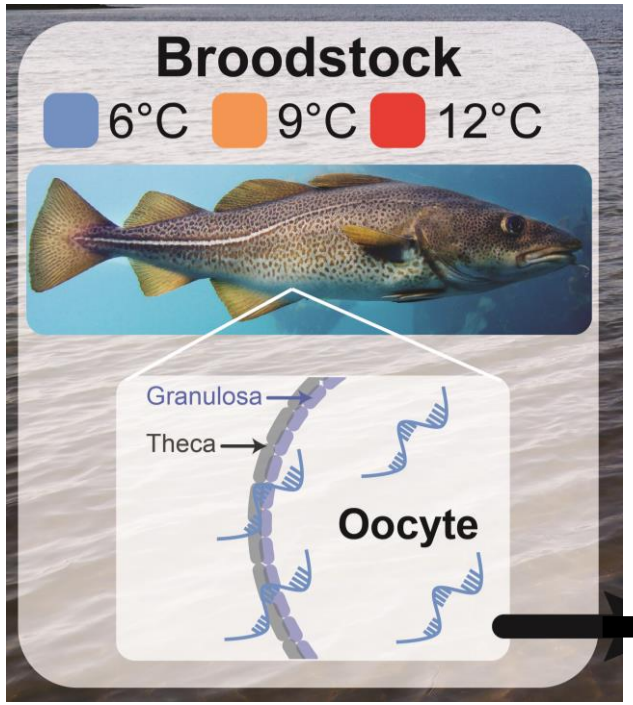
- Local cod (Bømlo)
- 200 individuals

Experimental design

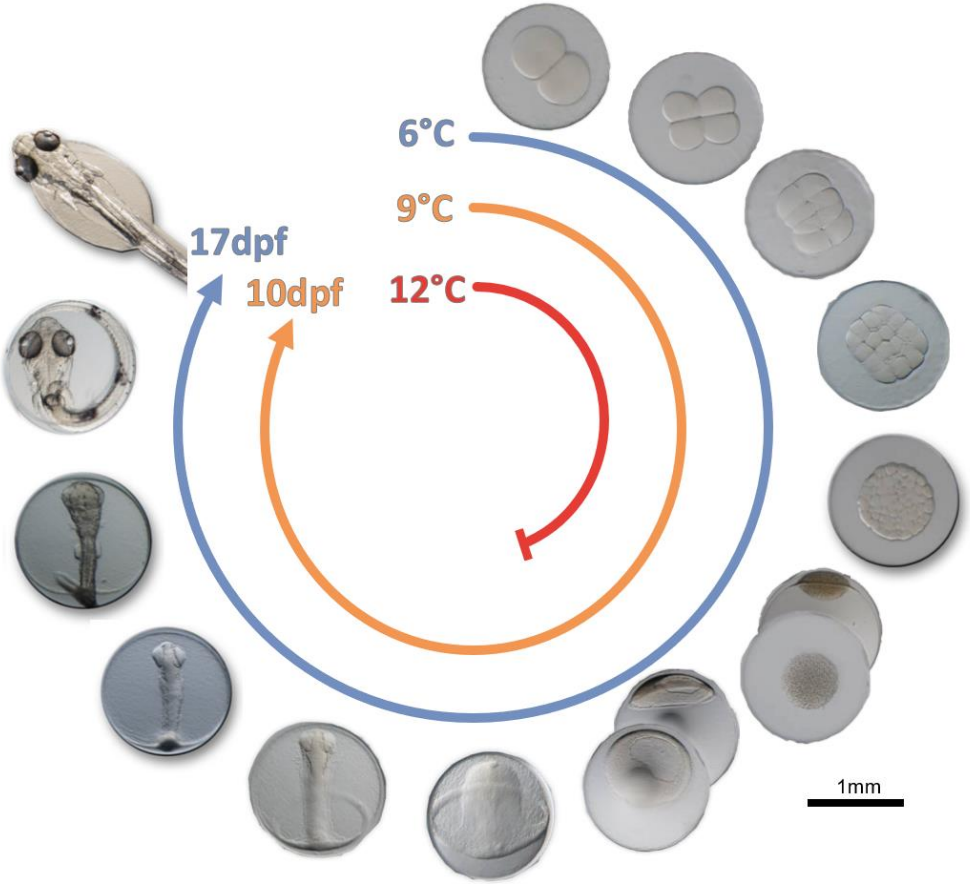


Broodstock temperature

Early embryoninc protein production relies exclusively on maternal molecules like messenger mRNAs incorporated into the ovarian follicles



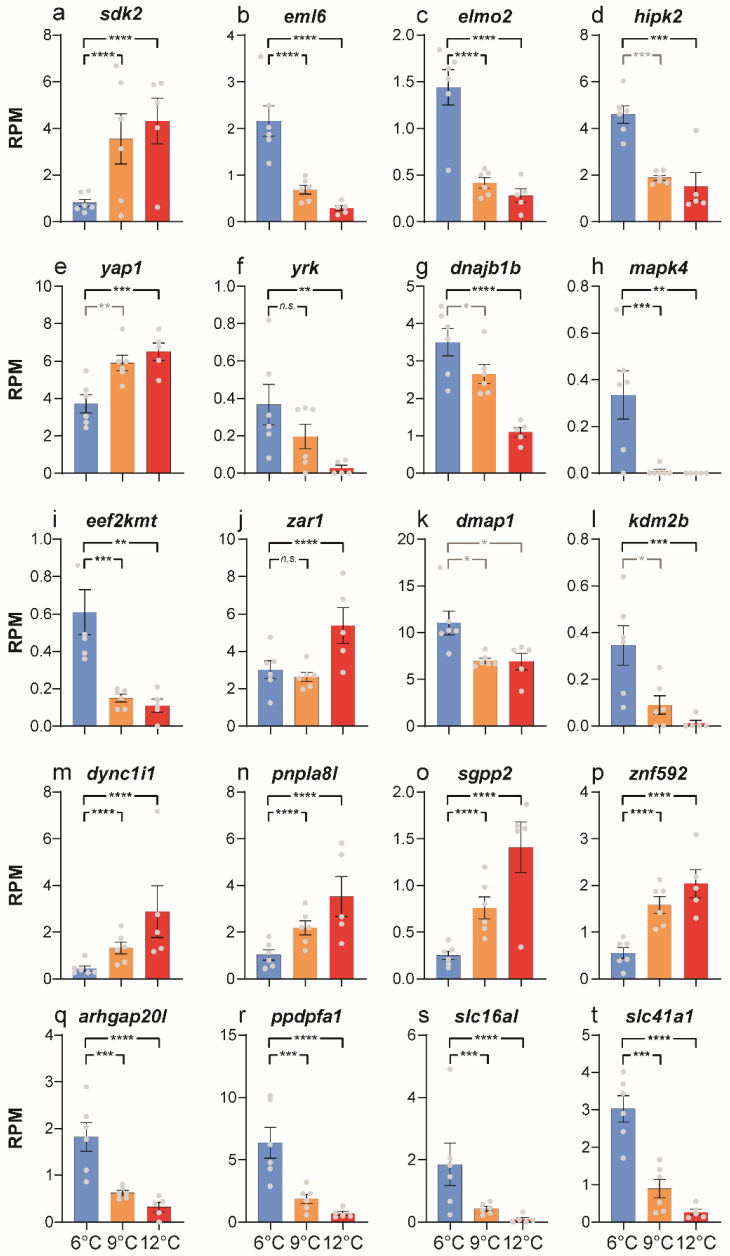
Thermally induced change in **maternal mRNAs**?



Elevated temperatures (9°C and 12°C vs. 6°C) during oogenesis
Influenced the next generation?
Targeting maternal mRNAs embryos, in view of up- and down-regulated genes in ovarian follicles of pre-spawning adults

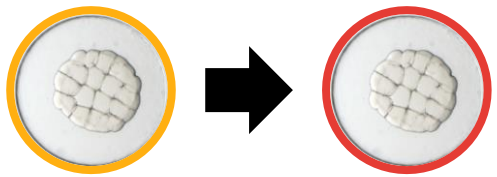
Broodstock temperature modulates maternal mRNA in offspring

- **mRNAs functions in embryonic development:**
  cytoskeleton assembly: *sdk2* , *eml6* , *elmo2*
  cell fate: *hipk2* , *yap1* , and *yrk*
  folding of proteins: *dnajb1b*
  transcriptional regulator and mitosis: *mapk4*
  protein methylation: *eef2kmt*
  translation: *zar1*
  chromatin configuration: *smarce1* and *kdm2b*

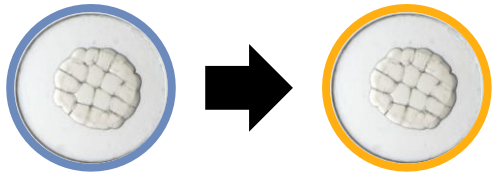


Temperature-induced maternal mRNAs adjustments in embryos

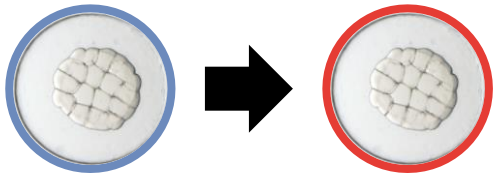
n = 6 egg batches per °C → RNA sequencing



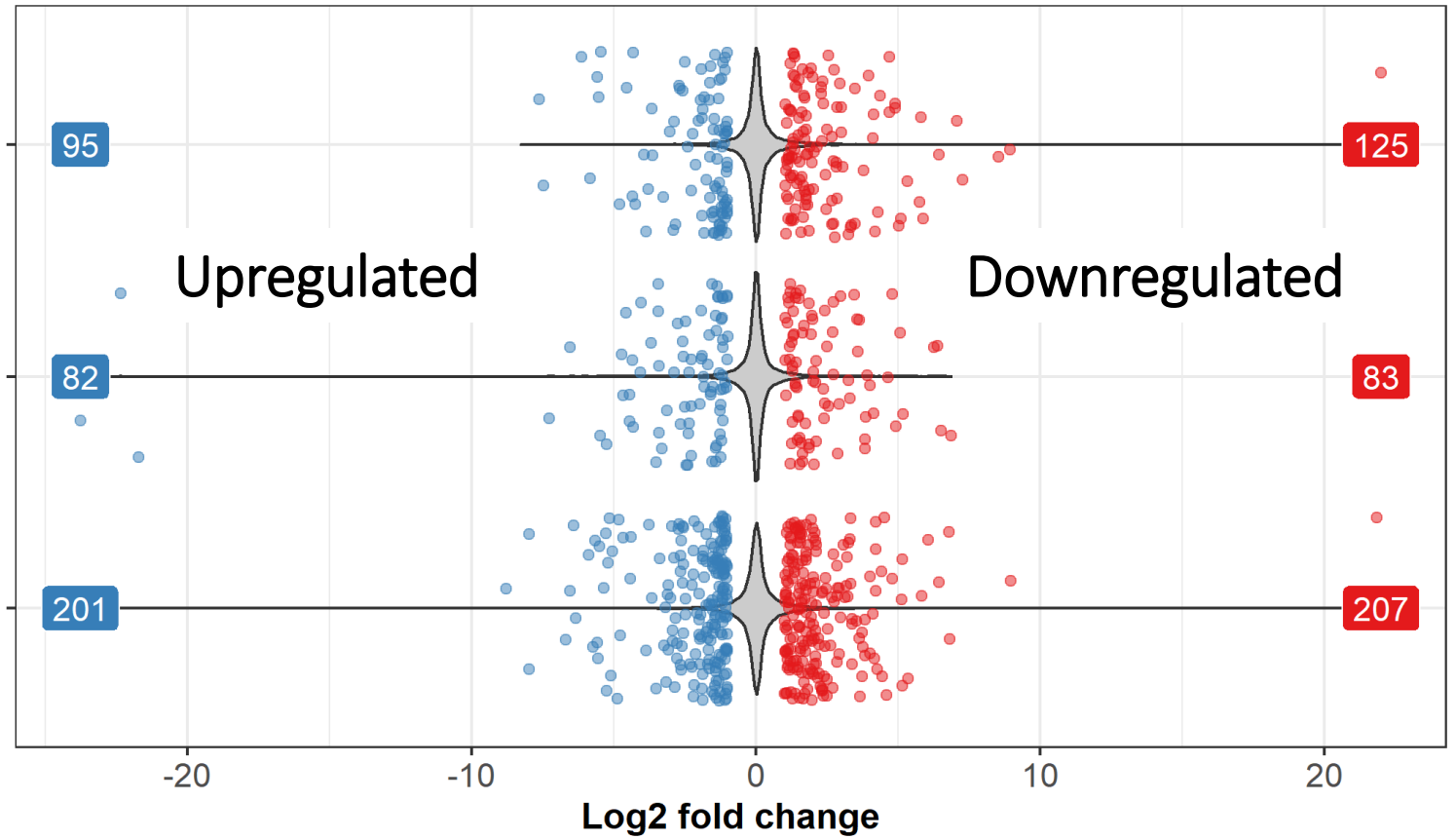
9 °C *vs* 12°C



6 °C *vs* 9°C



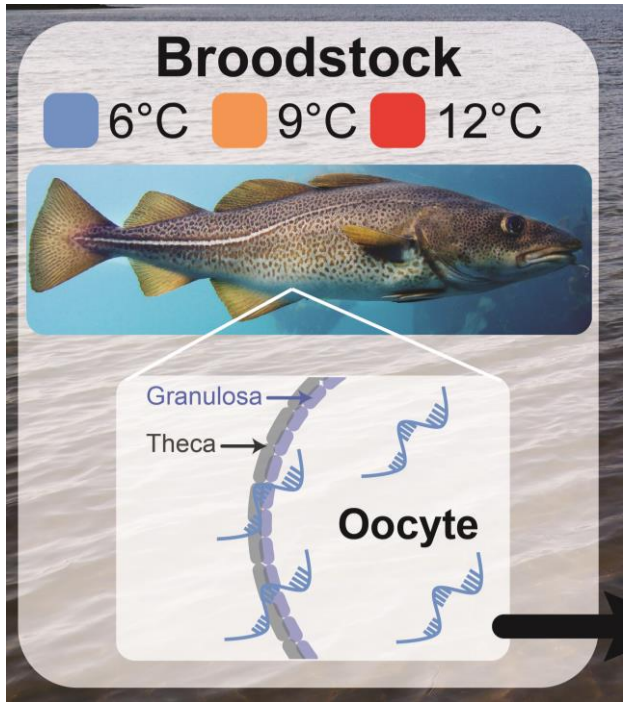
6 °C *vs* 12°C

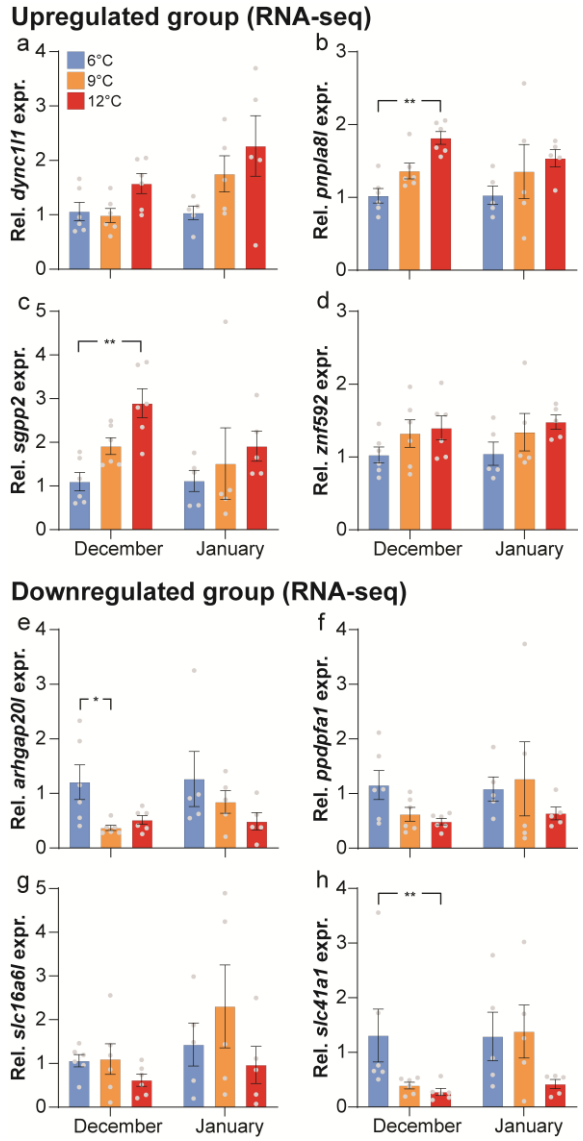


6
9
12

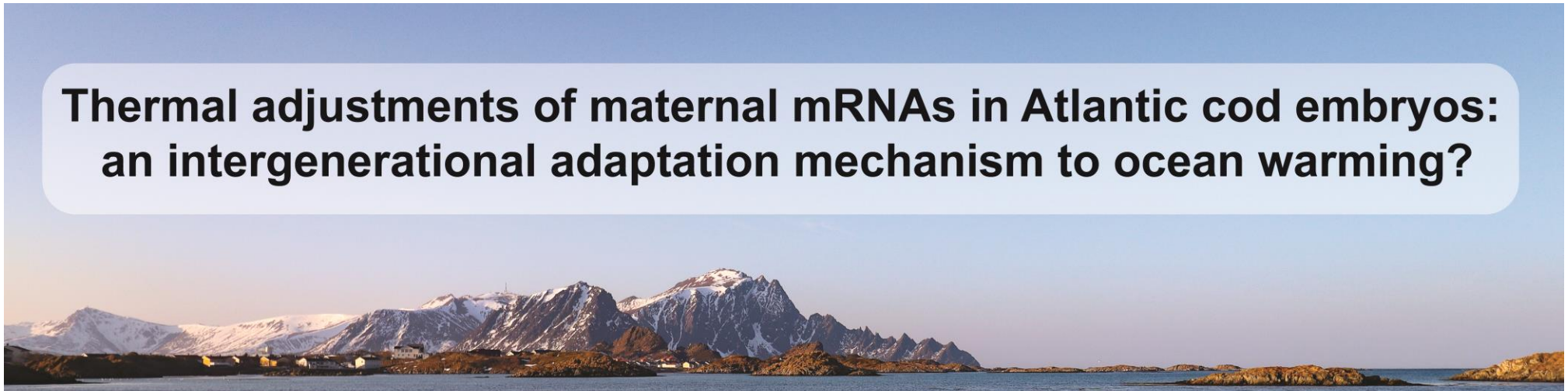
Number of Differentially expressed genes is proportional to temperature difference

Change in transcripts in oocytes for embryo development months ahead of spawning



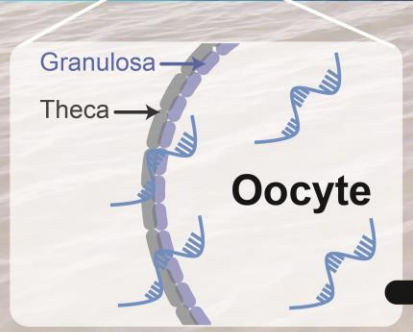


Thermal adjustments of maternal mRNAs in Atlantic cod embryos: an intergenerational adaptation mechanism to ocean warming?



Broodstock

6°C 9°C 12°C



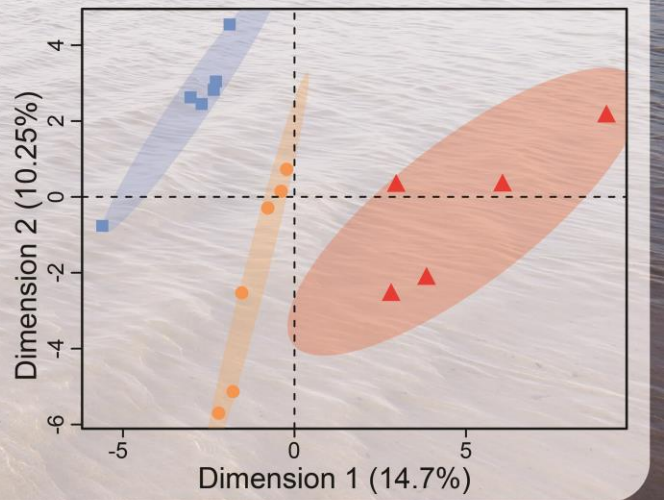
82 DEGs involved in e.g., cell fate, folding of protein, chromatin configuration

83

201 DEGs involved in e.g., cell fate, folding of protein, blood vessel formation, translation, chromatin configuration, histone tail modification

207

Maternal mRNA



Maternal temperature history

- **maternal temperature history:**
  contributes to egg quality and embryogenesis via maternal mRNAs

- **mRNAs functions in embryonic development:**
  cytoskeleton assembly: *sdk2* , *eml6* , *elmo2*
  cell fate: *hipk2* , *yap1* , and *yrk*
  folding of proteins: *dnajb1b*
  transcriptional regulator and mitosis: *mapk4*
  protein methylation: *eef2kmt*
  translation: *zar1*
  chromatin configuration: *smarce1* and *kdm2b*

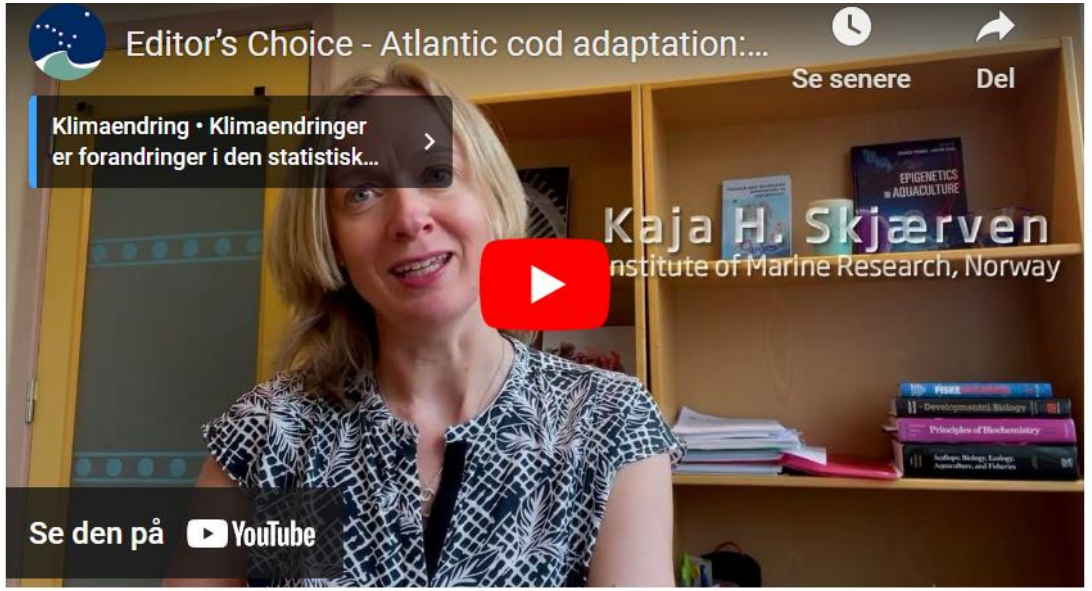
- mRNAs: may change developmental gene regulatory networks, causing a ‘domino effect’ through subsequent embryonic tissue architecture, growth, and development?

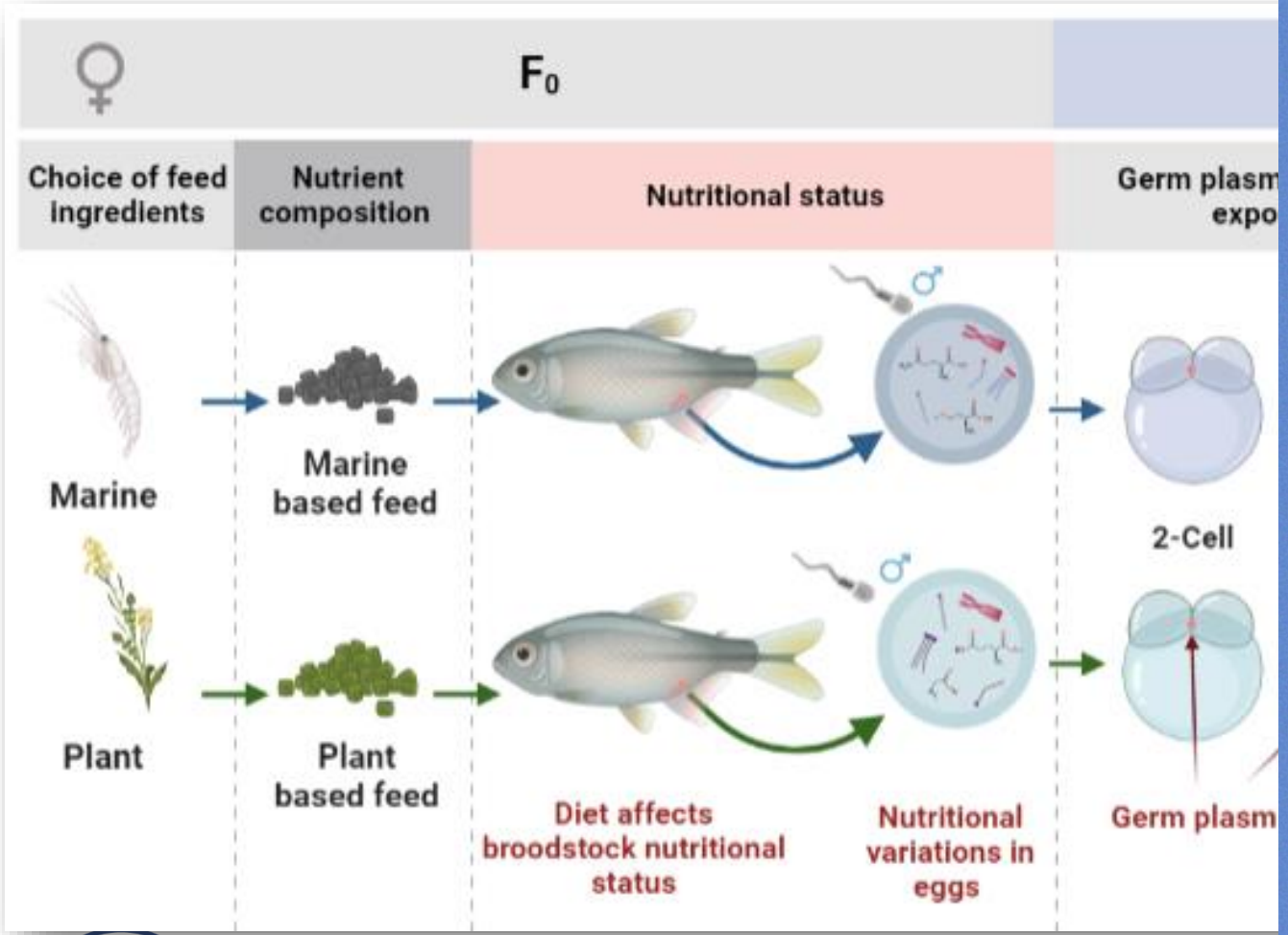
NEWS

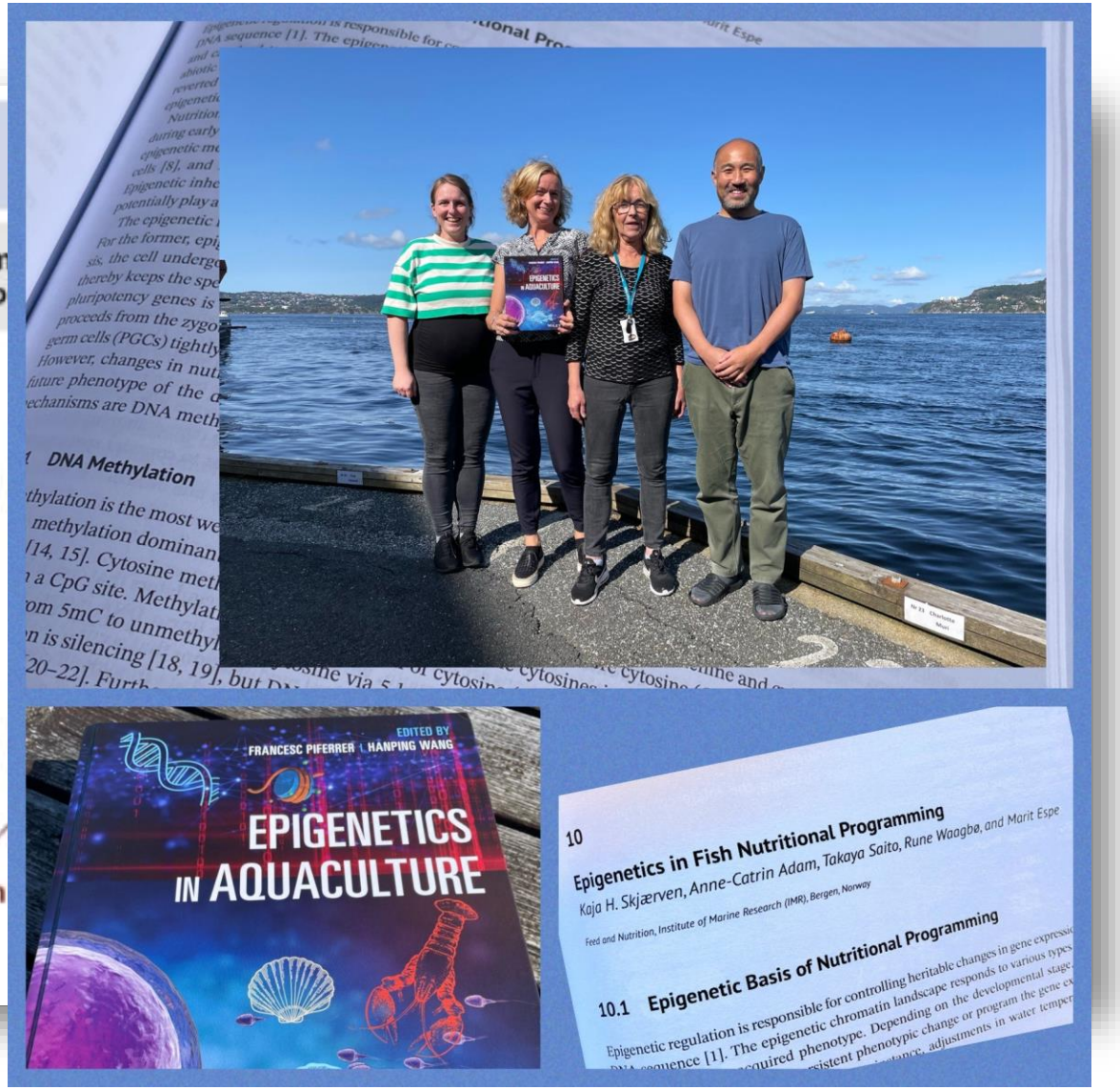
Editor’s Choice- Atlantic cod adaptation: Genetic insights into climate resilience

The latest Editor’s Choice in ICES Journal explores climate adaptation in fish. The study looked at genetic adaptation of Atlantic cod to rising sea temperatures, providing a deeper understanding of marine species’ response to climate change.

Published: 19 March 2024

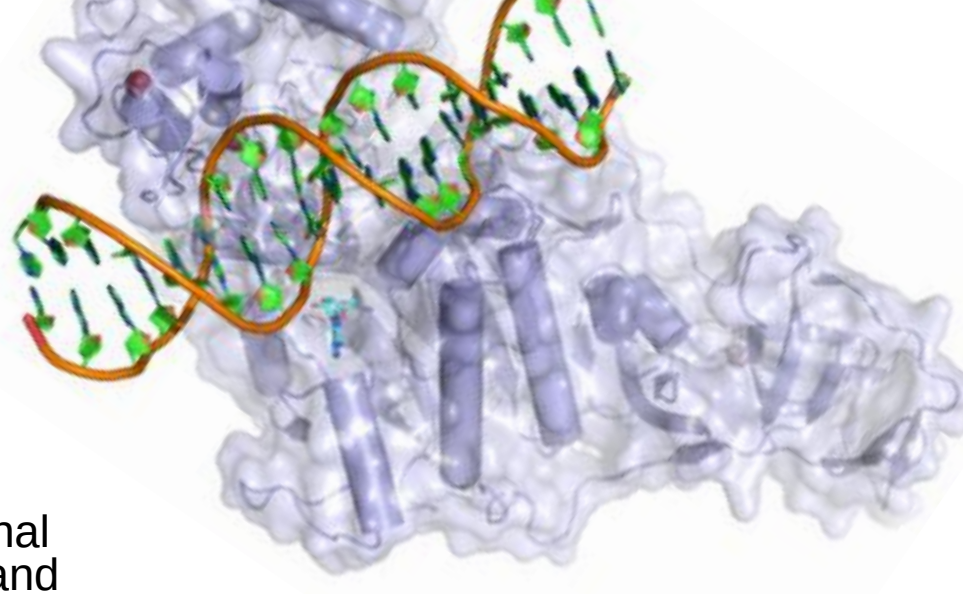




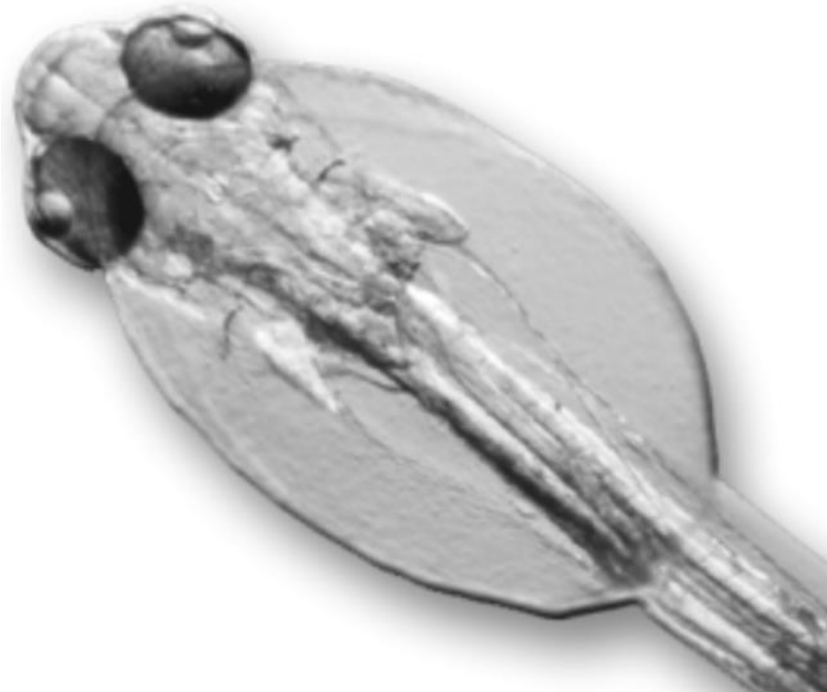


Epigenetics in aquaculture. Skjærven et al., 2023

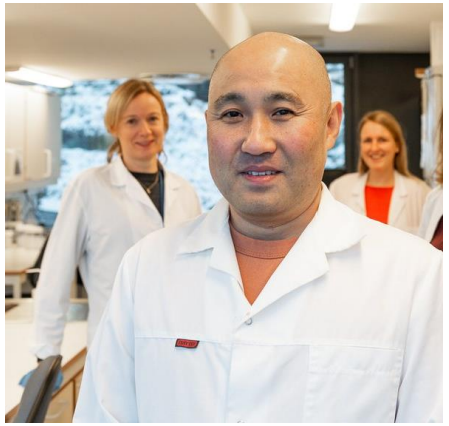
Summary:



- The metabolism interacts with the (epi-)gene regulation
- Broodstock handling affects the nutrient status of eggs- like SAM –، is needed for DNA methylation
- Atlantic salmon:
  - Broodstock spawning season manipulation changes the nutritional status of broodstock, and their offspring (Skjærven et al., 2020 and 2022). Altered spawning seasons transcriptionally and epigenetically influence cell cycle and lipid mediated regulations in their offspring (Saito et al., in review)
- Atlantic cod:
  - Temperature (Ocean warming) shapes embryonic developmental prospects of the next generation in Atlantic cod by altering maternal mRNA in offspring, these where regulated months earlier in the ovarian tissue (Skjærven, Maud, Kleppe et al.,Kjesbu 2024)



  - Further studies:
  - mRNAs: may change developmental gene regulatory networks, causing a ‘domino effect’ through subsequent embryonic tissue architecture, growth, and development?



The Research Council of Norway

267787 (NutrEpi)
295118 (EpiFishGrowth)

Co-workers and collaborators:

IMR: Anne-Catrin Adam, Eystein Oveland
Marit Espe, **Takaya Saito**, Eva Mykkeltvedt

Olav Kjesbu, Lene Kleppe and Maud Alix

Cambridge: Audrey Putman, Erik Miska
Nord Uni: Jorge M.O. Fernandes
CeMM: Christoph Bock