



A Current Review of Epigenetic Effects Associated with Salmonid Supplementation and Domestication

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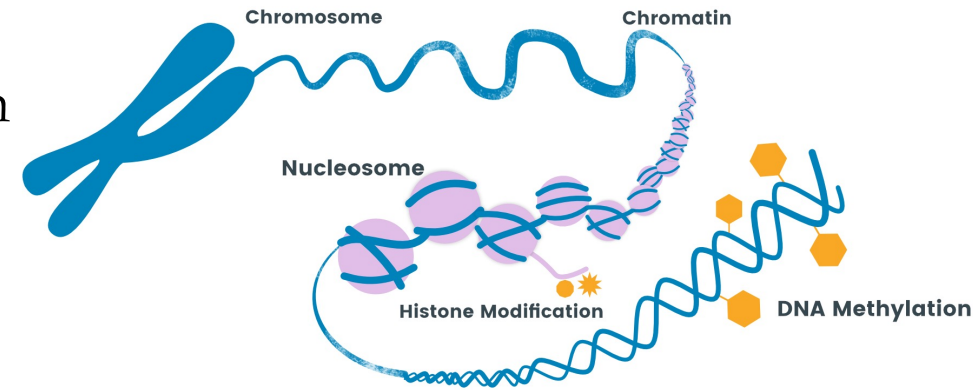
Supportive Breeding



- Multiple species of Pacific salmon with populations experiencing drastic declines
- Salmonid supplementation hatchery programs:
 - Rear and release hatchery-origin fish to supplement naturally spawning populations
 - Concerns of supportive breeding programs:
 - Captive-born individuals released into the wild may exhibit lower survival and/or produce lower numbers of offspring
- To date, limited evidence for genetic differences in salmonids directly related to domestication selection during hatchery rearing
- **Could rapid and heritable epigenetic changes in response to hatchery rearing present an explanation for fitness differences?*

Basic Epigenetic Concepts

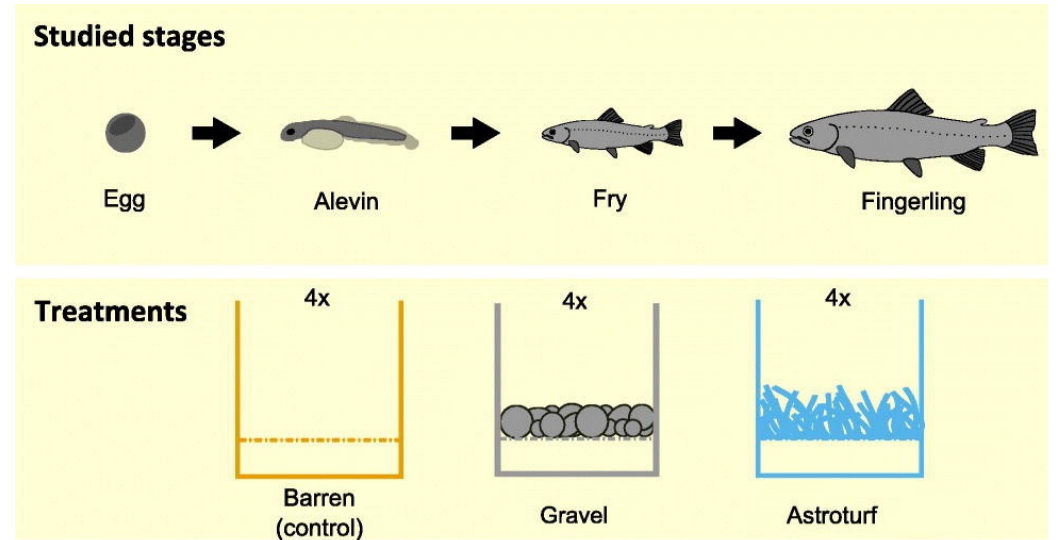
- Epigenetics: external modifications to DNA structure that impact gene expression but do not change the underlying DNA sequence (A,C,T,G)
- The epigenome is the collection of all the epigenetic marks in the cells.
- Primary types of epigenetic modifications:
 - Histone modification
 - Non-coding RNA gene silencing
 - **DNA methylation**: an epigenetic mechanism in which a methyl group is added to the DNA
 - Depending on placement, the methyl group can turn on or off gene expression.
- Epigenetic marks incorporated into the germline can be stable and heritable.



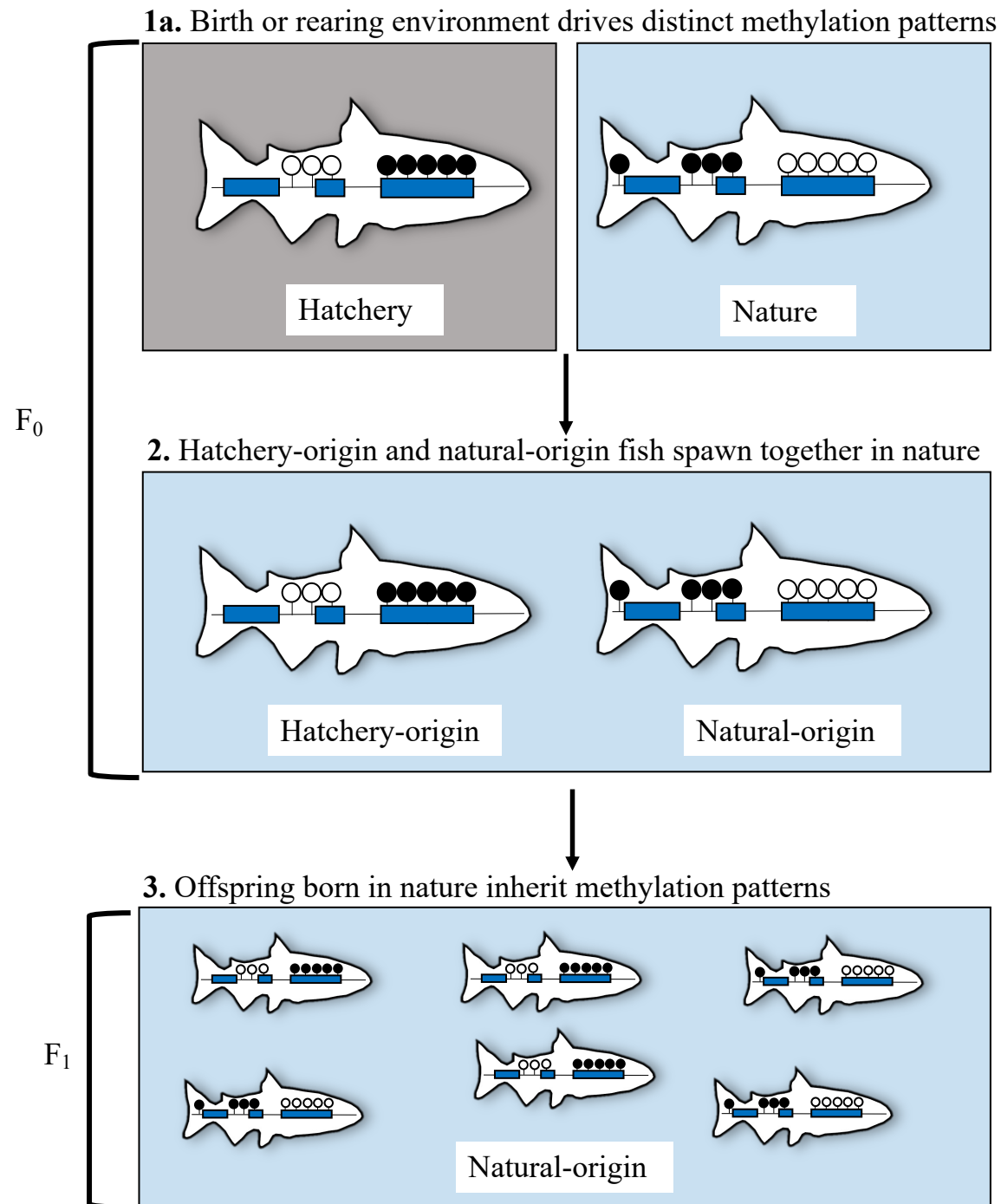
Epigenetic Studies in Fish

- Many epigenetic studies in both captive and natural marine environments
- Potential early environmental stressors during development that can alter the epigenome:
 - Temperature
 - Density
 - Predation stress
 - Water quality parameters
 - Environmental enrichment
- Example: Reiser et al. 2021
 - Rainbow trout reared in different types of substrate
 - Enrichment affected global DNA methylation in the brain at the egg and alevin stage.

**Hatchery vs.
Natural
Environment**



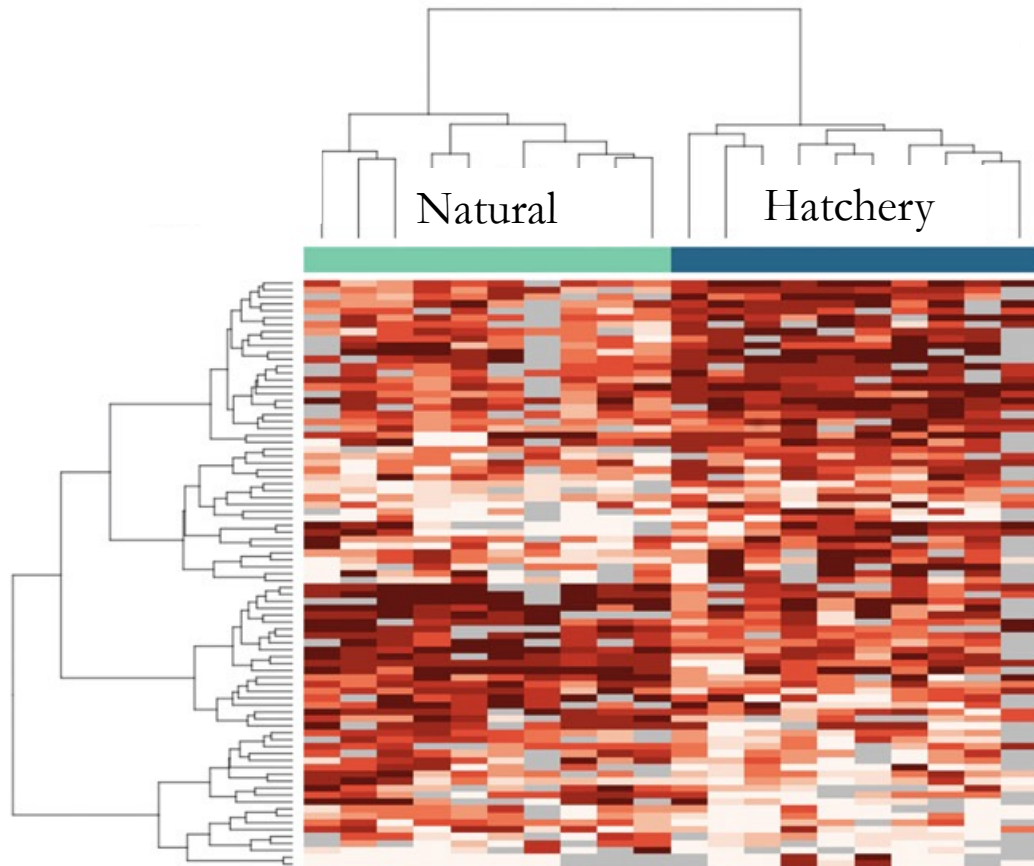
Potential Transmission of Epigenetic Modifications



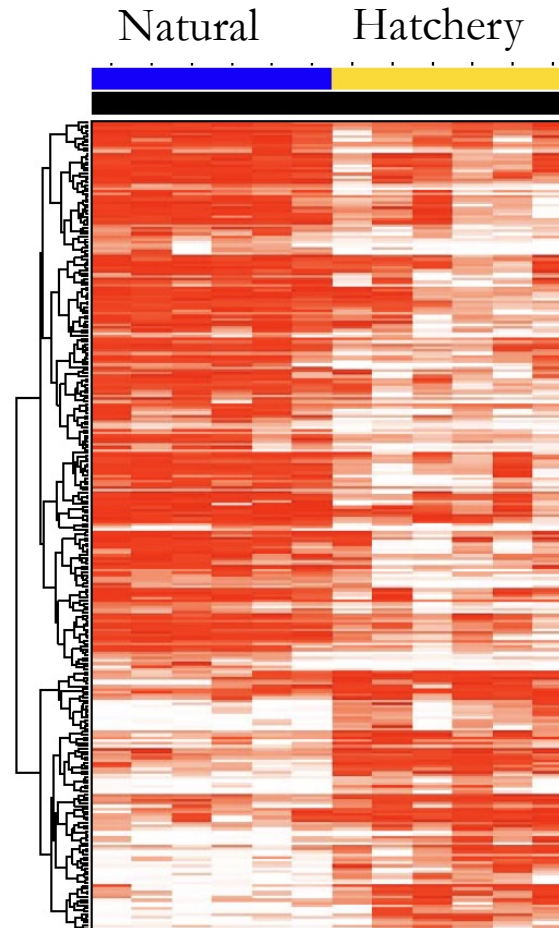
Empirical Studies

- Since 2010, **ten** published studies directly compared methylation differences between hatchery-origin and natural-origin salmonids:
- **Steelhead Trout:** Blouin et al. 2010; Gavery et al. 2018, 2019; Nilsson et al. 2021
- **Coho Salmon:** Le Luyer et al. 2017; Leitwein et al. 2021, 2022
- **Atlantic Salmon:** Rodriguez Barreto et al. 2019; Wellband et al. 2021; Venney et al. 2023
- Range of life stages (fry to adult), tissue types (liver, sperm, whole body, muscle, blood), geographical regions, and methodological approaches

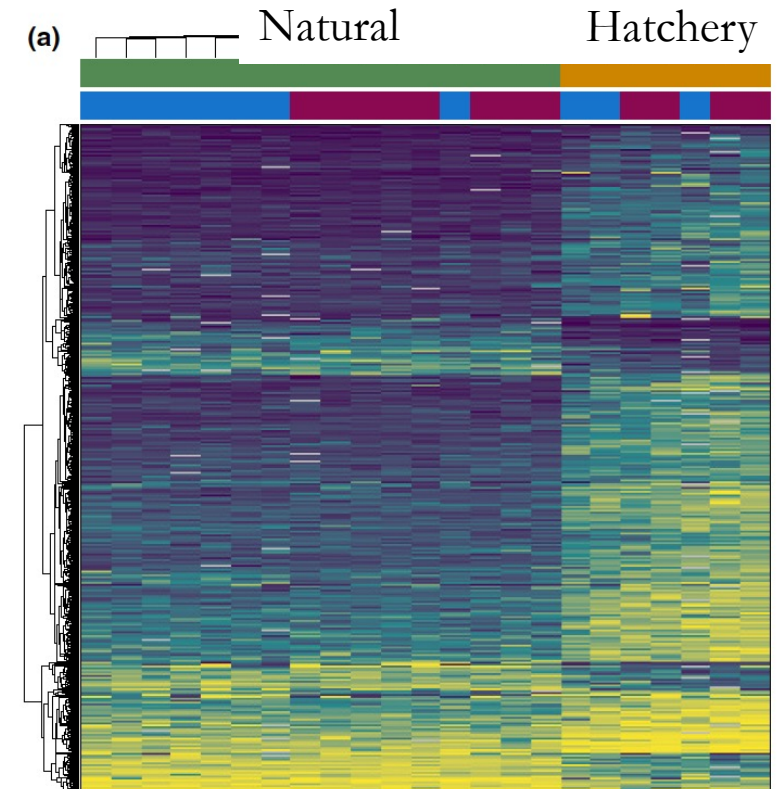
Key Finding 1: Patterns of methylation are different in hatchery- and natural-origin fish



Gavery et al. 2018



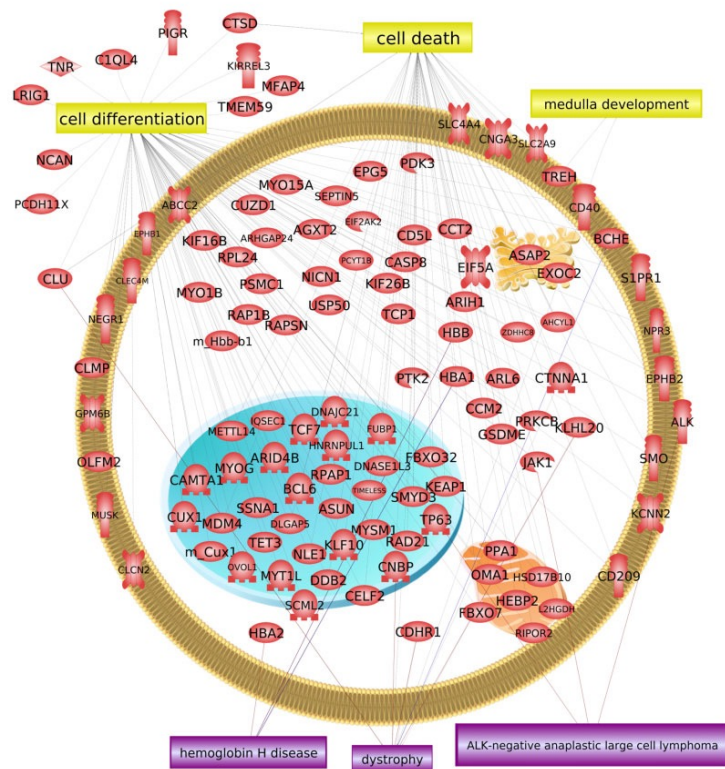
Wellband et al. 2021



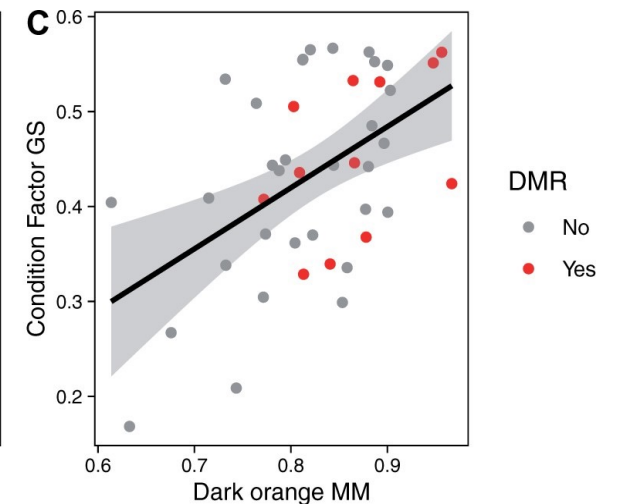
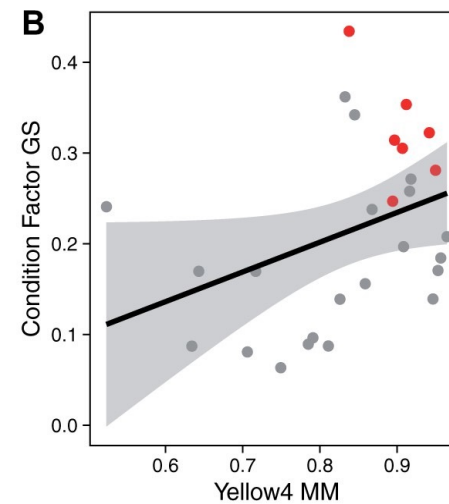
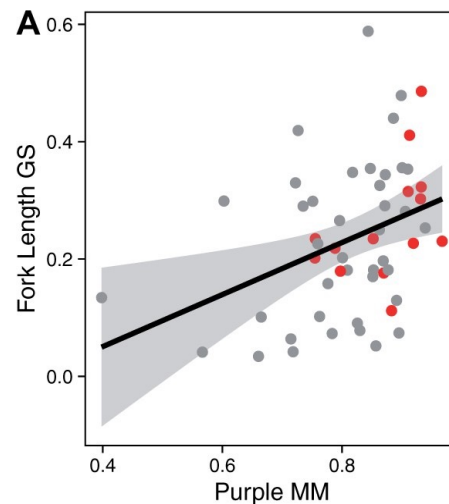
Venney et al. 2023

Key Finding 2: Overlap in functional genomic regions between hatchery- and natural-origin fish

Genes located in differentially methylated regions between hatchery- and natural-origin fish consistently included those involved in embryonic development, growth, smoltification, stress, and immune response.

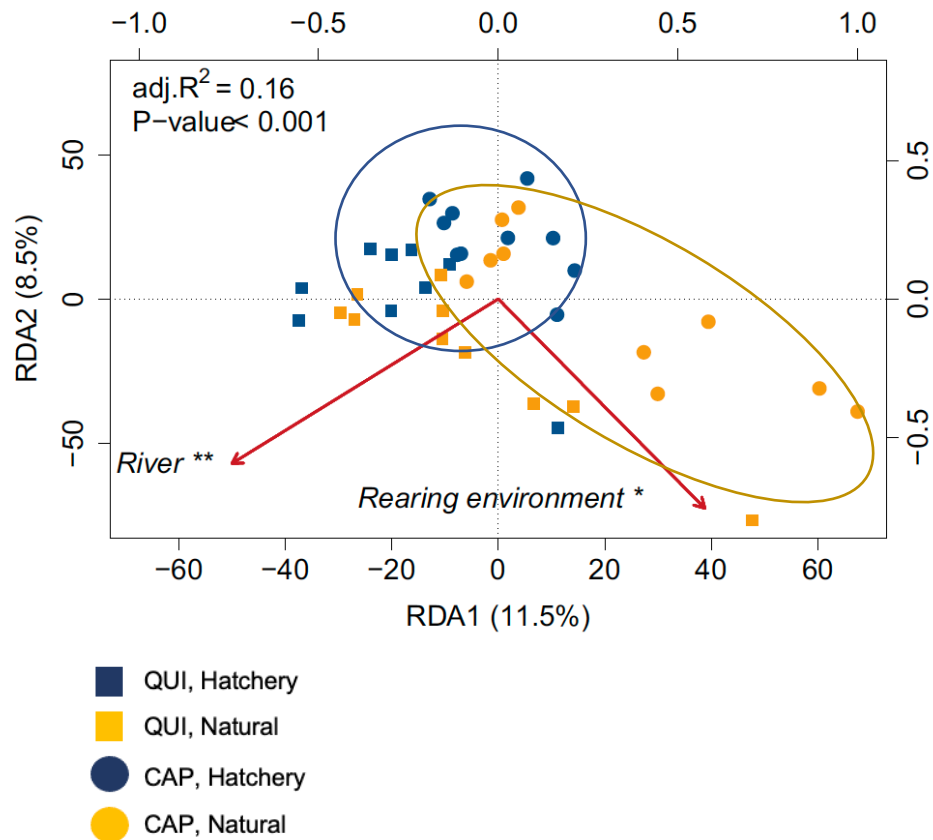


Nilsson et al. 2021

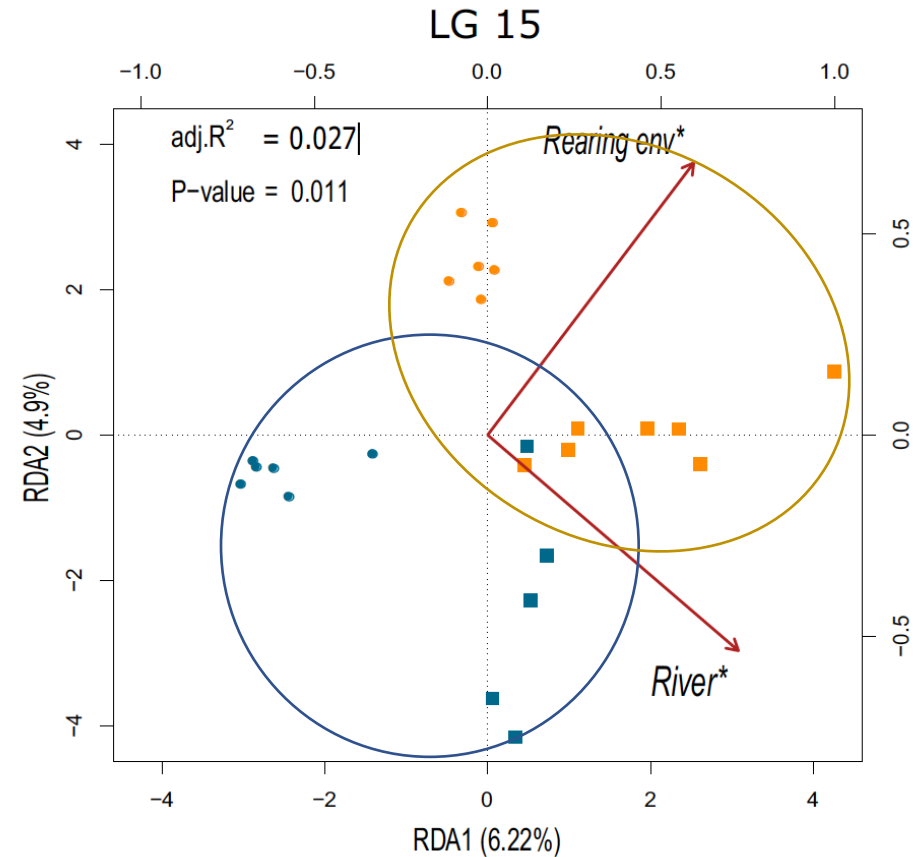


Wellband et al. 2021

Key Finding 3: Epigenetic changes are replicated in parallel across geographical locations

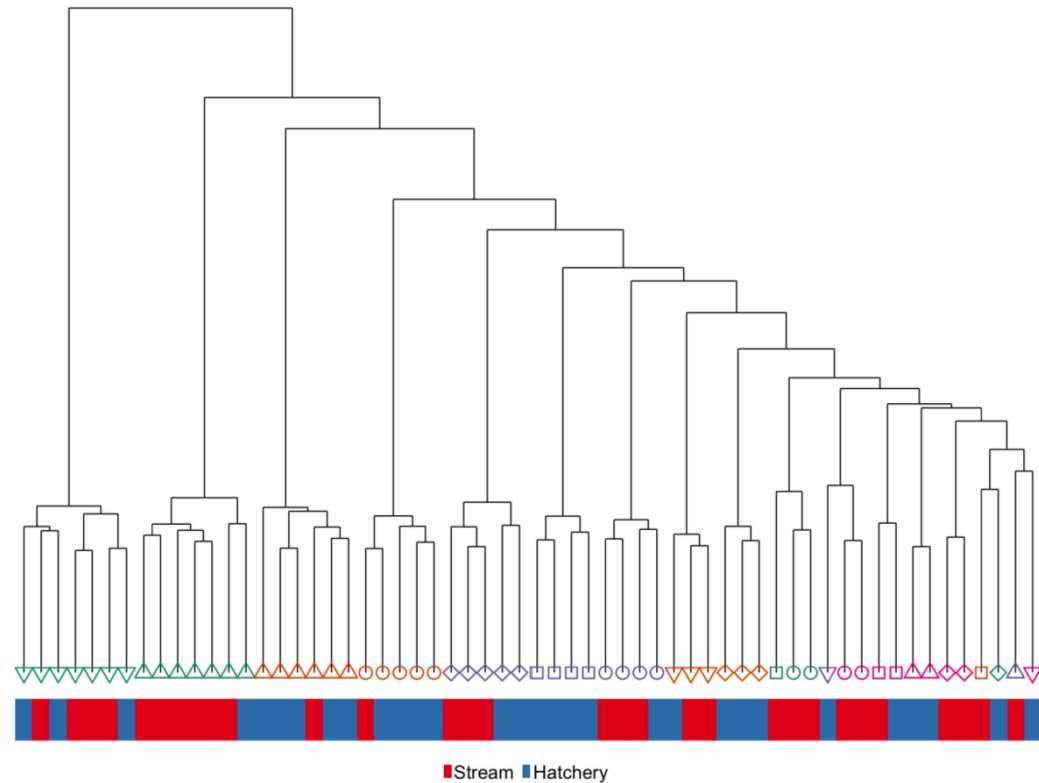


Le Luyer et al. 2017



Leitwein et al. 2021

Key Finding 4: Epigenetic marks are found in the sperm of hatchery- and natural-origin fish which may persist to offspring



Gavery et al. 2019

↓

DMRs sperm fathers		DMRs sperm offspring		Shared DMR
WvsH1	55	W_Off vs H1_Off	346709	2
WvsH2	298980	W_Off vs H2_Off	31130	167
H1vsH2	22563	H1_Off vs H2_Off	8564	105

Rodriguez Barreto et al. 2019

Do epigenetic modifications affect gene expression?

- **Christie et al. (2016)**: differential expression of hundreds of genes in offspring reared in a common environment from parents of different ancestry (hatchery- vs natural-origin)
- **Bull et al. (2022)**: synthesized results from multiple salmonid domestication studies and found clear patterns of differential gene expression
- **Christensen et al. (2021)**: little overlap between genes that were differentially methylated and expressed between fish reared in simulated stream vs tank environment
- **Leitwein et al. (2022)**: thousands of genes differentially expressed in parallel across river systems of hatchery- vs natural-origin fish
 - Weak relationship between gene expression and methylation

Additional Future Questions

- What are the specific environmental factors that are driving these epigenetic differences in hatcheries?
- How long do epigenetic changes persist both within a generation and across generations?
- What are the other epigenetic mechanisms besides methylation that could be driving hatchery versus natural fitness differences?
- What is the role of both maternal and paternal epigenetic effects (egg vs sperm)?

Examples of Practical Applications

- How can epigenetics be used to inform breeding practices and potentially reduce the fitness gap between hatchery-origin and natural-origin fish?
- Top-Down Approach:
 - Simulating the natural environment in the hatchery setting as much as possible
- Bottom-Up Approach:
 - Targeted selection on epigenetic markers that are linked to fitness-enhancing traits
 - Requires an in-depth understanding of the epigenetic association with fitness-related traits and the stability of epigenetic marks