



## **Геномная селекция в аквакультуре**

Мюге Н.С., ВНИРО

# Аквакультура в мире:

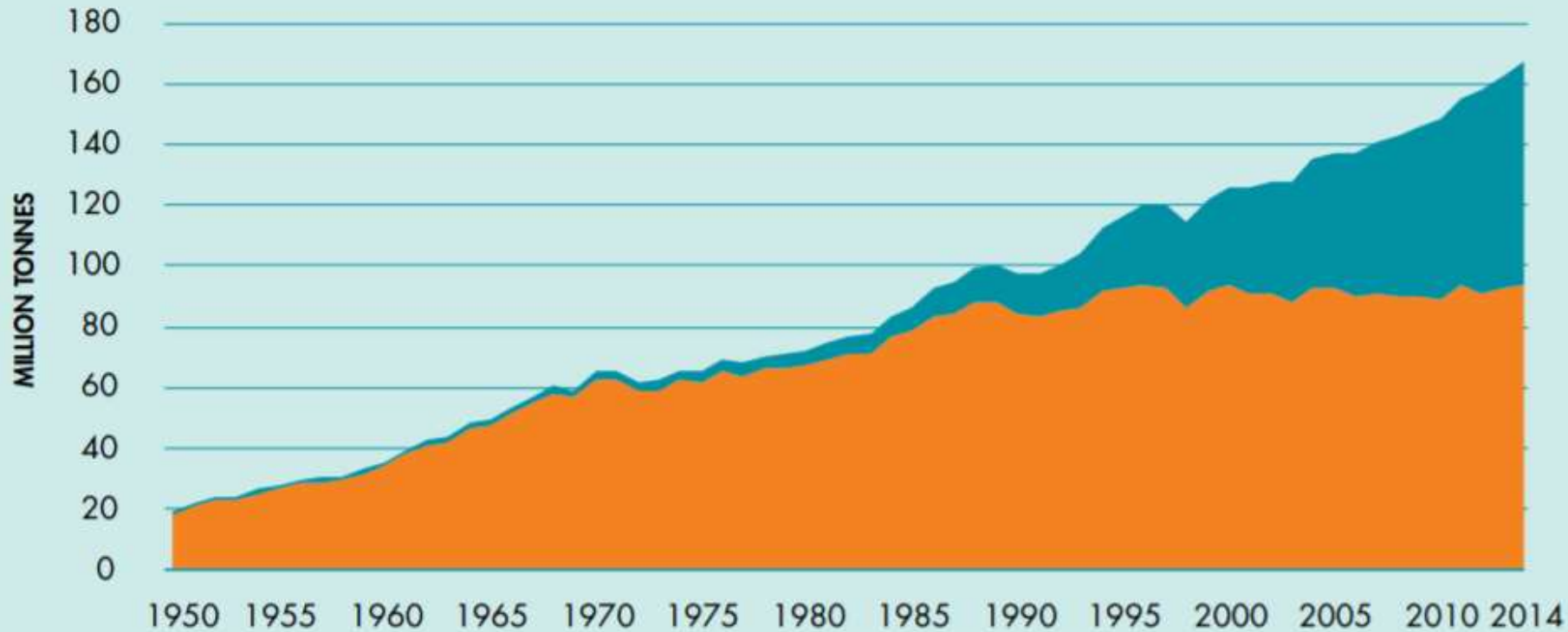
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- ▶ Продукция аквакультуры в мировом масштабе растет на 10% ежегодно.
- ▶ Общая продукция в мире >60 миллион тонн в год.
- ▶ Быстрое распространение и рост производства за последние 30 лет.
- ▶ 90% продукции аквакультуры – Китай и Юго-Восточная Азия.
- ▶ Подавляющее большинство используемых пород – результат “традиционного” одомашнивания.

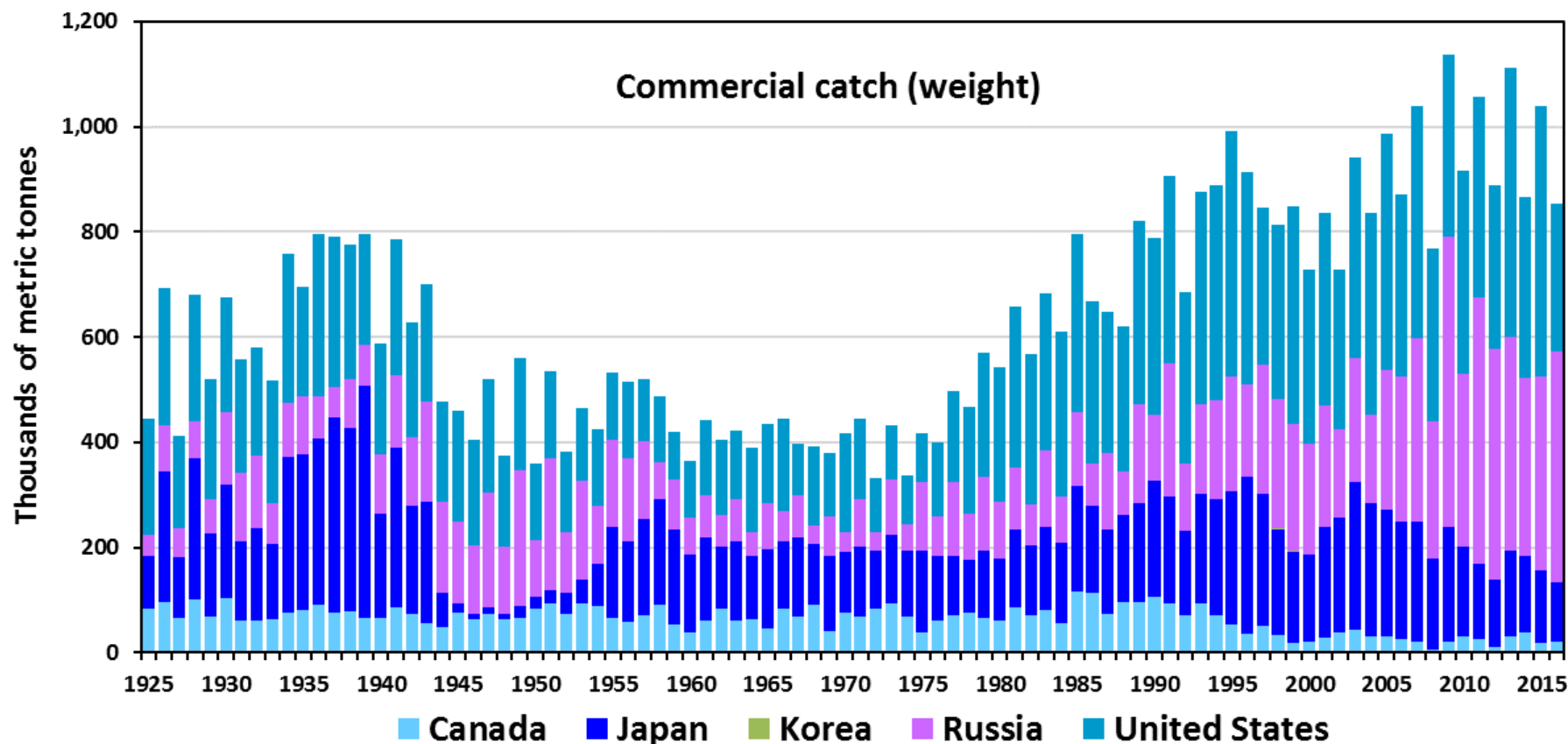


# Данные ФАО (суммарно вылов и аквакультура, в мире)

## WORLD CAPTURE FISHERIES AND AQUACULTURE PRODUCTION

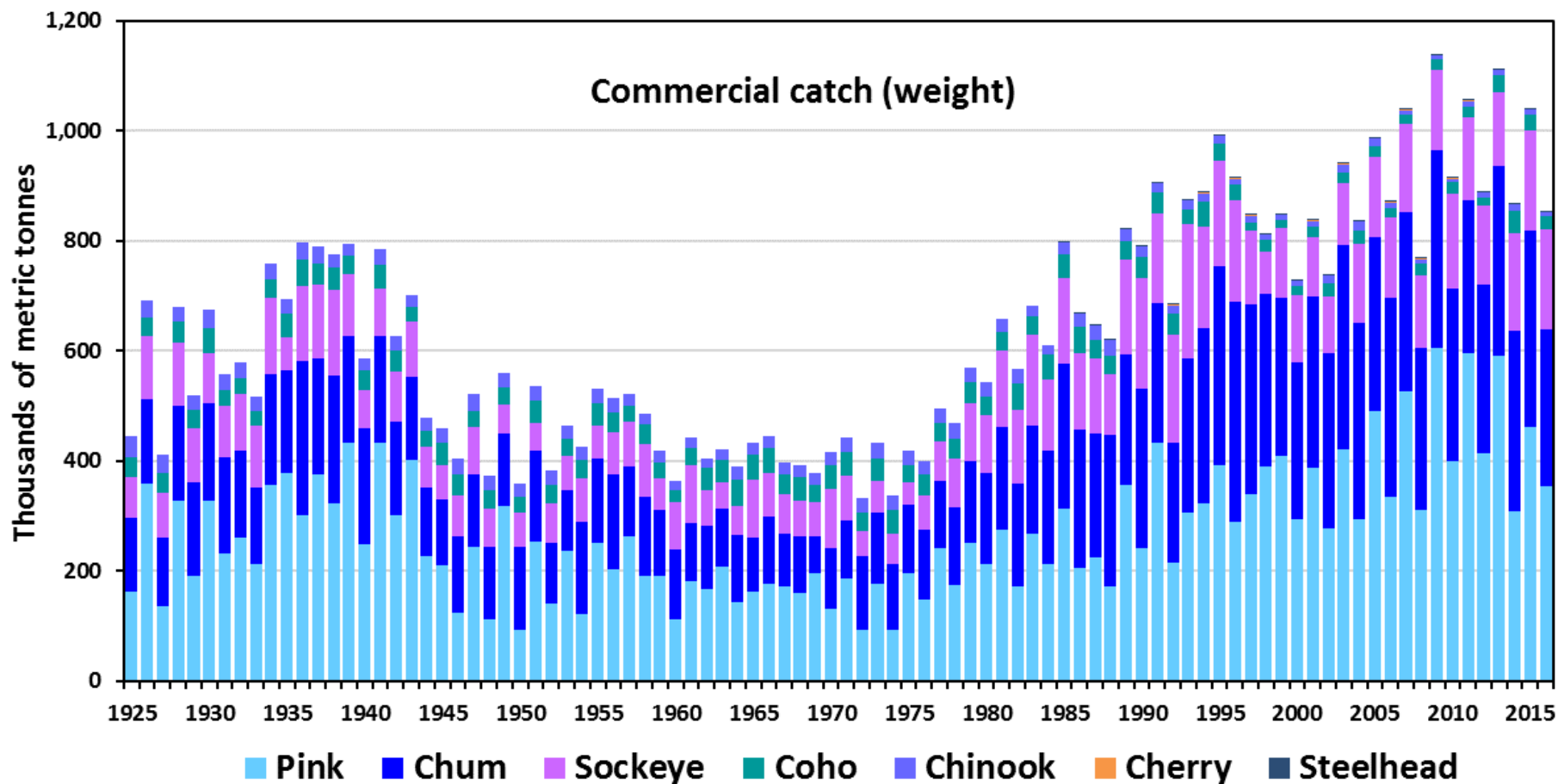


# Вылов тихоокеанских лососей (по странам)



Data Source: North Pacific Anadromous Fish Commission (NPAFC). 2017. NPAFC Pacific salmonid catch statistics (updated 31 July 2017). North Pacific Anadromous Fish Commission, Vancouver. Accessed July, 2017. Available: [www.npafc.org](http://www.npafc.org)

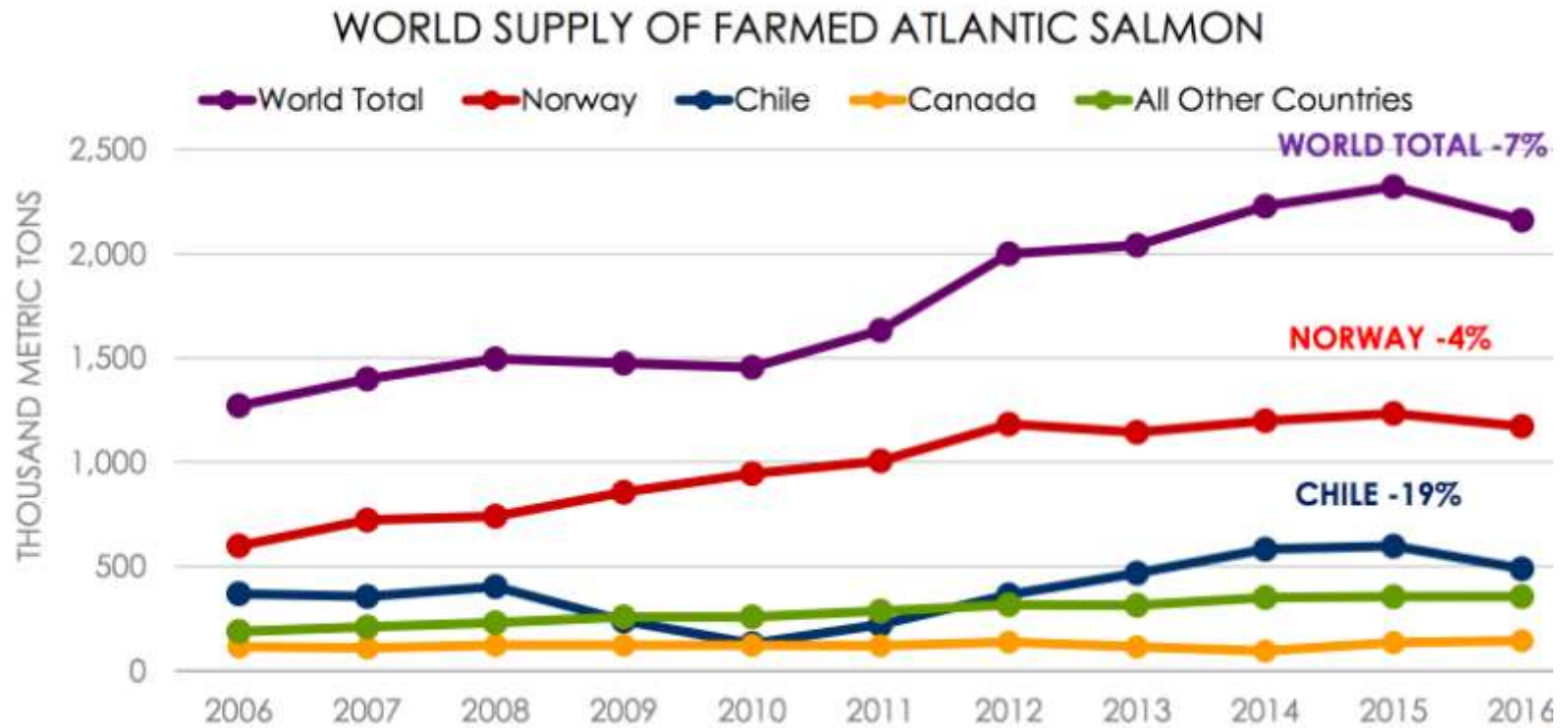
# Вылов тихоокеанских лососей (по видам)

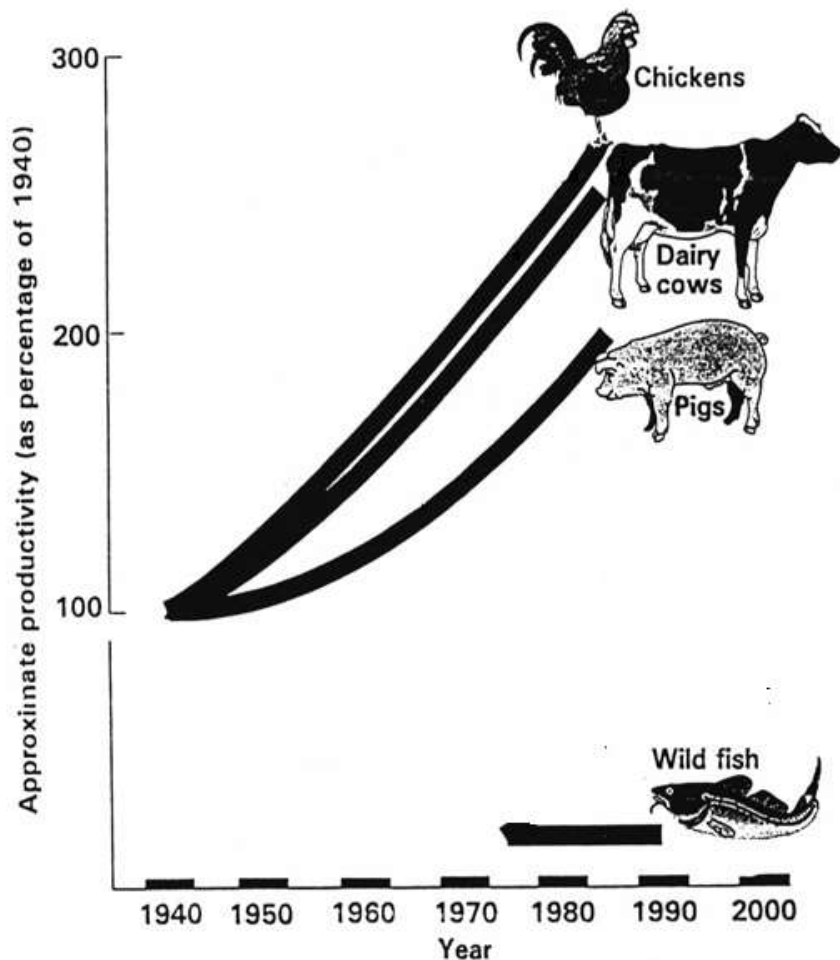


Data Source: North Pacific Anadromous Fish Commission (NPAFC). 2017. NPAFC Pacific salmonid catch statistics (updated 31 July 2017). North Pacific Anadromous Fish Commission, Vancouver. Accessed July, 2017. Available: [www.npafc.org](http://www.npafc.org)

# Мировая продукция лосося в аквакультуре

World farmed Atlantic salmon supply fell by 7% in 2016

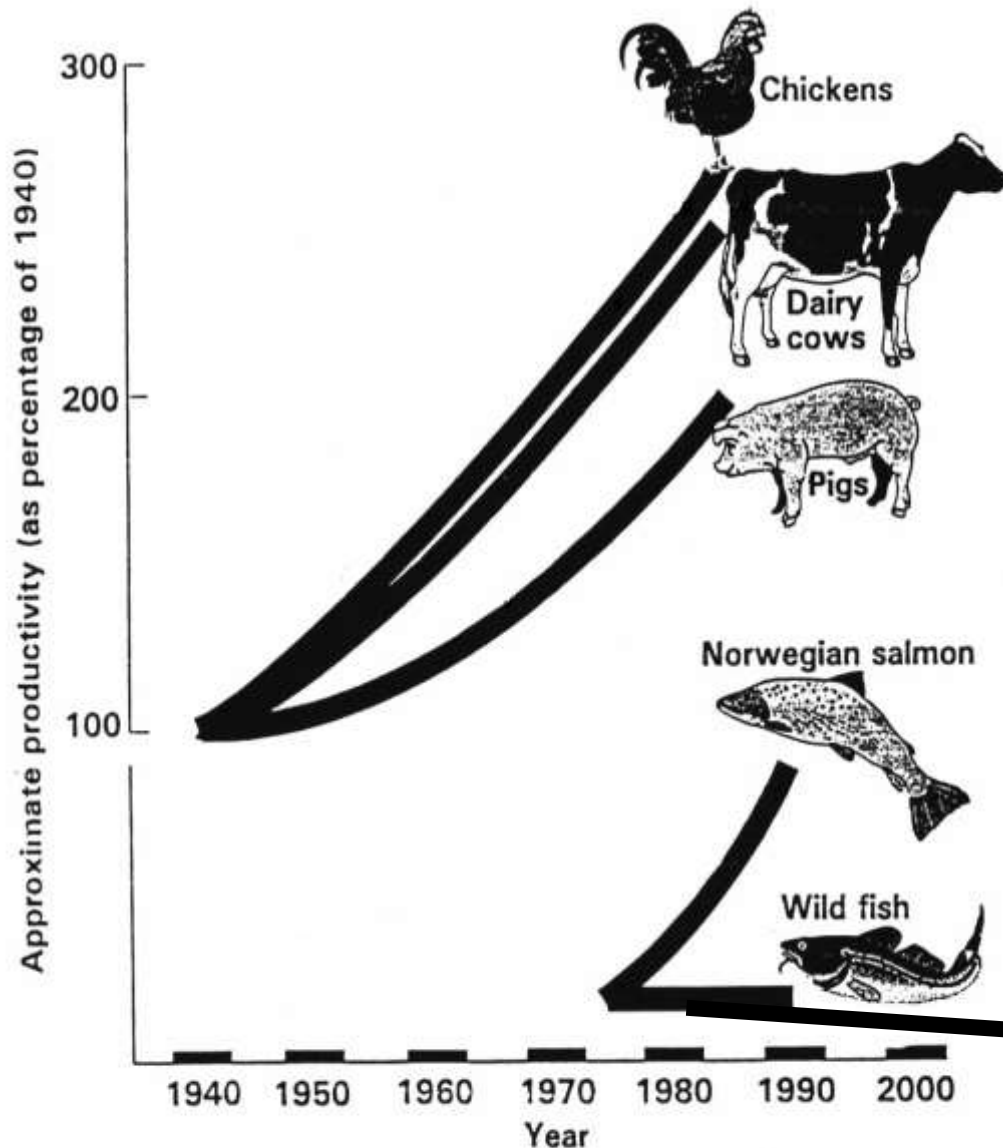




Development of productivity in farm animals and finfishes.

- ▶ Без применения генетических методов, качество пород, используемых в аквакультуре с времени понижается.
- ▶ ВСЕ другие отрасли (животноводство и птицеводство) используют генетически улучшенные породы (не путать с ГМО)
- ▶ Примеры применения современных генетических методов в аквакультуре пока редки

# Динамика роста продуктивности



Development of productivity in farm animals and finfishes.

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# Роль генетики в аквакультуре

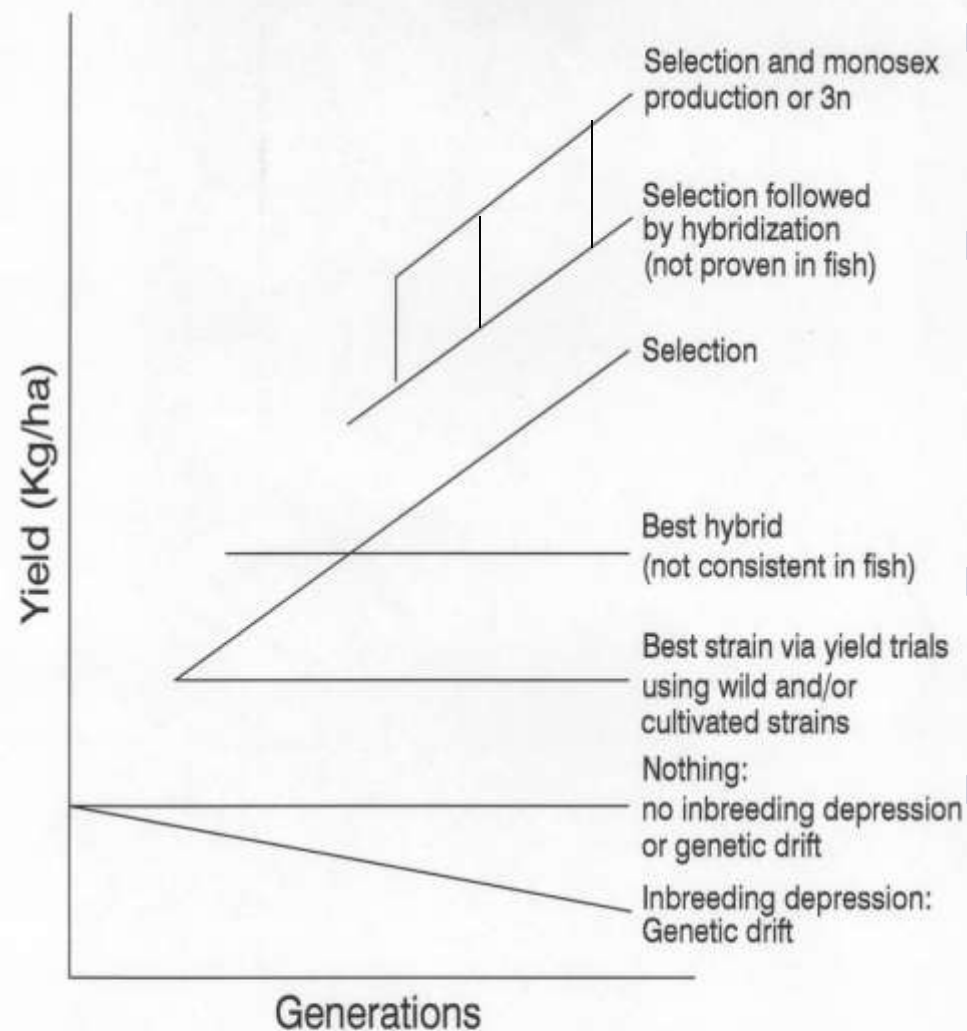
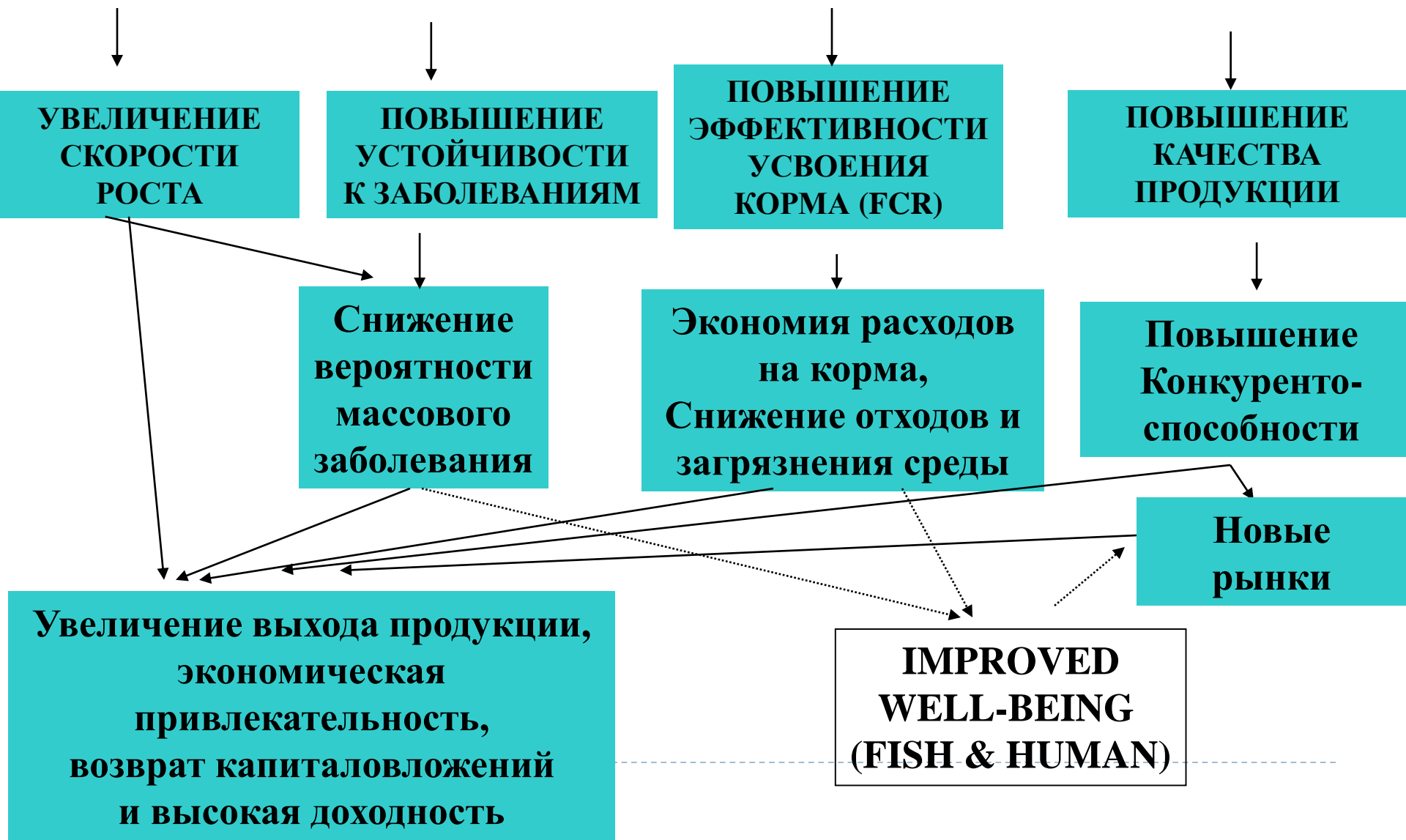


Схема изменения продуктивности пород при различных методах селекции (по Tave, 1986)

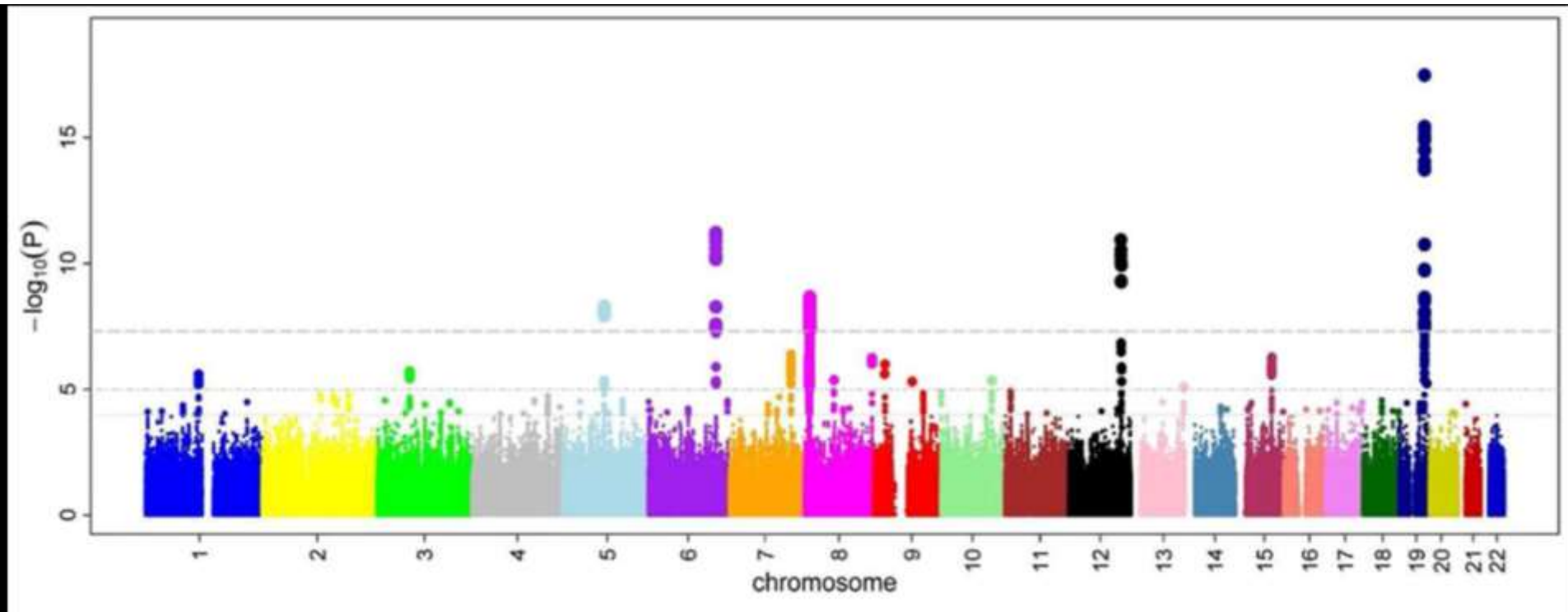
- ▶ Существует много различных подходов улучшения пород с использованием генетики.
- ▶ Улучшение пород за счет селекции основано на использовании полигенной природной генетической изменчивости (эффект совокупности аллелей).
- ▶ Гибридизация основана на доминировании признаков и гетерозисе (эффект пар аллелей).
- ▶ Генетические манипуляции обычно являются «разовыми» (т.е. создание однополых или триплоидных рыб). Однако продолжительное применение генетических методов бывает необходимо для раскрытия полного потенциала вида как объекта аквакультуры.

# Четыре основных критерия при селекции в аквакультуре



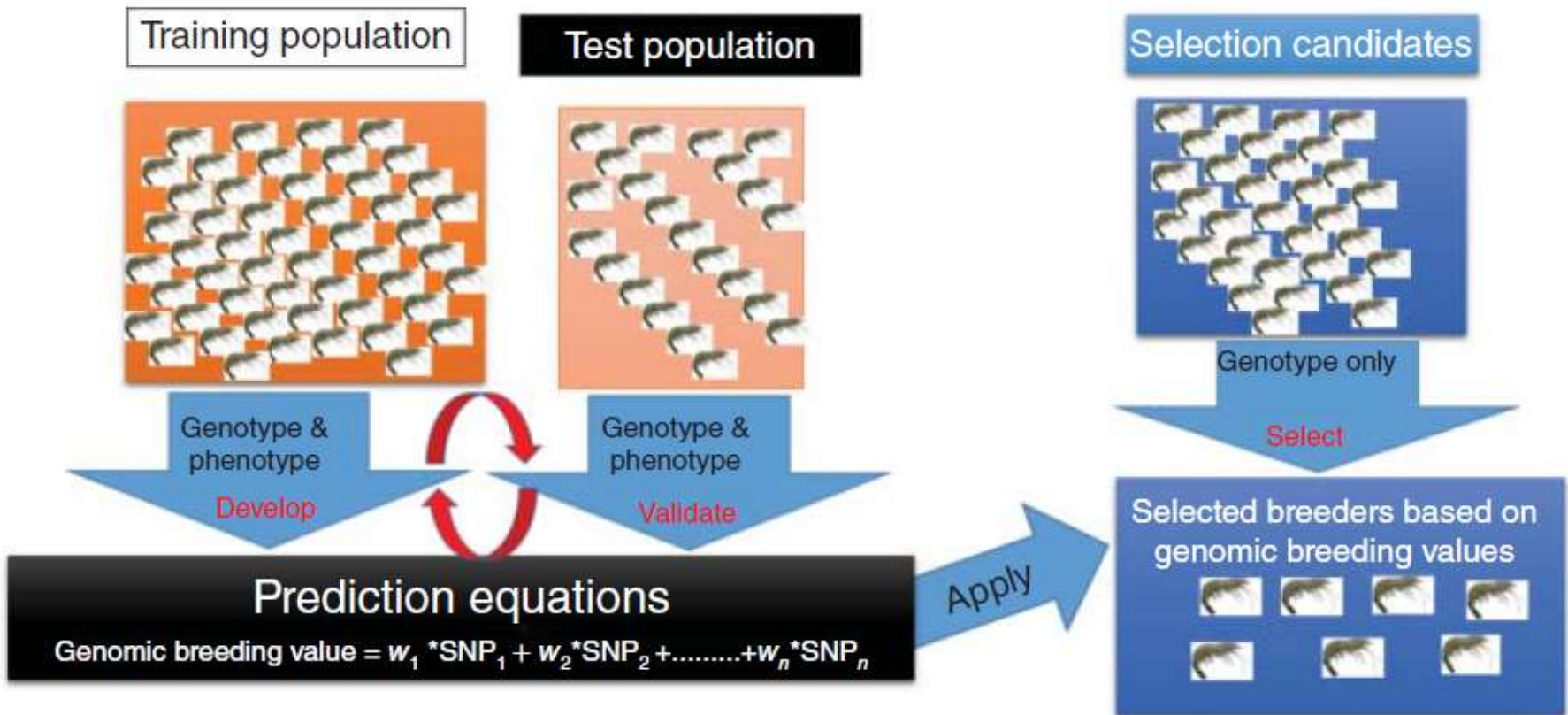
# GWAS

Полногеномный поиск ассоциаций (англ. **GWAS**, Genome-Wide Association Studies) — направление биологических исследований, связанных с исследованием ассоциаций между геномными вариантами и фенотипическими признаками.



# Принцип применения геномной селекции (MAS – marker-assisted selection)

21 Genomic selection in Aquaculture breeding program



## Genomic Selection in Aquaculture

Sho HOSOYA\*<sup>1</sup>, Kiyoshi KIKUCHI\*<sup>1</sup>, Hiroshi NAGASHIMA\*<sup>2</sup>, Junichi ONODERA\*<sup>2</sup>,  
 Kouishi SUGIMOTO\*<sup>2</sup>, Kou SATOH\*<sup>2</sup>, Keisuke MATSUZAKI\*<sup>2</sup>, Masaki YASUGI\*<sup>3</sup>,  
 Atsushi J. NAGANO\*<sup>3,4</sup>, Akira KUMAGAYI\*<sup>2</sup>, Kenichi UEDA\*<sup>2</sup>, and Tadahide KUROKAWA\*<sup>5</sup>

**Table 1.** Summary of species, traits, genotyping platform and prediction method researches about genomic selection for aquaculture

Species	Trait	Genotyping platform	Prediction method	Citation
Atlantic salmon ( <i>Salmo salar</i> )	parasite resistance	SNP array	GBLUP	Ødegård <i>et al.</i> (2014)
	fillet color			
	body size	SNP array	GBLUP	Tsai <i>et al.</i> (2015)
	parasite resistance	SNP array	GBLUP	Tsai <i>et al.</i> (2016)
Rainbow trout ( <i>Oncorhynchus mykiss</i> )	disease resistance	SNP array, RAD	ssGBLUP, wssGBLUP, BayesB, BayesC	Vallejo <i>et al.</i> (2016)
Yellow croaker ( <i>Larimichthys crocea</i> )	body size	Genotyping-by-Sequencing	GBLUP, emBayesB	Dong <i>et al.</i> (2106)
	fatty acid composition	(GBS)		
Yesso scallop ( <i>Patinopecten yessoensis</i> )	body size	2d RAD-seq	GBLUP, LASSO, Bayesian LASSO, BayesA, BayesB, rrBLUP	Dou <i>et al.</i> (2016)
Coho salmon ( <i>Oncorhynchus kisutch</i> )	body size	ddRAD-seq	GBLUP	Hosoya <i>et al.</i> (submitted)



INDY/EATS

# PLAGUES OF PARASITIC SEA LICE

# DEPLETING WORLD'S SALMON STOCKS

Aquaculture sector loses \$1 billion a year to outbreaks of tiny crustaceans infesting and devouring fish farmed for human consumption

# Морская вошь *Lepeophtheirus salmonis*. –Эктопаразит лосося

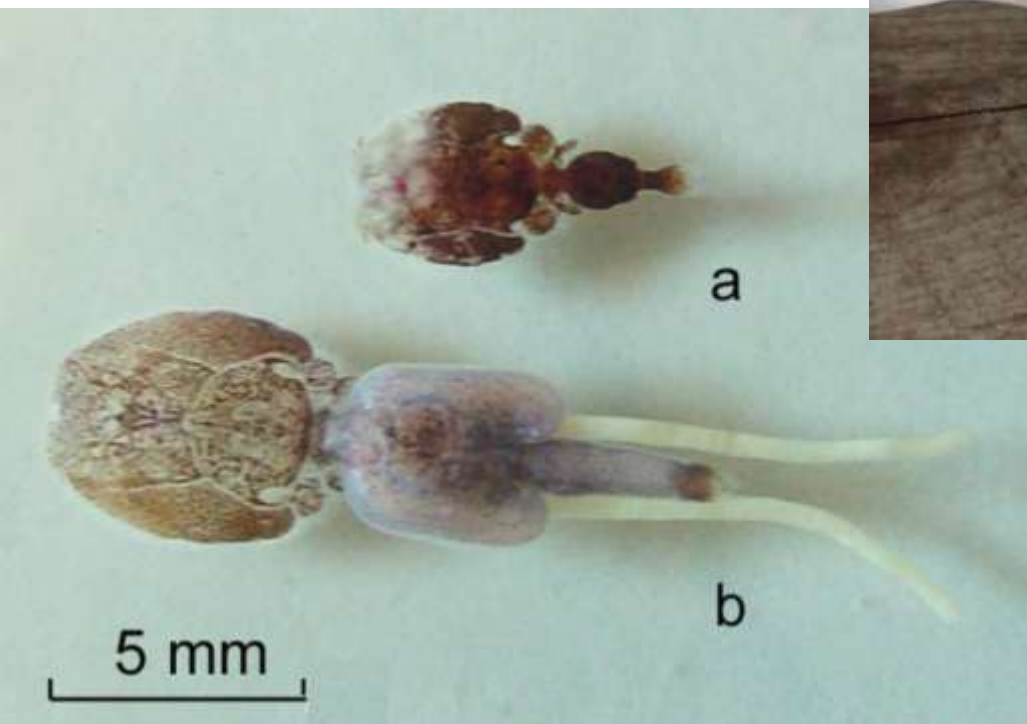
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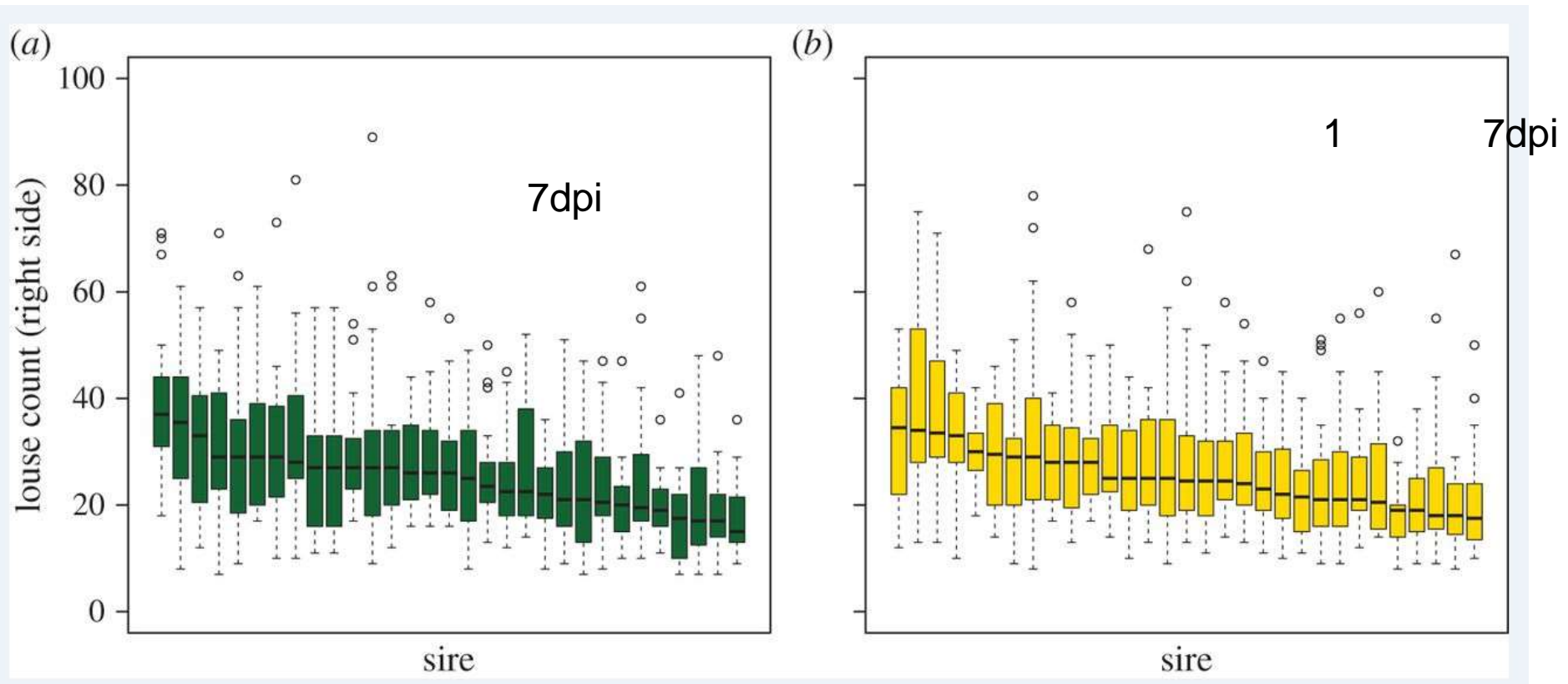
## ■ The control of sea lice in Atlantic salmon by selective breeding

Karim Gharbi, Louise Matthews, James Bron, Ron Roberts, Alan Tinch, Michael Stear

Published 19 August 2015. DOI: [10.1098/rsif.2015.0574](https://doi.org/10.1098/rsif.2015.0574)



# Генетическая составляющая устойчивости к морской вши в семьях лосося

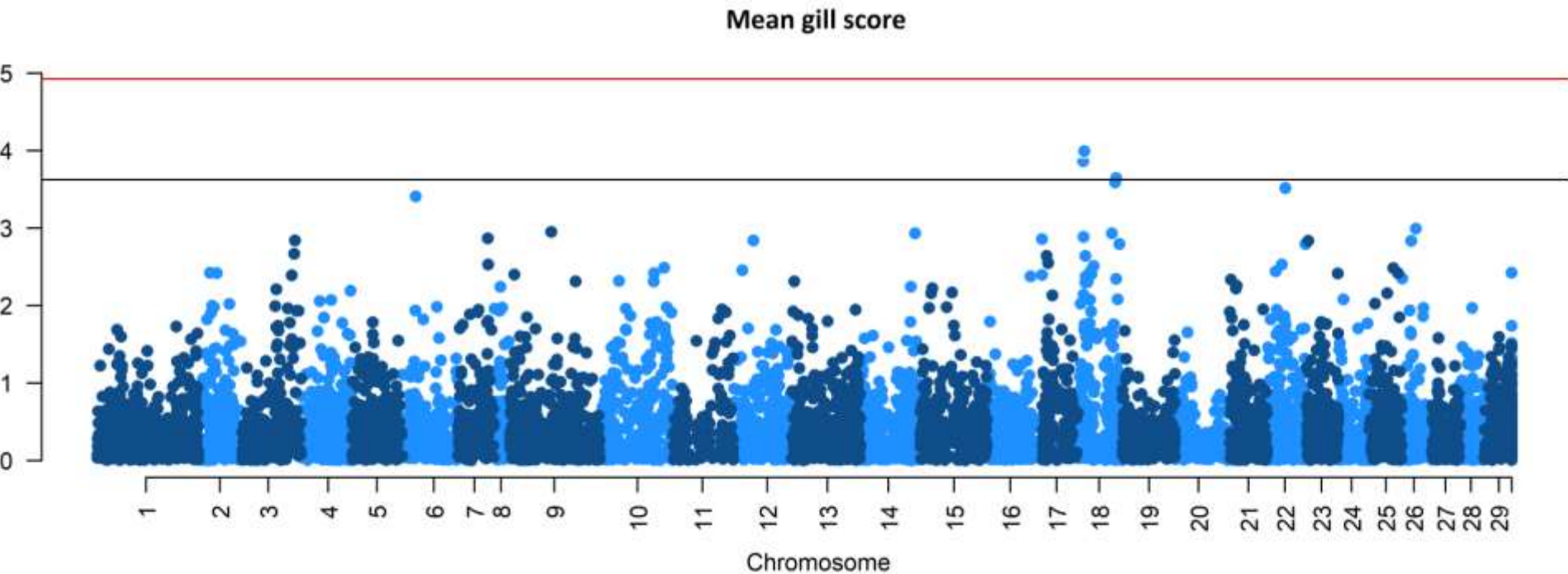




# Genome-Wide Association and Genomic Selection for Resistance to Amoebic Gill Disease in Atlantic Salmon

Diego Robledo, Oswald Matika, Alastair Hamilton and Ross D. Houston

G3: GENES, GENOMES, GENETICS *Early online February 2, 2018; <https://doi.org/10.1534/g3.118.200075>*



# FILLET QUALITY AND YIELD OF FARMED ATLANTIC SALMON (*salmo salar* L.): variation between families, gender differences and the importance of maturation

NORWEGIAN UNIVERSITY OF LIFE SCIENCES

Department of ANIMAL AND AQUACULTURAL SCIENCE  
Master Thesis 60 credits 2011

## Генетический контроль качества филе



Fig. 2. 2. Roche SalmoColour Fan™ (Source: <http://www.focs.ca/fishfarming/index.asp>)



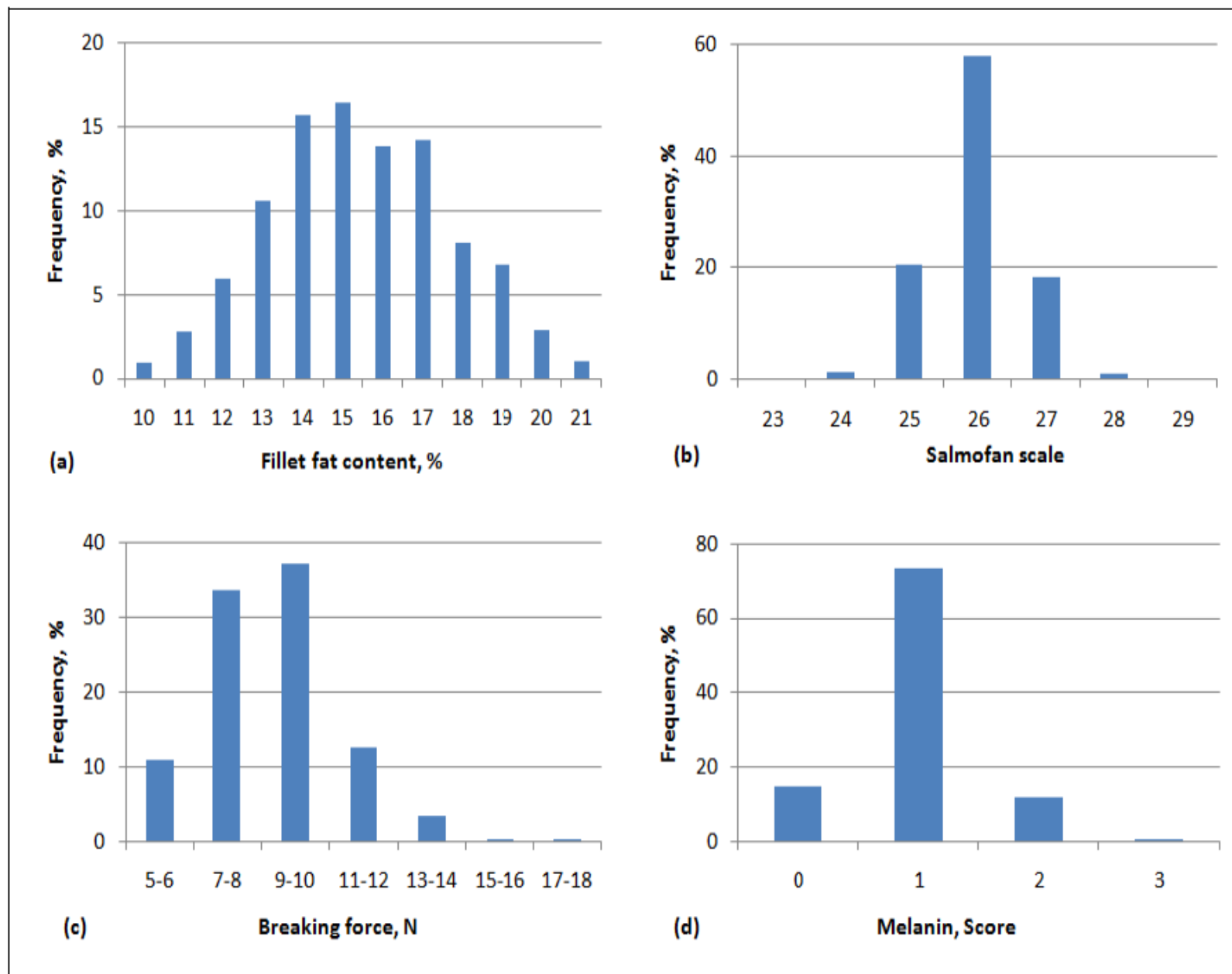


Fig. 4.2. Distribution of (a) fillet fat content (%), (b) SalmoFan score, (c) breaking force (N) and

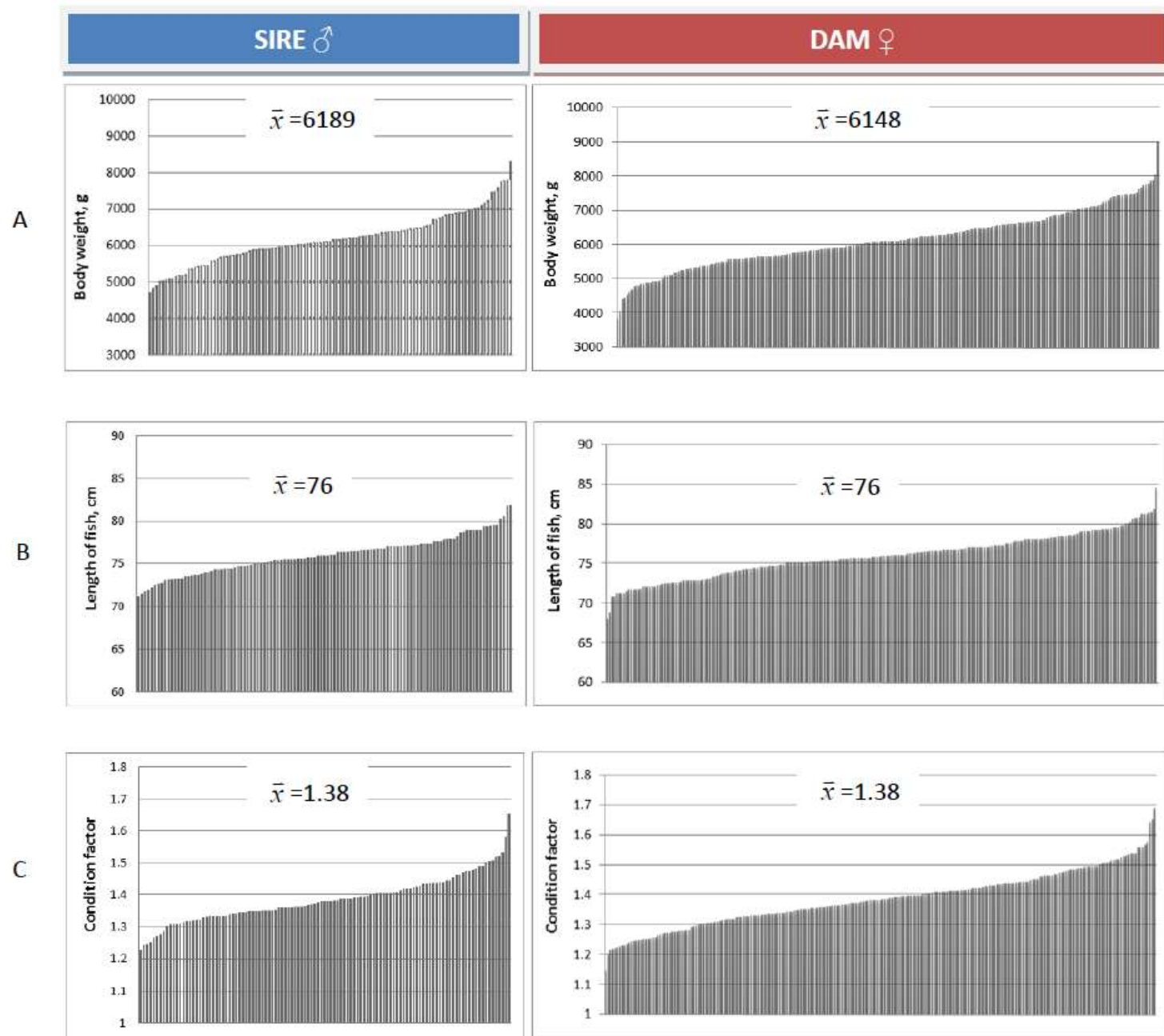


Fig. 4.4. Body weight (A), body length (B) and condition factor (C) of Atlantic salmon families.



# Broodstock Genetics Management

Xelect offers a complete service for broodstock genetics management covering finfish, shrimp and shellfish species.



Stock Program Support

Client sends samples



Fin punches sent to Xelect in St Andrews

Xelect carries out analysis



Genotyping  
Parentage Assignment  
Genetic Calculations  
Breeding Values

Results returned and evaluated



Selection, On-growing  
Spawning, Broodstock  
Selection

Send a Stocklist

Request a Quote

Request a Quote

Request a Quote

Request a Quote

Request a Quote

Request a Quote

Request a Quote

Send a Stocklist to St Andrews

Parentage Assignment Genetic Calculations Breeding Values

Spawning, Broodstock Selection

RAD-Seq

ddRAD/MISeq

Read Mapping /SNP Calling

dDocent Pipeline

Select Suitable SNPs/QC

Custom Scripts

SNP Assay Design

Eliminate Null Alleles

Experimental Crosses / Training Panel

Independent Validation

Final Panel Selection

Xelect Pipeline

[Home](#)[Projects](#)[FISHBOOST](#)

# FISHBOOST

**Improving European aquaculture by advancing selective breeding to the next level for the six main finfish species**

Breeding and genetics

The European research project FISHBOOST will advance European aquaculture to the next level. Nofima is coordinating this FP7 project.

Time:

1. February 2014 – 31. January 2019

<https://nofima.no/en/prosjekt/fishboost-2/>



# AquAdvantage salmon

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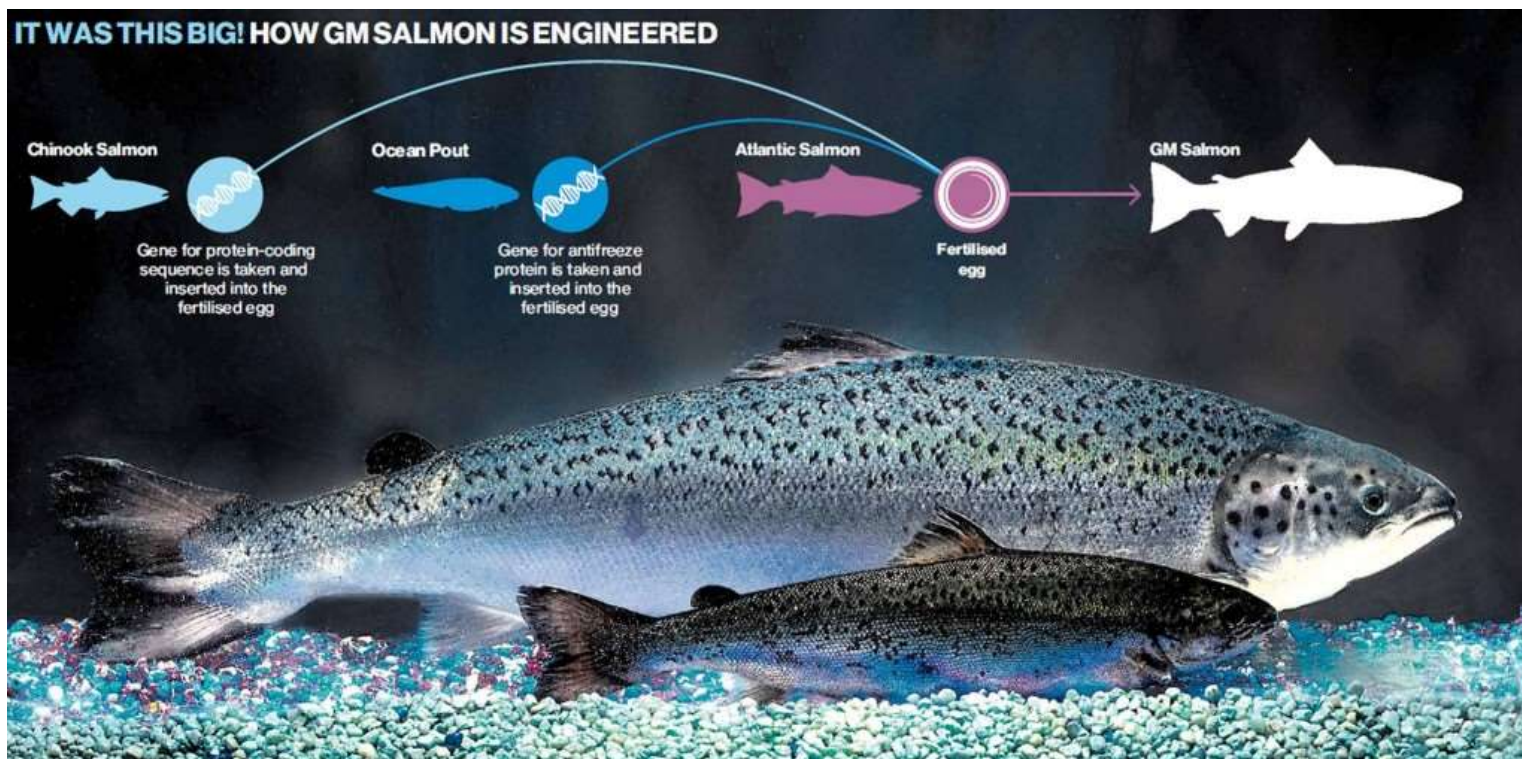
- ▶ Ген гормона роста кижуча с промотором от бельдюги (1 ген из 40,000, остальные – гены лосося)
- ▶ Растет круглогодично, товарного размера достигает за 18 мес. (обычный – за 3 года)
- ▶ Разрешен к выращиванию и продаже пока только в Канаде и только в УЗВ



- ▶ 100% самки, триплоид
  - ▶ Чтобы вывести GM сорт на рынок – нужно в среднем 13 лет и 130 млн.\$
-



# AquAdvantage salmon

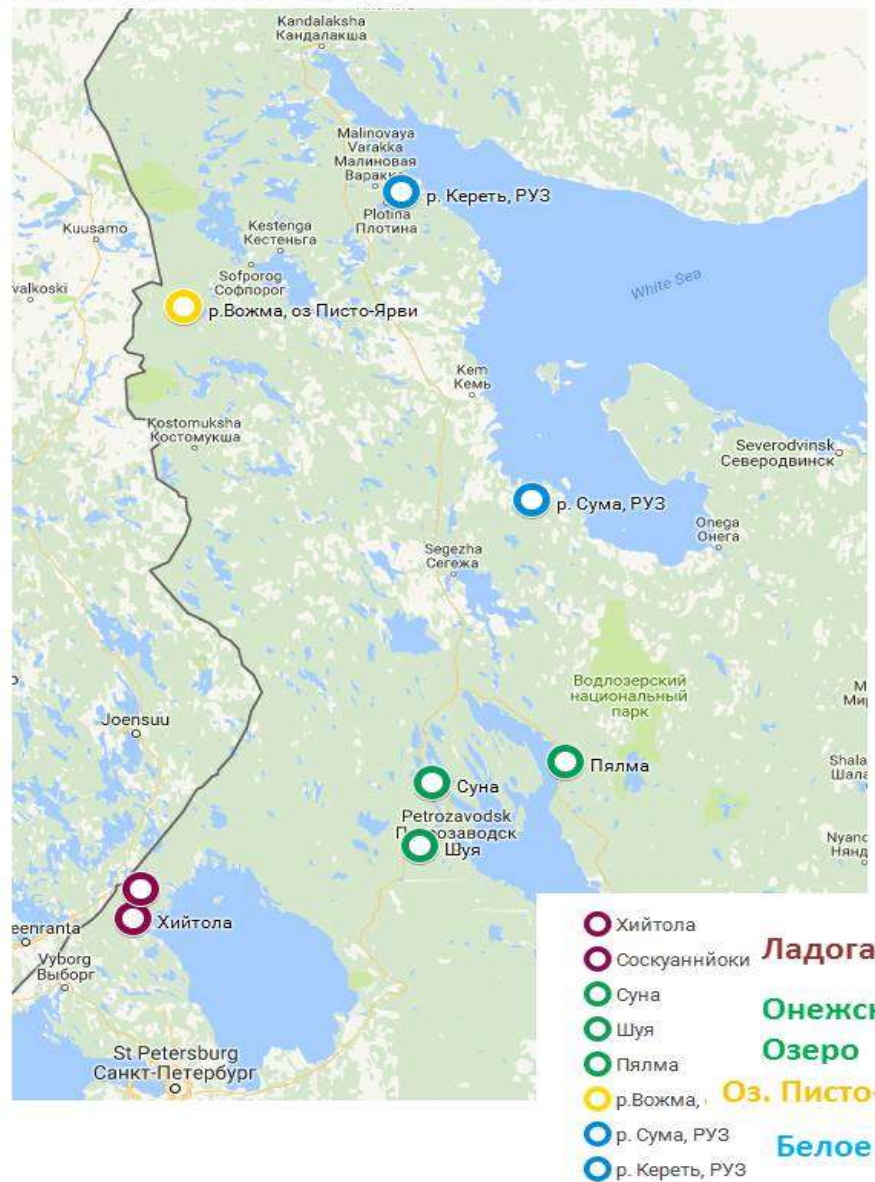


**AquAdvantage salmon** is a [genetically modified](#) (GM) [Atlantic salmon](#) developed by [AquaBounty Technologies](#). A [growth hormone](#)-regulating [gene](#) from a Pacific [Chinook salmon](#), with a [promoter](#) from an [ocean pout](#), was added to the Atlantic salmon's 40,000 genes. This gene enables it to grow year-round instead of only during spring and summer. The purpose of the modifications is to increase the speed at which the fish grows without affecting its ultimate size or other qualities. The fish grows to market size in 16 to 18 months rather than three years. The latter figure refers to varieties whose growth rate has already been improved by 2:1 as a result of traditional [selective breeding](#).



# Озерный лосось и морской лосось (семга)

Карта сбора *Salmo salar* для геномного секвенирования  
с указанием популяционной принадлежности



Keret_A12	WGS	White sea
Keret_B12	WGS	White sea
Keret_F12	WGS	White sea
Keret_H11	WGS	White sea
Suma_A10	exome	White sea
Suma_B10	exome	White sea
Suma_C10	exome	White sea
Suma_D10	exome	White sea
Suma_G10	exome	White sea
Hiitola_A01	exome	Landlocked
Hiitola_B01	exome	Landlocked
Hiitola_C02	exome	Landlocked
Hiitola_D02	exome	Landlocked
Hiitola_E02	exome	Landlocked
Palma_C06	exome	Landlocked
Palma_E06	exome	Landlocked
Palma_E07	exome	Landlocked
Palma_F06	exome	Landlocked
Palma_F07	exome	Landlocked
Shuya_A05	exome	Landlocked
Shuya_A06	exome	Landlocked
Shuya_B05	exome	Landlocked
Shuya_C05	exome	Landlocked
Soskuannjoki_A04	exome	Landlocked
Soskuannjoki_B04	exome	Landlocked
Soskuannjoki_D03	exome	Landlocked
Soskuannjoki_D04	exome	Landlocked
Soskuannjoki_E03	exome	Landlocked
Vozhma_A08	exome	Landlocked
Vozhma_A09	exome	Landlocked
Vozhma_B09	exome	Landlocked
Vozhma_D08	exome	Landlocked
Vozhma_F09	exome	Landlocked



# Геномное (экзомное) секвенирование на Illumina HiSeq4000

- Отсеквенировано 33 особи из 7 выборок
- Получено
  - WGS – (4экз) 822 млн 100 bp pair-end reads,
  - Exome (29 экз) 1,260 млн чтений
- Число маркеров ( $p < 0,2$  в море,  $p > 0,8$  в одном из озер) – 5190
- Число несинонимичных SNP ~ 2500
- В системно-биологический анализ включено ~500 генов с NS мутациями



# Аннотация всех 5190 SNPs

Chr	Pos	State	Ref	Hiitol	Palma	Shuya	Sosku	Gene	Func
ssa01	307098	nonsynony	A		C			LOC106566220	forkhead box protein 11c-like
ssa01	2307157	synonymo	C		T				
ssa01	2581798	synonymo	C	T	T			LOC106586969	coiled-coil domain-containing protein 177-like%2C transcript variant X1LOC
ssa01	2581800	synonymo	G	T	T			LOC106586969	coiled-coil domain-containing protein 177-like%2C transcript variant X1LOC
ssa01	2582578	nonsynony	C	G	G			LOC106586969	coiled-coil domain-containing protein 177-like%2C transcript variant X1LOC
ssa01	3008905	synonymo	A				G	LOC106594936	nucleolar and spindle-associated protein 1-like%2C transcript variant X2LOC
ssa01	5581773	nonsynony	T		C	C	C	xdh	xanthine dehydrogenase
ssa01	6696243	synonymo	T			C		LOC106606907	zinc finger protein 239-like%2C transcript variant X1
ssa01	6731492	synonymo	G			T		LOC106607016	zinc finger protein 11-like%2C transcript variant X2LOC106607016
ssa01	6731671	nonsynony	A			C		LOC106607016	zinc finger protein 11-like%2C transcript variant X2LOC106607016
ssa01	6732370	nonsynony	T			C		LOC106607016	zinc finger protein 11-like%2C transcript variant X2LOC106607016
ssa01	8476259	synonymo	G	A				klhdc2	kelch domain containing 2%2C transcript variant X1klhdc2
ssa01	8479791	nonsynony	C	A				klhdc2	kelch domain containing 2%2C transcript variant X1klhdc2
ssa01	10977344	synonymo	C			T	T	LOC106562352	lysine-specific histone demethylase 1A-like%2C transcript variant X3LOC10
ssa01	11530706	synonymo	C		T	T		LOC106563602	SH3 and cysteine-rich domain-containing protein-like%2C transcript variant
ssa01	11628003	synonymo	C			T		LOC106564204	saposin-C-like%2C transcript variant X2LOC106564204
ssa01	11790200	nonsynony	T	C			C	LOC106564129	uncharacterized LOC106564129
ssa01	11790828	synonymo	C	A			A	LOC106564129	uncharacterized LOC106564129
ssa01	12271151	synonymo	T			A		LOC106565104	interphotoreceptor matrix proteoglycan 1-like%2C transcript variant X4LOC
ssa01	12333568	nonsynony	C		T			LOC106565365	unconventional myosin-VI-like%2C transcript variant X1LOC106565365
ssa01	13933568	synonymo	G				T	LOC106566340	kinase D-interacting substrate of 220 kDa-like%2C transcript variant X4LOC1
ssa01	14568895	nonsynony	C			G		LOC106567335	zinc finger protein 395-like%2C transcript variant X8LOC106567335
ssa01	14798429	synonymo	C				T	hnrnpu	heterogeneous nuclear ribonucleoprotein U (scaffold attachment factor A):
ssa01	15147387	synonymo	G		A		A	LOC106569575	consortin-like%2C transcript variant X2LOC106569575
ssa01	15150046	nonsynony	T				C	LOC106569575	consortin-like%2C transcript variant X2LOC106569575
ssa01	15171772	nonsynony	A			G	G	LOC106569909	saccharopine dehydrogenase-like oxidoreductase

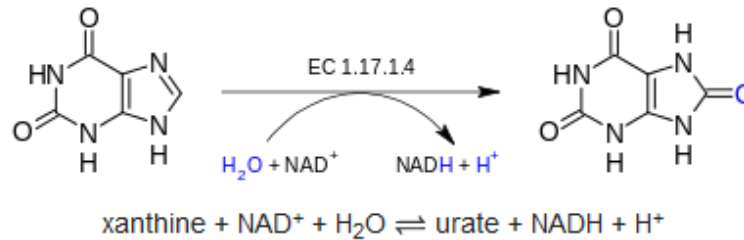
# Xanthine dehydrogenase

## ssa01:5581773 T->C

Function [\[ edit \]](#)

Xanthine dehydrogenase belongs to the group of [molybdenum-containing hydroxylases](#) involved in the oxidative metabolism of [purines](#). The enzyme is a homodimer. Xanthine dehydrogenase can be converted to [xanthine oxidase](#) by reversible sulfhydryl oxidation or by irreversible proteolytic modification.<sup>[5]</sup>

Xanthine dehydrogenase [catalyzes](#) the following [chemical reaction](#):



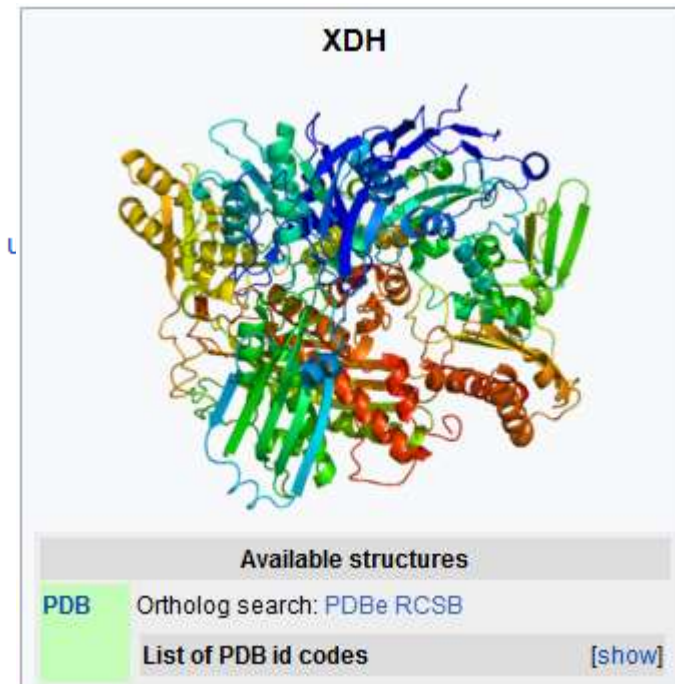
The three [substrates](#) of this enzyme are [xanthine](#), [NAD<sup>+</sup>](#), and [H<sub>2</sub>O](#), whereas its three [products](#) are [urate](#), [NADH](#), and [H<sup>+</sup>](#). This enzyme participates in [purine metabolism](#).



Comparative Biochemistry and Physiology Part B:

Comparative Biochemistry

Volume 54, Issue 1, 1976, Pages 117-119

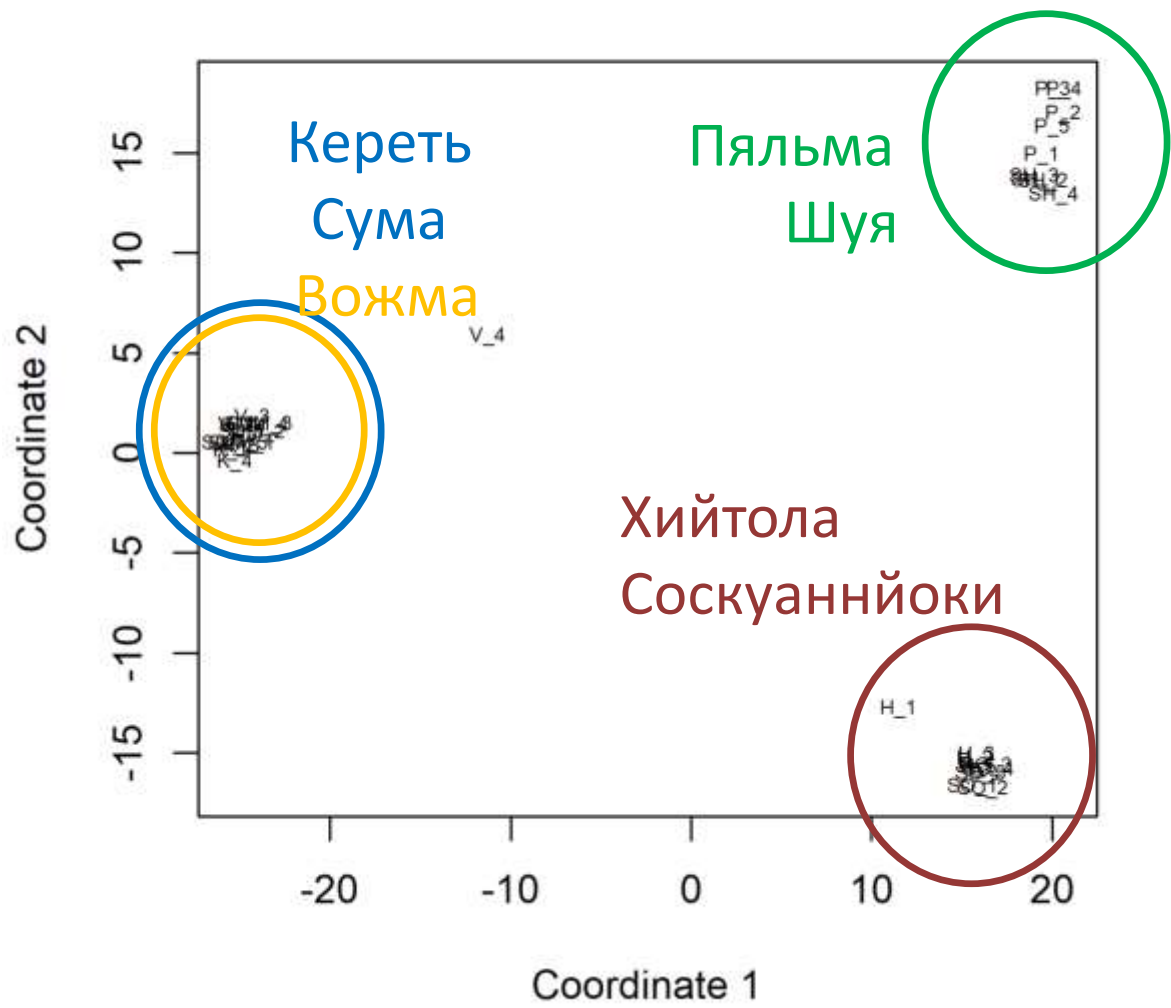


Urate oxidase and xanthine dehydrogenase activities in liver extracts from fish caught in Irish waters



# Распределение образцов в многомерном шкалировании

MetricMDS



# Gene Set Enrichment Analysis

Представленность набора генов по функциональным категориям, метаболическим и регуляторным каскадам



Molecular Signatures Database v6.0



## Overview

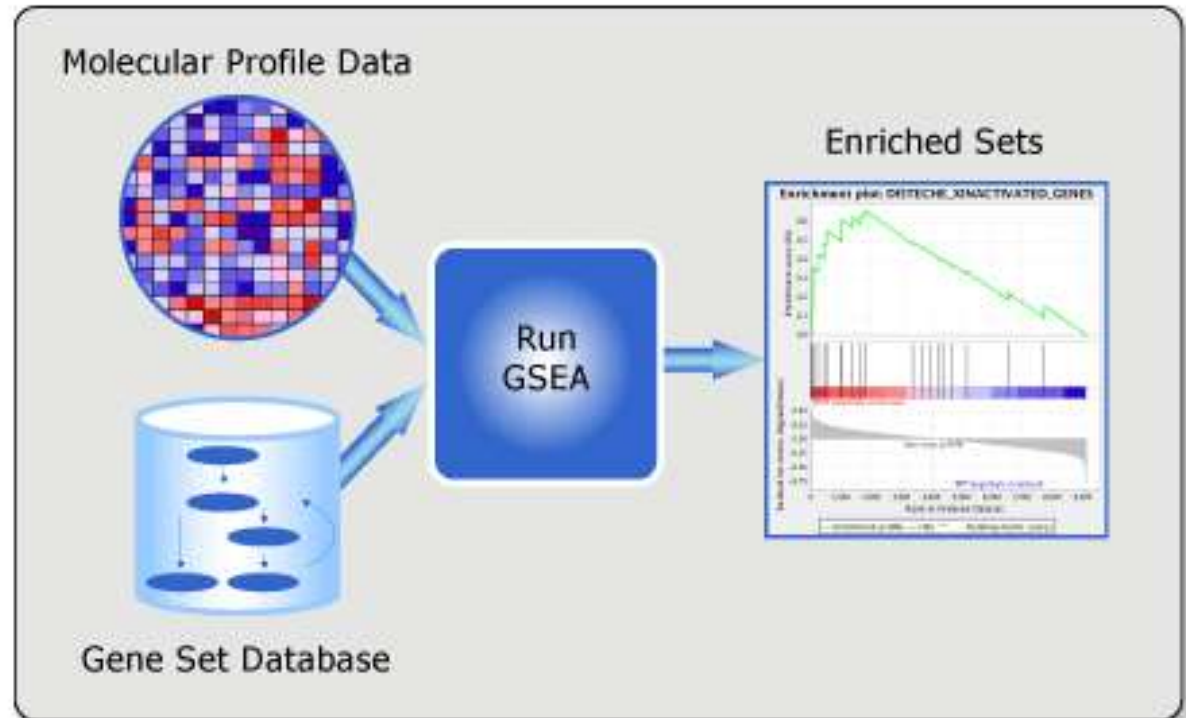
The Molecular Signatures Database (MSigDB) is a collection of annotated gene sets for use with GSEA software. From this web site, you can

- ▶ **Search** for gene sets by keyword.
- ▶ **Browse** gene sets by name or collection.
- ▶ **Examine** a gene set and its annotations. See, for example, the [GO\\_NOTCH\\_SIGNALING\\_PATHWAY](#) gene set page.
- ▶ **Download** gene sets.
- ▶ **Investigate** gene sets:
  - ▶ **Compute overlaps** between your gene set and gene sets in MSigDB.

## Collections

The MSigDB gene sets are divided into 8 major collections:

**hallmark gene sets** are coherently expressed







# GO (GSEA) analysis

# Genes in Gene Set (K)	Description	# Genes in Overlap (k)	k/K	p-value	FDR q-value
275	Ensemble of genes encoding core extracellular matrix including ECM	28	0.1018	5.68E-15	7.83E-12
200	Genes important for mitotic spindle assembly.	23	0.1150	1.15E-13	6.87E-11
1028	Ensemble of genes encoding extracellular matrix and extracellular r	52	0.0506	1.49E-13	6.87E-11
196	Genes encoding structural ECM glycoproteins	22	0.1122	6.45E-13	2.22E-10
396	Genes involved in Developmental Biology	28	0.0707	4.16E-11	1.15E-8
113	Genes involved in Signaling by Rho GTPases	15	0.1327	2.79E-10	6.42E-8
251	Genes involved in Axon guidance	21	0.0837	5.56E-10	1.09E-7
200	Genes defining late response to estrogen.	18	0.0900	2.97E-9	5.11E-7
46	Regulation of RhoA activity	9	0.1957	3.27E-8	5.01E-6
40	Genes encoding structural components of basement membranes	8	0.2000	1.6E-7	2.21E-5
413	Genes involved in Transmembrane transport of small molecules	23	0.0557	1.84E-7	2.31E-5
74	Genes involved in G alpha (12/13) signalling events	10	0.1351	2.23E-7	2.56E-5
933	Genes involved in Immune System	37	0.0397	2.79E-7	2.86E-5
43	Genes involved in NUAGE signals death through JNK	8	0.1860	2.9E-7	2.86E-5
217	Genes involved in Signalling by NGF	16	0.0737	3.51E-7	3.23E-5
200	Genes defining early response to estrogen.	15	0.0750	6.53E-7	5.63E-5
84	ECM-receptor interaction	10	0.1190	7.46E-7	6.05E-5
66	Beta1 integrin cell surface interactions	9	0.1364	8.34E-7	6.39E-5
328	Pathways in cancer	19	0.0579	1.18E-6	8.59E-5
39	Aurora B signaling	7	0.1795	2.1E-6	1.45E-4
478	Genes involved in Metabolism of lipids and lipoproteins	23	0.0481	2.27E-6	1.49E-4
200	Genes encoding cell cycle related targets of E2F transcription factors	14	0.0700	3.45E-6	2.16E-4
60	Genes involved in Cell death signalling via NUAGE, NRIF and NADE	8	0.1333	4.06E-6	2.43E-4
150	Genes involved in DNA repair.	12	0.0800	4.36E-6	2.51E-4
267	MAPK signaling pathway	16	0.0599	5.29E-6	2.92E-4
241	Genes involved in SLC-mediated transmembrane transport	15	0.0622	6.57E-6	3.48E-4
466	Genes involved in Hemostasis	21	0.0451	1.65E-5	8.45E-4



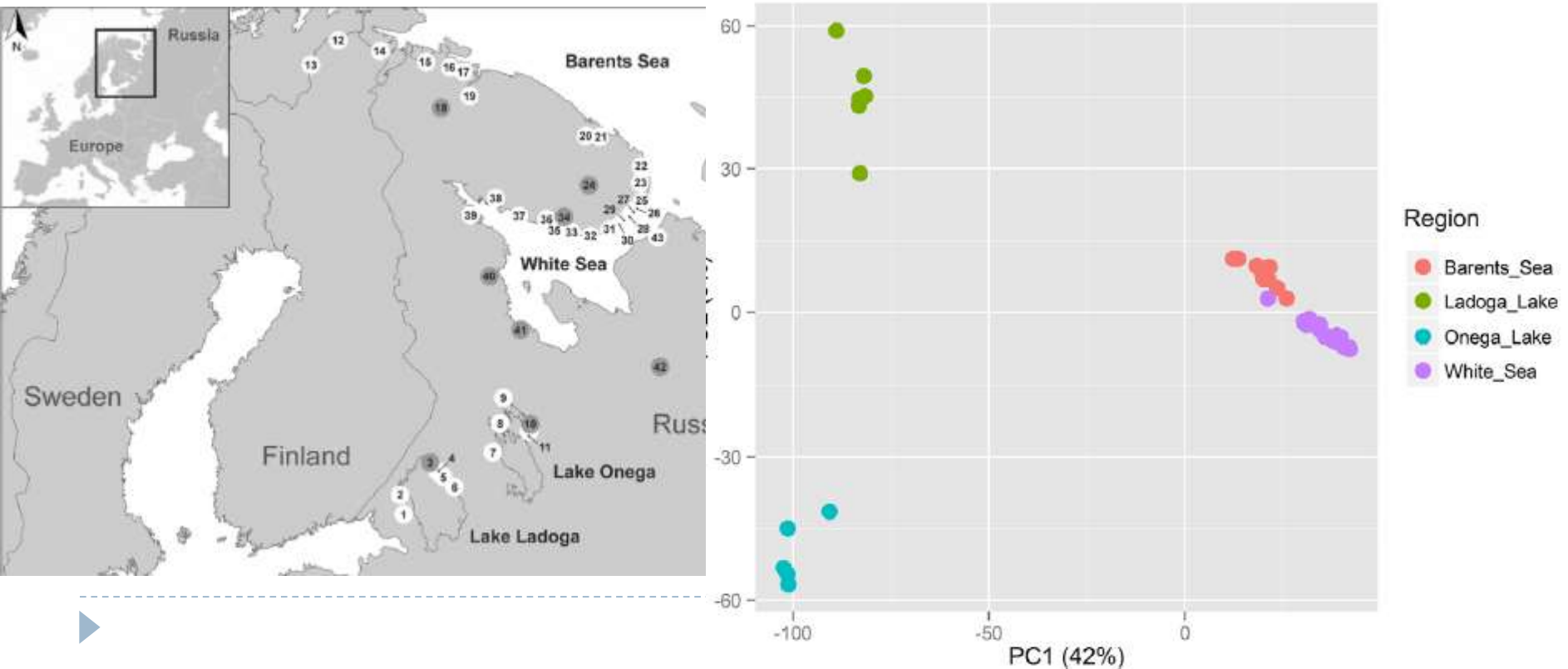
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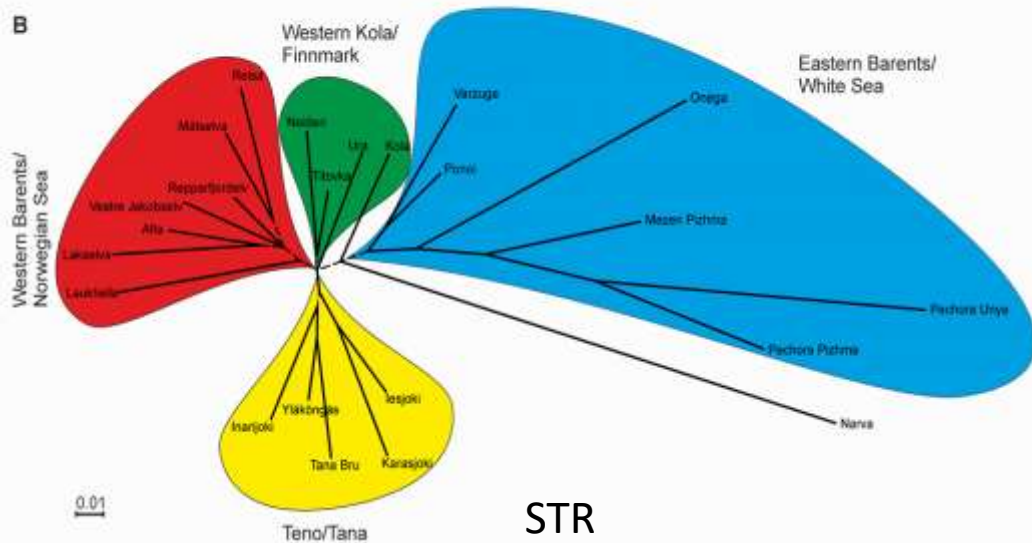
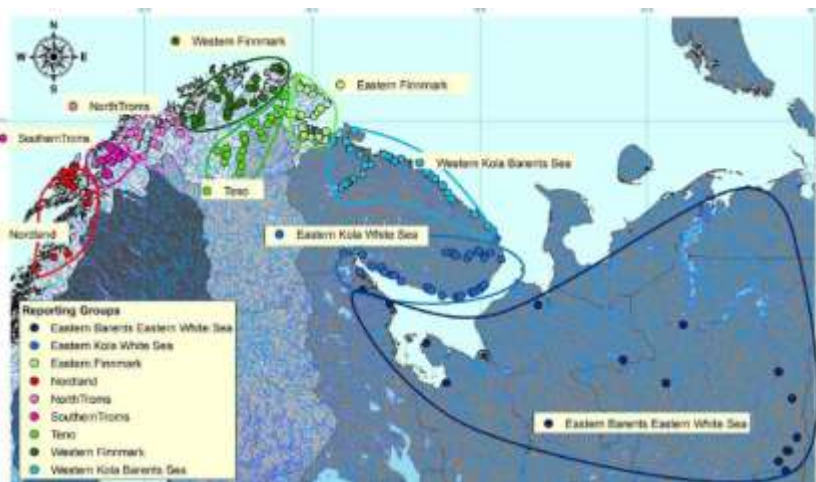
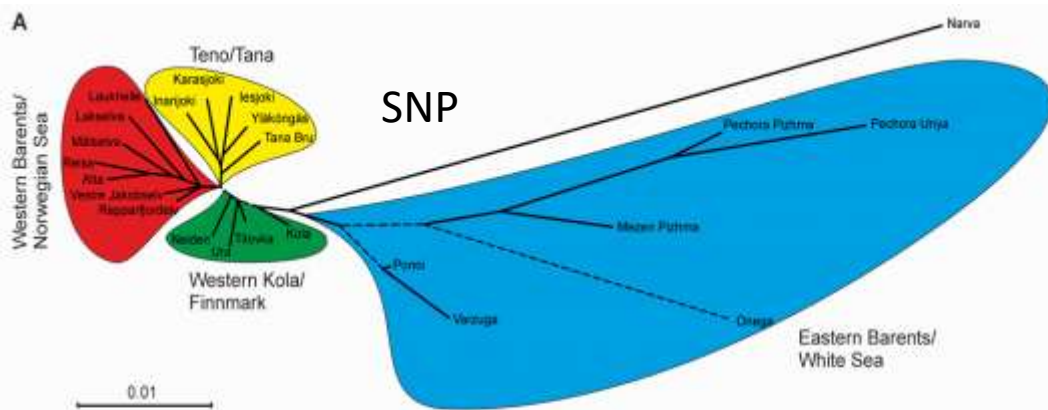
journal homepage: [www.elsevier.com/locate/margen](http://www.elsevier.com/locate/margen)

Research paper

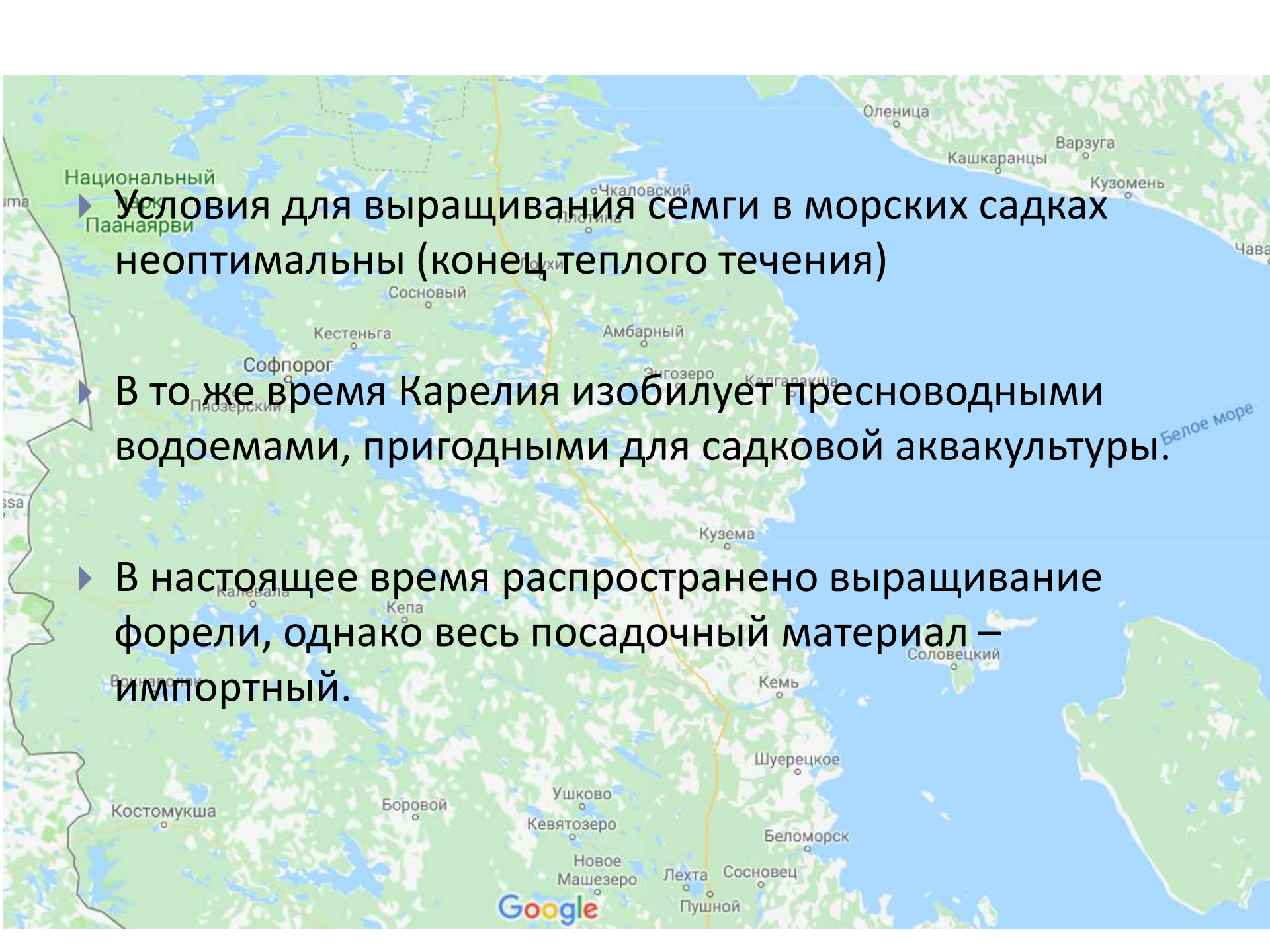
Genomic signatures of parasite-driven natural selection in north European Atlantic salmon (*Salmo salar*)Ksenia J. Zueva<sup>a</sup>, Jaakko Lumme<sup>b</sup>, Alexey E. Veselov<sup>c</sup>, Matthew P. Kent<sup>d</sup>, Craig R. Primmer<sup>a,e,f,\*</sup>



# Генетическая дифференциация семги



Дополнительное секвенирование балтийского лосося - Невский ЛРЗ

A satellite-style map of the Karelia region in Russia, showing a dense network of lakes and rivers. The map is overlaid with text and arrows. The text is in Russian and discusses salmon farming conditions. The map includes labels for various locations such as Оленица, Варзуга, Кашкаранцы, Кузомень, Чкаловский, Национальный парк Паанаярви, Сосновый, Кестеньга, Амбарный, Софпорог, Ангозеро, Кузема, Кемь, Шуерецкое, Ушково, Кевятозеро, Новое Машезеро, Лехта, Пушной, Сосновец, Беломорск, Костомукша, Боровой, Кепа, Калевала, Кузема, Соловецкий, and Чавань. The White Sea (Белое море) is visible on the right side. The Google logo is at the bottom center.

▶ Условия для выращивания семги в морских садках неоптимальны (конец теплого течения)

▶ В то же время Карелия изобилует пресноводными водоемами, пригодными для садковой аквакультуры.

▶ В настоящее время распространено выращивание форели, однако весь посадочный материал – импортный.



# «Карельский супер-лосось»

- Адаптации к пресной воде и климатическим условиям Карелии, устойчивость к некоторым заболеваниям – от озерного лосося
- Быстрый рост, высокая конверсия корма, стрессоустойчивость – от современных коммерческих линий семги
- Использование genome-assisted selection в сочетании с современными методами семейной селекции

Благодарю за внимание!

# Вопросы?

