UNIVERSITY OF STIRLING

Universidad Complutense De Madrid

nutreco AQUACULTURE RESEARCH CENTRE

CRIPESA

Cria de Pescado SA

Cloning and functional analysis of fish Peroxisome Proliferator-Activated Receptors: The transcriptional control of lipid metabolism in farmed fish species (fPPARs)

EU Fifth Framework Q5RS-2000-30360

PARTICIPANTS

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- 2. University of Stirling-Institute of Aquaculture (UK).
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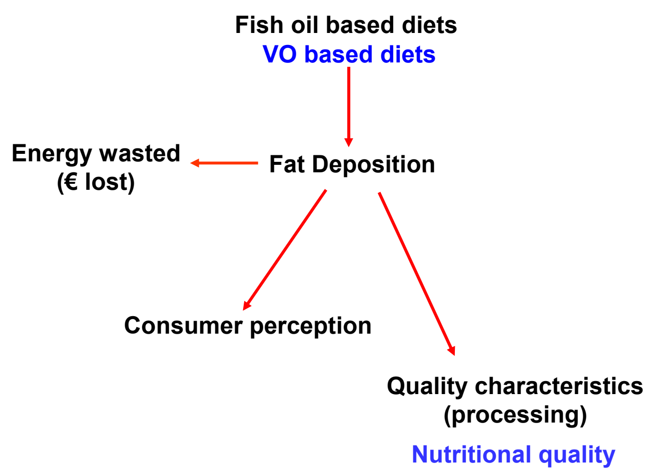
- 4. Nutreco Aquaculture Research Centre (ARC, Norway).
- 5. Cria de Pescado (Spain).

Fatty acid metabolism-associated problems in aquaculture



Need a better understanding of underlying physiology

Peroxisome proliferator-activated receptors (PPARs)

Ligand-induced Transcription factors

- •Activated by PUFA and their eicosanoid derivatives (fatty acid sensors)
- •Functions in lipid and carbohydrate metabolism, inflammation, cell cycle and differentiation
- •Discovered in 1990, to date >3000 publications

Three isotypes in mammals, birds, amphibians

α	β/δ	γ
Peroxisomal and mitochondrial fatty acid β-oxidation. Liver, muscle.	Widespread regulator of fat burning. Ubiquitous.	Fat accumulation/ Adipogenesis. Adipose tissue, spleen.

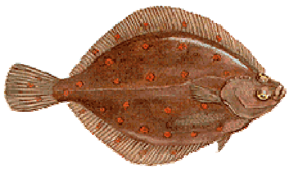
Questions:

- **Do fish have PPARs?**
- **Functional properties of PPARs in fish (expression, DNA and ligand binding, transactivation), i.e. the role of PPARs in fatty acid metabolism in fish?**

Aim:

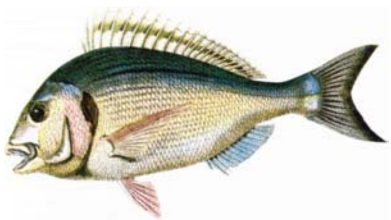
- **Manipulate fish fatty acid metabolism *via* PPARs.**

Looked for PPARs in:

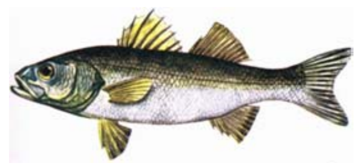


Plaice (Pleuronectes platessa)

Atlantic salmon (Salmo salar)



Sea bream (Sparus aurata)



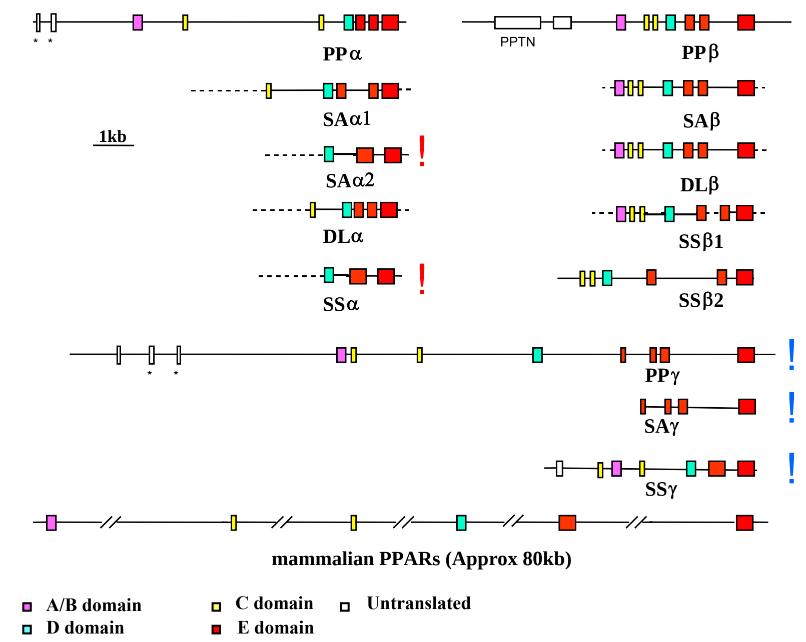
Sea bass (Dicentrarchus labrax)

Found:

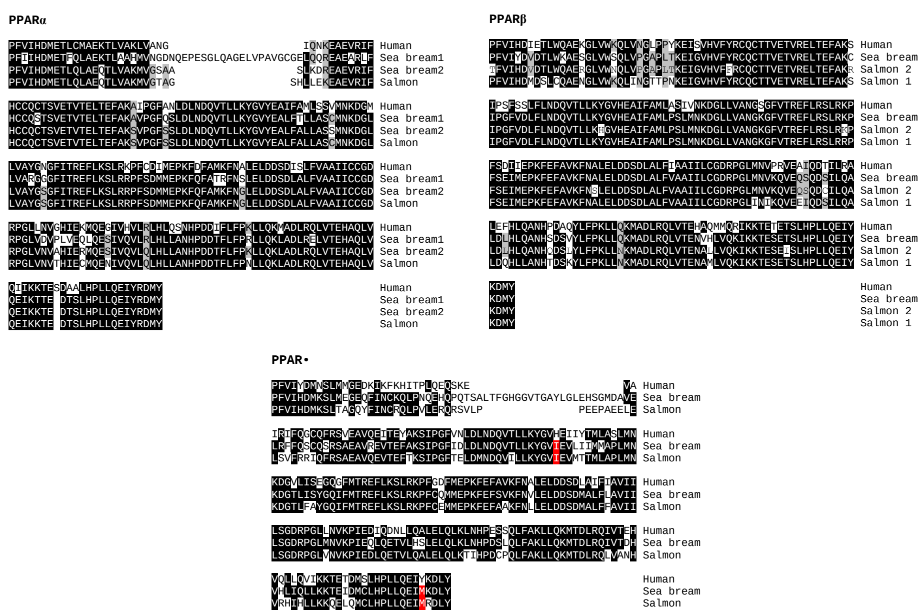
- **Genes and corresponding cDNAs encoding 3 distinct PPAR isotypes in plaice and sea bass.**
- **In sea bream, 2 PPARα isoforms, each encoded by a distinct gene, were identified in addition to the PPAR β and γ isotypes.**
- **In Atlantic salmon, 2 PPARβ isoforms, each encoded by a distinct gene, were identified in addition to the PPARα and γ isotypes.**

=> More complex level of PPAR isotype variety in fish than in mammals

Fish PPAR genomic organization



Alignment of the Ligand Binding Domain of PPARs



Conclusions from the molecular characterization of the fish PPARs

Likely that PPARα1 and β fulfill the same functions in marine fish as in mammals, i.e. important regulators of fatty acid catabolism in fish.

Questions remaining:

- What does PPARγ do?
- PPARα2?

Nutritional stimuli and gene expression

- Qualitative aspects of diet and gene expression
  - 6 experimental diets tested in sea bream and Atlantic salmon (FO replacement, CLA supplementation)
  - PPAR, CPT I, ELO, and DES gene expression
- Effects of fasting/feeding on gene expression in sea bream.
  - PPAR, CPT I, α-amylase gene expression

The Partners

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