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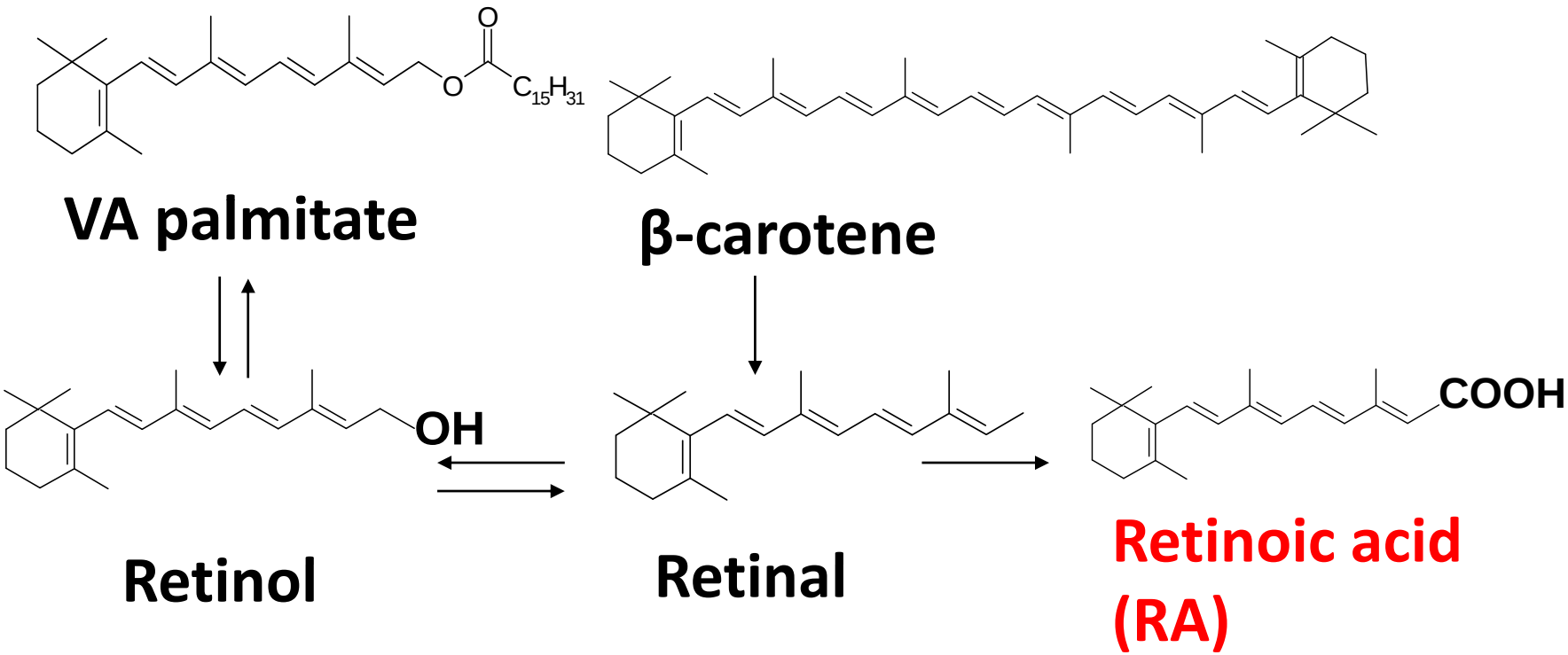
Analysis of skeletal deformity in fish using vitamin A-induced bone deformity model

Yutaka Haga (TUMSAT), Shao Jun Du (COMB), Shuichi Satoh (TUMSAT), Tomonari Kotani (Fukuyama Univ.), Hiroshi Fushimi (Fukuyama Univ.), Toshio Takeuchi (TUMSAT)

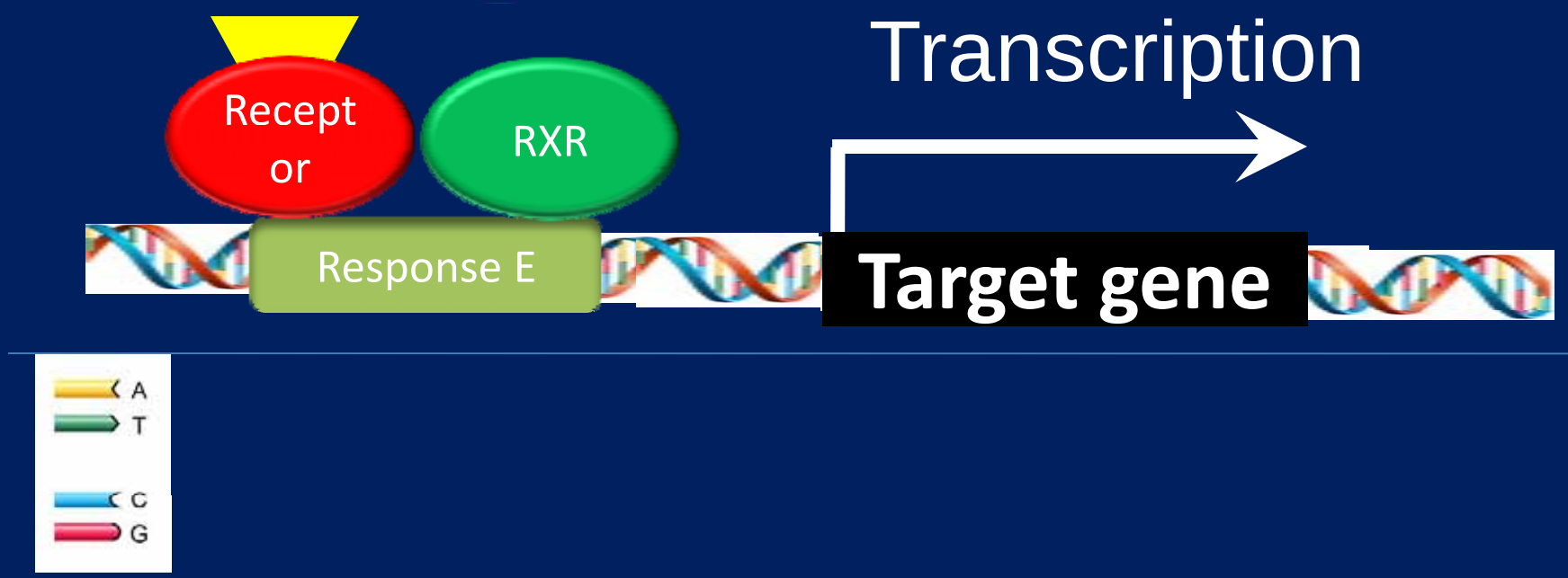
Contents of presentation

- Molecular mechanism of bone deformity induced by retinoid receptor agonist
- Vertebral deformity in fish larvae induced by retinoic acid

Metabolic pathway of vitamin A (VA)



Mode of action of nuclear receptors



Two classes of retinoid receptors

RAR :*Retinoic Acid Receptor*

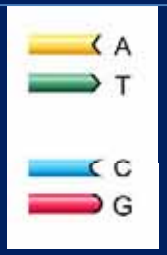
(*RAR* α, β, *and* γ)

RXR :*Retinoid X Receptor*

(*RXR*α, β, *and* γ)

Mode of action of RARs/RXRs

Q1. Which of RAR/RXR is important?



Q2. Which kind of gene is important?

QUESTION 1

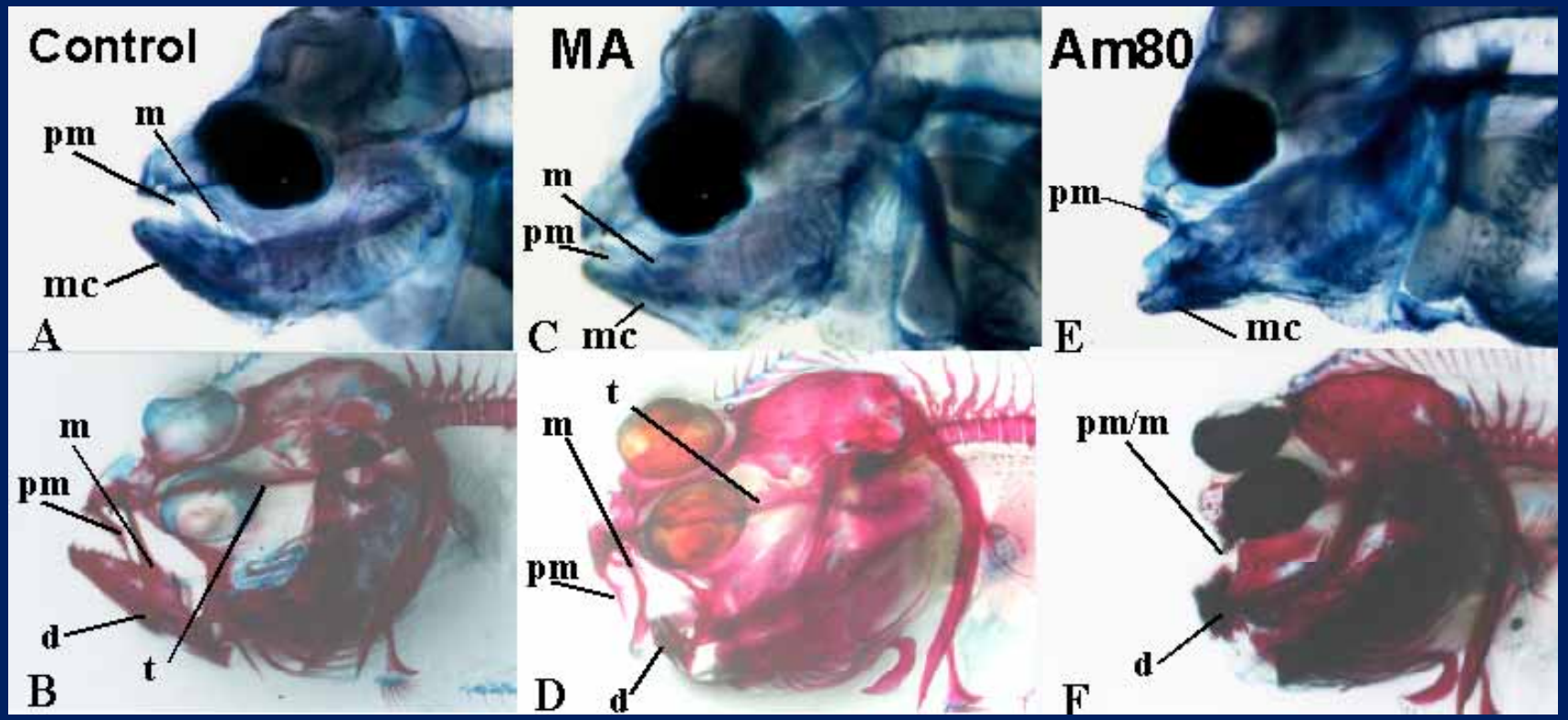
Which of RAR/RXR is responsible for bone deformity?

Binding affinity of retinoids used in the experiment

All-trans RA (atRA)	RAR
9-*cis*-RA (9cRA)	RAR/RXR
Am80	RAR
Methoprene acid (MA)	RXR

Lower jaw deformity in flounder at 9 and 58 dph

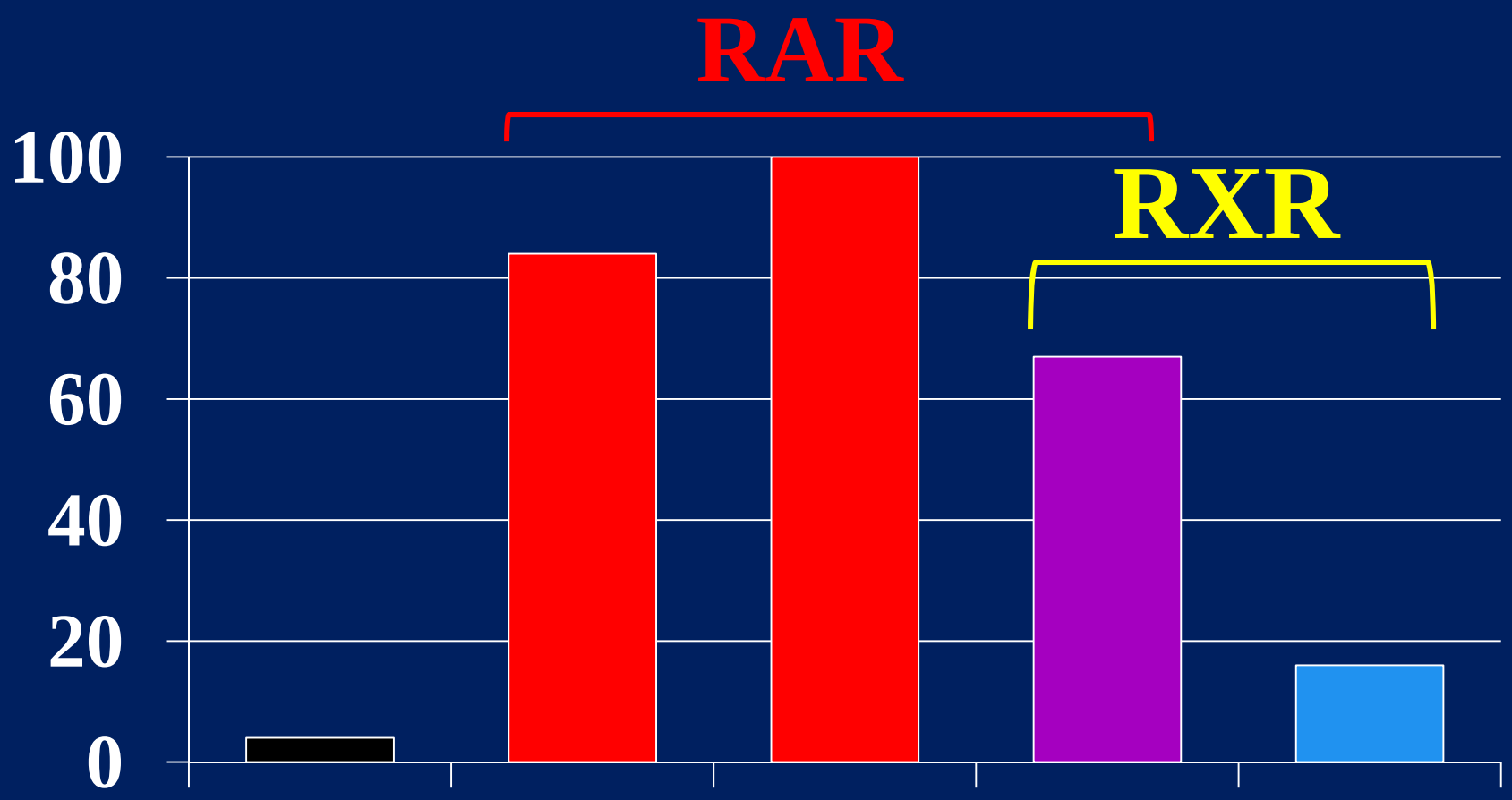
RXR ligand **RAR ligand**



9 dph (A, C, E) and 58 dph(B, D, F)

Haga *et al*. 2003

Jaw deformity in flounder by RAR/RXR ligands



Modified from Haga et al. 2002. & Haga et al. 2003.

Two classes of retinoid receptors

RAR :*Retinoic Acid Receptor*

(*RAR* α, β, *and* γ)

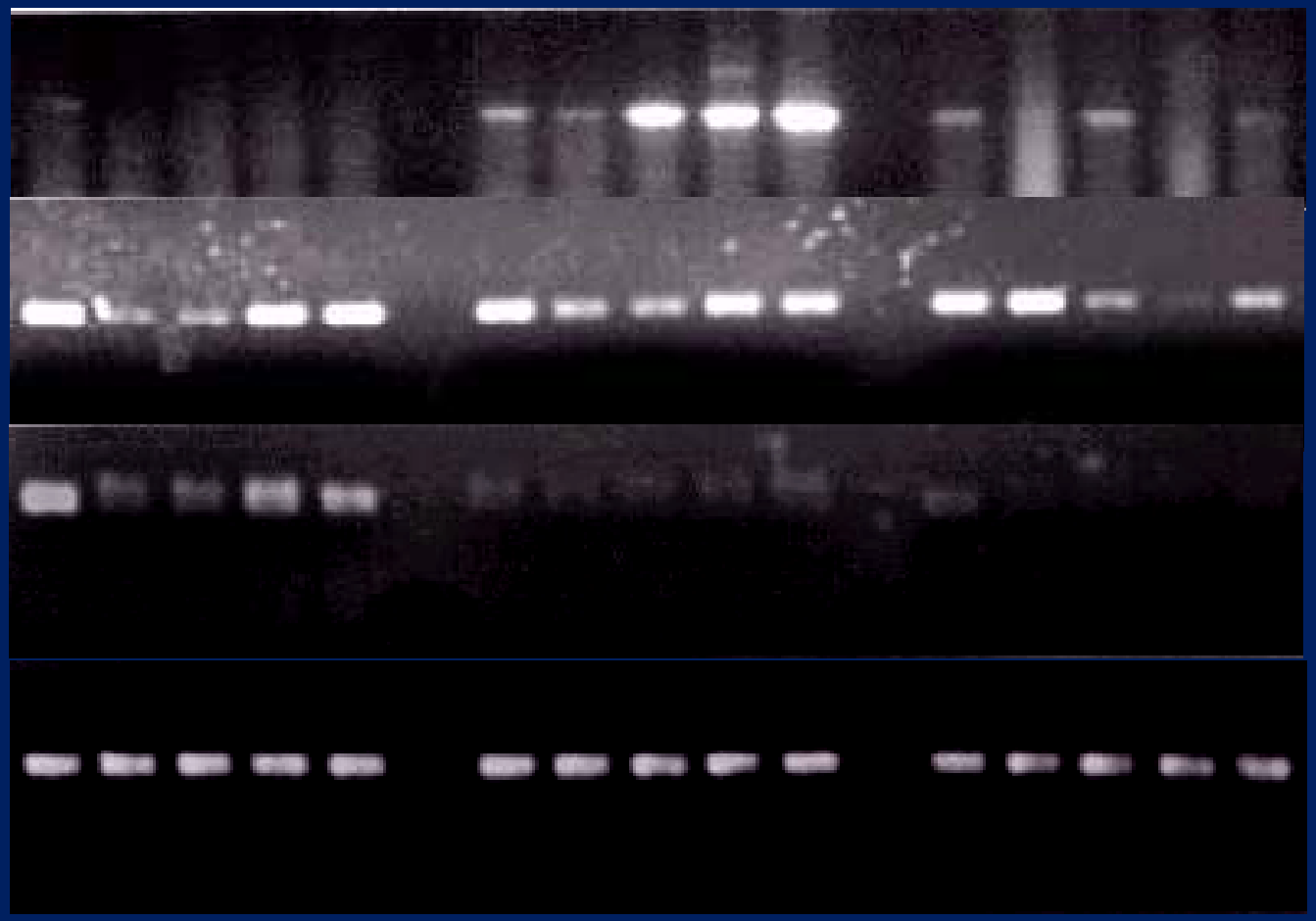
RXR :*Retinoid X Receptor*

(*RXR*α, β, *and* γ)

QUESTION 2

Which kind of the genes are downstream of RAR/RXR?

Expression of *RAR/RXR* and *patched* in the lower jaw

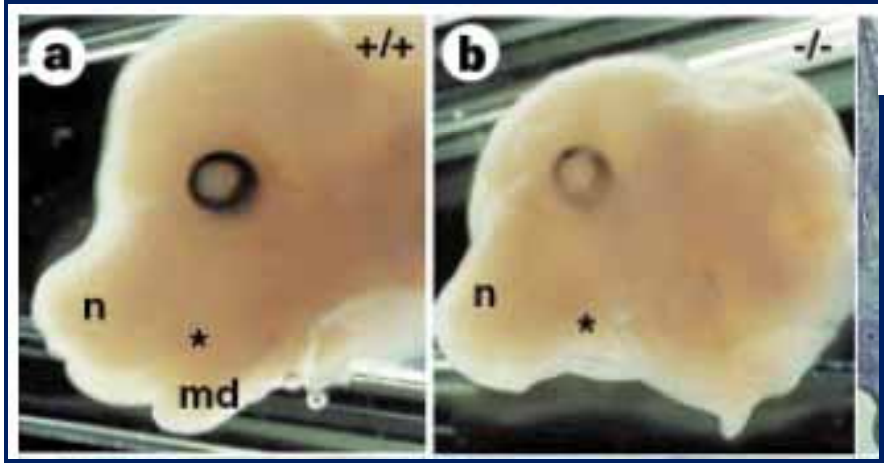


Expression of *pitx-2* in the jaw

Control

RAR ligand
atRA

RAR/RXR ligand
9*c*RA

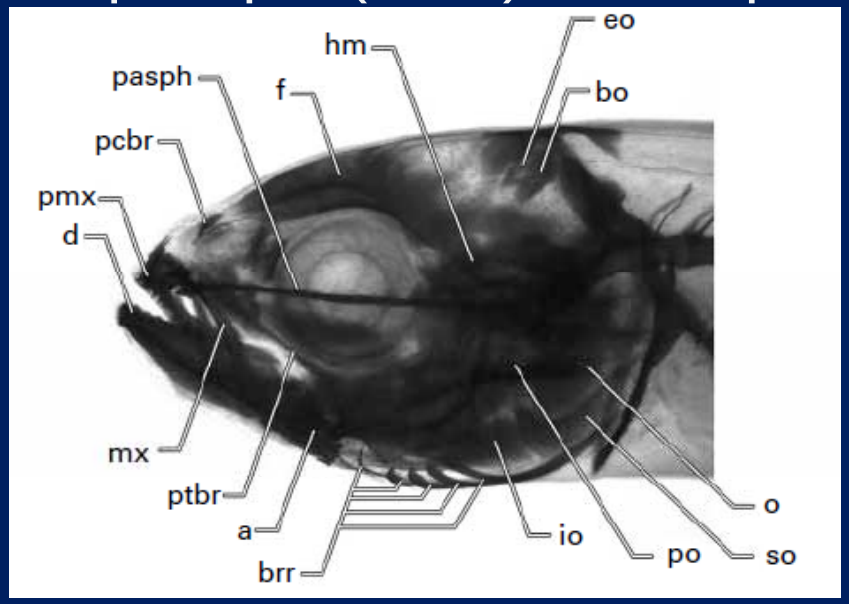


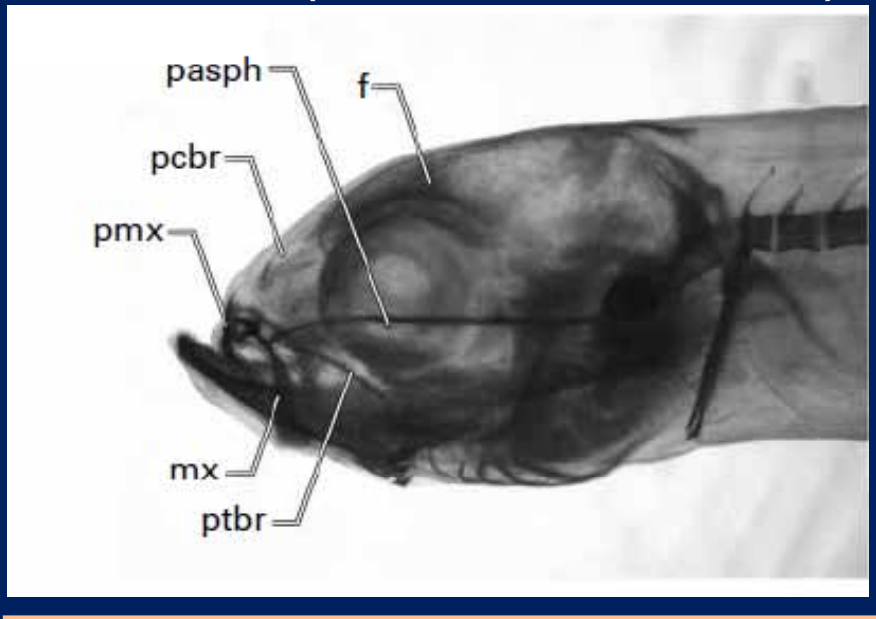
letters to nature

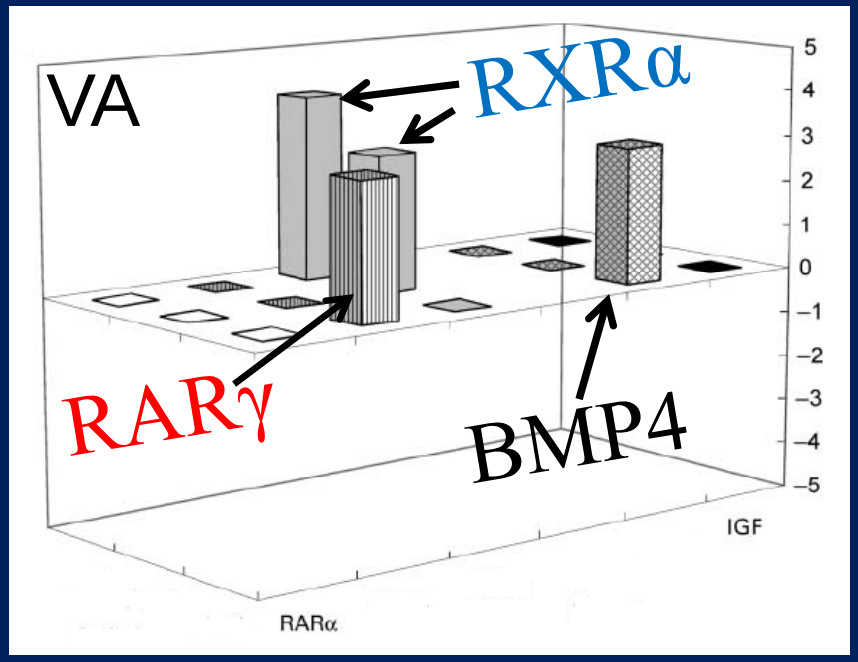
Function of Rieger syndrome gene in left–right asymmetry and craniofacial development

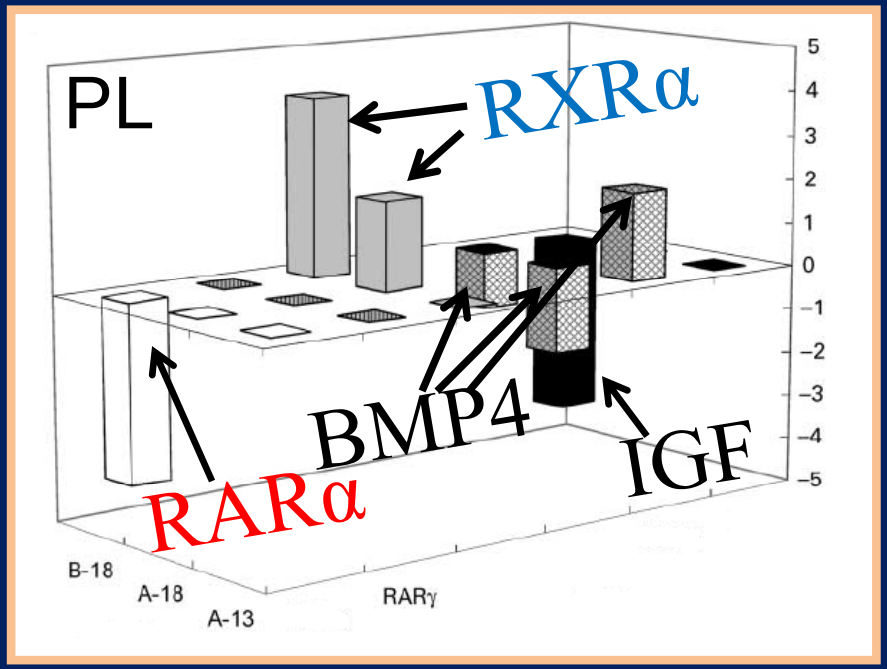
Mei-Fang Lu*, Carolyn Pressman†, Rex Dyer*, Randy L. Johnson† & James F. Martin*

Deformity and altered gene expression induced by VA and phospholipid (DHA) in European sea bass (Villeneuve et al. 2006)



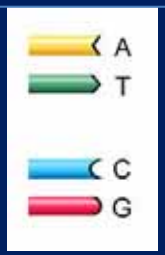






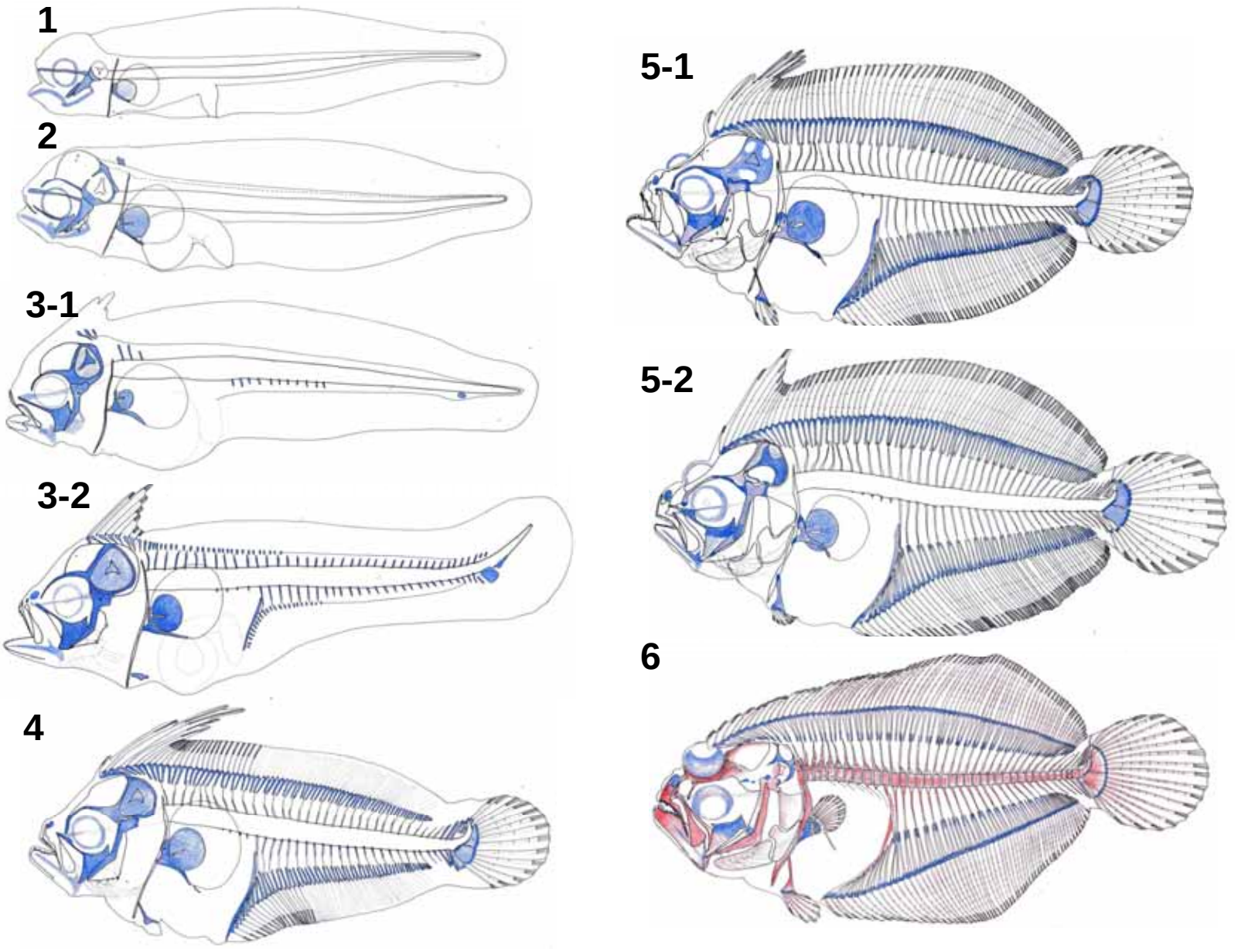
Mode of action of RARs/RXRs

Q1. Which of RAR/RXR is important?



Q2. Which kind of gene is important?

Stages and skeletal development of Japanese flounder (Fushimi)

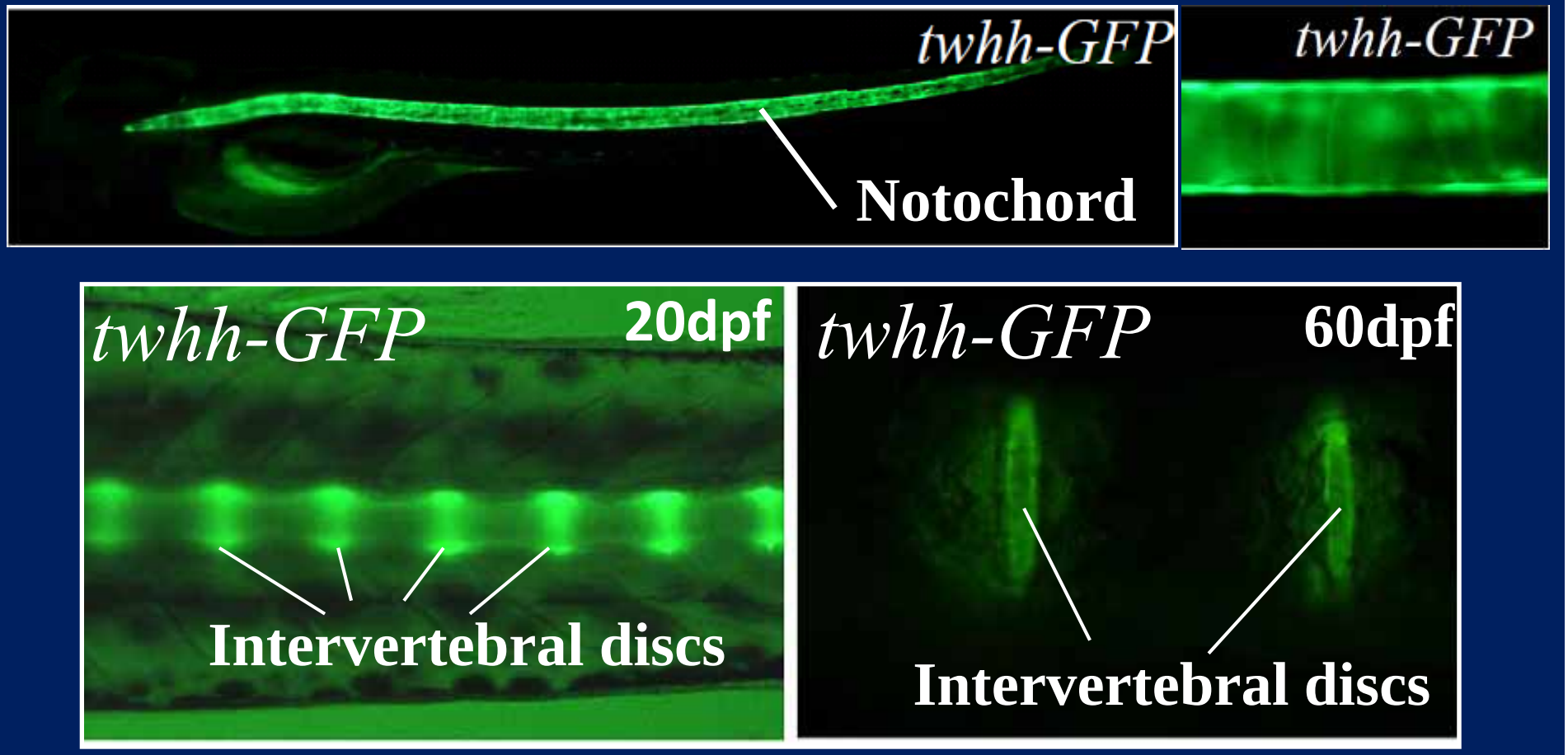


Loss of the intervertebral discs in fused vertebrae in red sea bream

How do intervertebral discs develop?

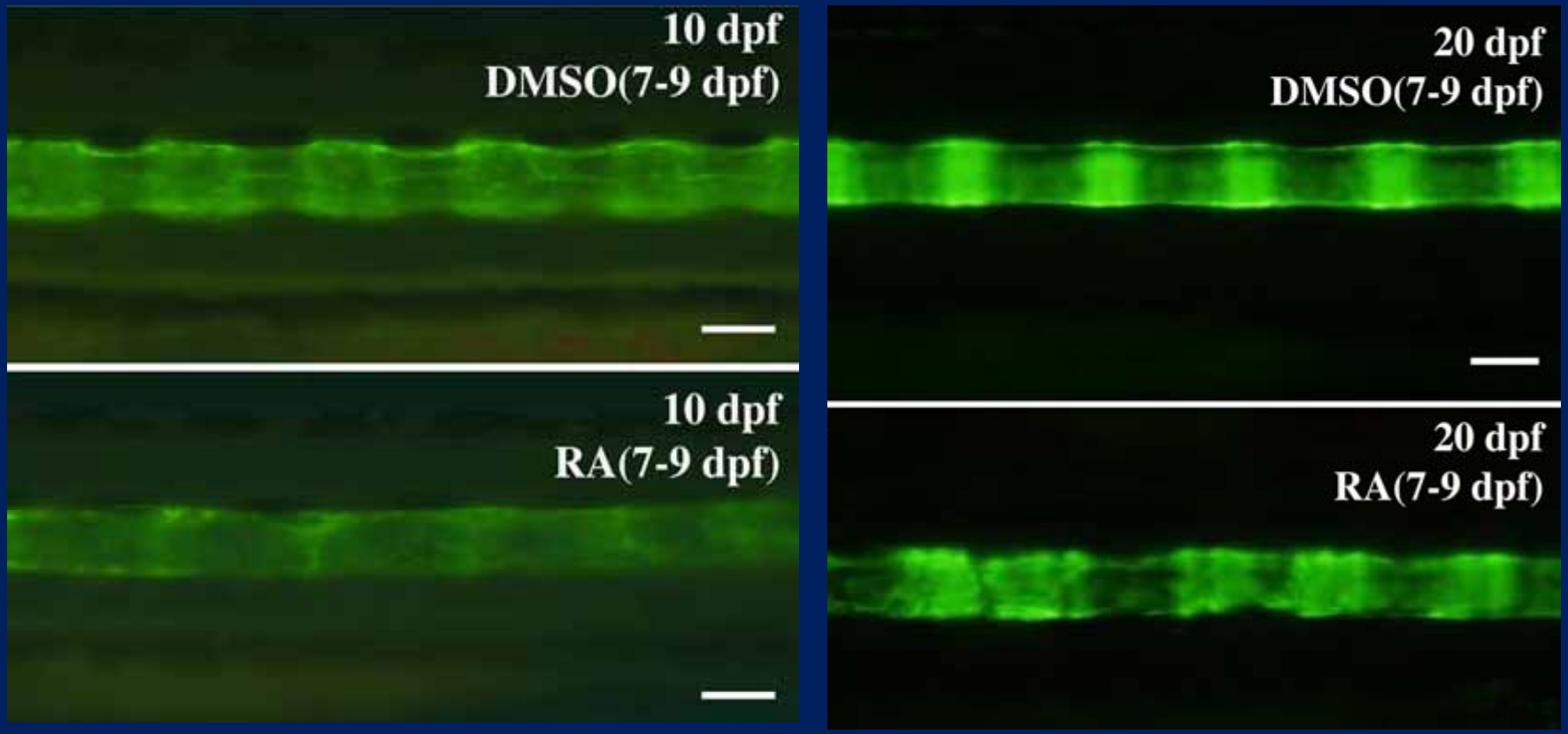
Production of zebrafish carrying GFP in intervertebral disc

GFP expression in *twhh*-GFP transgenic zebrafish



Haga *et al*. 2009. Transgenic Res. in press

RA induced disruption of GFP expression pattern in *twhh*-GFP zebrafish



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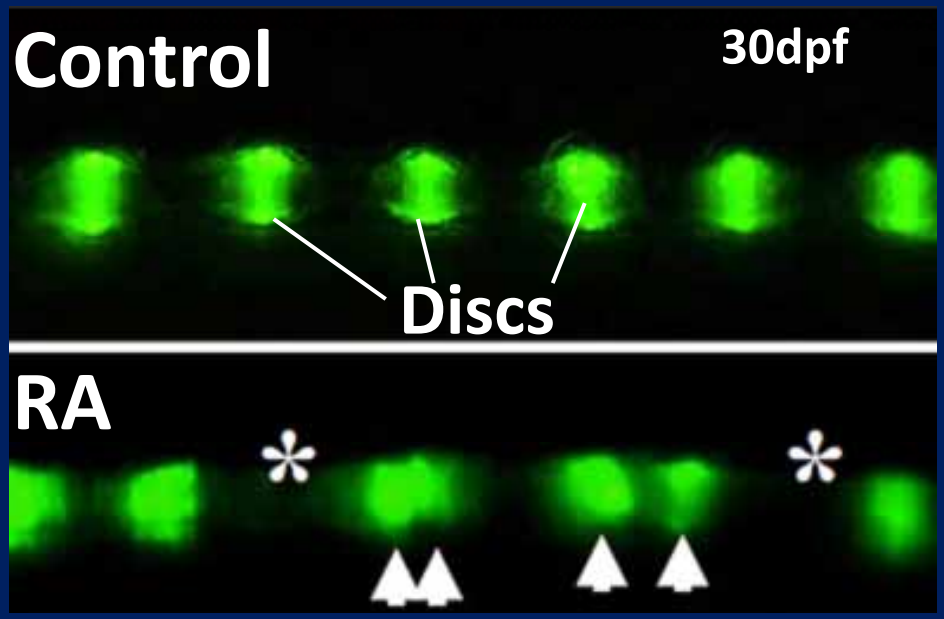
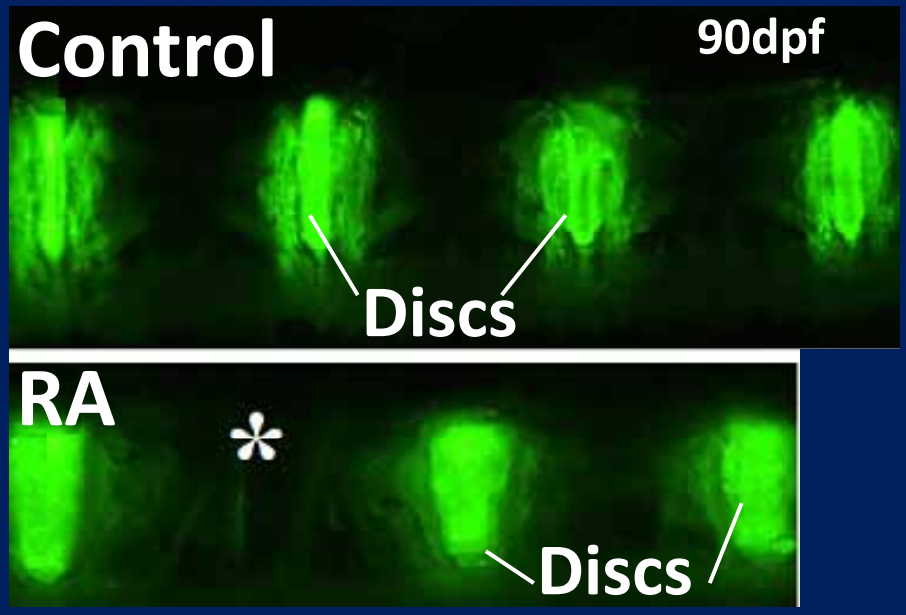
RA induced disruption of GFP expression pattern in twhh-GFP zebrafish





Haga *et al*. 2009. Transgenic Res. in press

Summary

- Altered gene expression was demonstrated in larvae showing high percentage of deformity
- *Twhh*-GFP transgenic zebrafish is useful resource to study intervertebral disc development and vertebral fusion in fish

Perspective

Process of production of cultured fish