# Vertebral fusion as a developmental, evolutionary and pathological process

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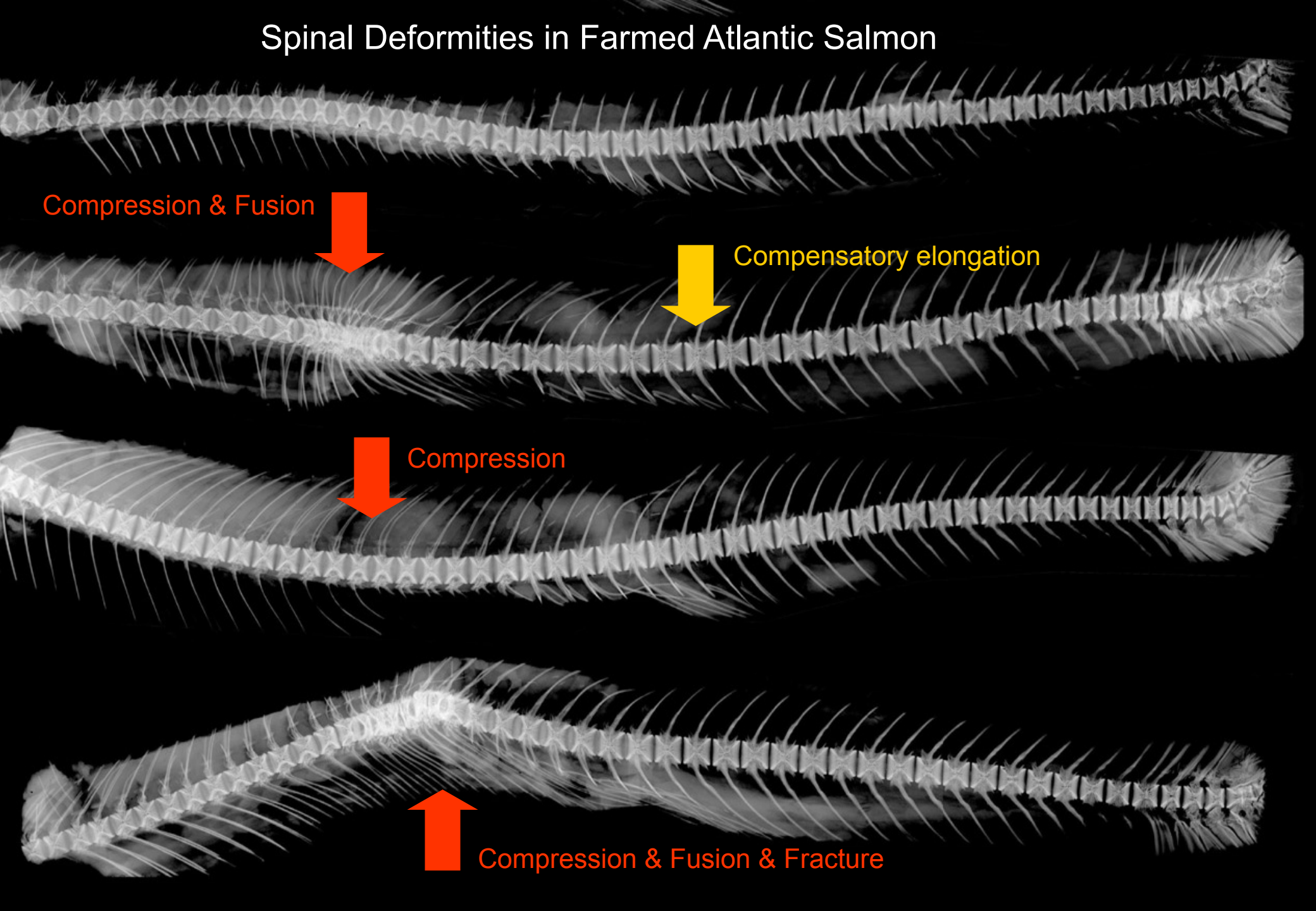
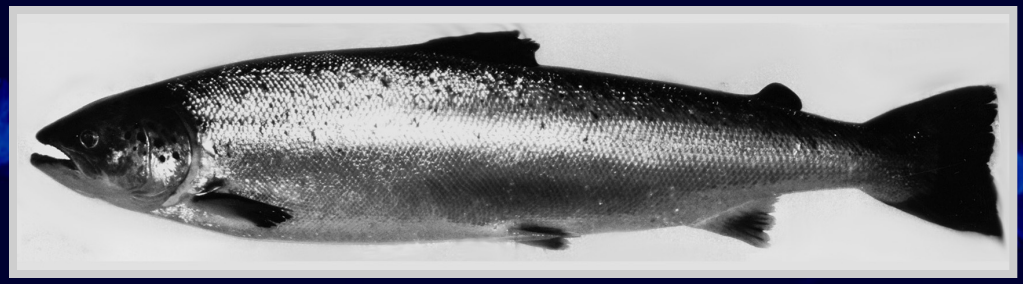
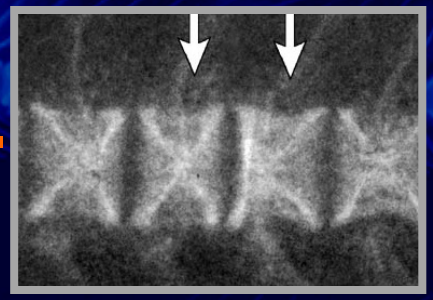
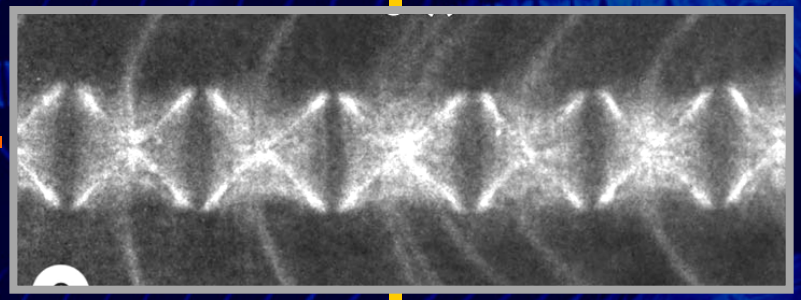
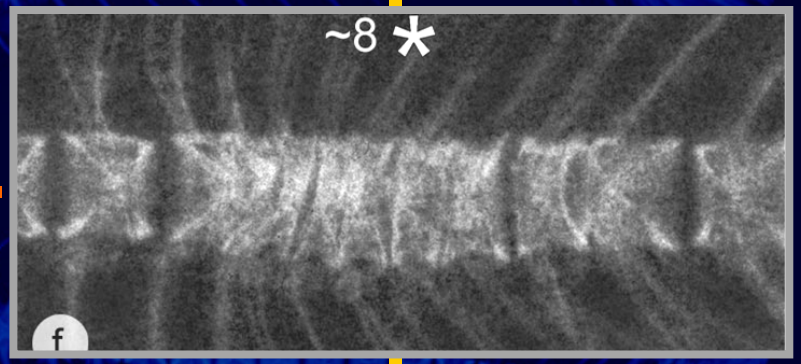

Spinal Deformities in Farmed Atlantic Salmon
Compression & Fusion
Compensatory elongation
Compression
Compression & Fusion & Fracture





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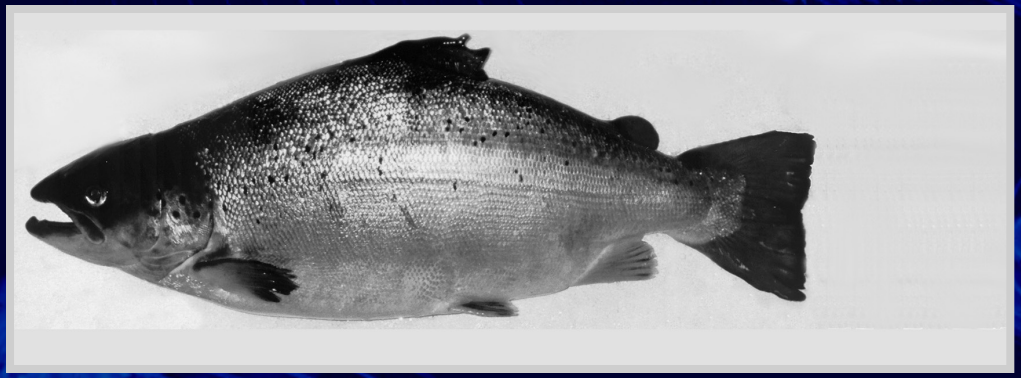
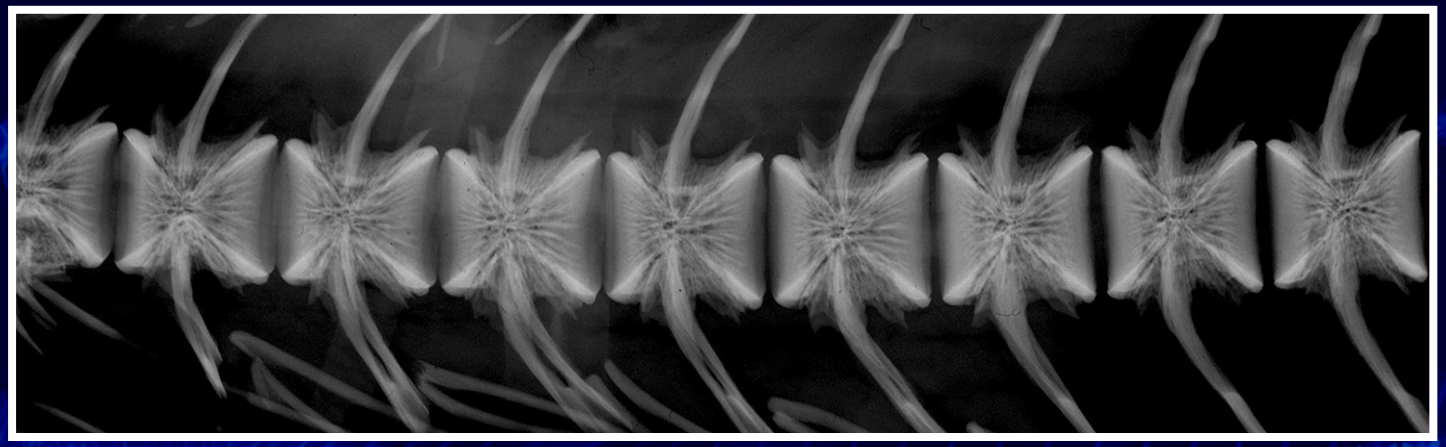
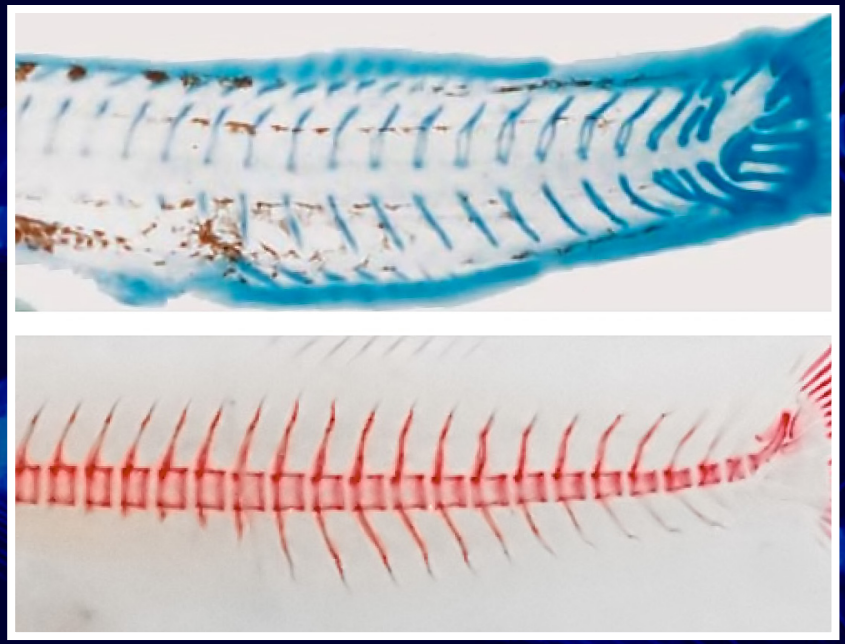
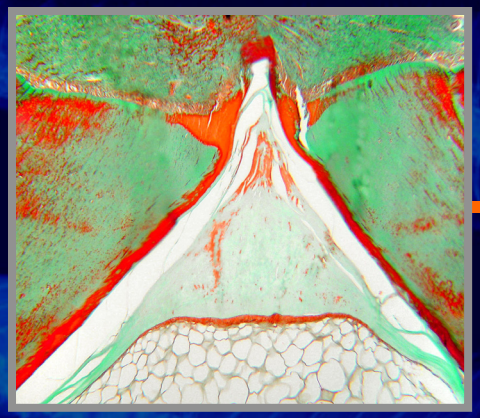


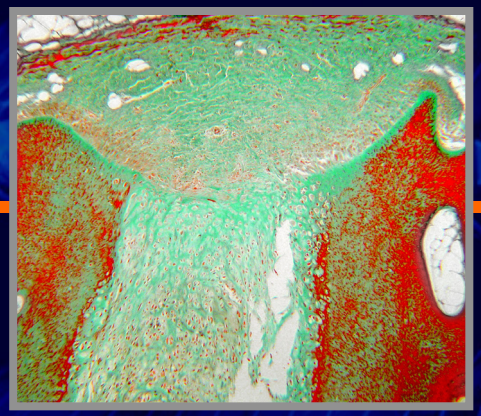


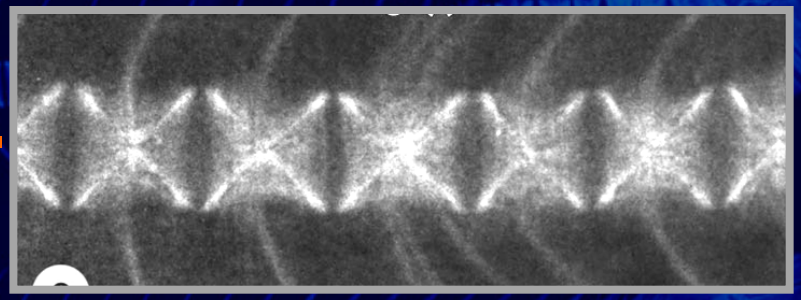
Teleost vertebral centra have no cartilaginous precursor

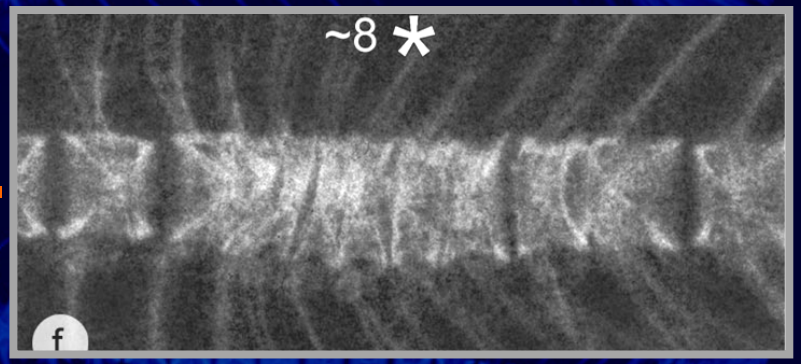


Witten & Villwock 1997





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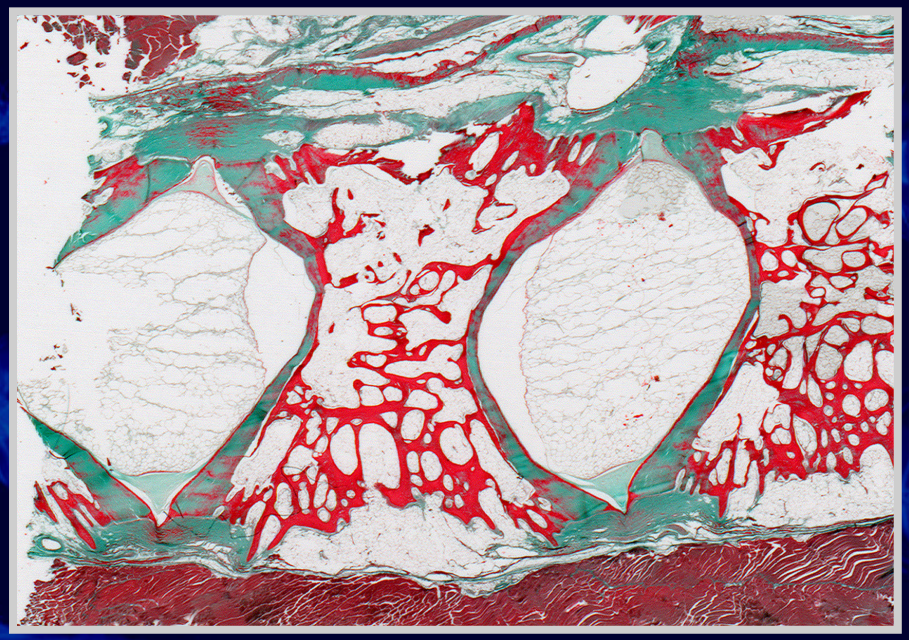
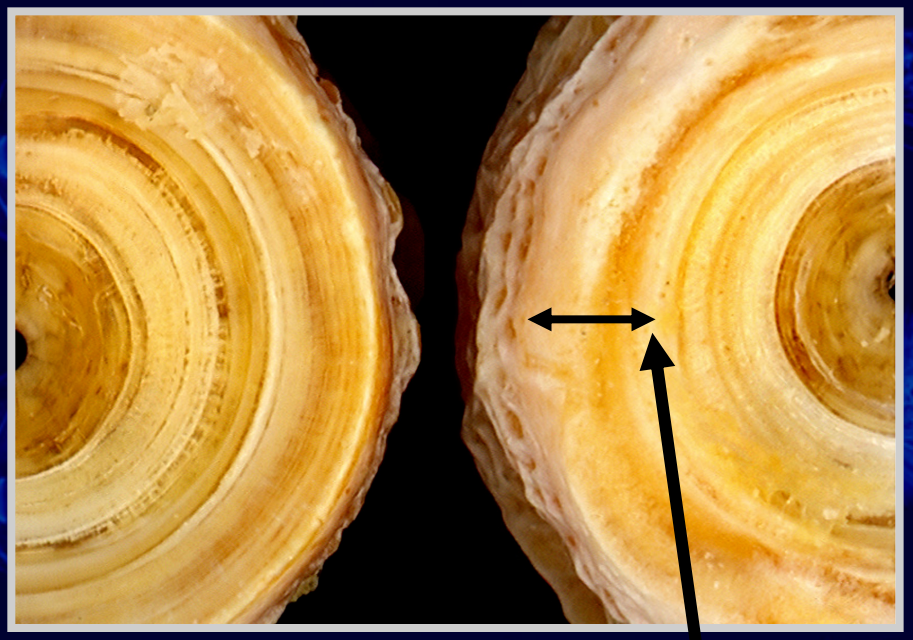
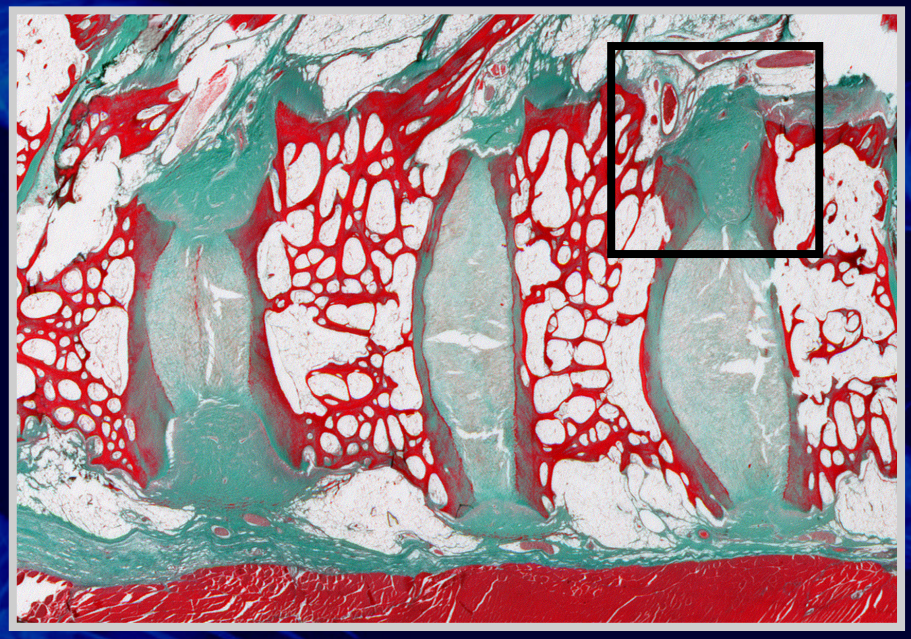
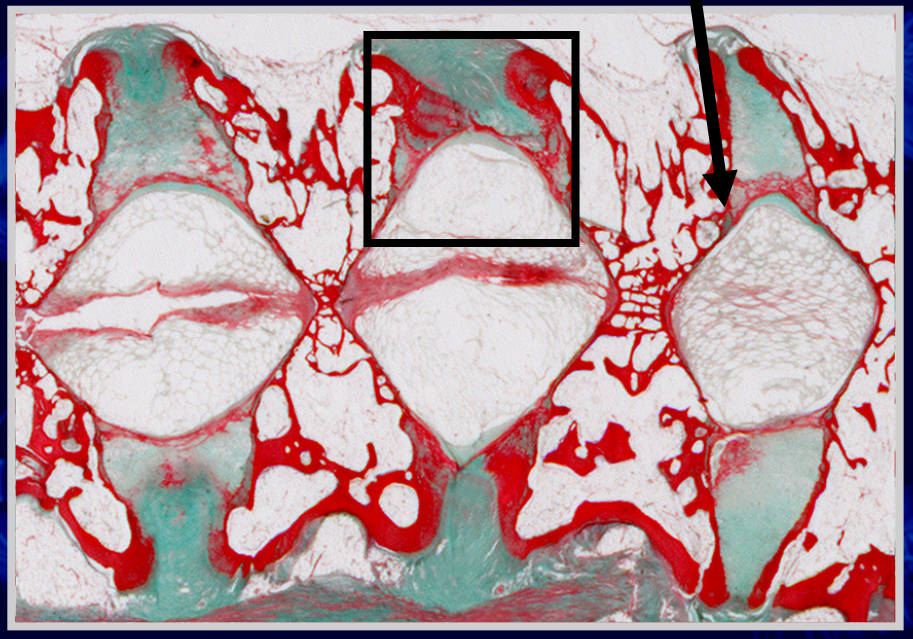
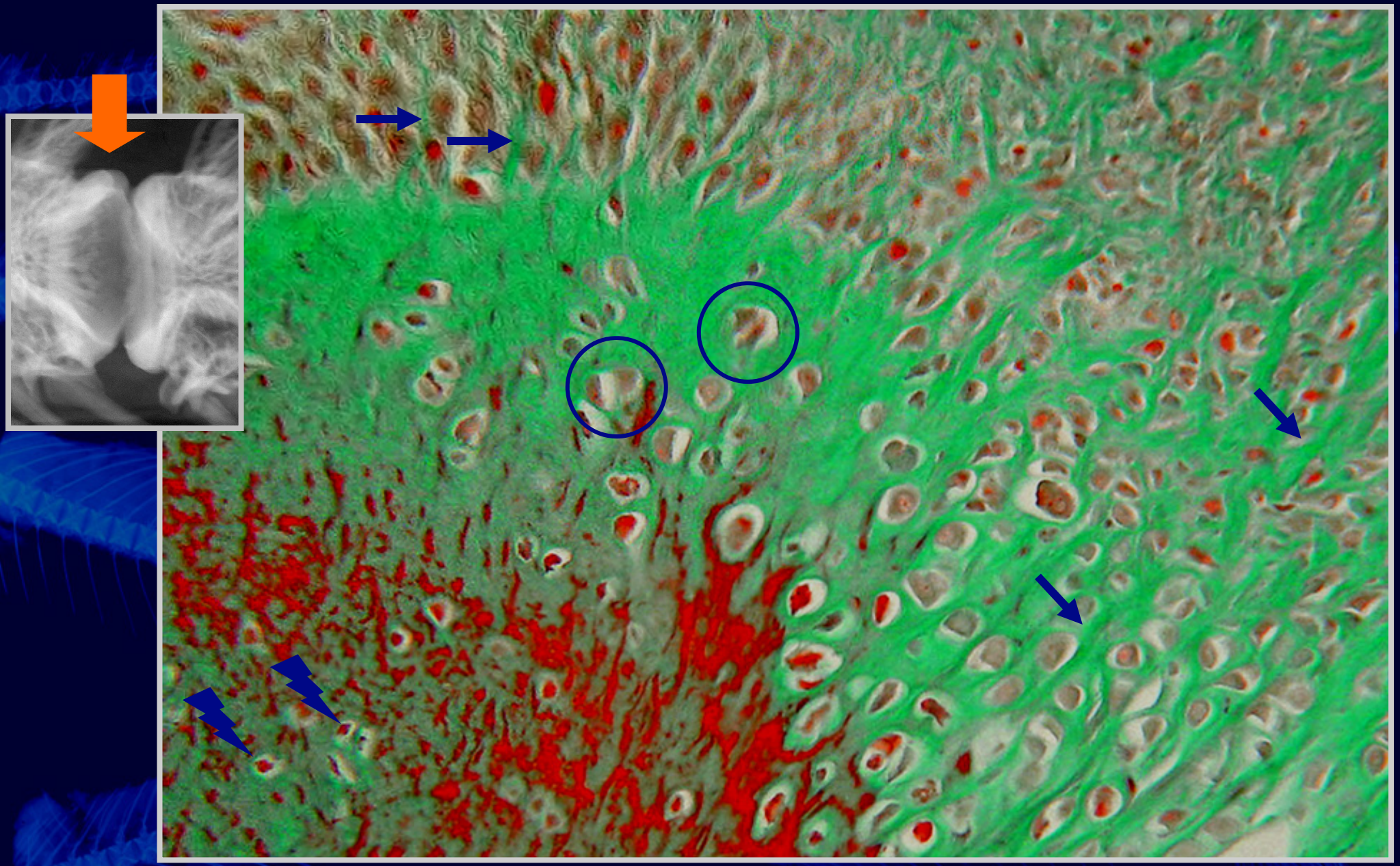


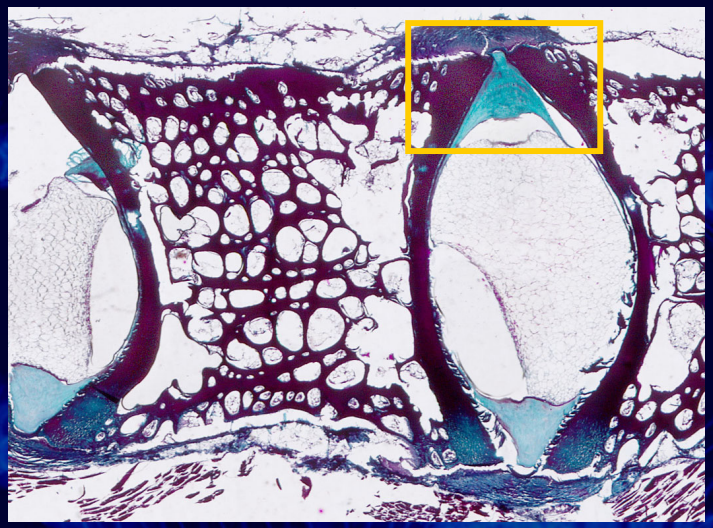
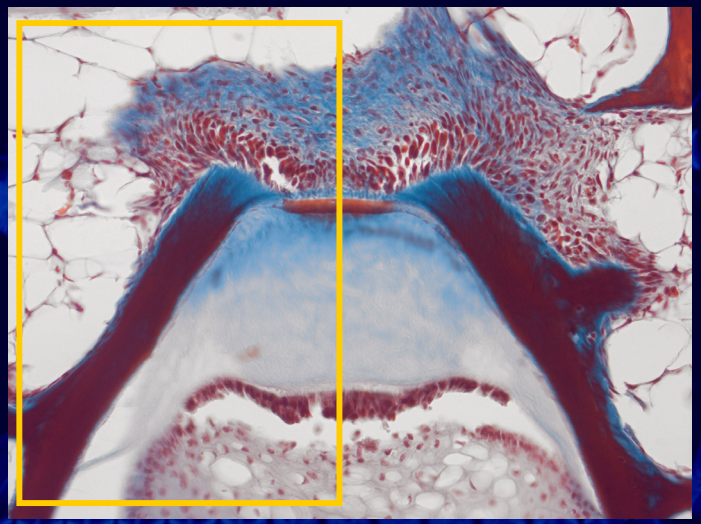
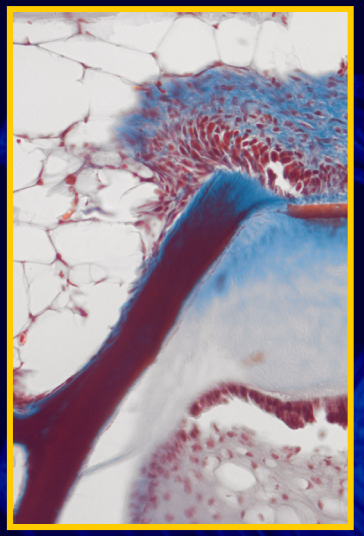
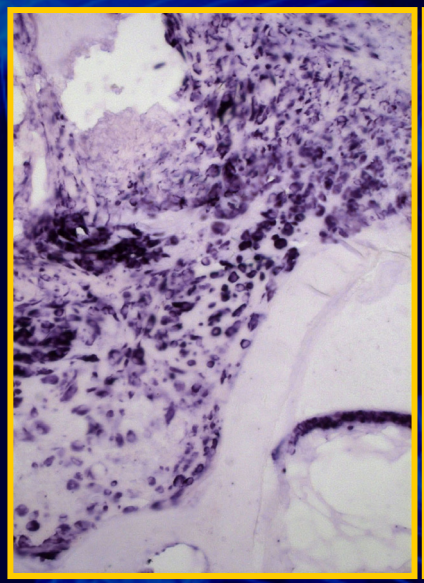
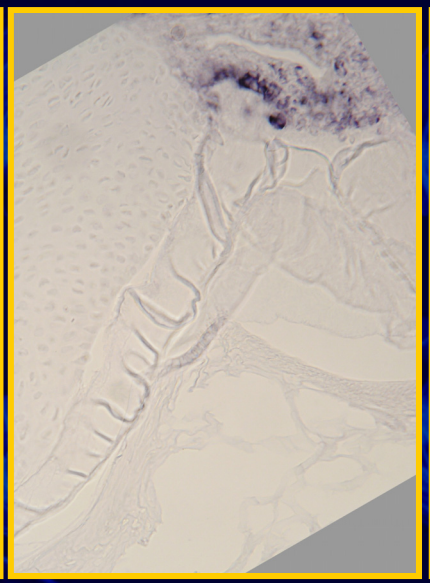
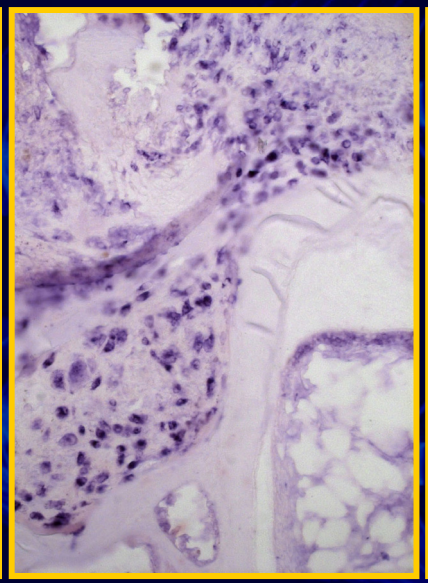
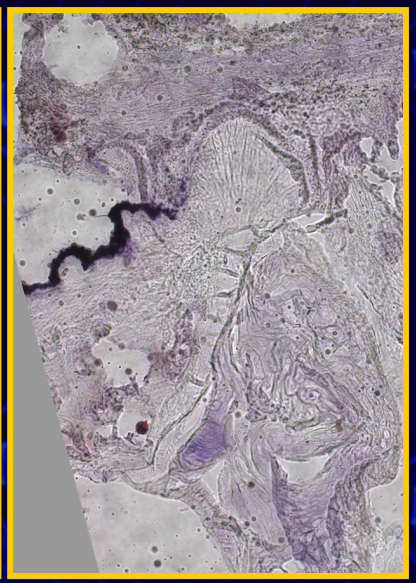
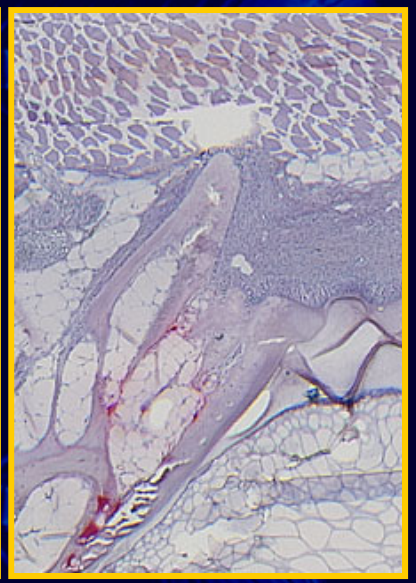








Witten et al. 2005

Sox9 Col I Col II Osteocalcin TRAP

# Changes in the intervertebral disk due to compressive loading

**Sox9**
master transcription factor
for chondrogenic differentiation

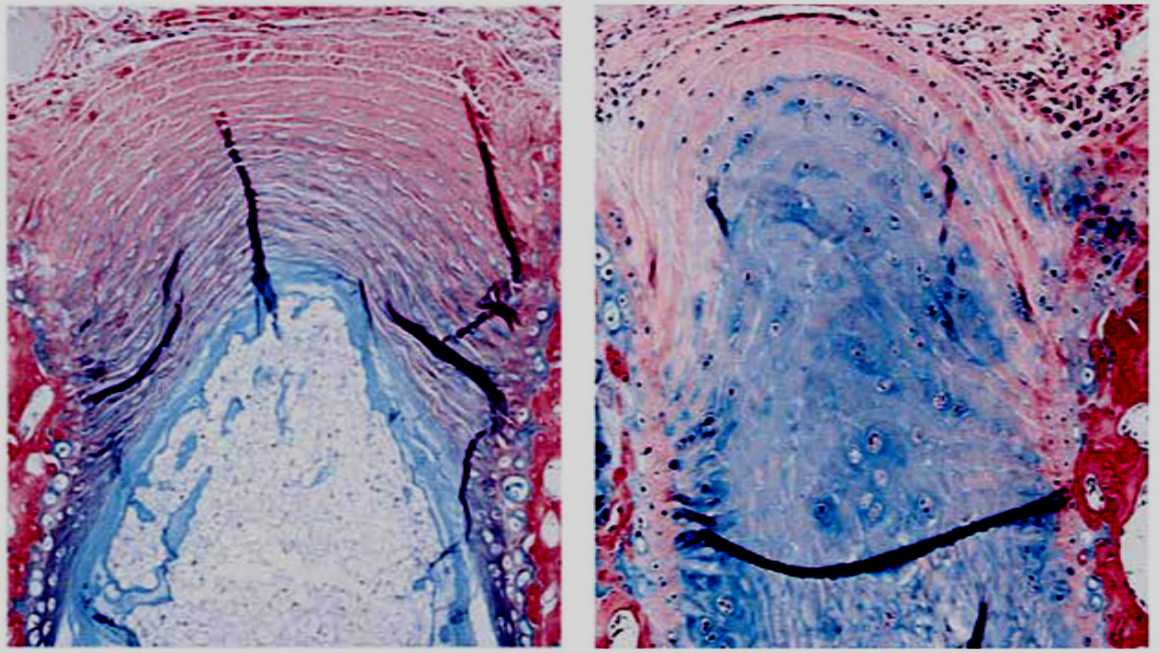
**collagen type II**
major cartilage collagen

**collagen type I**
major bone &
connective tissue collagen

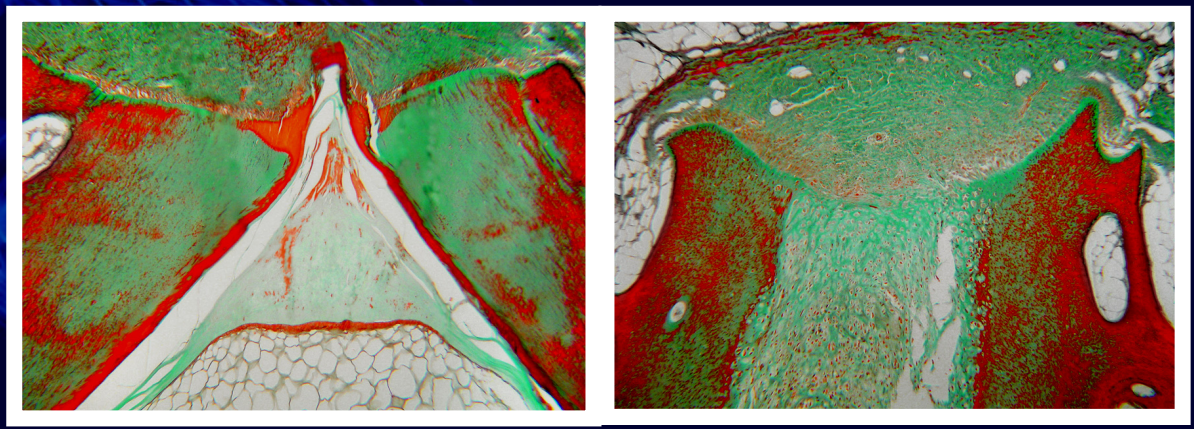
**Sox5 and Sox6**
transcription factors that
control maturation
(chondrogenesis) of
notochord cells

Mouse

Smits & Lefebvre 2003



Histology of the normal and degenerated murine tail intervertebral disc

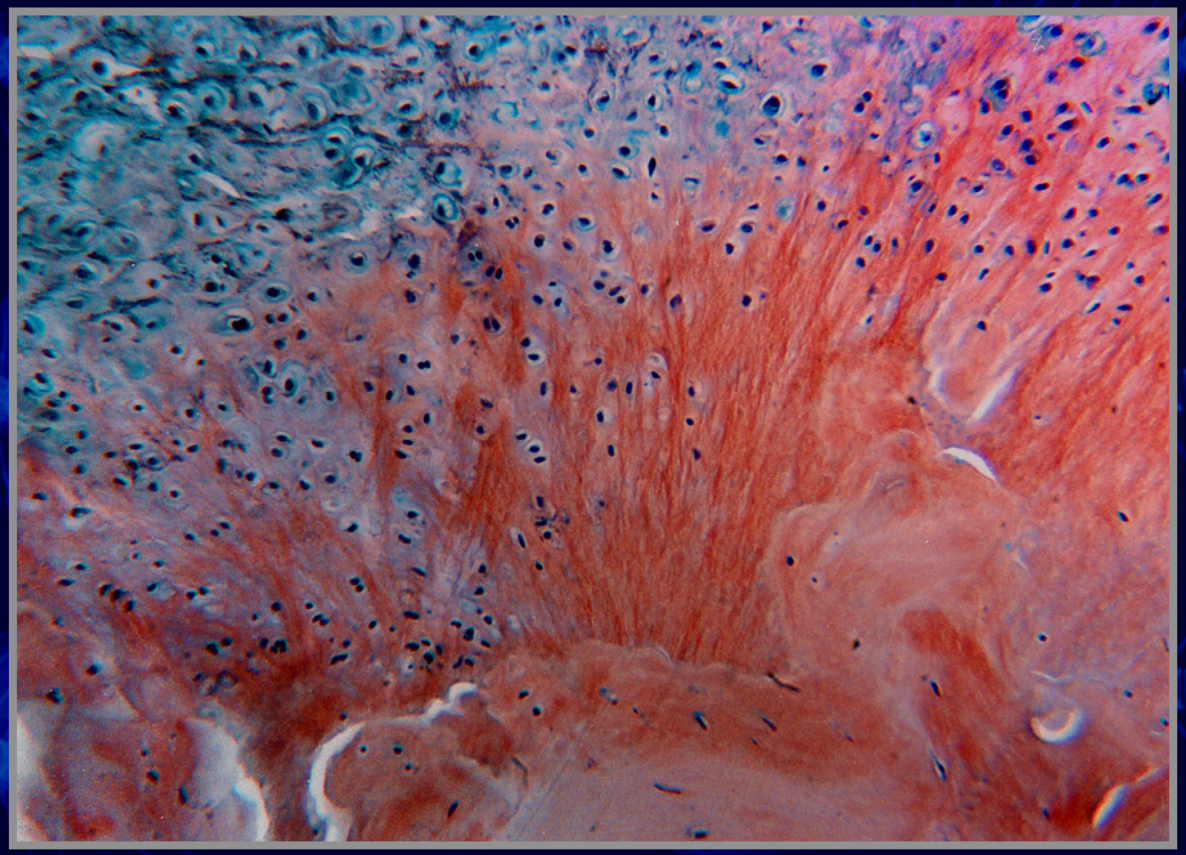


Salmon

Patt & Patt 1969, Hall 1977, 2005, Oegema 2002, Hunter et al. 2003, Beresford 1981, de la Fuente & Helms 2005

Sox9

Cartilage

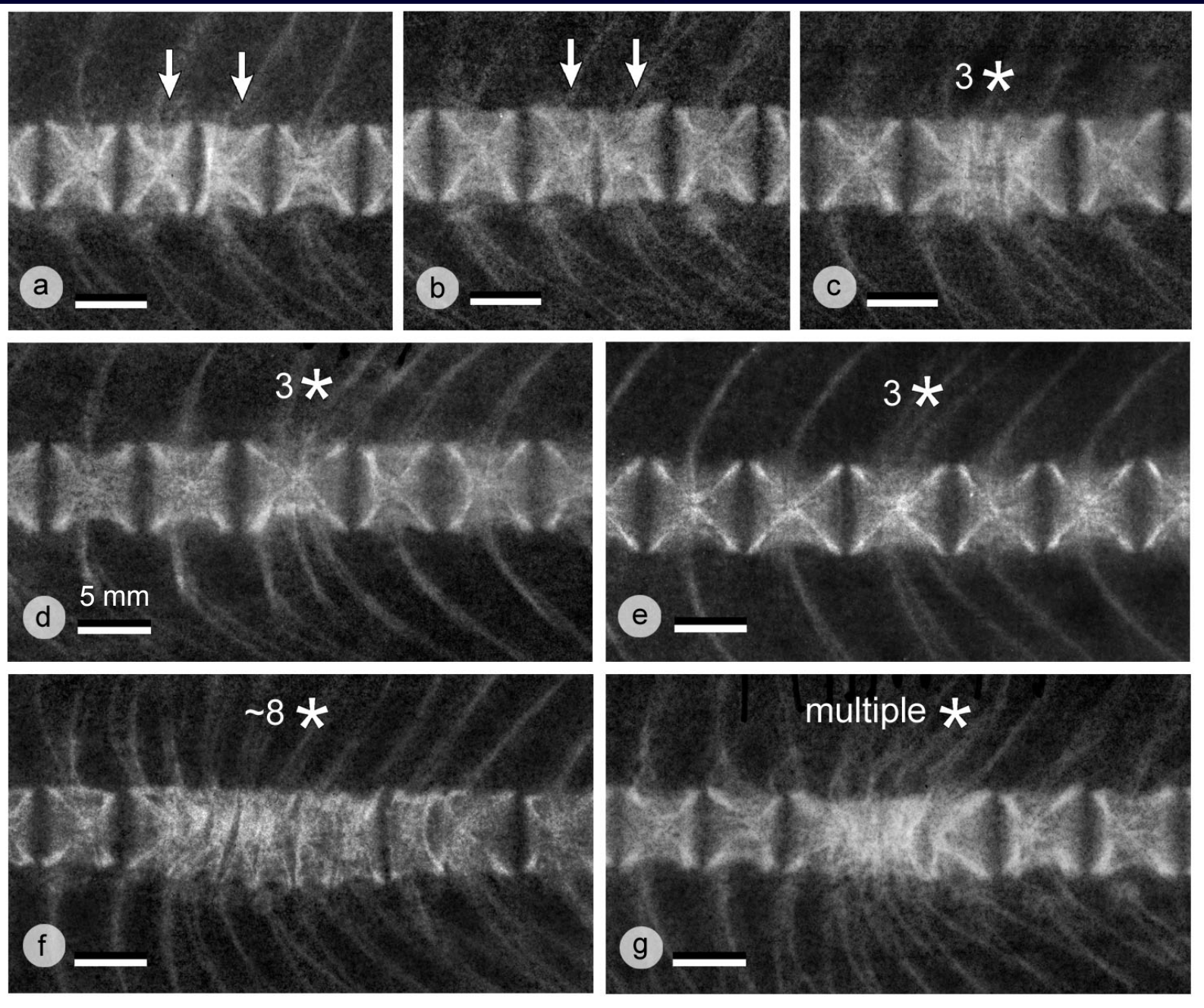


Bone

PTHrp

Cbfa-1/ Runx2

- slow growth - tension - high oxygen - fixed -
- fast growth - pressure - low oxygen - motion -




Witten et al. 2006

★ fused vertebrae
➡ vertebrae in the process of fusion
➤ haemal arches

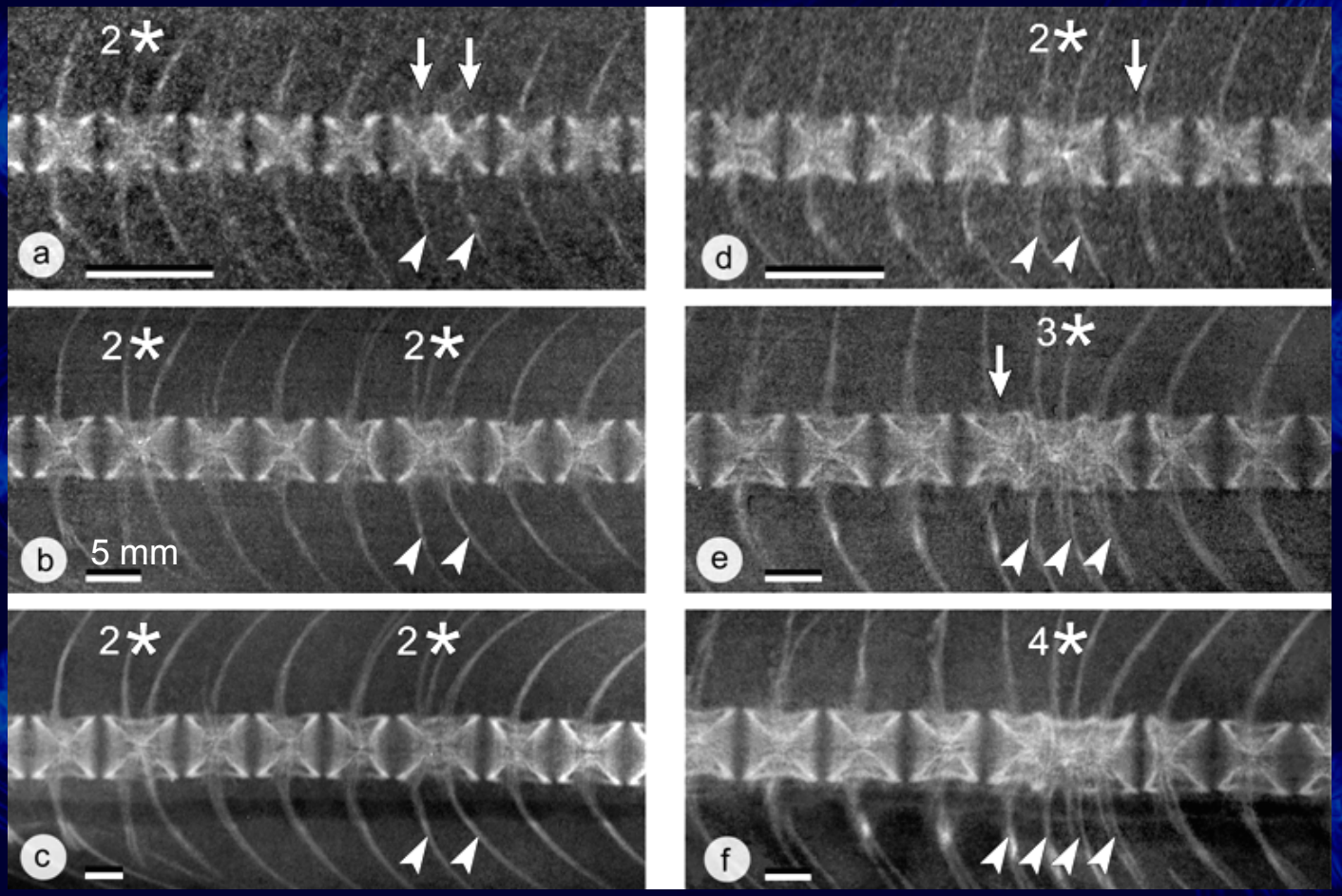
**Complete fusion of vertebrae, starting early (a, left) or late (a, right) during the animals' freshwater phase**

**Fusion of vertebrae that elicits further amalgamation of neighbouring vertebral bodies**

**juveniles (pre-smolts)**

**after 6 months in seawater**

**after 12 months in seawater**

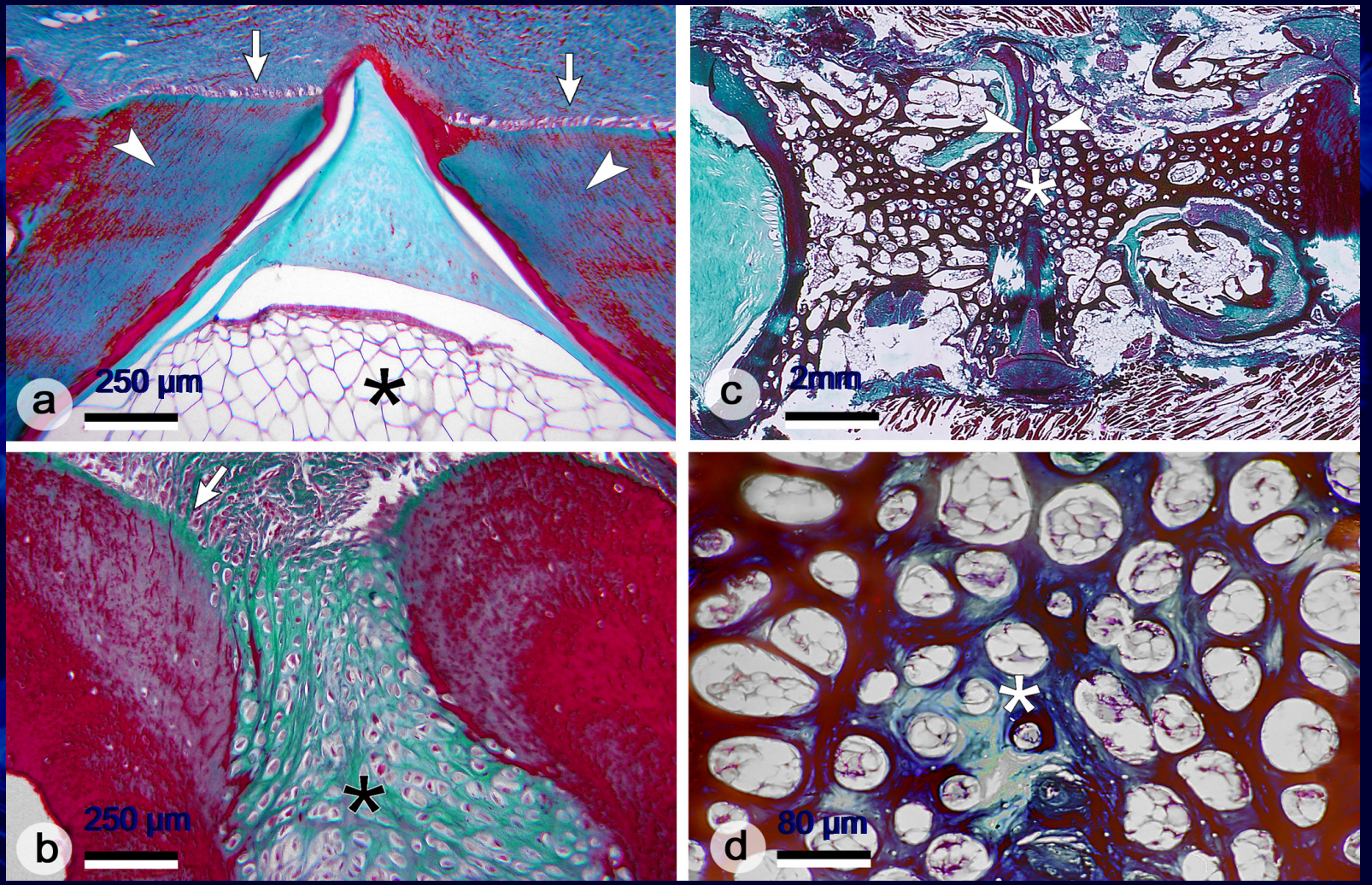



Witten et al. 2006

bone growth zone
notochord or cartilage
end plate
former intervertebral space

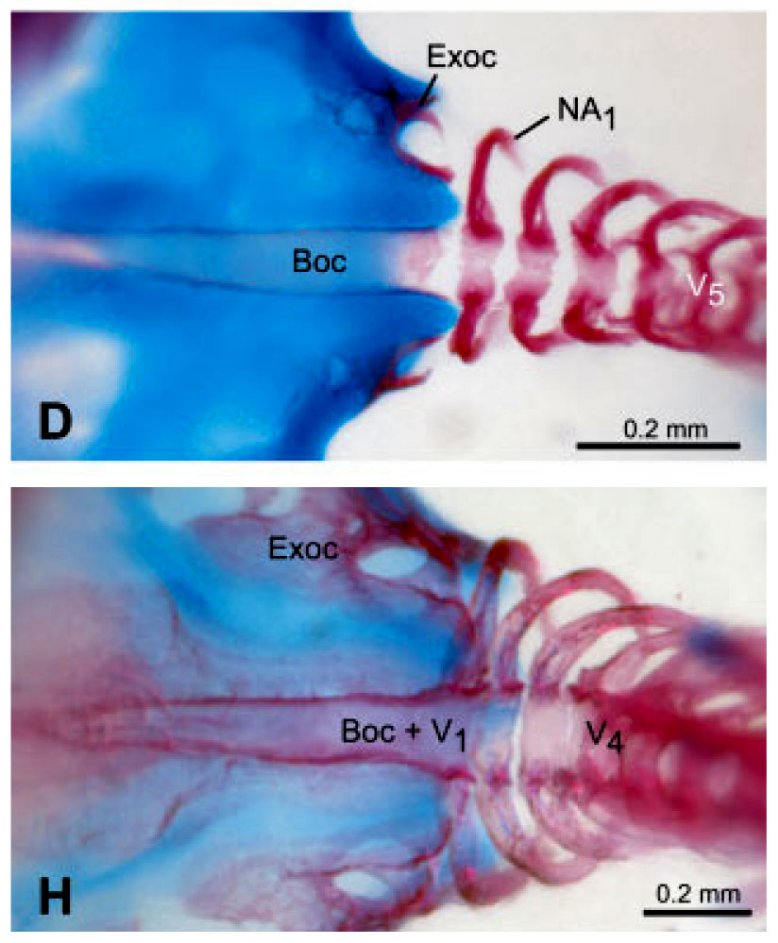
**Between two vertebrae, notochord tissue (a) is replaced by cartilaginous tissue (b)**

**Cartilaginous tissue in the former intervertebral space (c) is completely remodelled into bone (d)**



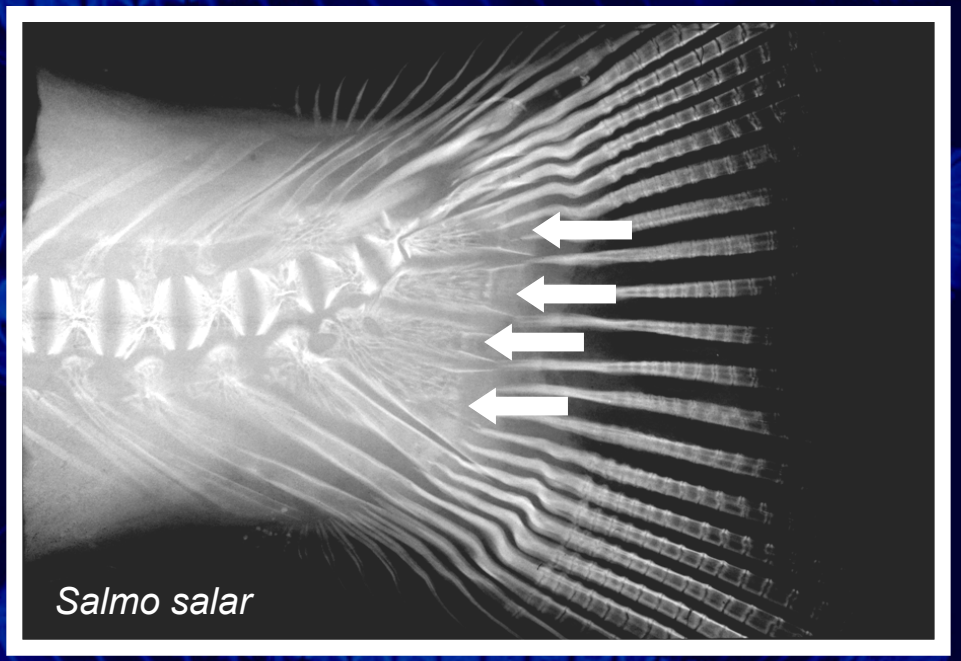

Witten et al. 2006

## Occipito-Vertebral Fusion in Ocean Sunfishes



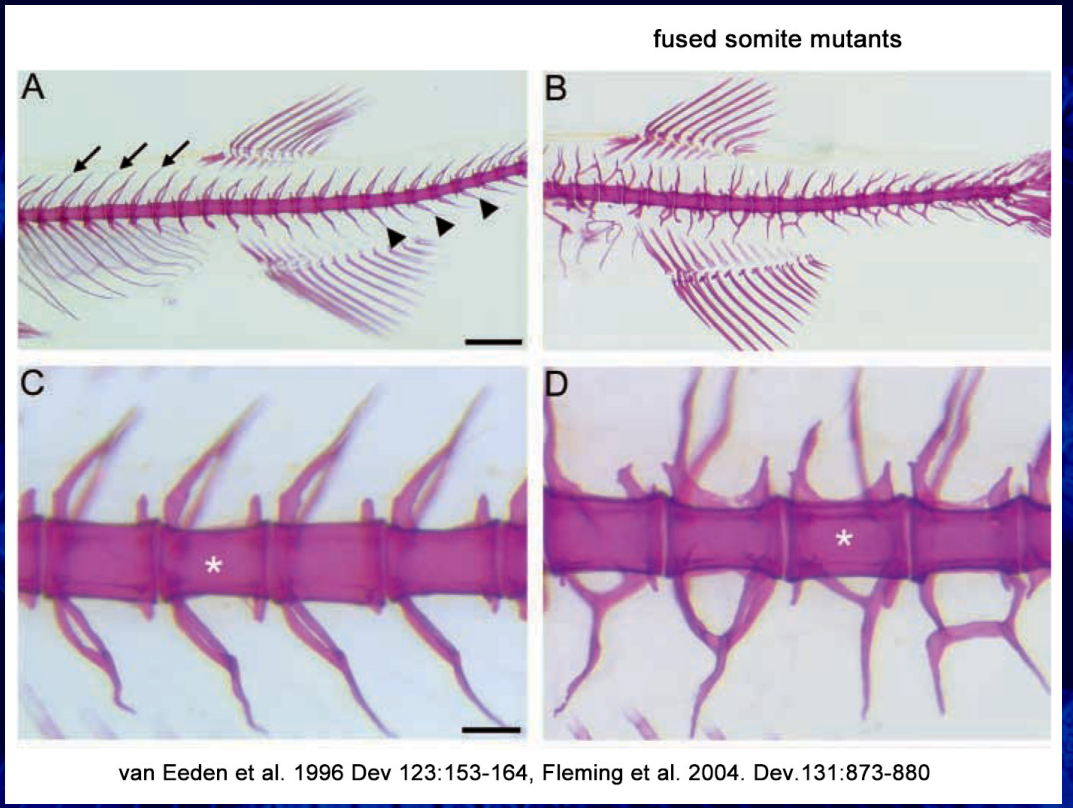

Ralf Britz and G. David Johnson 2005

In evolution and in development, fusion of vertebral body anlagen causes multiple arches which become regular elements of the caudal fin endoskeleton

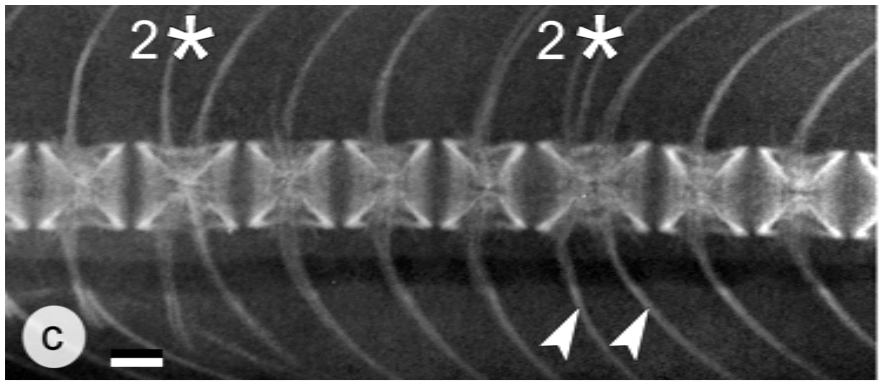


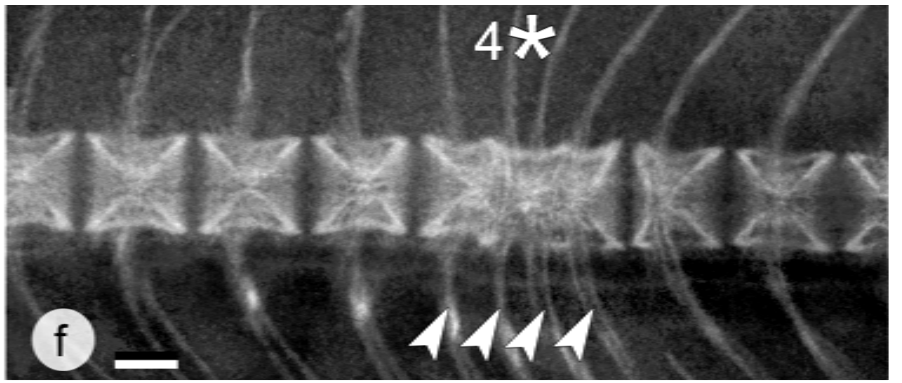

Witten & Huysseune 2007

Vertebral bodies and neural arches as independent developmental modules




van Eeden et al. 1996 Dev 123:153-164, Fleming et al. 2004. Dev.131:873-880

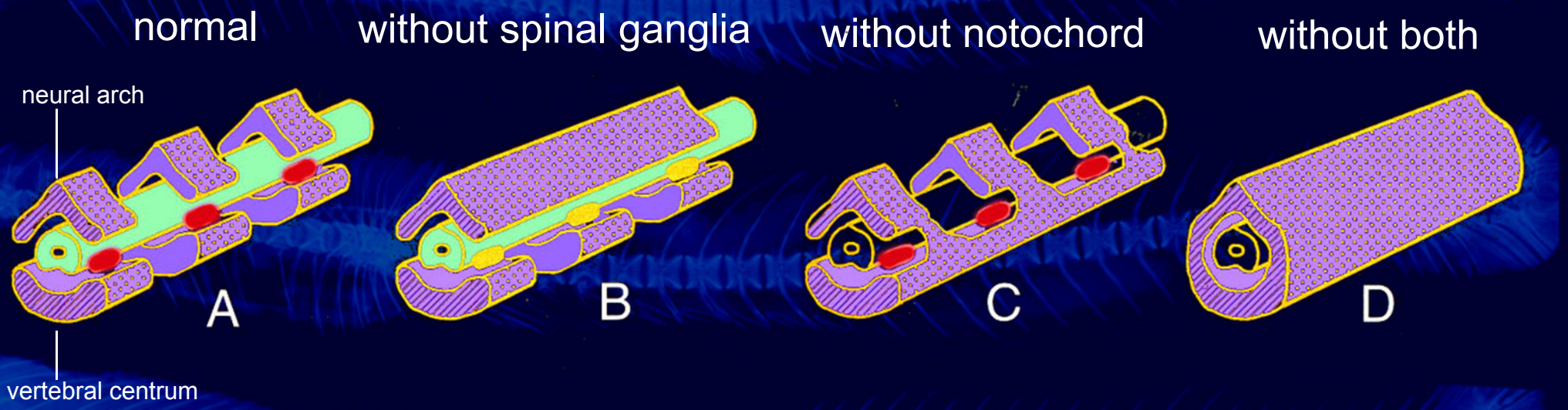



fused vertebral bodies

# Vertebral bodies and arches as developmental modules

Hall BK (1975) after Holtzer H (1951) and Strudel (1953, 1955)



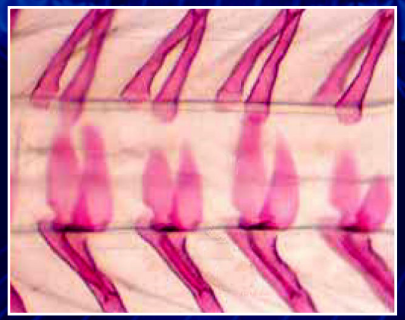

The teleost notochord induces segmentation and mineralisation of vertebral bodies in teleosts

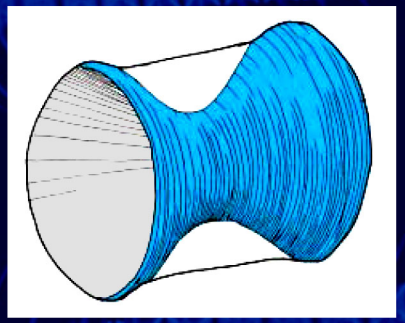
Grotmol et al. (2003, 2005), Fleming et al. (2004), Nordvig et al (2005)

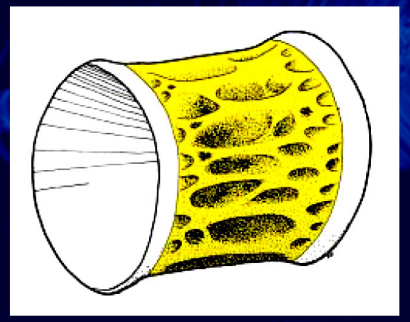
As late as has been tested, notochords remain inductively active but spinal cords do not Hall BK (2005) Bones and Cartilage, p520

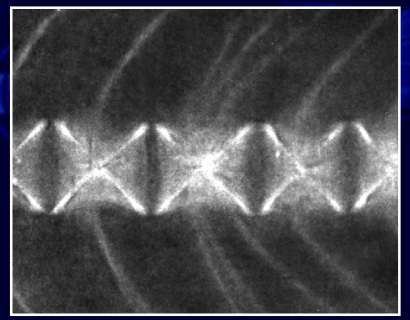
# Ontogeny of vertebral fusion in Zebrafish

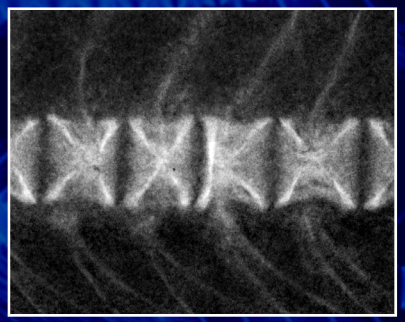
Ph.D project of
Anabela B. Brito
(Portugal)

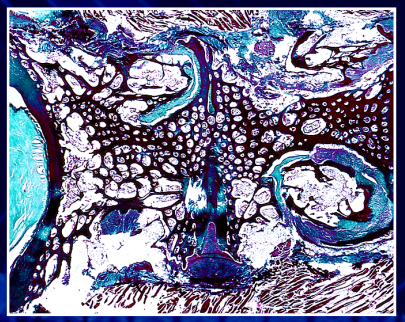












Ph.D. project of
Laura Gil-Martens
(Norway)

## Vertebral fusion as response to inflammation

1. Fusion of vertebral bodies involves transdifferentiation (Jasper Dewit) of osteoblasts into chondroblasts in the vertebral growth zone and remodelling of heterotopic intervertebral cartilage and notochord into trabecular bone. Laura Gil-Martens is currently testing if inflammatory factors promote shape alterations and fusion of vertebral bodies.

2. Vertebral fusion can generate a centre of malformation, causing the amalgamation of adjacent vertebral bodies. Alternatively vertebral fusion can be contained by complete fusion and reshaping of (max 3) vertebral bodies into one normally shaped element.

3. Early development and adult reshaping (regeneration?) of vertebral bodies generates the same skeletal element, raising the question about genetic versus epigenetic (biomechanical) control of vertebral body formation. Anabel B. Brito is currently investigating how vertebral bodies fuse and stay apart in early normal development.

4. As in early development, signalling from the notochord may be lifelong required to maintain the vertebral body identity.

# Acknowledgments

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