

# Characterization of a Scoliosis Model in FGFR3 -/- Mice

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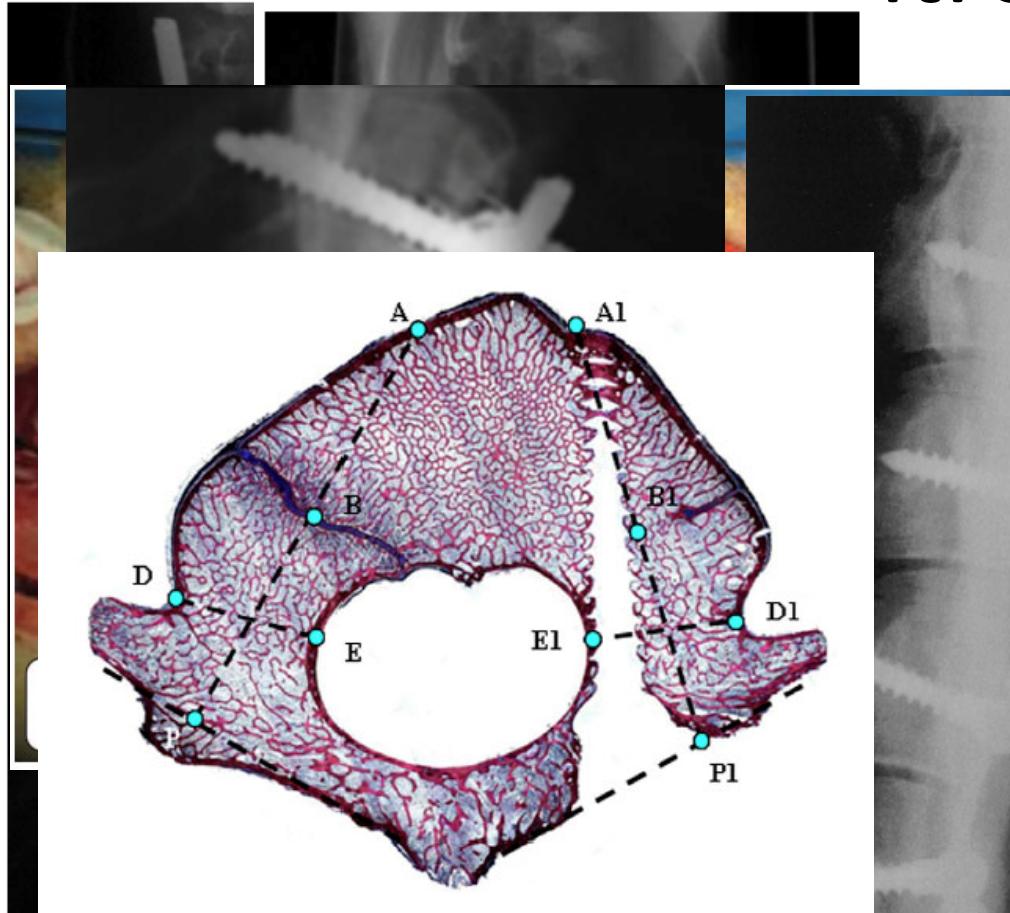
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# Disclosures

- Michael B Sullivan – none
- Ali Esmaeel – none
- Janet E Henderson – none
- Jean A Ouellet
  - Synthes – Consultant
  - Depuy Spine – Educational Grant
  - AO Spine – Educational Grant
- Neil Saran
  - Depuy Spine – Research Grant

# Intro



Newton et al Spine 2001

Braun et al Spine

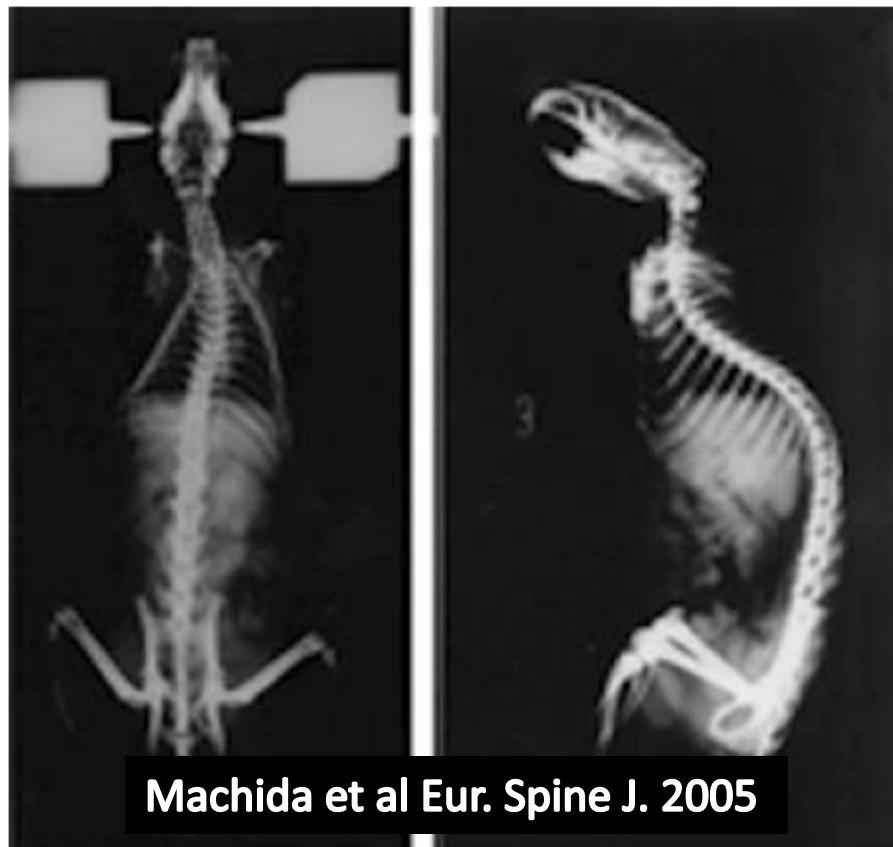
Braun et al Spine 2005



- some may be useful in assessing mechanical intervention; however, most of them may be difficult to use in assessing pharmaceuticals on the scoliosis progression.

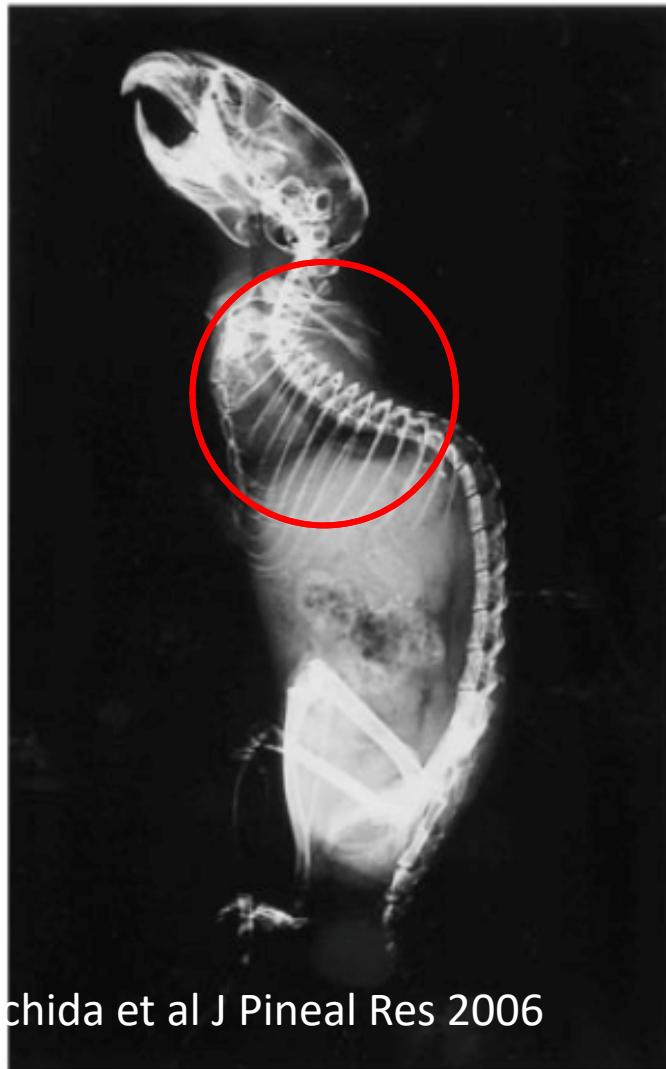
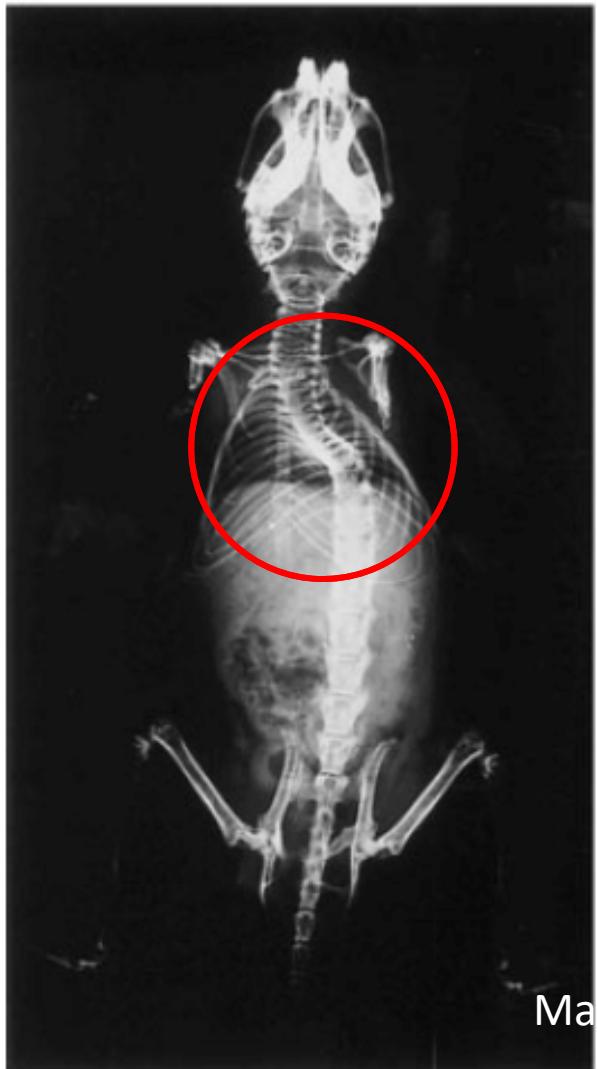


Machida et al Spine 1999



Machida et al Eur. Spine J. 2005

# C57BL/6J mice – genetically melatonin deficient

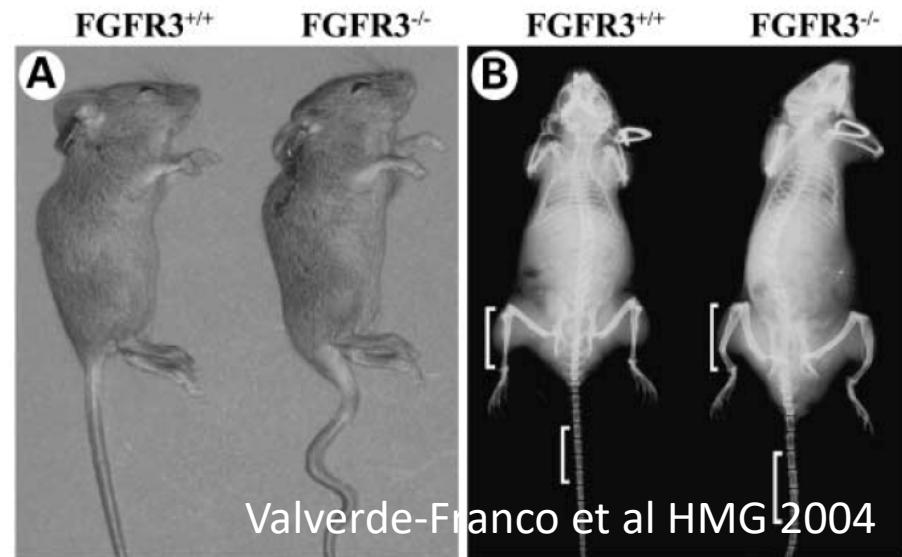


Machida et al J Pineal Res 2006

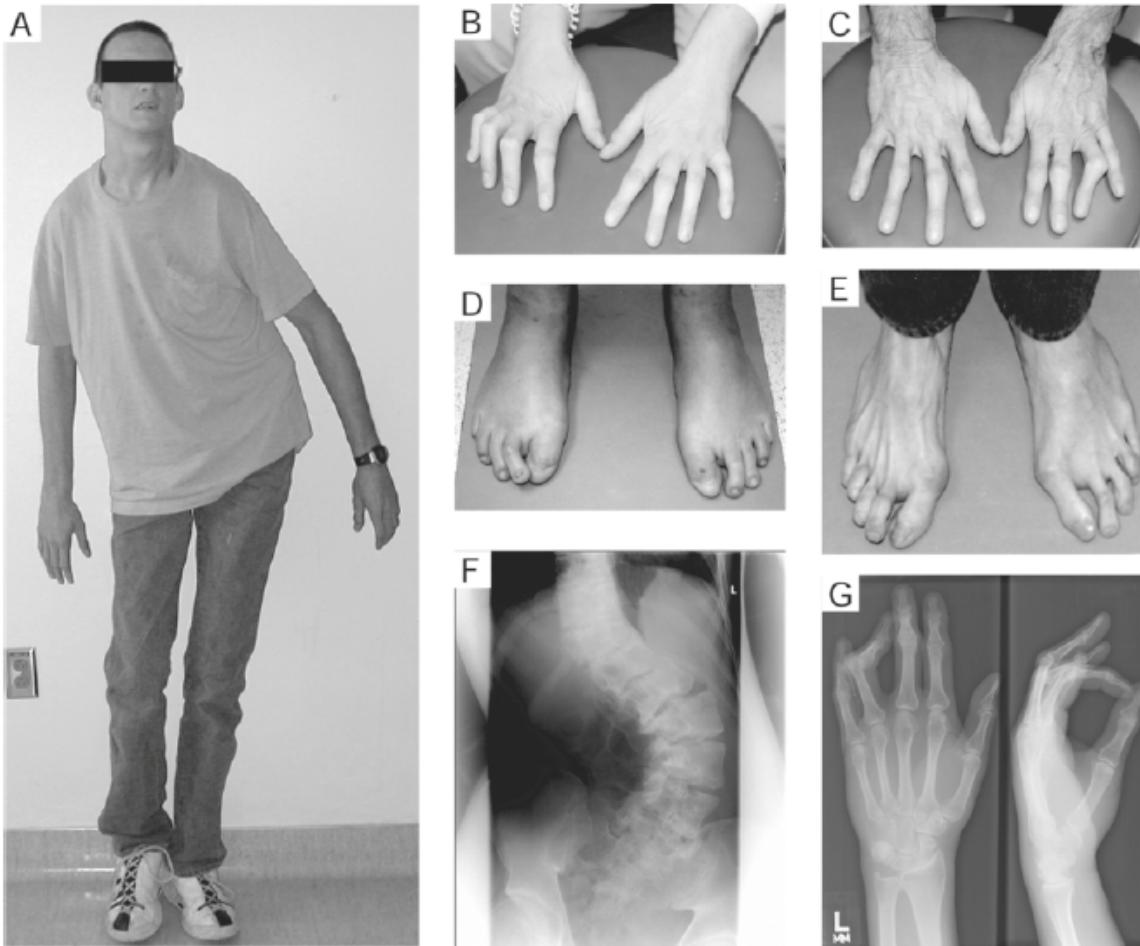
Melatonin treats the Scoliosis

In Humans, while the melatonin pathway may play a role, it is not the end determinant

- FGFR3  $-/-$  mice on C3H background
  - Prolonged endochondral bone growth with expansion of proliferative and hypertrophic zones of growth plate
  - Longer than normal long bones
  - Kinked tails
  - Osteopenia
  - Deafness
  - Kyphoscoliosis



# Aside: CATSHL Syndrome



Camptodactyly  
Tall Stature  
Hearing Loss

FGFR3 mutation

Toydemir et al AJHG 2006

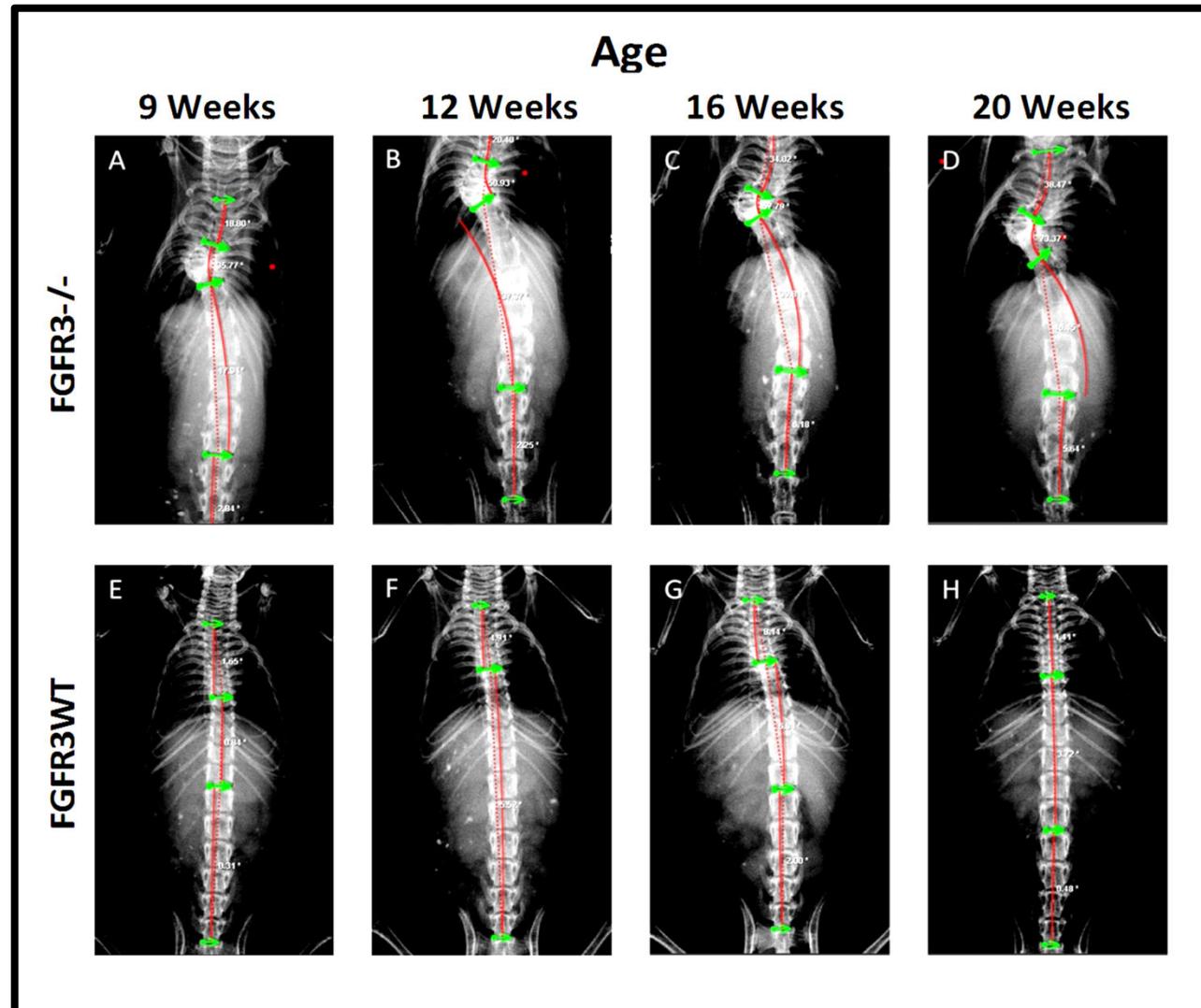
# Objective

- *Radiographic and Morphometric Characterization of the spinal deformity that develops in the FGFR3-/- mouse*
- Enable testing of asymmetrically expressed genes/proteins in these mice on the progression/development of scoliosis

# Methods

- 47 FGFR3-/-
- 47 WT
- Euthanized between 4-25 weeks
- Radiographs at multiple time points
  - Cobb angles
  - Femur length
- Micro-CT
  - Vertebral and disc morphology
  - Bone density
- Histology
  - Basic stains, ALP, TRAP, TUNNEL Assay

# Results



Progressive  
scoliosis  
(46/47 KO)  
(0/47 WT)  
Apex ~T9  
R=L

Thoracic  
hyperlordosis

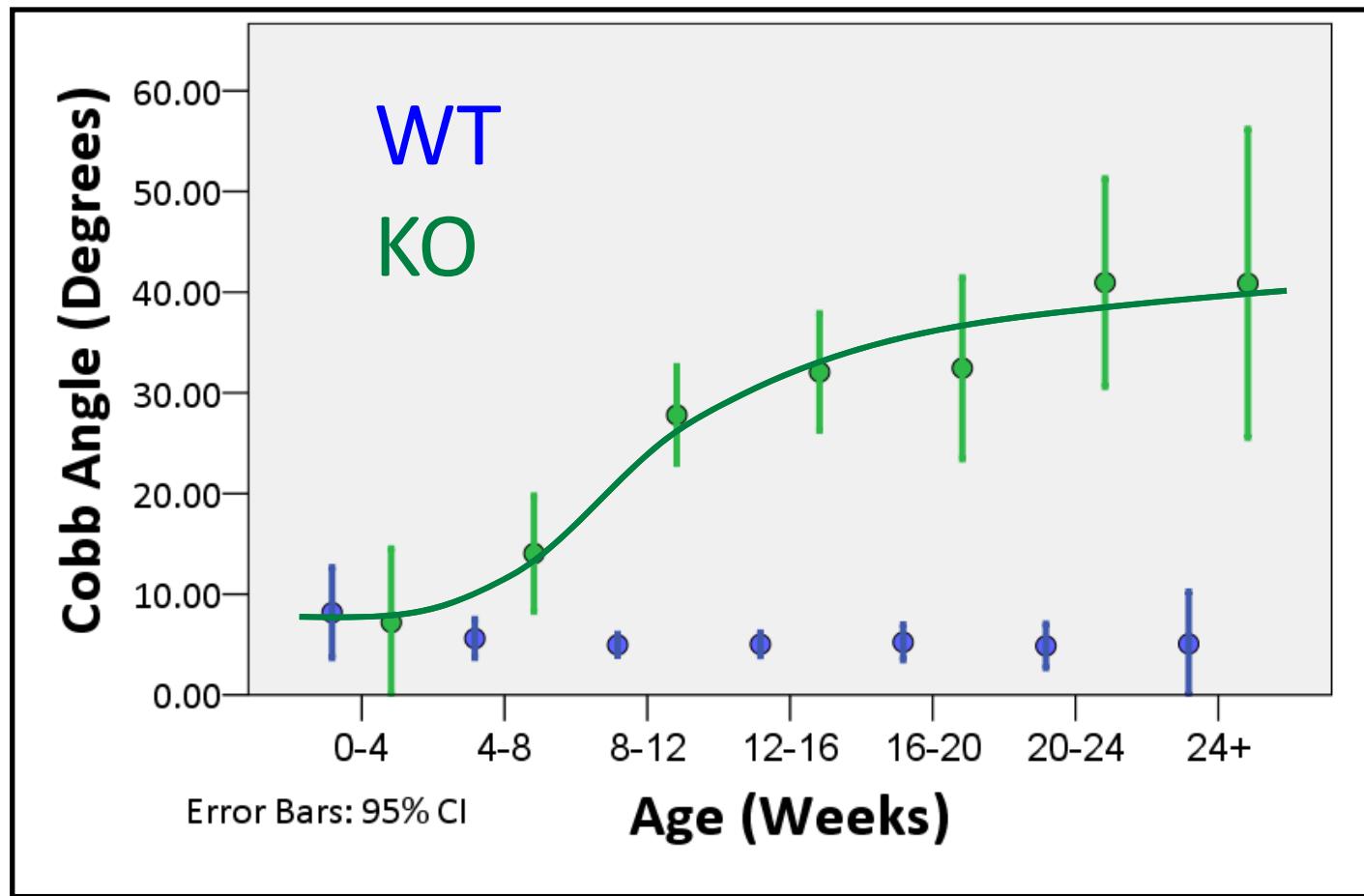
Thoracolumbar  
kyphosis



KO

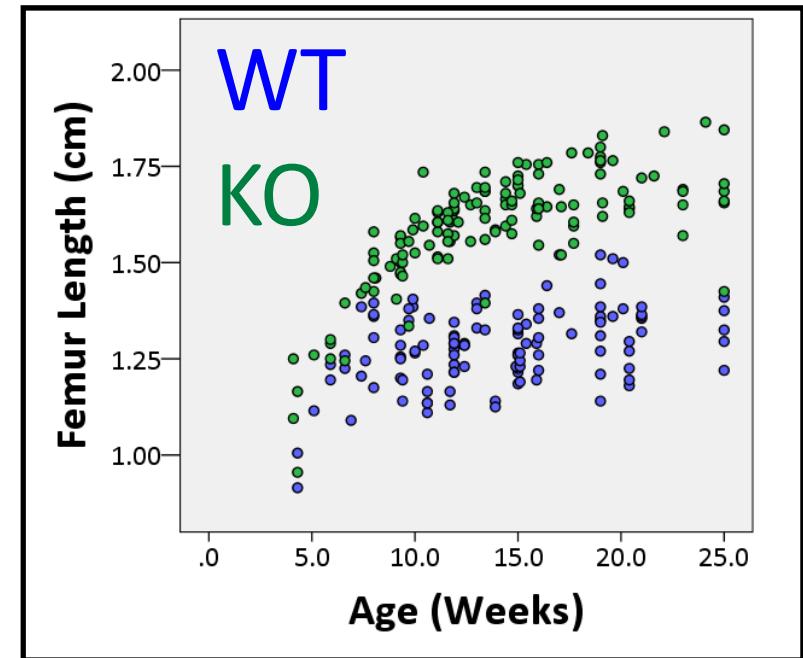
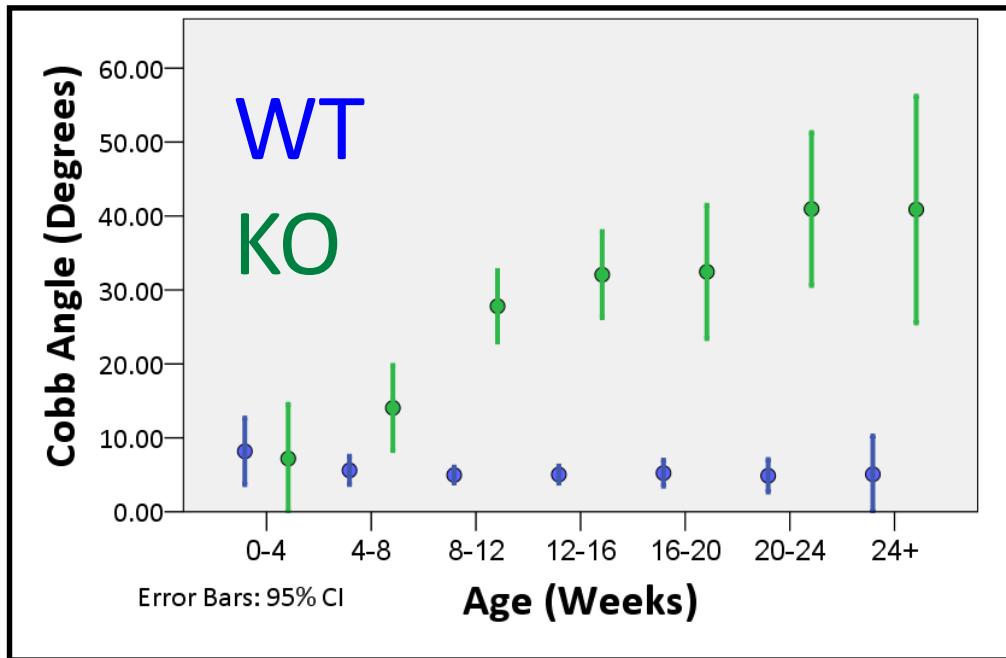


WT

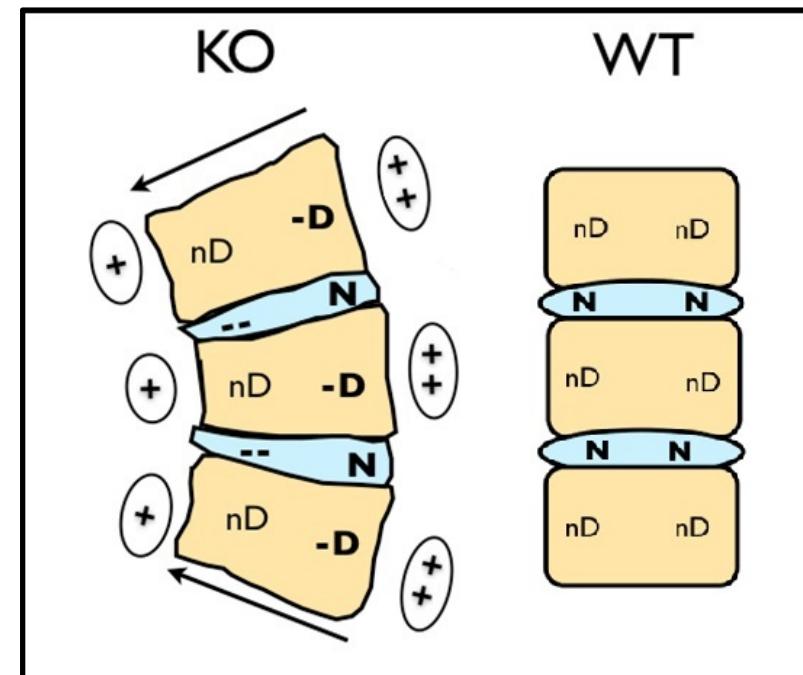
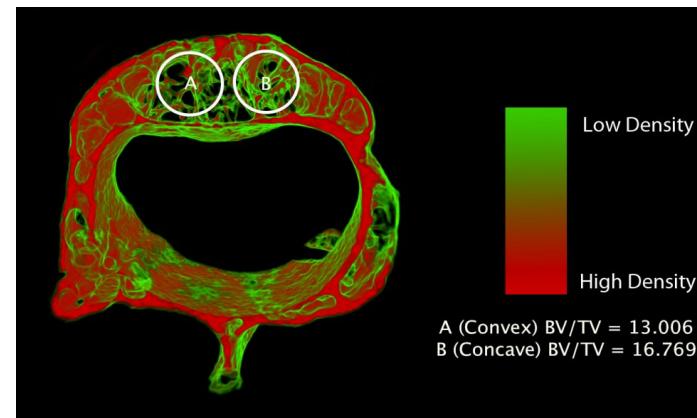
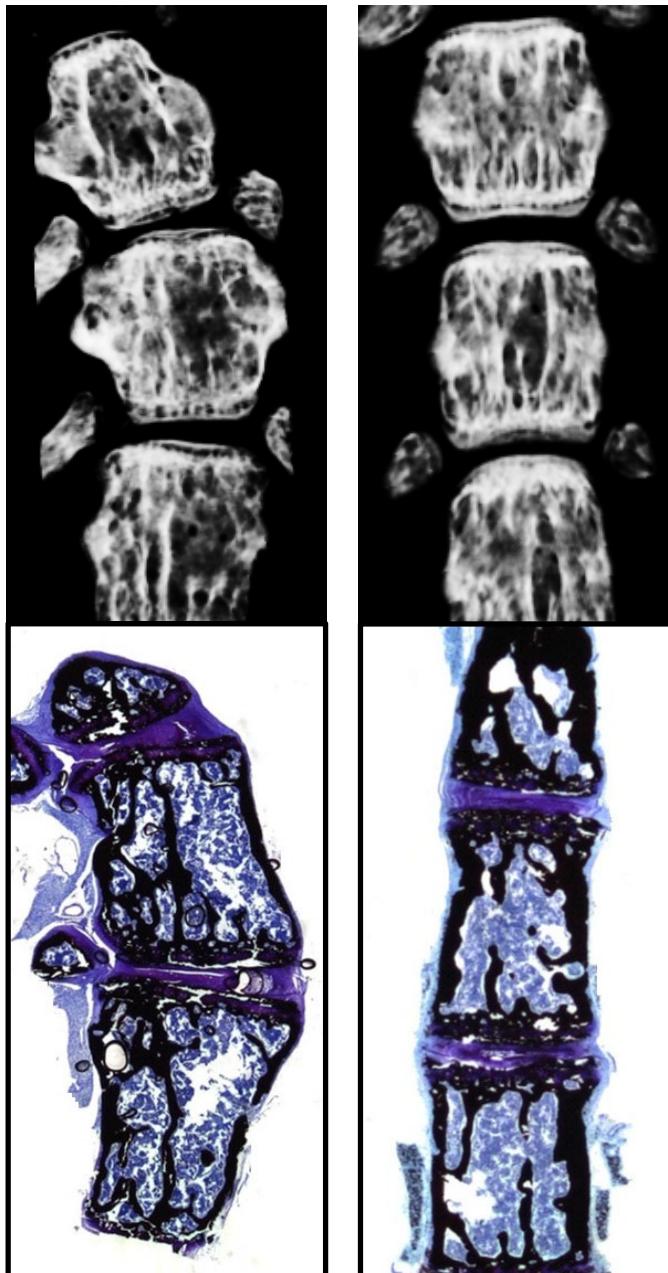


4-8 wks: scoliosis apparent

8-12 wks: progression of scoliosis

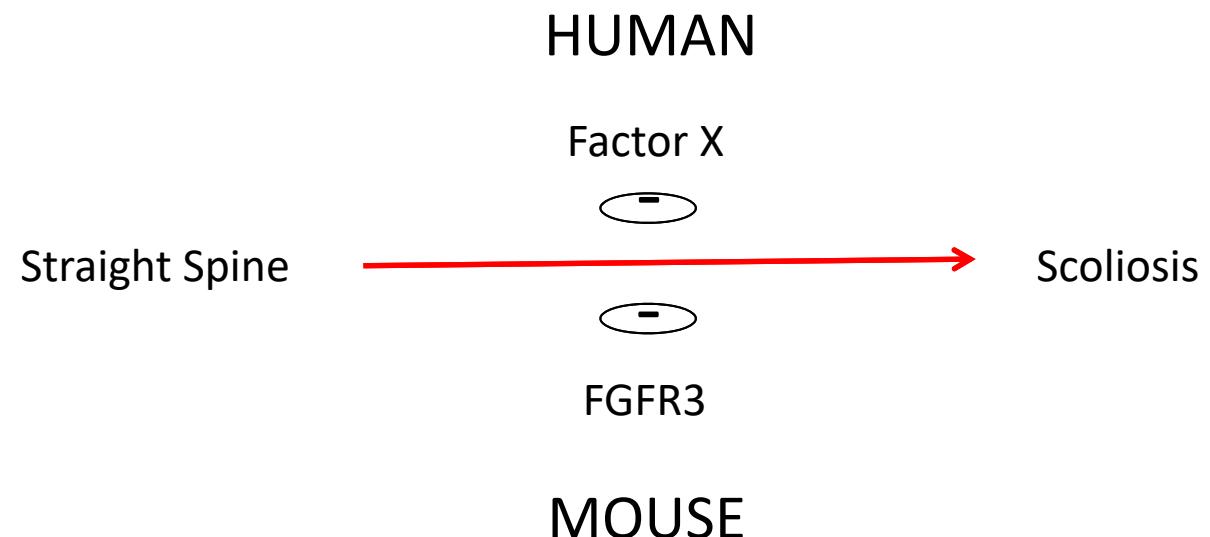
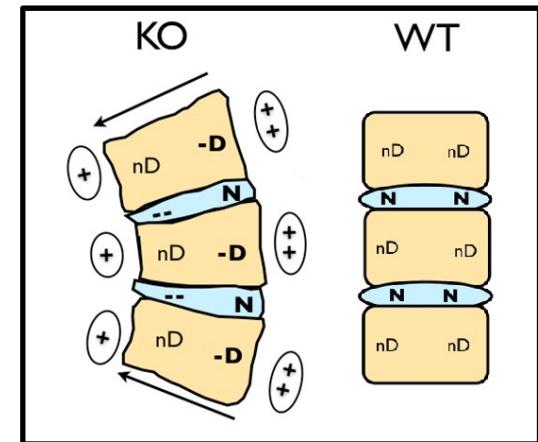


Scoliosis magnitude correlates with femoral growth



# Limitations

- Osteopenia
- Pinealectomized bipedal rats
- C57BL/6J bipedal mice
- Common pathway



# Conclusions & Future Direction

- FGFR3-/- mice consistently develop a progressive scoliosis that correlates with skeletal growth
- To assess the osteopenia theory for scoliosis development in the FGFR3 -/- mice
- To test various growth factors in the FGFR3 -/- mice for scoliosis progression



# Thanks