



HAL
open science

Autocrine/paracrine IGF-1 plays a critical role in determining bone size prenatally and early postnatally

Sébastien Elis, Hayden-William Courtland, Yingjie Wu, Hui Sun, Karl J. Jepsen, Shoshana Yakar

► To cite this version:

Sébastien Elis, Hayden-William Courtland, Yingjie Wu, Hui Sun, Karl J. Jepsen, et al.. Autocrine/paracrine IGF-1 plays a critical role in determining bone size prenatally and early postnatally. 91. Annual Conference on endocrine System Diseases, The Endocrine Society. USA., Jun 2009, Washington, United States. hal-02751334

HAL Id: hal-02751334

<https://hal.inrae.fr/hal-02751334>

Submitted on 3 Jun 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



MOUNT SINAI
SCHOOL OF
MEDICINE

Elevated levels of serum IGF-1 restore peak bone properties and mechanical functionality in the absence of autocrine/paracrine IGF-1



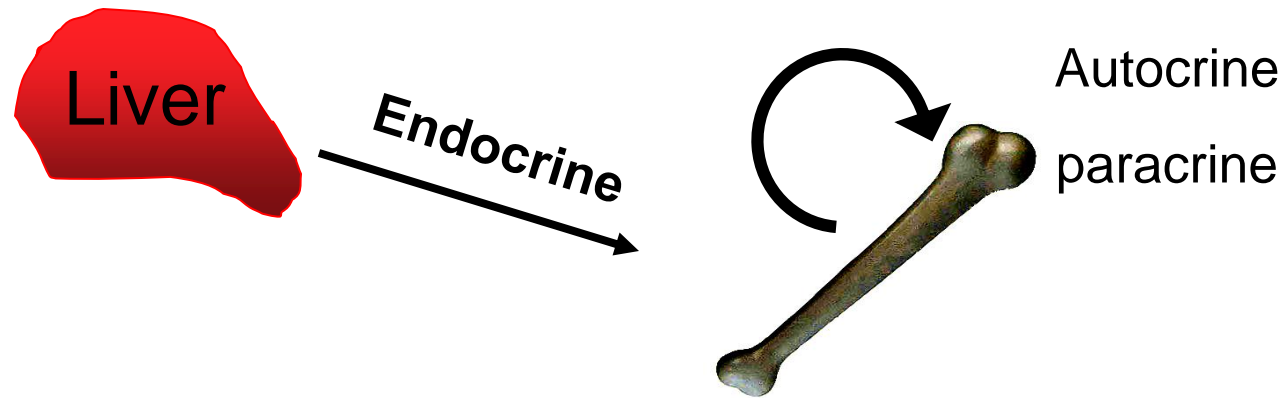
MOUNT SINAI
SCHOOL OF
MEDICINE

Sebastien Elis, Hayden-William Courtland,
Yingjie Wu, Hui Sun, Karl J Jepsen and
Shoshana Yakar

Mount Sinai School of Medicine
Department of Medicine
Division of Endocrinology, Diabetes and Bone Diseases

ENDO 09, Washington, 6.12.09

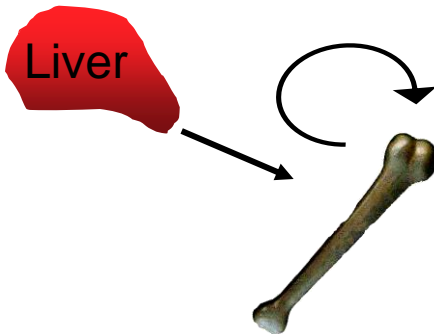
IGF-1 is an endocrine, and autocrine/paracrine modulator of growth and metabolism



Aim:

To test whether elevated serum IGF-1 levels can support skeletal growth and integrity in the complete absence of tissue IGF-1

Control



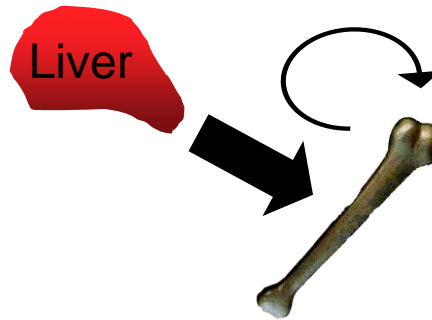
Normal serum IGF1 levels
Normal tissue IGF1 levels

HIT

Hepatic IGF-1 Transgene



TTR promoter



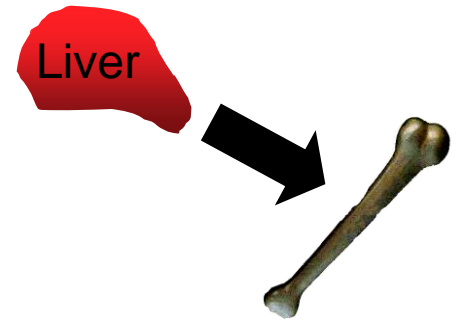
High serum IGF1 levels
Normal tissue IGF1 levels

KO-HIT

Total IGF-1 KO+
Hepatic IGF-1 Transgene



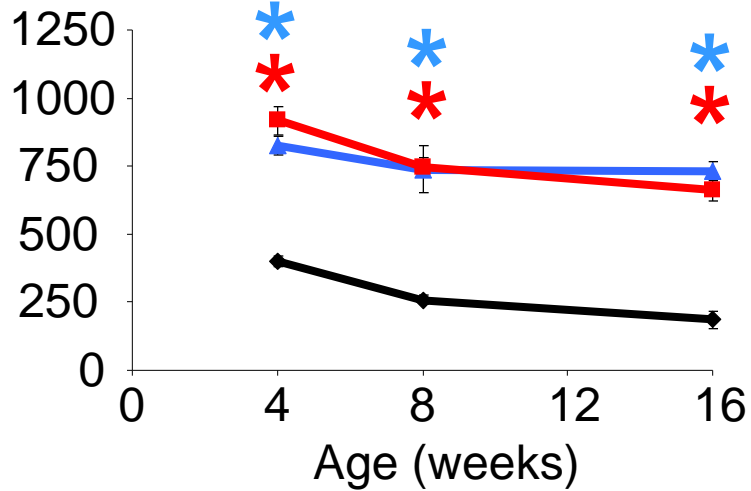
TTR promoter



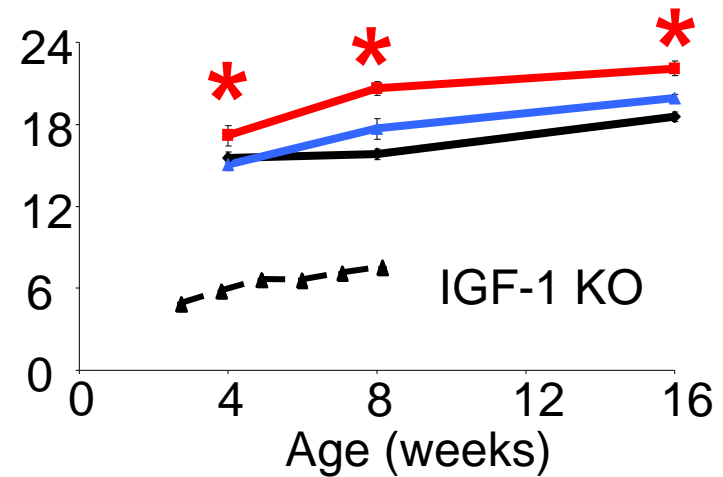
High serum IGF1 levels
NO tissue IGF1

High levels of endocrine IGF-1 increase body weight

Serum IGF-1 (ng/mL)

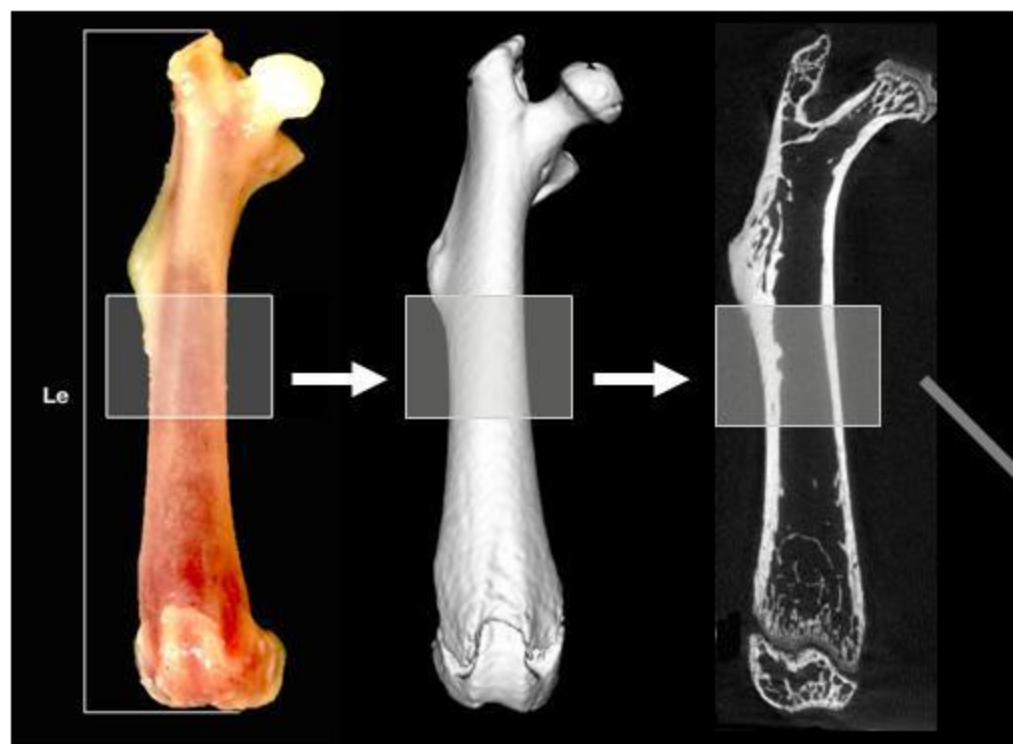


Body Weight (g)



Legend		Serum	Tissue
	Control	✓	✓
	HIT	✓	✓
	KO-HIT	✓	✗

Micro Computational Tomography

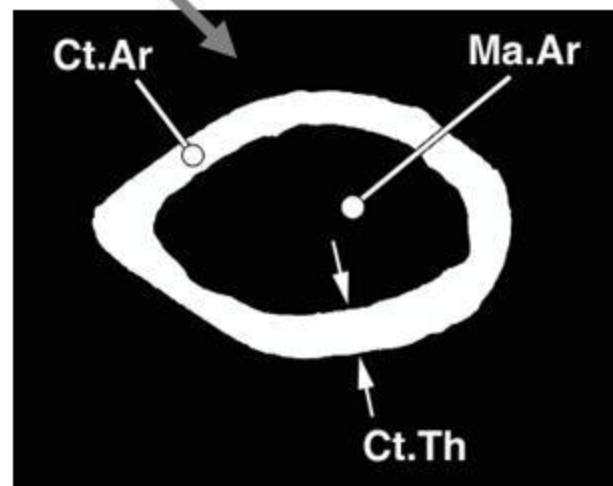


Morphology

Dynamic μ CT

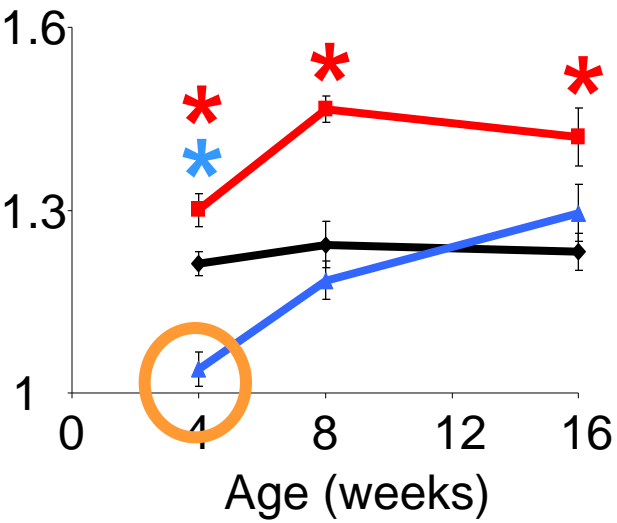
Midshaft of femur

Bone Compartment size

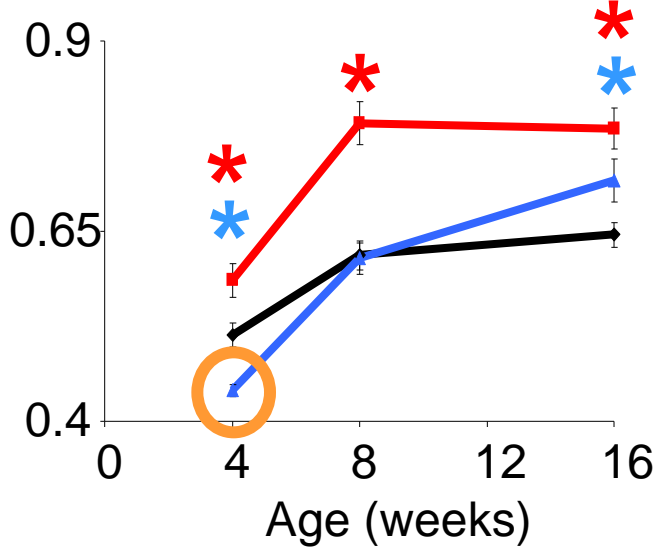


Cortical bone

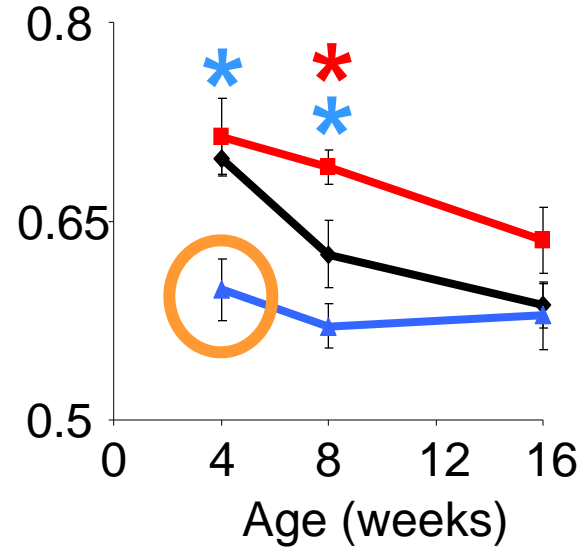
Total Area (mm²)



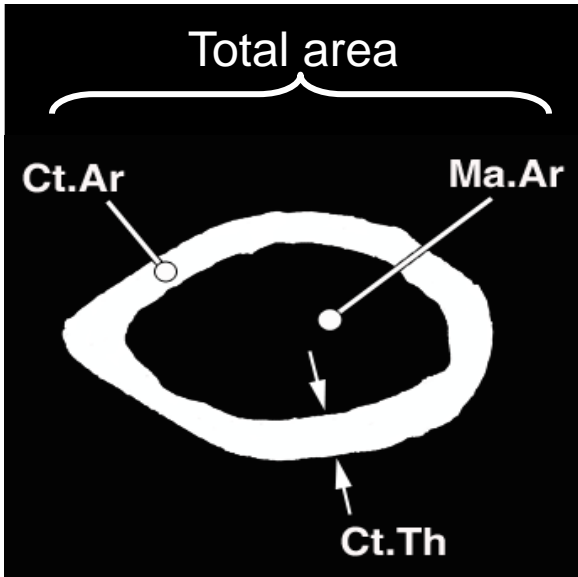
Cortical Area



Marrow Area



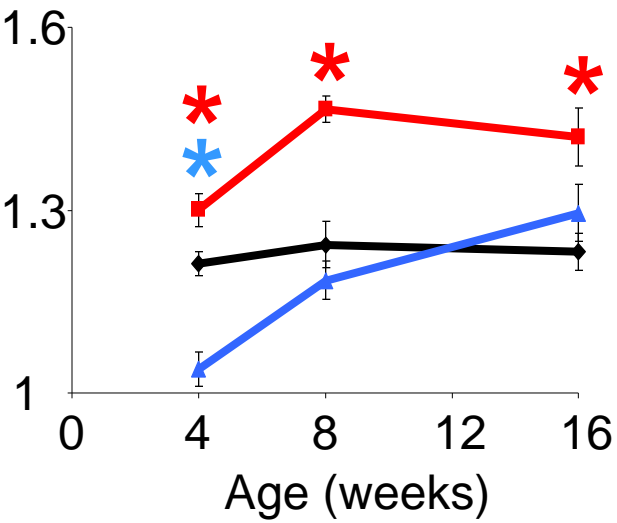
Autocrine/paracrine IGF-1 critical for early growth (before 4w)



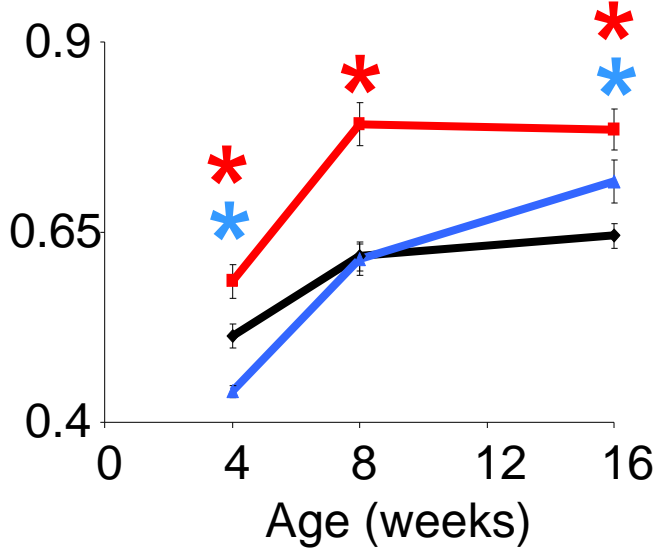
Legend		Serum	Tissue
—◆—	Control	✓	✓
—■—	HIT	✓	✓
—▲—	KO-HIT	✓	✗

Cortical bone

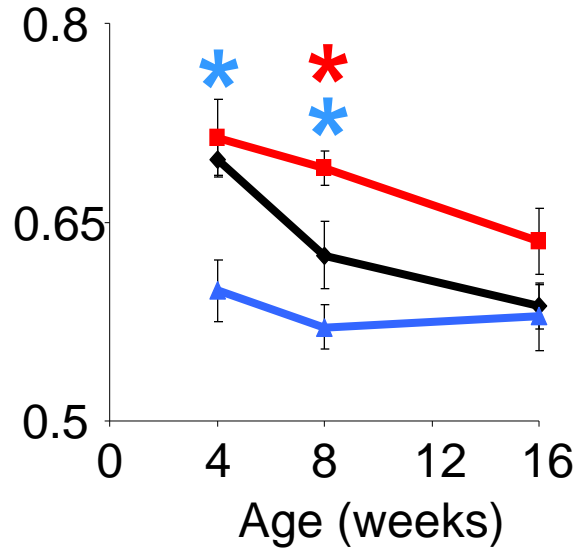
Total Area (mm²)



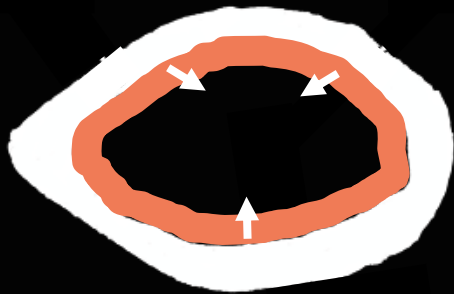
Cortical Area



Marrow Area



Marrow infilling



4 W

16 W

Control

Serum Tissue

✓ ✓

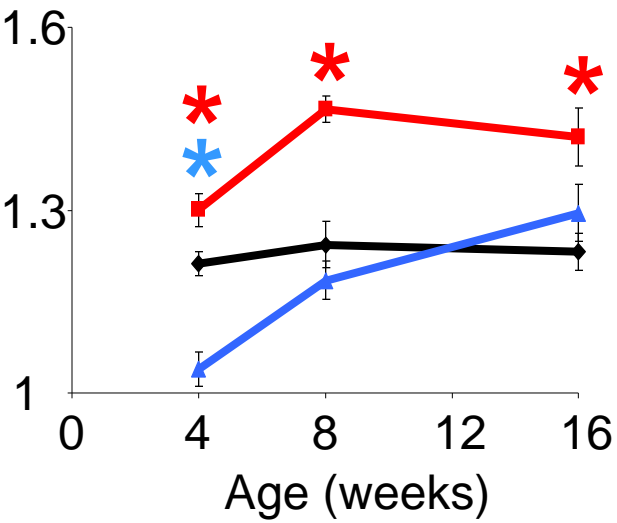
Legend

Serum Tissue

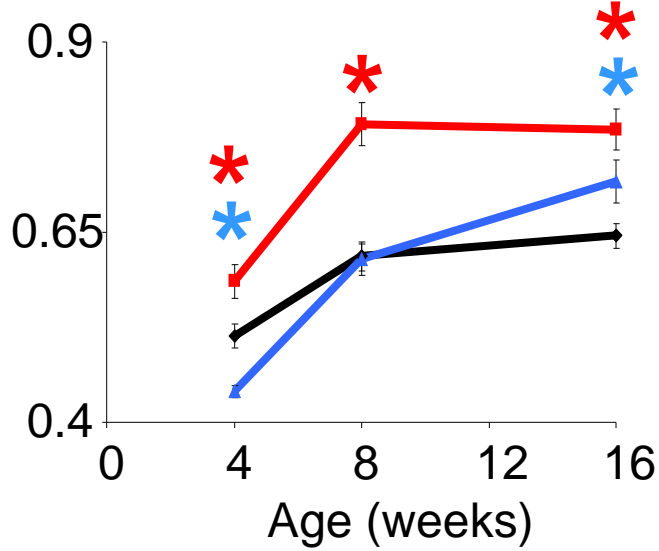
	Control	✓	✓
	HIT	✓	✓
	KO-HIT	✓	✗

Cortical bone

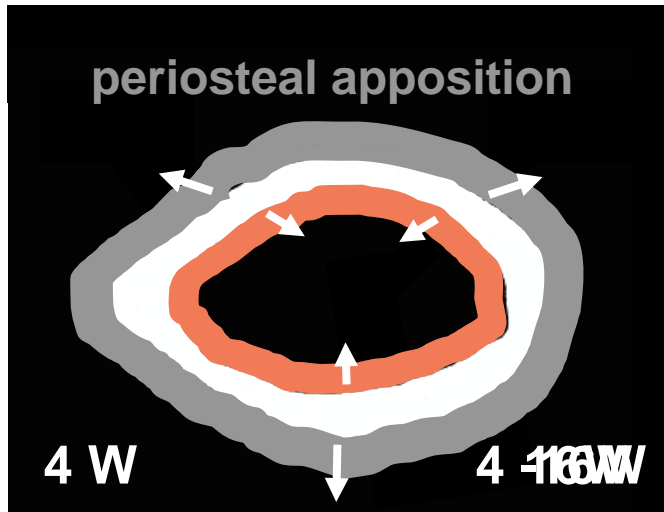
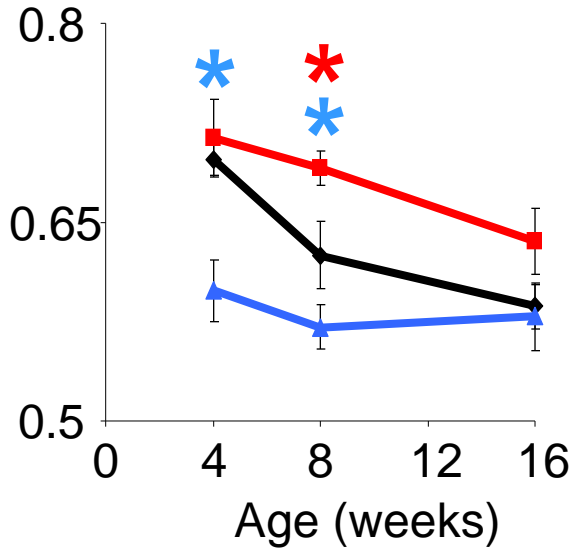
Total Area (mm²)



Cortical Area



Marrow Area

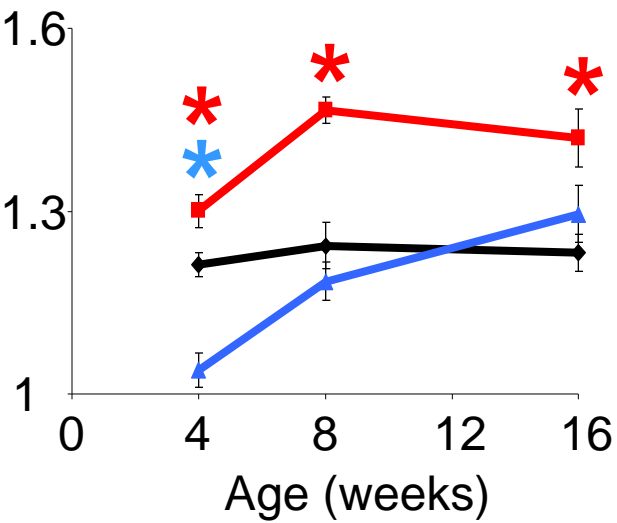


Control
Serum Tissue
✓ ✓

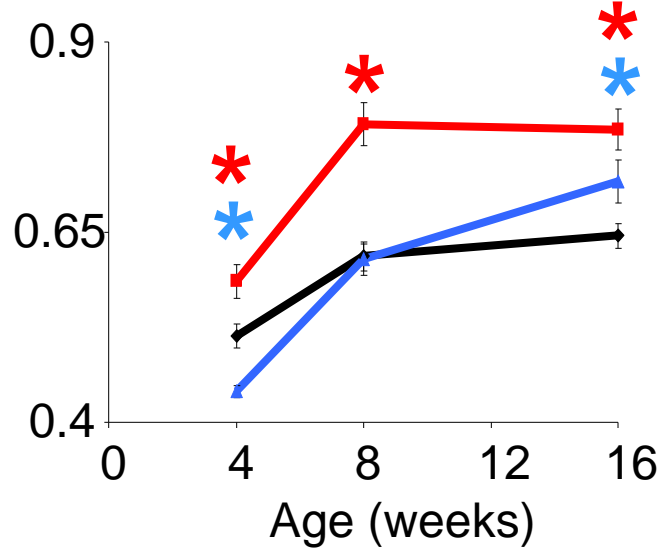
HIT
Serum Tissue
✓ ✓

Cortical bone

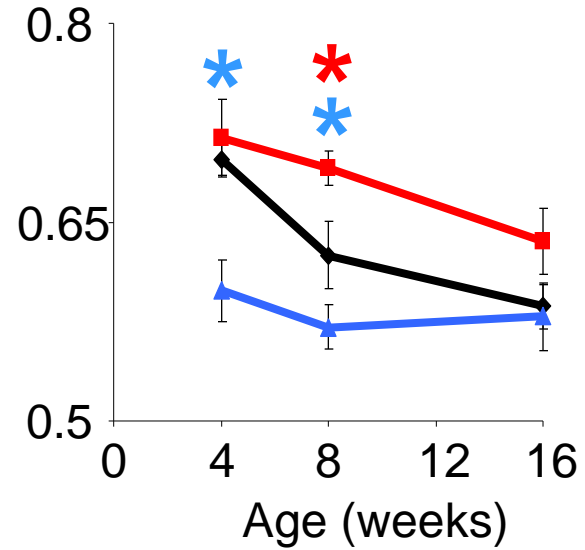
Total Area (mm²)



Cortical Area



Marrow Area



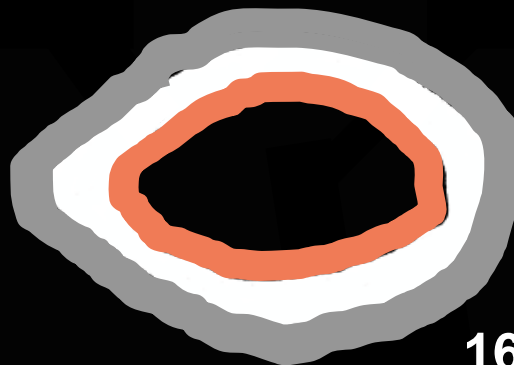
Marrow infilling



16W

Control
Serum ✓ Tissue ✓

Periosteal apposition



16W

HIT
Serum ✓ Tissue ✓

Periosteal apposition



4 W

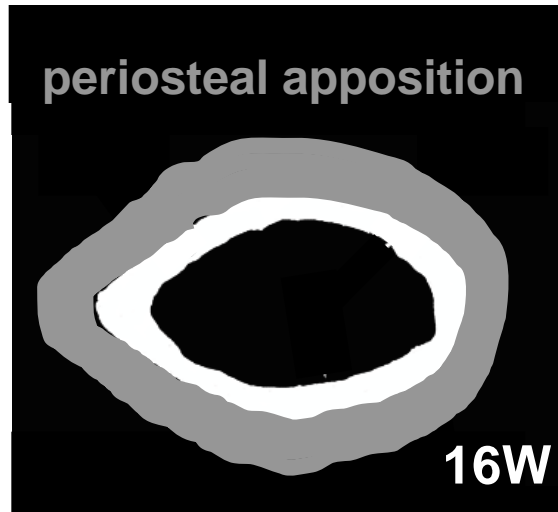
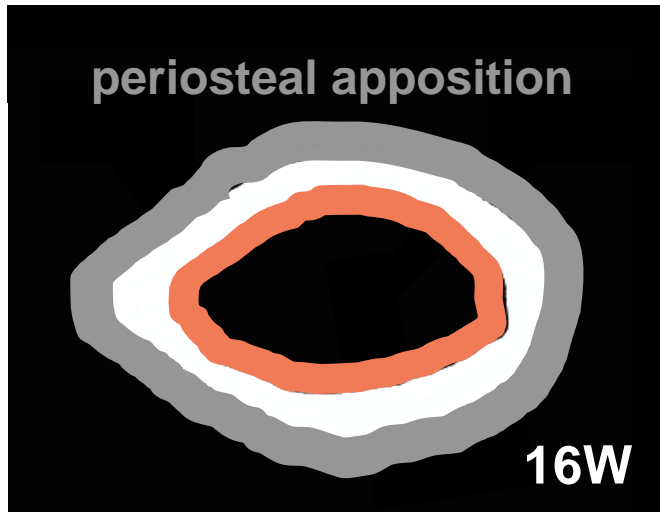
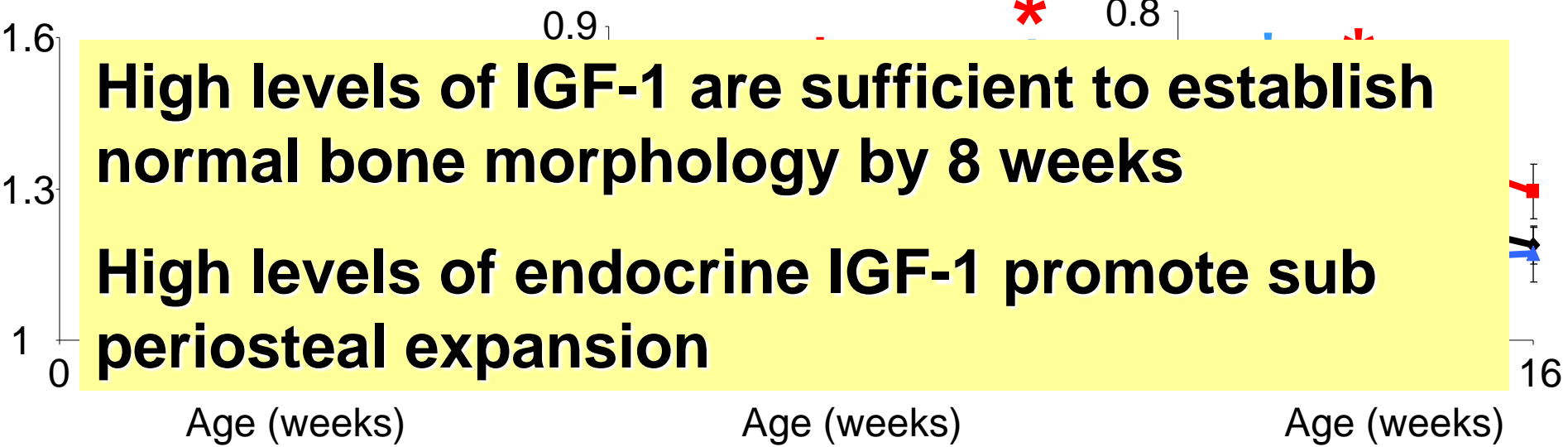
KO-HIT
Serum ✓ Tissue ✗

Cortical bone

Total Area (mm²)

Cortical Area

Marrow Area



Control

Serum Tissue



HIT

Serum Tissue

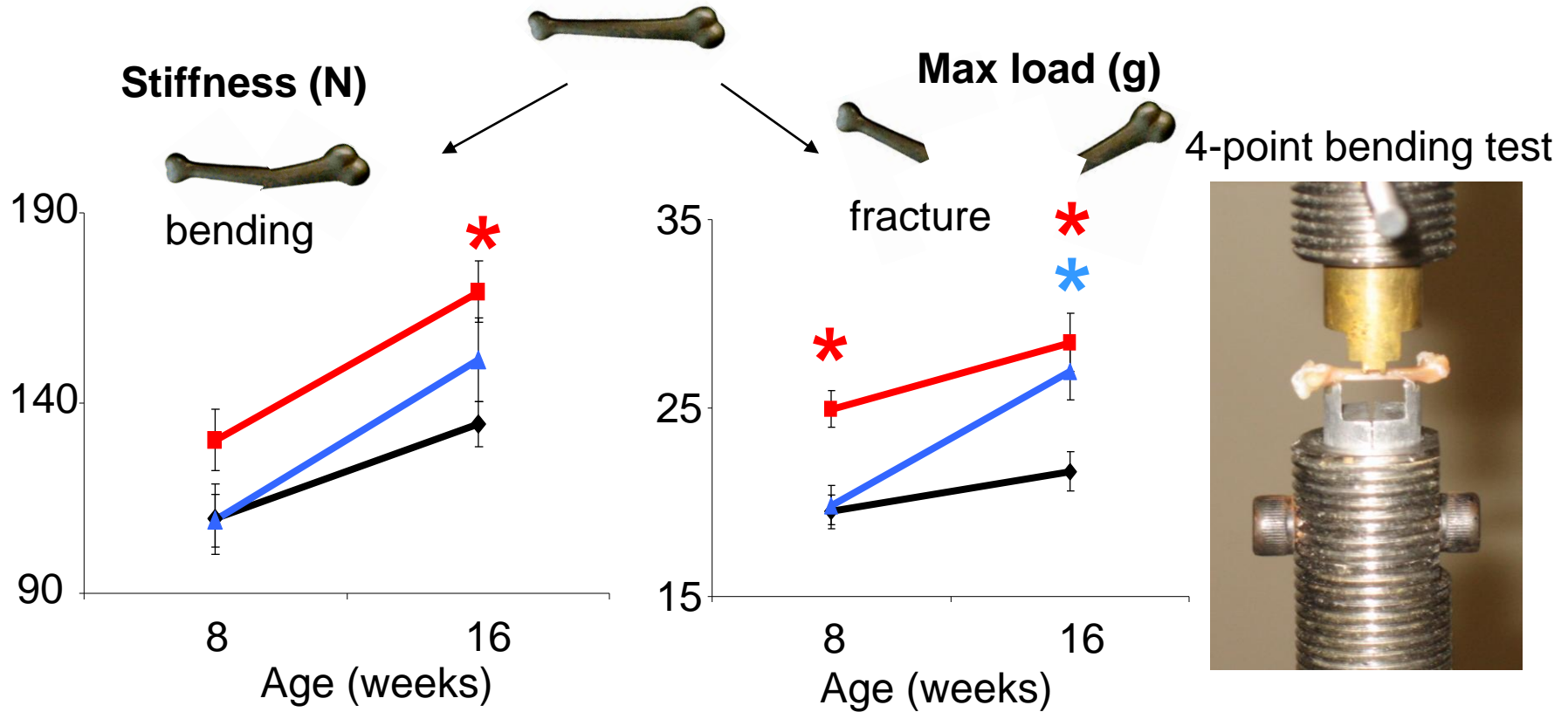


KO-HIT

Serum Tissue



Mechanical properties



8 weeks :

HIT

cortices



max load



KO-HIT

cortices

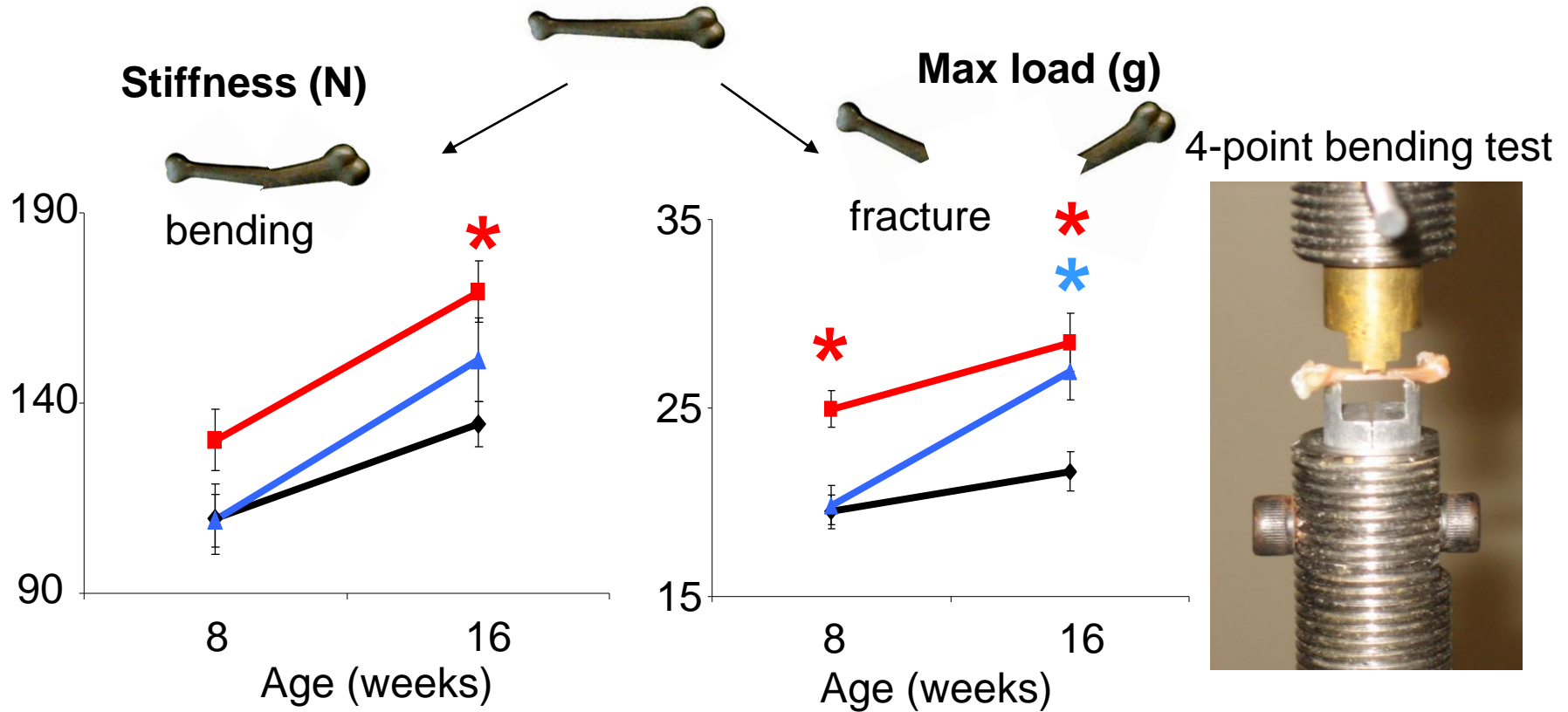


max load



Legend		Serum	Tissue
	Control	✓	✓
	HIT	✓	✓
	KO-HIT	✓	✗

Mechanical properties

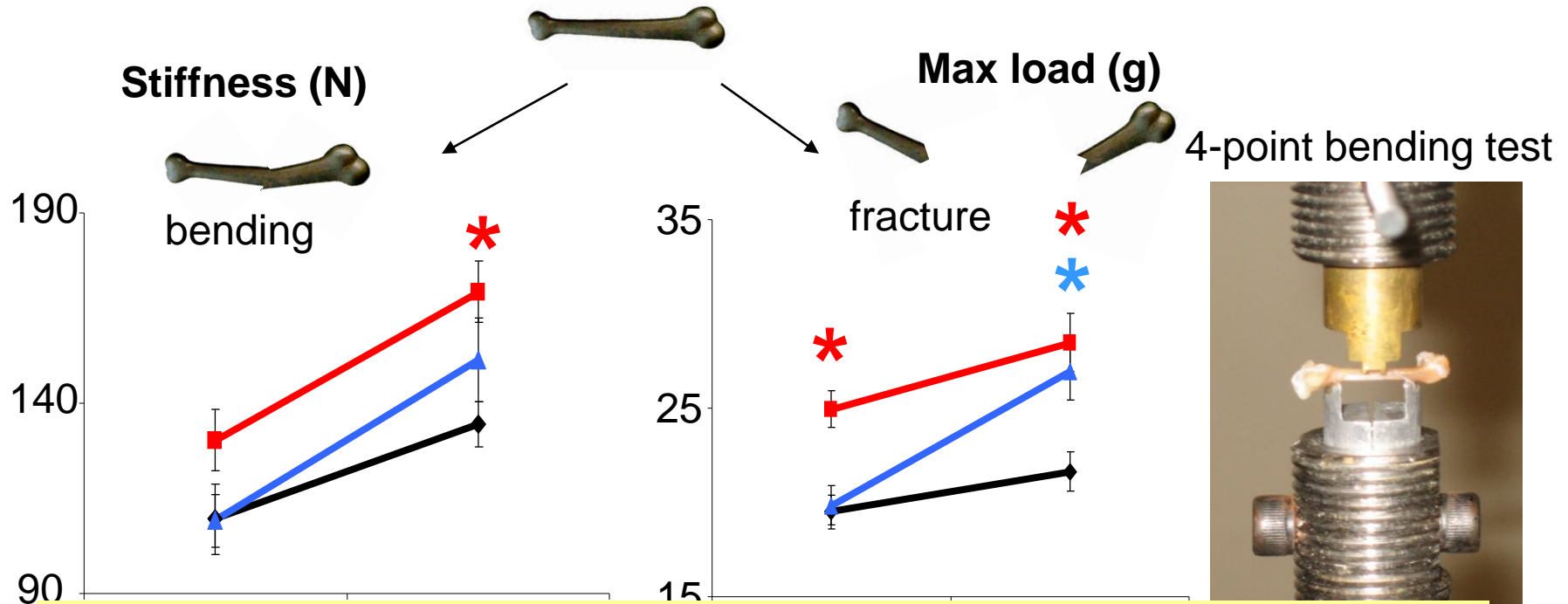


16 weeks :

HIT	cortices	↗	max load	↗
KO-HIT	cortices	↗	max load	↗

Legend		Serum	Tissue
—◆—	Control	✓	✓
—■—	HIT	✓	✓
—▲—	KO-HIT	✓	✗

Mechanical properties



Elevated levels of IGF-1 in serum increase bone mechanical properties

Elevated levels of IGF-1 compensate for a lack of local IGF-1 both morphologically and mechanically

tissue

✓

✓

✗

Summary

Postnatally, elevated serum IGF-1 levels :

- increase in body weight.
- increase bone morphological traits
- increase in mechanical properties.

Tissue IGF-1 is critical for neonatal and early postnatal growth (before 4w).

Elevated serum IGF-1 levels fully compensate for a postnatal absence of tissue IGF-1 :

Morphologically & Mechanically

Acknowledgments

Endocrinology division, Mount Sinai School of Medicine



Shoshana
Yakar

Hayden-William
Courtland

Hui Sun

Yingjie Wu

Clifford
Rosen



Valerie Williams

Karl J Jepsen

**Orthopaedics department, Mount Sinai School
of Medicine**



U.S. Department of Health
and Human Services

Supported by the



**National
Institutes
of Health**

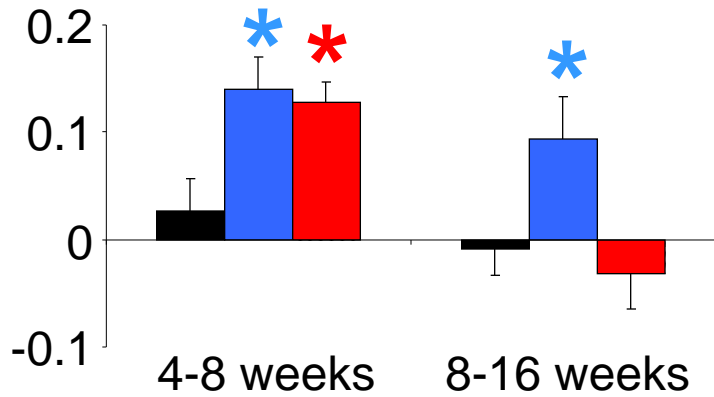


R01AR055141
R01AR054919

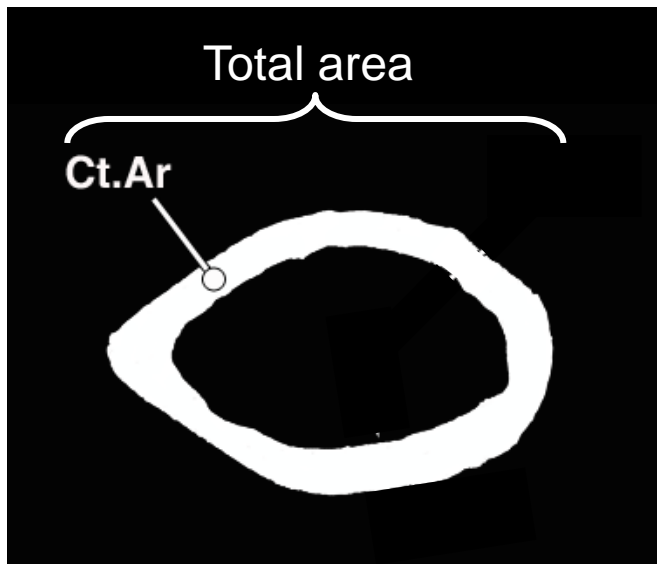
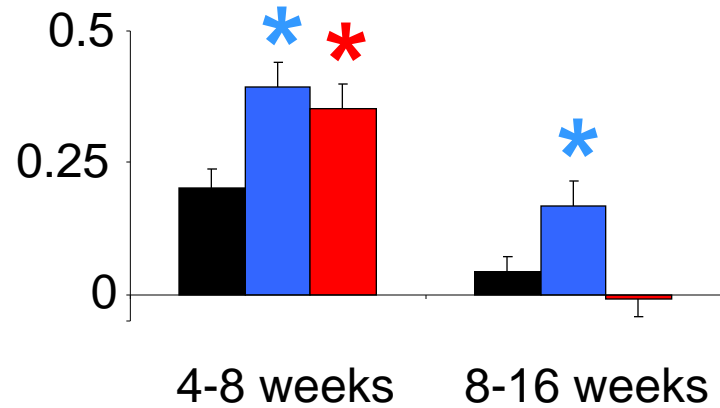
THANK YOU

Increased serum IGF-1 levels accelerate growth rate

Growth rate of TtAr



Growth rate of CtAr



Legend		Serum	Tissue
Black	Control	✓	✓
Red	HIT	✓	✓
Blue	KO-HIT	✓	x