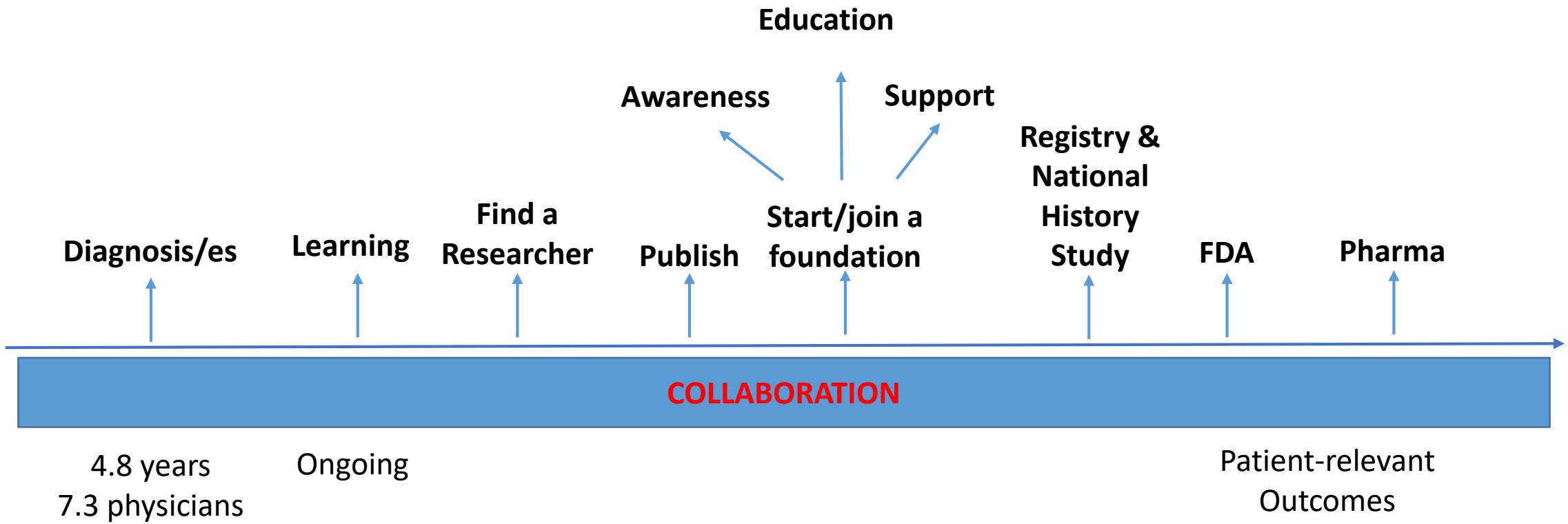
The Diagnostic Odyssey

- Dr. Neena Nizar

www.thejansensfoundation.org



Patient Pathway to Cures/Treatment

- A rare disease
- Miles and miles of desert sand
- No Google
- No “expert opinions”

Christmas, 2009

No Sign of Disease

Arshaan Adam (A Strong and Brave Man)

Christmas, 2010

A Diagnosis at last

Jahan Adam (Savior)

Jansen Metaphyseal Chondrodysplasia (JMC)

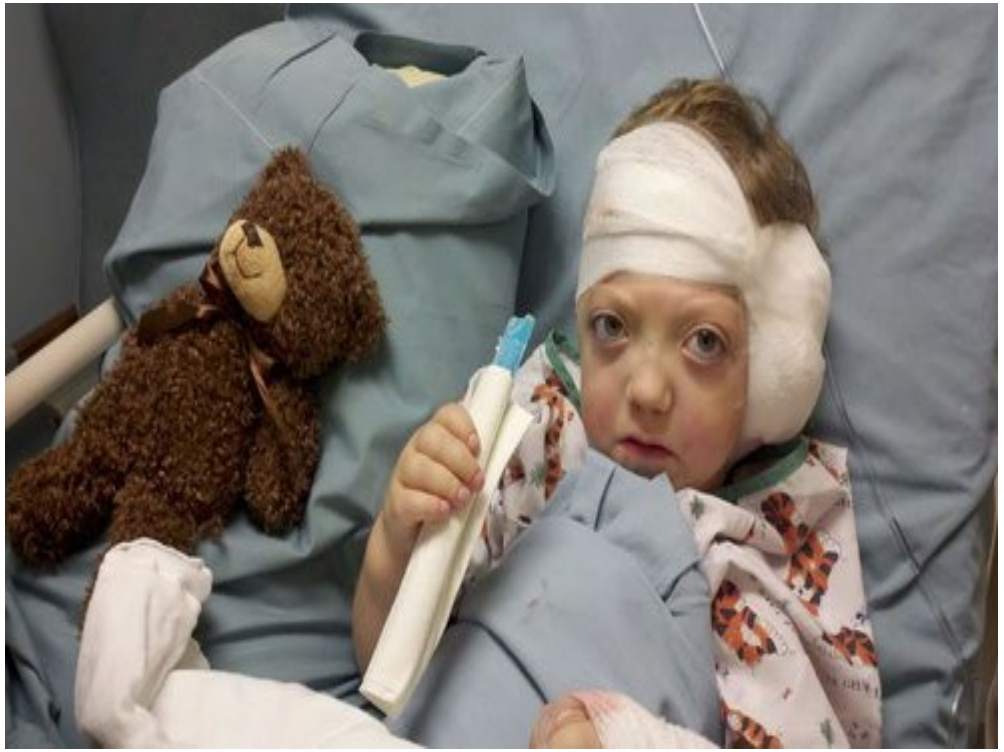
- A rare disease of bone and mineral ion physiology
- ~ 30 patients known to date
- Autosomal dominant, caused by activating mutations in the PTH/PTHrP receptor (PTHR1)
- Short stature, skeletal abnormalities, hypercalcemia/hypercalciuria, nephrocalcinosis, renal disease.

Dr. Harald Jueppner had been researching Jansen's Disease for 20 years, but ***never*** met a patient.

Rare Disease Day 2016, NIH

A.I. Dupont Hospital 2016, Delaware

The Jansen's Foundation formed in February, 2017.



Jansen's patient recovering from eardrum reconstruction, was born with craniosynostosis - the fusion of the skull's bones, and at two years old had to have his skull broken to make room for his brain to grow.

Text Source: National Organization for Rare Diseases website, https://rarediseases.org/rare-diseases/jansen-type-metaphyseal-chondrodysplasia/.
Picture Source: Jansen's Foundation website:

Jansen's Foundation and MGH

Connected with the research team at MGH, and has been supporting the research efforts.

ORIGINAL ARTICLE

Jansen Metaphyseal Chondrodysplasia due to Heterozygous H223R-PTH1R Mutations With or Without Overt Hypercalcemia

Sheela Nampoothiri, Eduardo Fernández-Rebollo, Dhanya Yesodharan, Thomas J. Gardella, Eric T. Rush, Craig B. Langman, and Harald Jüppner

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Context: Jansen's metaphyseal chondrodysplasia (JMC) is a rare skeletal dysplasia characterized by abnormal endochondral bone formation and typically severe hypercalcemia despite normal/low levels of PTH. Five different heterozygous activating PTH/PTHrP receptor (PTH1R) mutations that change one of three different amino acid residues are known to cause JMC.

Objectives: Establishing the diagnosis of JMC during infancy or early childhood can be challenging, especially in the absence of family history and/or overt hypercalcemia. We therefore sought to provide radiographic findings supporting this diagnosis early in life.

Patients and Methods: Three patients, a mother and her two sons, had radiographic evidence for JMC. However, obvious hypercalcemia and suppressed PTH levels were encountered only in both affected children. Sanger sequencing and endonuclease (*Sph*I) digestion of PCR-amplified genomic DNA were performed to search for the H223R-PTH1R mutation.

Results: The heterozygous H223R mutation was identified in all three affected individuals. Surprisingly, however, the now 38-year-old mother was never overtly hypercalcemic and was therefore not diagnosed until her sons were found to be affected by JMC at the ages of 28 months and 40 days, respectively. The presented radiographic findings at different ages will help diagnose other infants/toddlers suspected of having JMC.

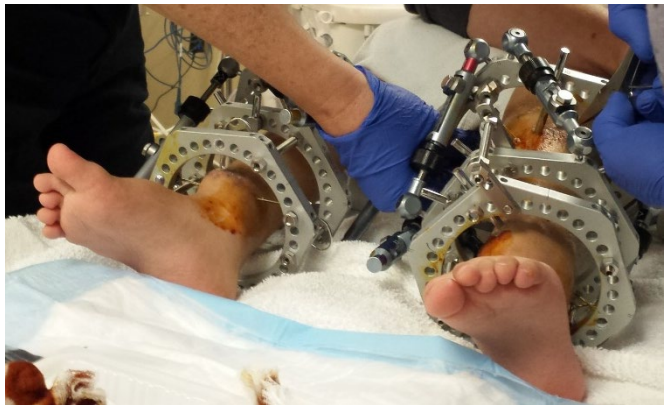
Conclusion: The H223R mutation is typically associated with profound hypercalcemia despite low/normal PTH levels. However, the findings presented herein show that overt hypercalcemia is not always encountered in JMC, even if caused by this relatively frequent mutation, which is similar to observations with other PTH1R mutations that show less constitutive activity. (***J Clin Endocrinol Metab*** **101: 4283–4289, 2016)**

Children Living with Jansen's

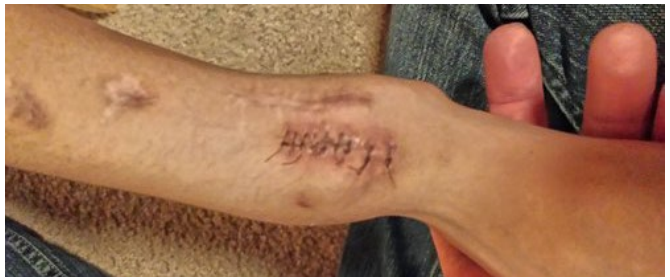
"During childhood, affected individuals may begin to exhibit progressive stiffening and swelling of many joints and/or an unusual 'waddling gait' and squatting stance."

Jansen's patient's legs pre-surgery

Post-Surgery Recovery



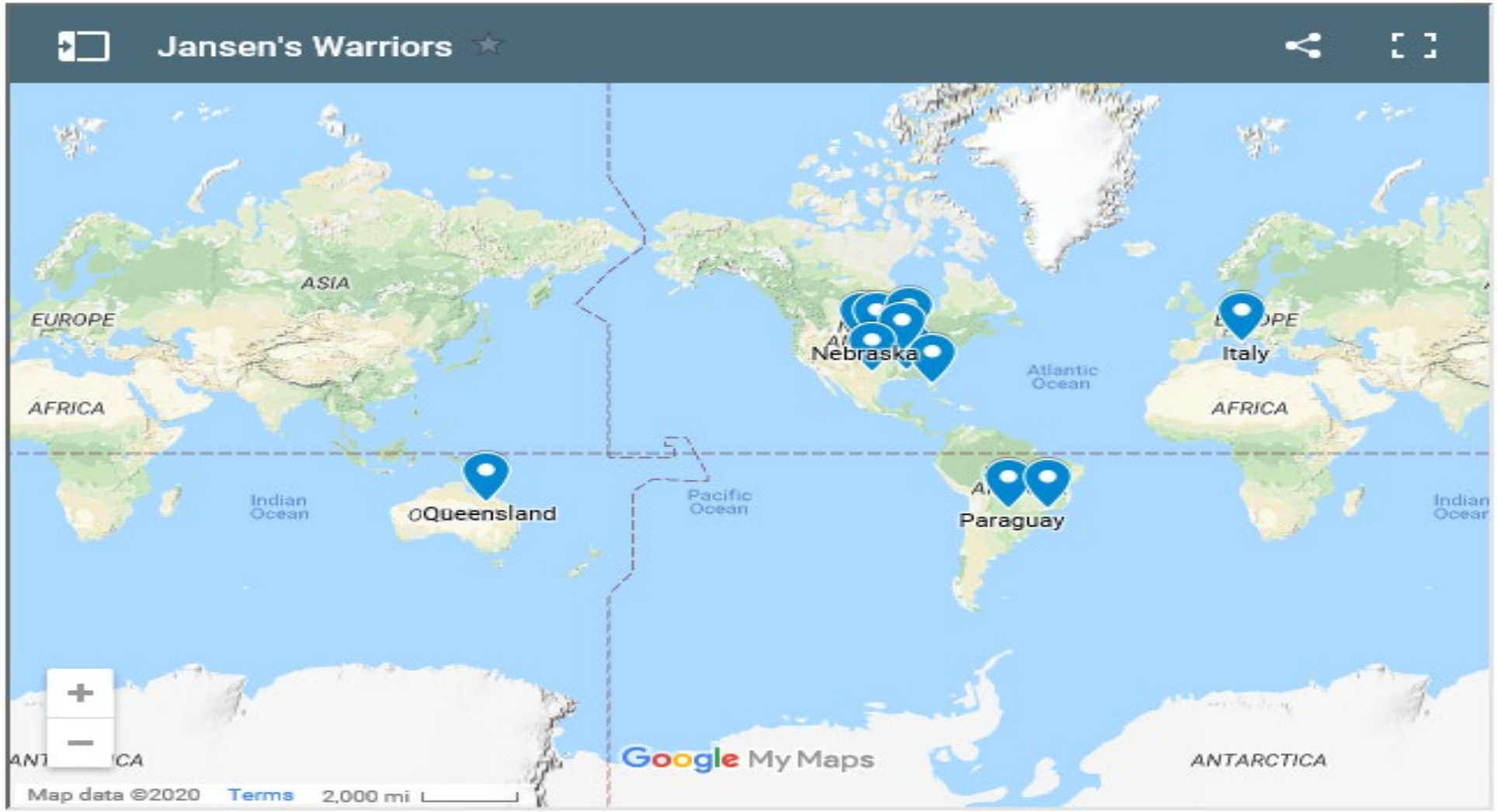
A few months post-surgery, the "Bends" are already back



Text Source: National Organization for Rare Diseases website, https://rarediseases.org/rare-diseases/jansen-type-metaphyseal-chondrodysplasia/.
Picture Source: Jansen's Foundation website:

The Monster Inside

See where our Jansen's Warriors Are At.



All 5 Jansen's warriors in America

Summer 2017

Creating Awareness for Jansen's

Nebraska's Neena Nizar Seeks Cure for Jansen's, One of World's Rarest Diseases

AUGUST 20, 2019 BY LARRY LUXNER IN NEWS.

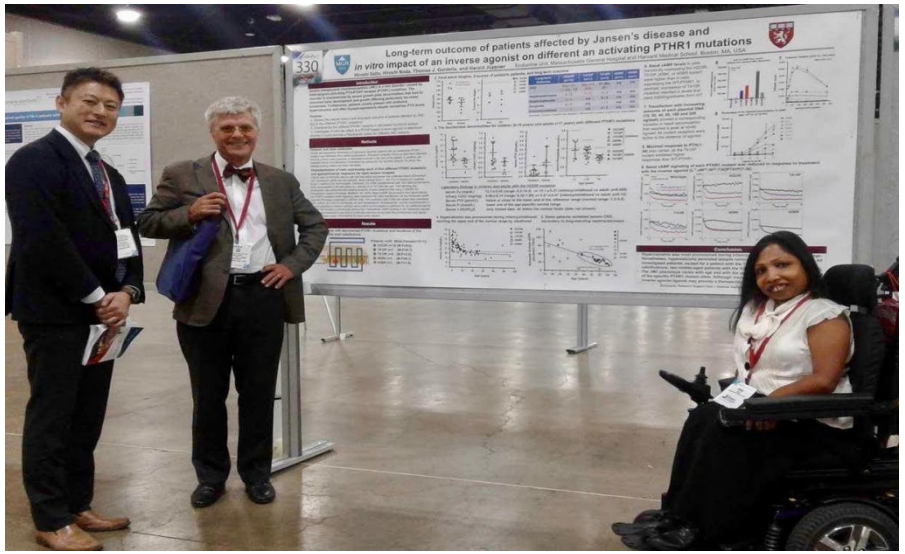
Meet the Rare Family Who Account for 10% of All Cases of Jansen's

There Are Just 30 Known Cases of Jansen's Metaphyseal Chondrodysplasia Worldwide

Neena Nizar
February 11, 2019

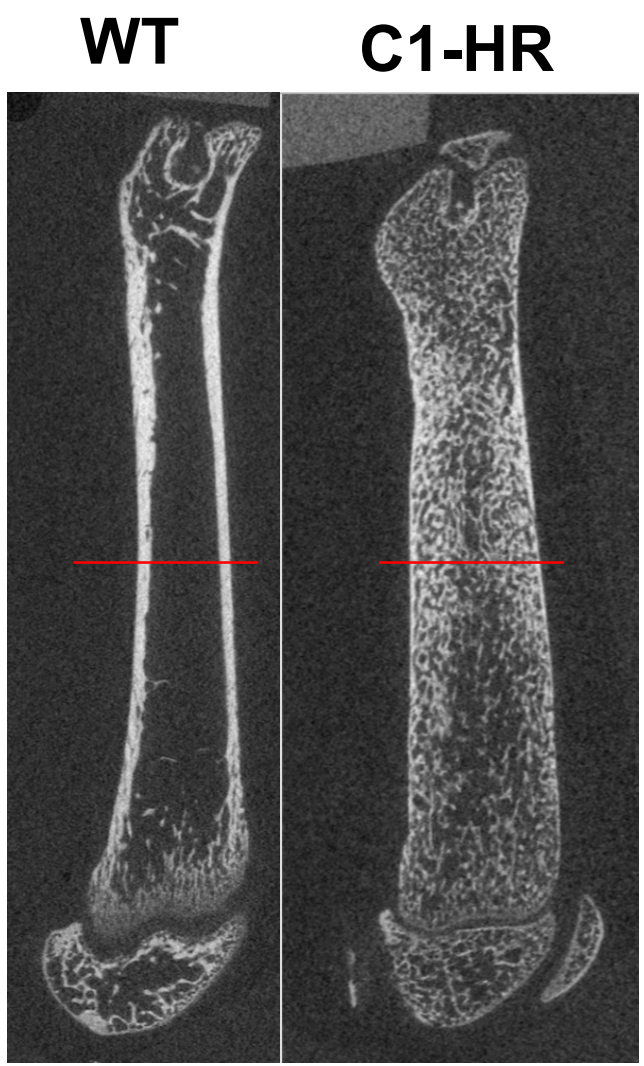
Tweet Share

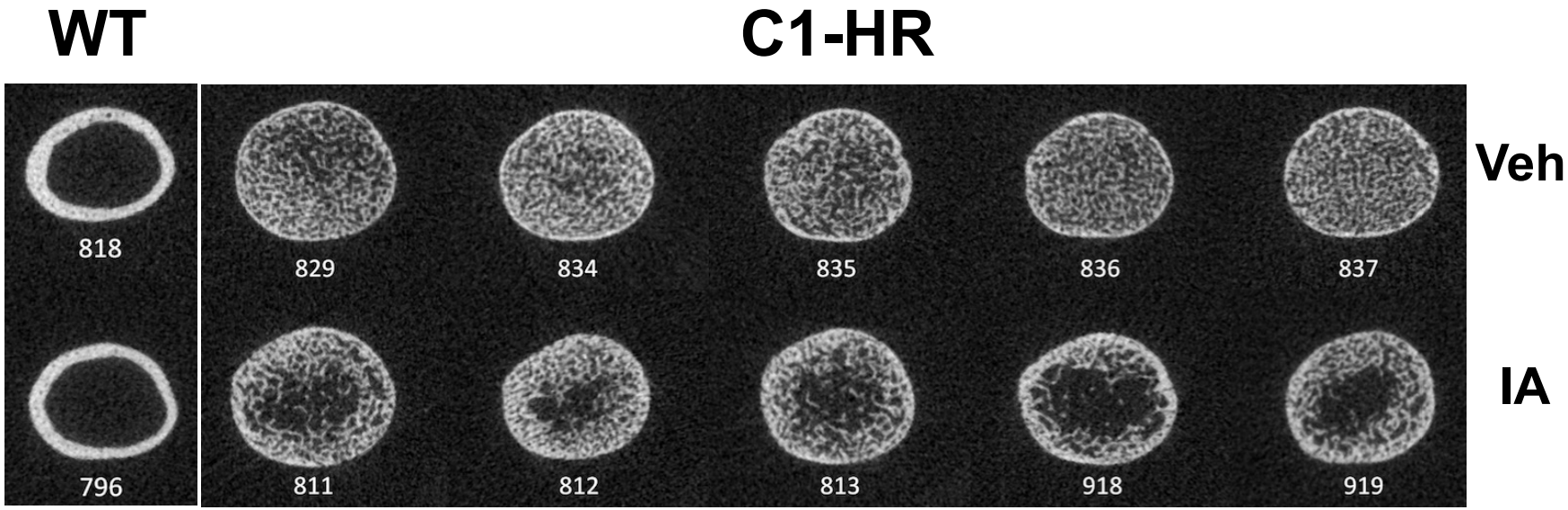
MGH Research Team

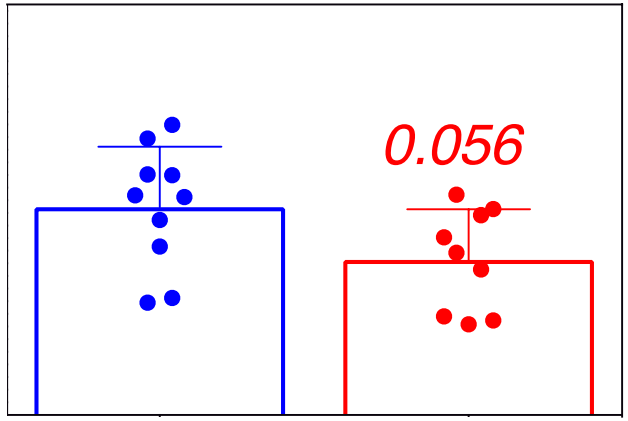


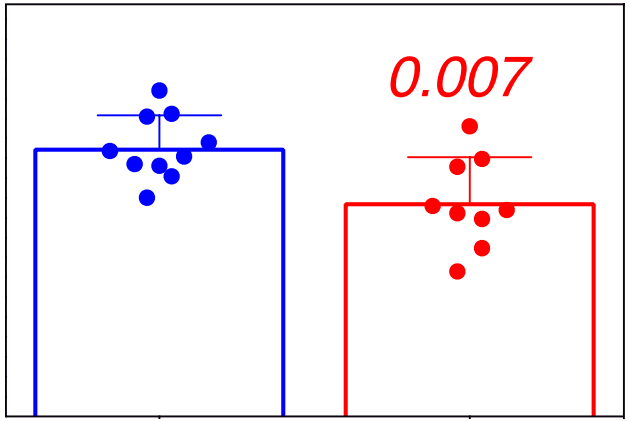
ASMBR Conference, Colorado, 2017

Inverse agonist (IA) improves bone parameters of C1-HR mice









The Jansen's Foundation Mission

The Jansen's Foundations goal is to speed up research process, obtain all the necessary approvals, and to start the first testing of a disease-modifying peptide in an adult patient with Jansen's disease.

- **Nov. 2017 – RO1 NIH grant – pre-clinical studies**
- **June 2018 – Pre-IND meeting with FDA**
- **Sept 2018 – Patient Registry**
- **2019 – NCATS TRND grant**

2022 – FIH PROTOCOL TO FDA

Never doubt that a small group of thoughtful, committed people can change the world.

Warriors of Hope!

Thank You!