

THE JOURNAL OF BONE & JOINT SURGERY



PERSPECTIVES: SPECIALTY UPDATES

What's New in Musculoskeletal Basic Science

 Bahney, Chelsea S. PhD¹;  Stoddart, Martin J. PhD²;  Miclau, Theodore MD^{1,a};  Marcucio, Ralph S. PhD¹

[Author Information](#) 

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Chelsea S Bahney, PhD

Associate Professor, Orthopaedic Trauma Institute

University of California San Francisco (UCSF)

April 2026



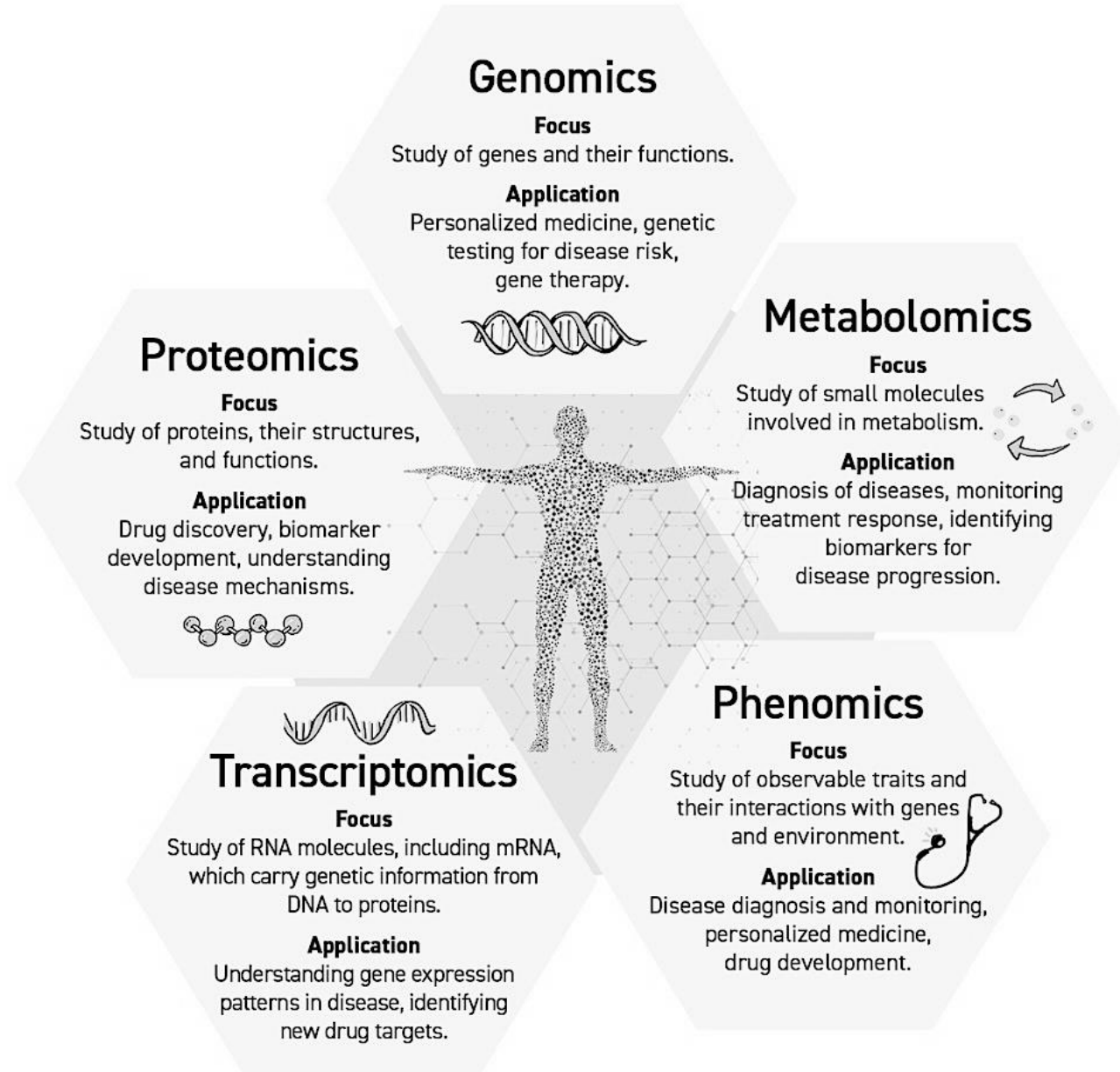
Orthopaedic Trauma Institute

UCSF + SAN FRANCISCO GENERAL HOSPITAL

Disclosures

- None

Advancing Orthopaedic Research with Multi-Omics

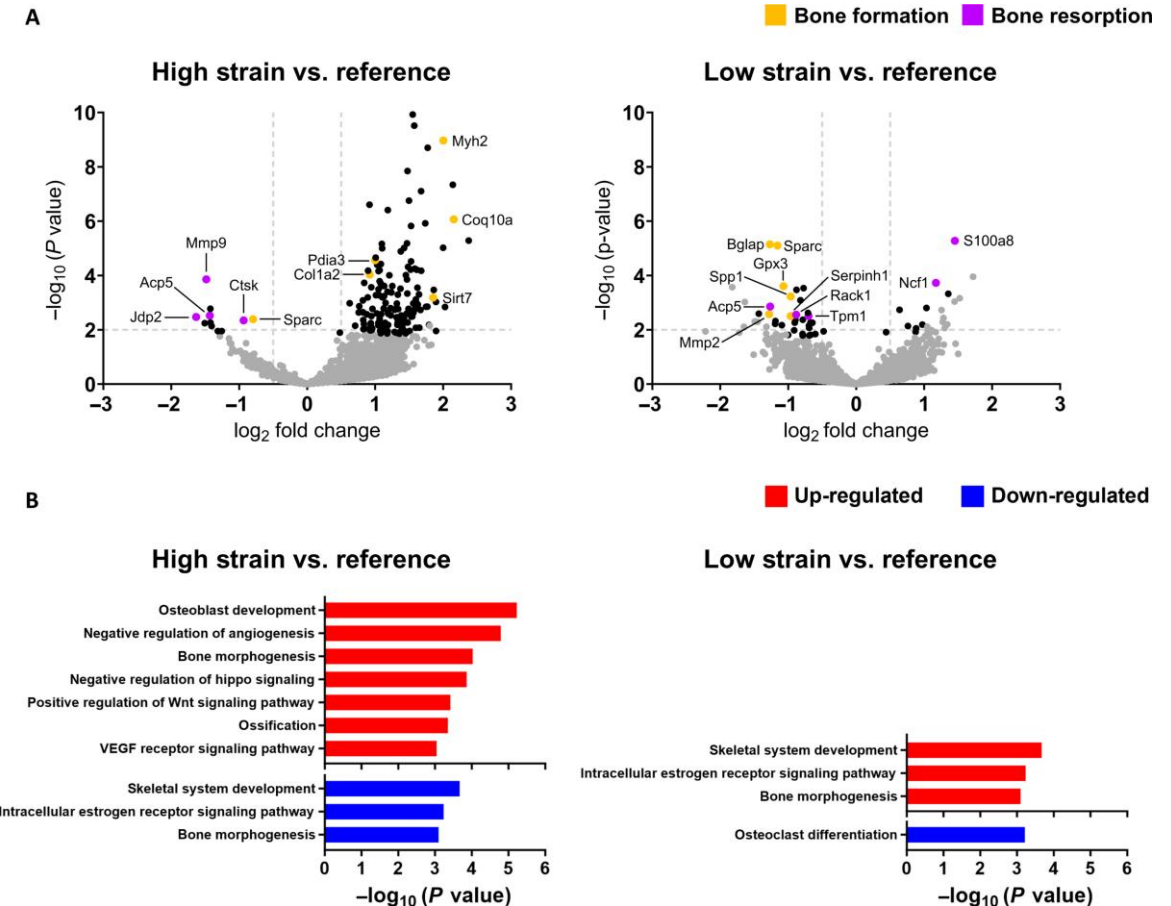
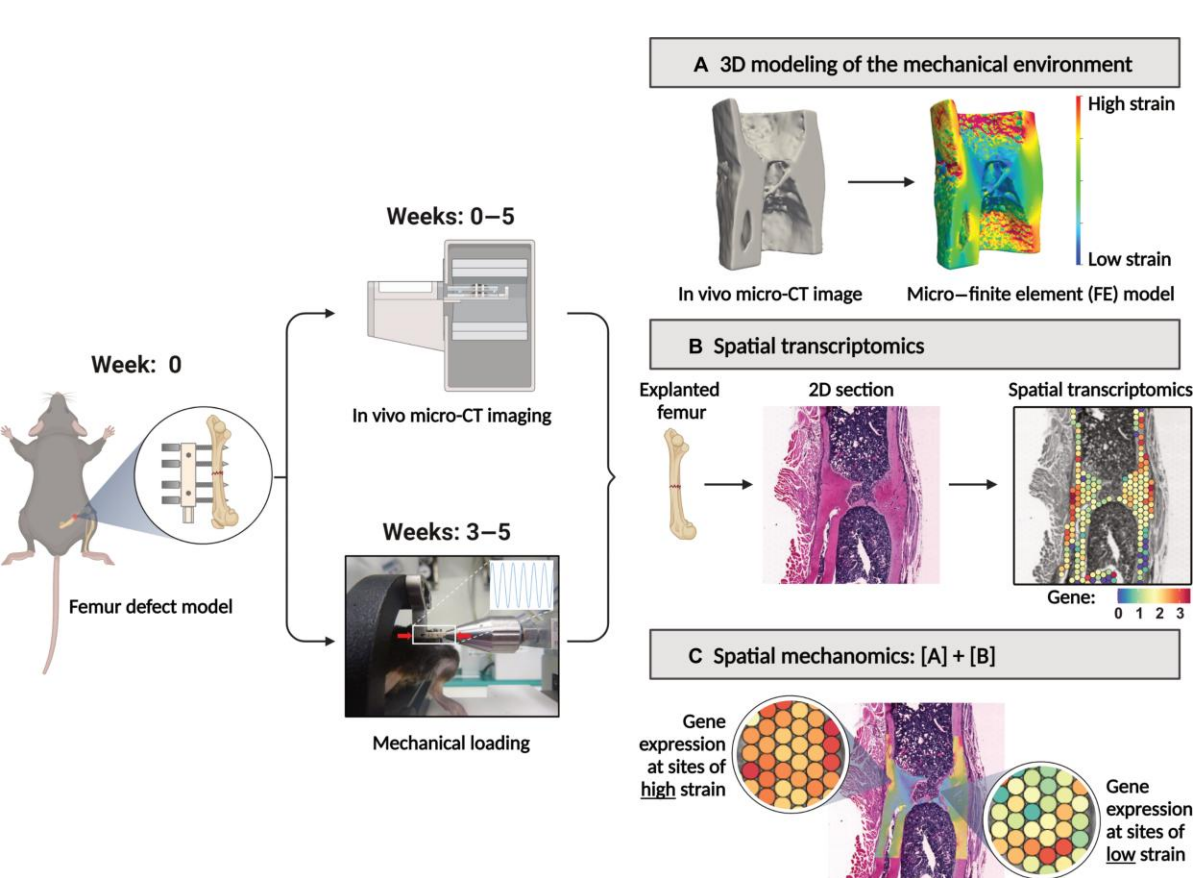


Transcriptomics Identifies Mechanoresponsive Genes

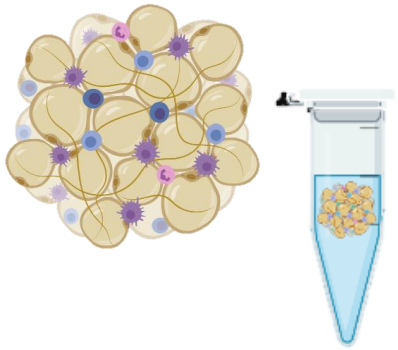


Spatial transcriptomics in bone mechanics: Exploring the mechanoregulation of fracture healing in the era of spatial omics

NEASHAN MATHAVAN , AMIT SINGH, FRANCISCO CORREIA MARQUES , DENISE GÜNTHER , GISELA A. KUHN, ESTHER WEHRLÉ , AND RALPH MÜLLER



Fat Talks To Cartilage: Adipokines Induce Pain & Destruction

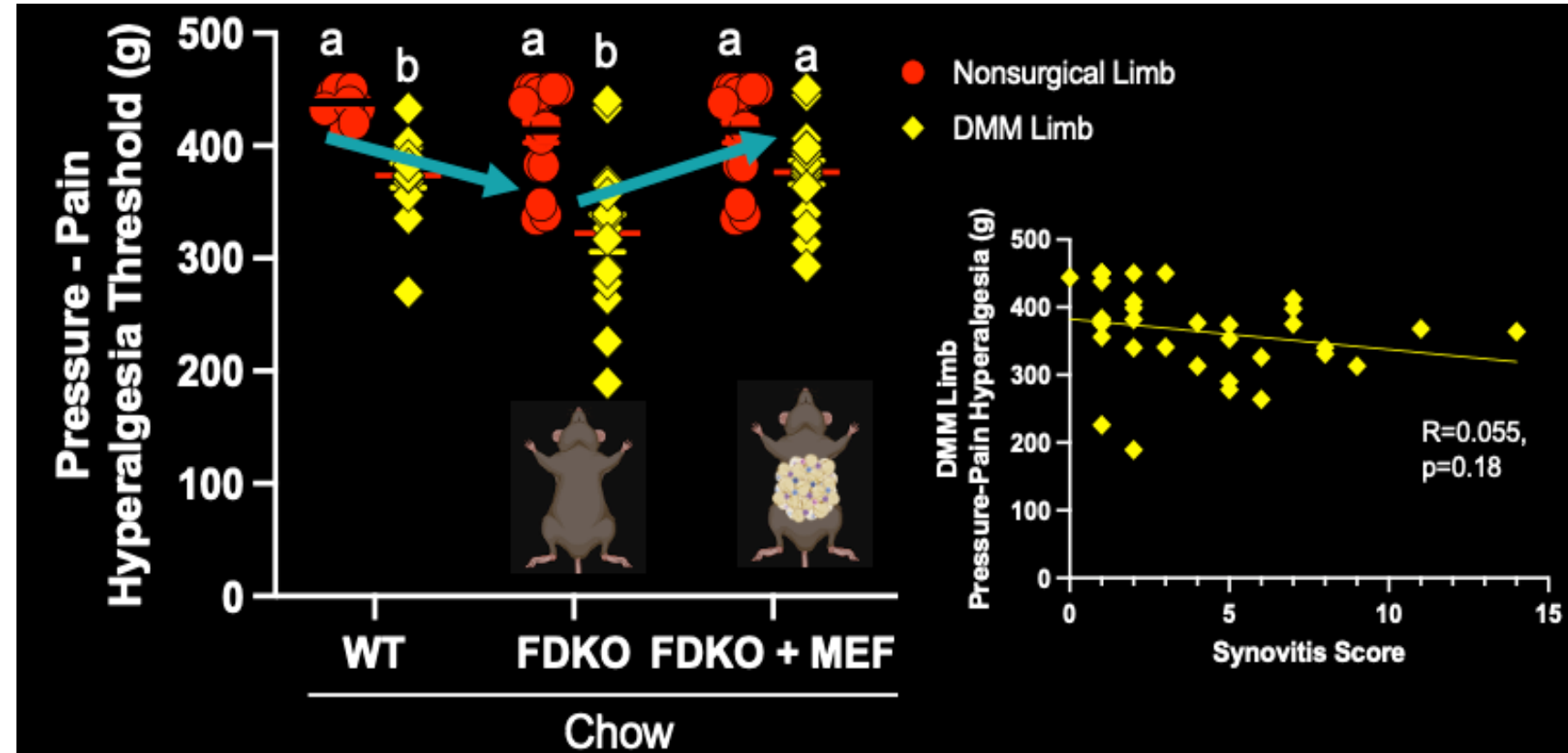
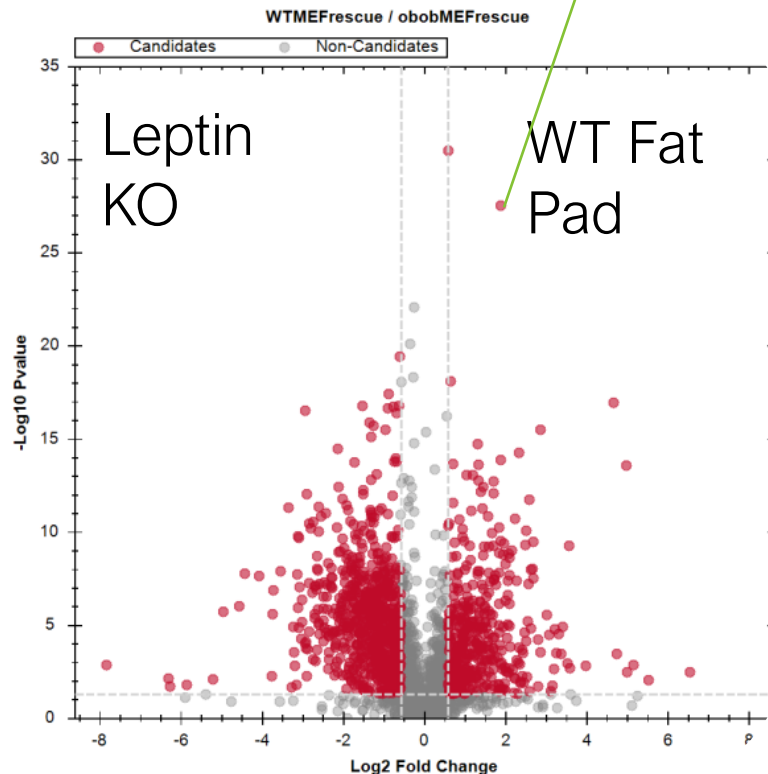


Complement
Factor D

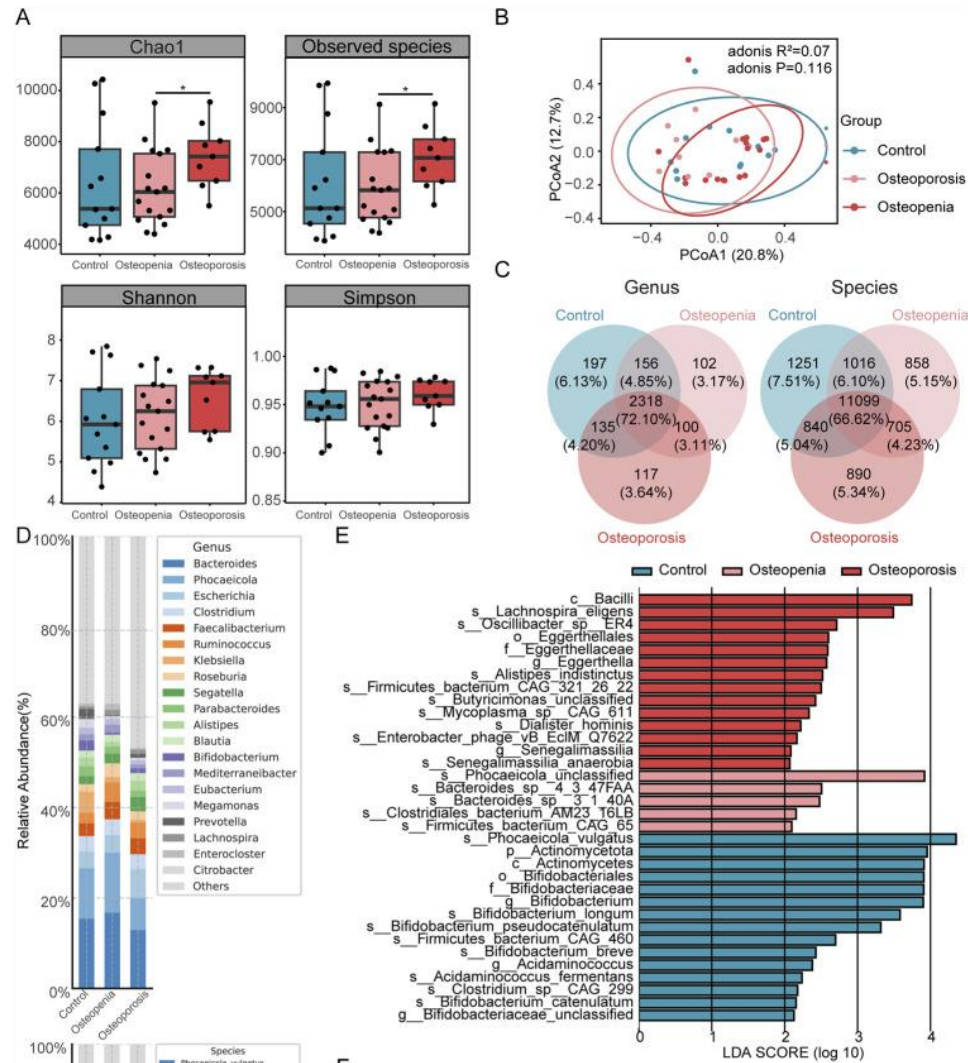


Adipose-derived leptin and complement factor D mediate osteoarthritis severity and pain

KELSEY H. COLLINS , KRISTIN L. LENZ , HOPE D. WELHAVEN , ERICA ELY , LUKE E. SPRINGER , SOPHIE PARADI , RUHANG TANG , LAURYN BRAXTON
ANTONINA AKK , [...], AND FARSHID GUILAK +7 authors [Authors Info & Affiliations](#)



Gut-Bone Axis: Microbiome-Metabolome in Fracture Repair



Front Mol Biosci. 2025 Sep 1;12:1646361. doi: [10.3389/fmolb.2025.1646361](https://doi.org/10.3389/fmolb.2025.1646361)

Gut microbiota-metabolome remodeling associated with low bone mass: an integrated multi-omics study in fracture patients

Intermittent fasting alleviates obesity-associated impairments in bone fracture healing: Exploring the role of gut microbiome

Honey Hendesj^{a,*}, Dana A Godfrey^a, Ana Ferreira Ruble^a, Aaron M Tran^b, David A Villani^a, Samantha H Landgrave^{a,c}, Nur A Hasan^d, Douglas J Adams^a, Michael J Zuscik^a

- Unique microbiota-metabolome axis in fracture patients with low bone mass
- Microbiome as a possible non-invasive biomarkers for assessing skeletal health.
- Microbiome “correction” can improve fracture repair

Limitations of Current Methods of Monitoring Healing

CURRENT METHODS



X-ray: late detection



Clinical observation: subjective



CT scan: radiation, expensive

} *Qualitative*

RESEARCH



Biomarkers correlating to progression of healing have not been identified



Sensors to measure tissue properties

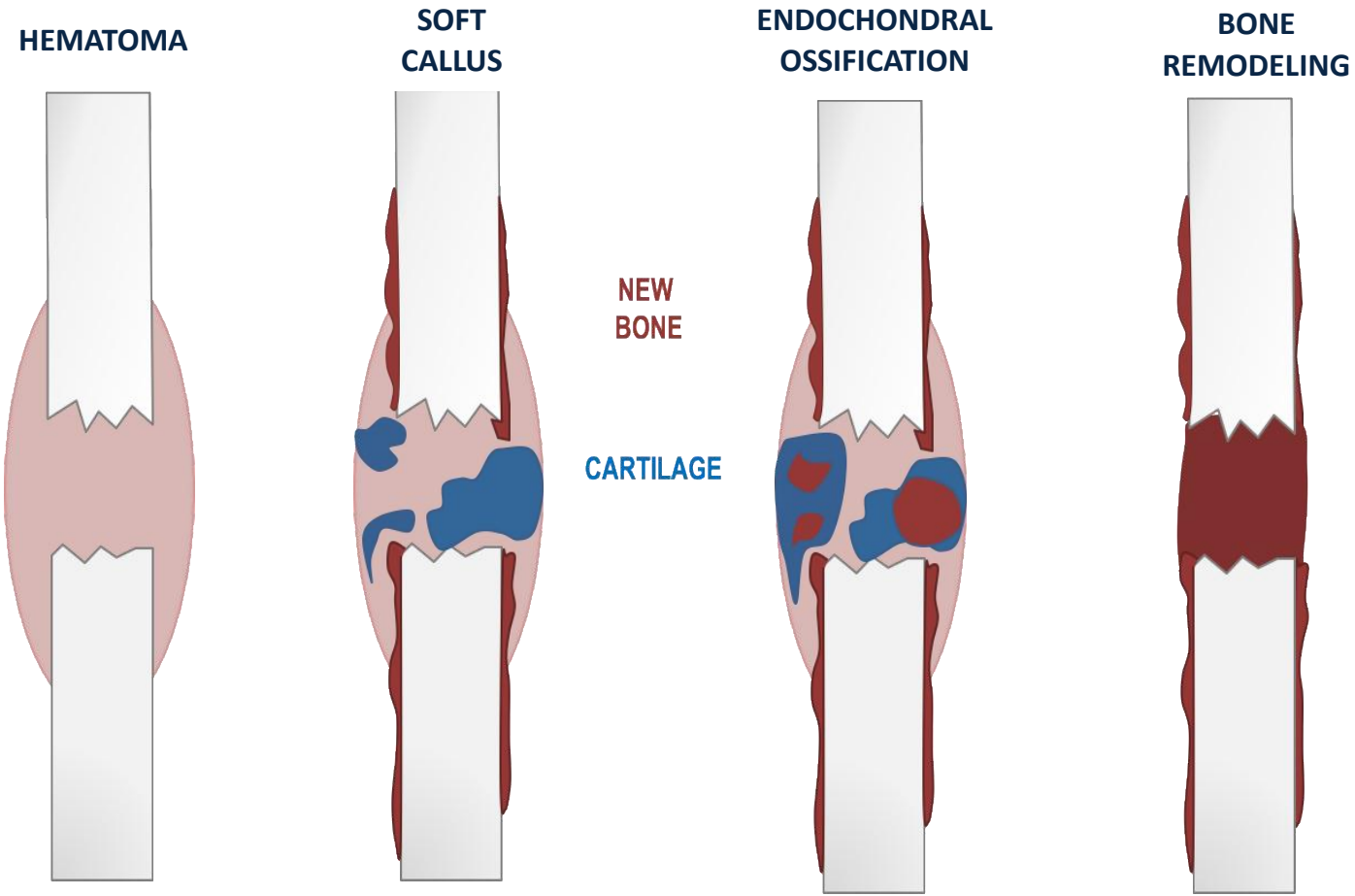
Smart bone plates can monitor fracture healing

SCIENTIFIC
REPORTS
nature research

Monica C. Lin ^{1,4*}, Diane Hu ², Meir Marmor ², Safa T. Herfat ², Chelsea S. Bahney ^{1,2,3}, Michel M. Maharbiz ^{1,4,5}

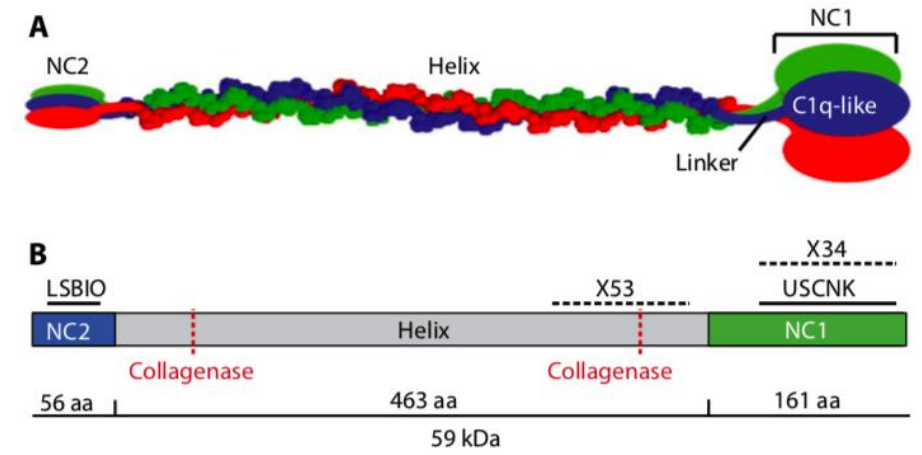
Clinical Need: A method to quantify fracture healing and identify predictive healing patterns

New Biomarker for Fracture Repair



Bahney et al. Frontiers Endocrin 2017

Collagen X Degradation (CXM)



BILL & MELINDA
GATES foundation

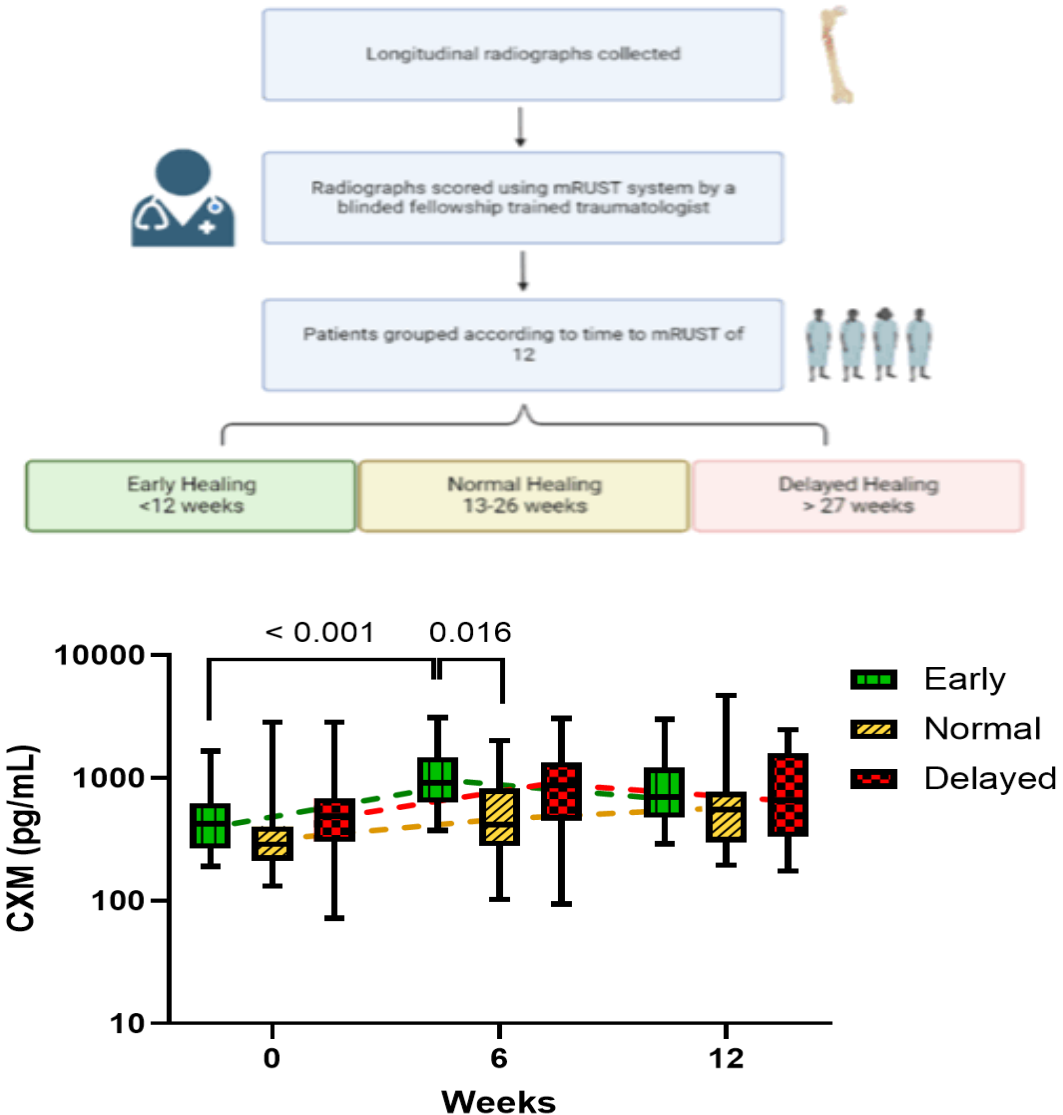
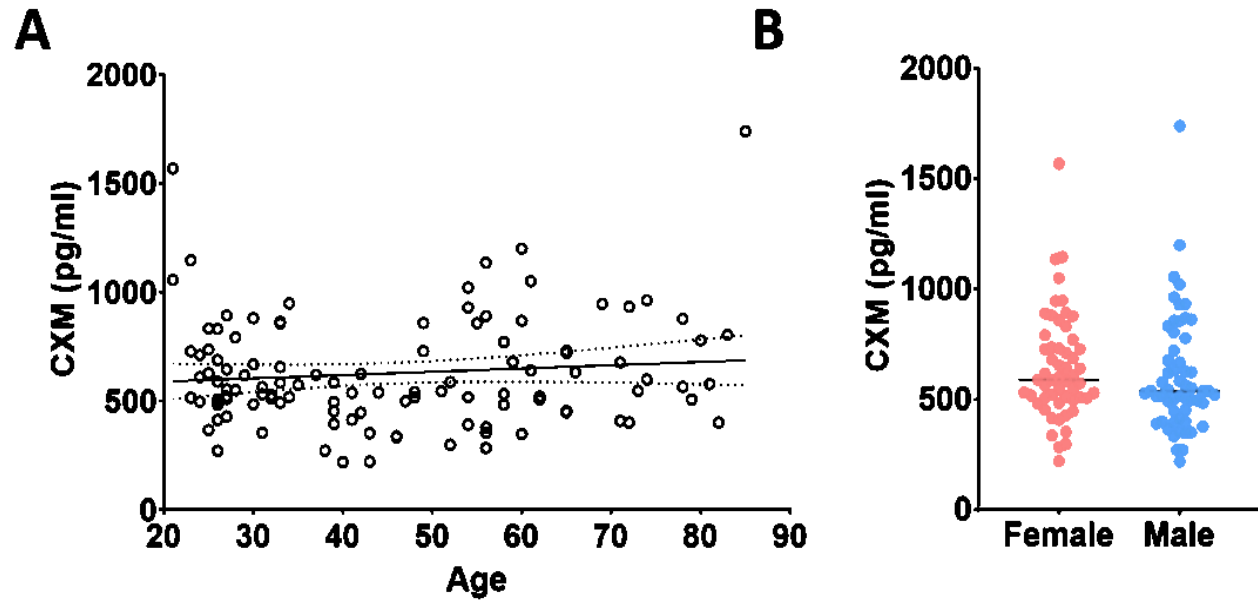
Science
Translational Medicine



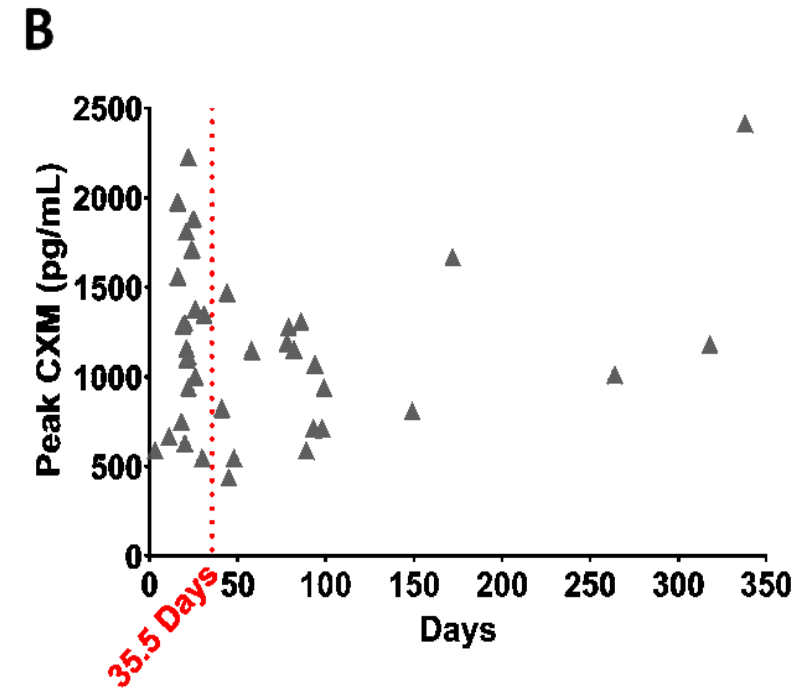
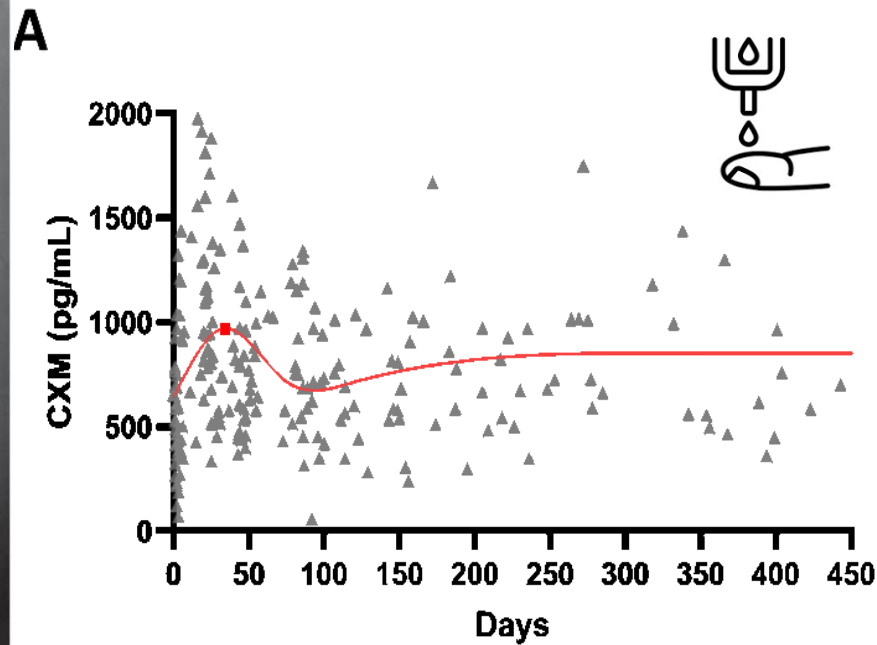
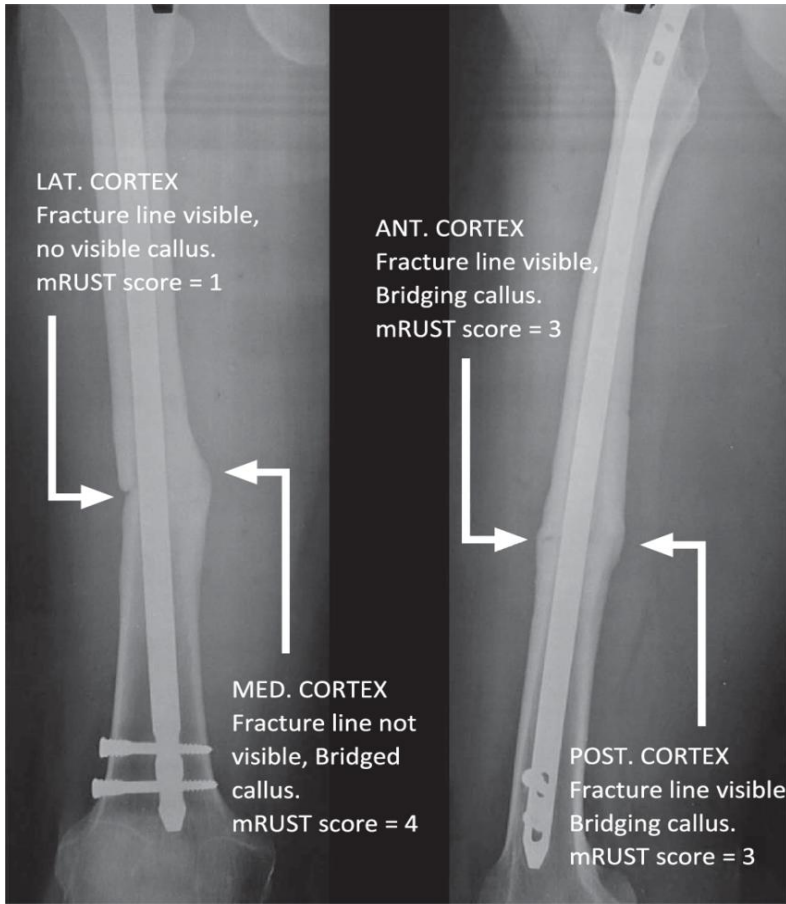
Coughlan et al. Sci Trans Med 2017

CXM Peaks at 6 Weeks and is Elevated in Early Healers

CXM in Healthy Individuals No Age or Sex Differences



CXM Peaks Between 25-35 Days Much Earlier than Radiographic Bone Healing



Early Healing <12 weeks

Normal Healing 13-26 weeks

Delayed Healing > 27 weeks



Efficacy of biomarkers in the endochondral phase of fracture repair and healing in long bones: A clinical observational study

Zachary M. Working, Molly E. Czachor, Anna Laura Nelson, Kelsey M. O'Hara, Karalynn Lancaster, Justin E. Hellwinkel, Kaitlyn Whitney, Lucas S. Marchand, Sofia Bzovskys, Graham J. DeKeyser, Darin M. Friess, Theodore Miclau, William A. Horton, Sheila A. Sprague, Nathan N. O'Hara, Brian Johnstone, Lauren A. Pierpoint, Gerard P. Slobogean, Chelsea S. Bahney. On behalf of the Vita-Shock Investigators [view less]

mRNA as Next Generation Fracture Therapeutic

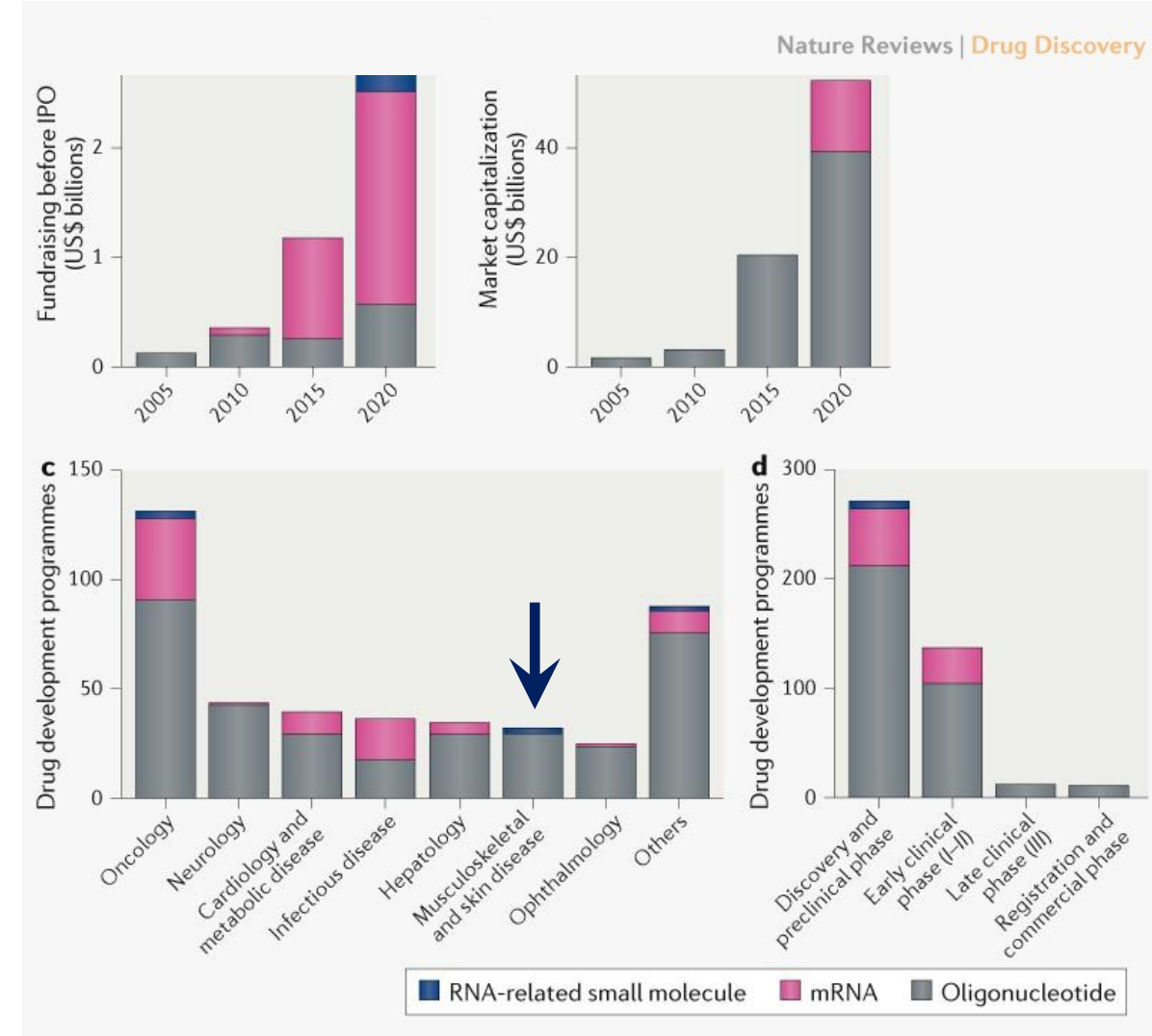
Business: The billion-dollar biotech

Elie Dolgin

Nature 522, 26–28 (2015) | [Cite this article](#)

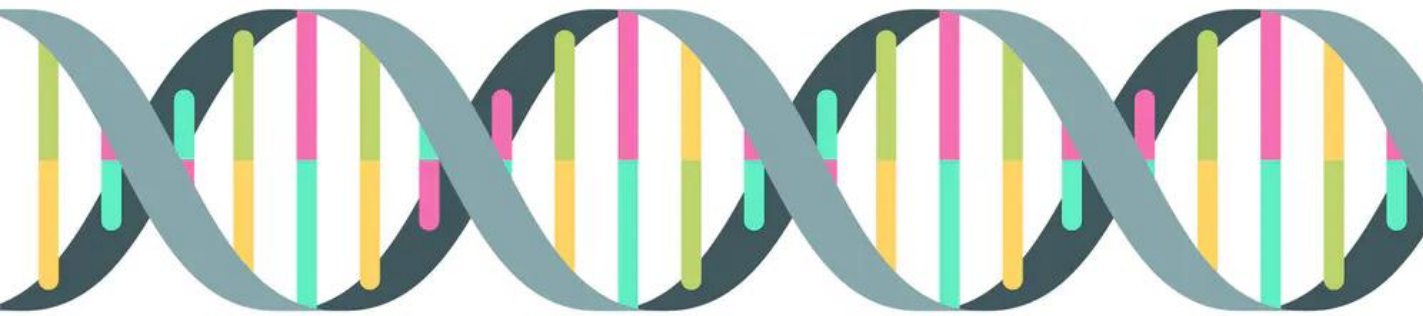
741 Accesses | 9 Citations | 272 Altmetric | [Metrics](#)

Moderna Therapeutics has big ambitions and a bankroll to match. How a fledgling start-up became one of the most highly valued private drug firms ever.



Wang F, et al. *Nature Reviews Drug Discovery*.

Therapeutic Advantages of mRNA



DNA

TRANSCRIBED



mRNA



TRANSLATED

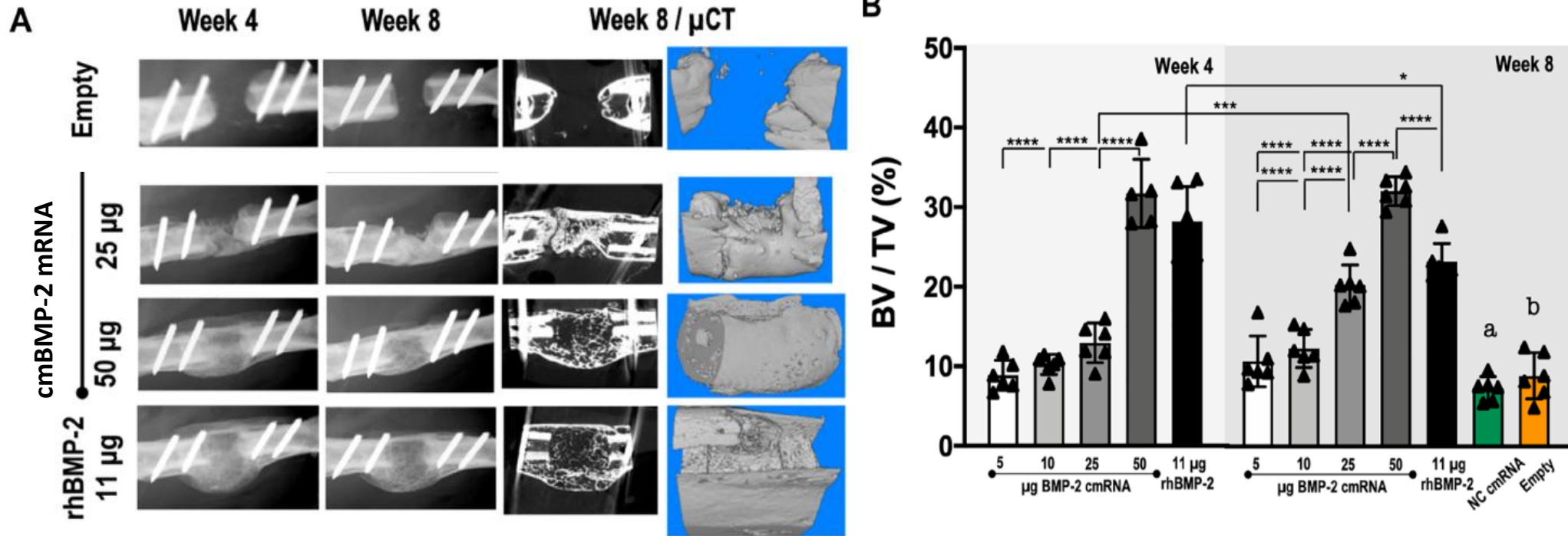


Protein

- Safety concerns (genomic integration)
- Difficult in non-dividing cells

- Short half life
- Limited activity → high doses
- Expensive to manufacture

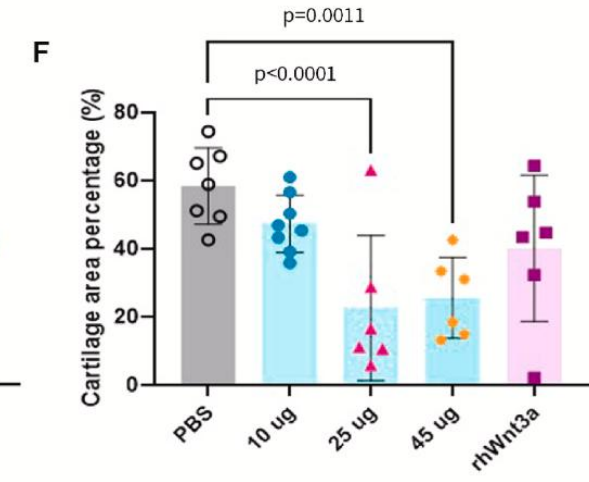
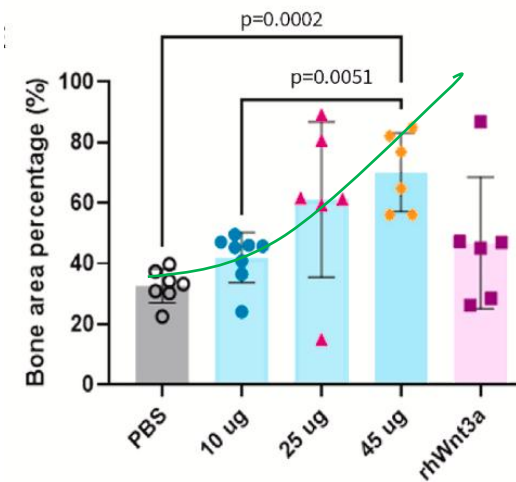
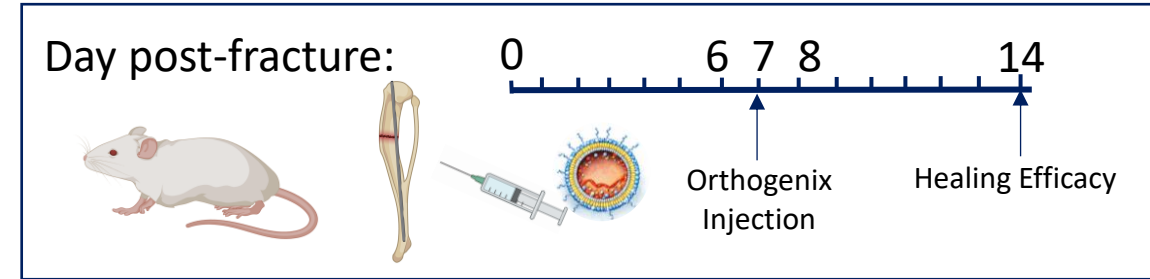
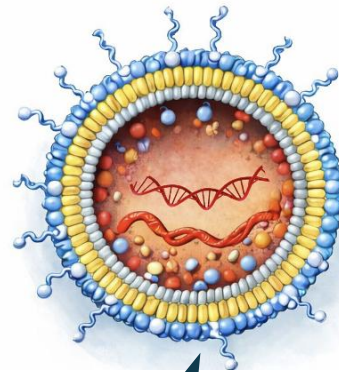
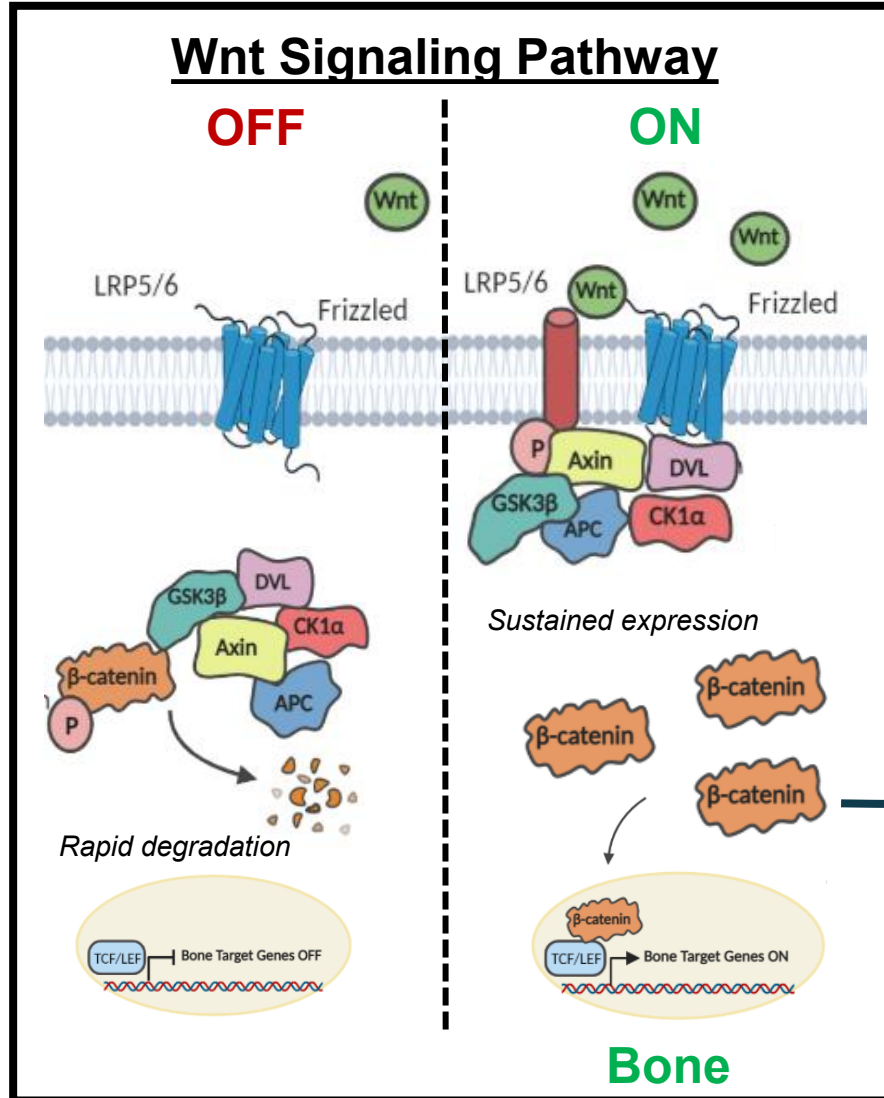
BMP2 RNA as a Therapeutic is Promising in Bone Repair



Efficient healing of large osseous segmental defects using optimized chemically modified messenger RNA encoding BMP-2 PMID: 35171668

Rodolfo E. De La Vega^{1,2}, Martijn van Griensven^{1,2}, Wen Zhang³, Michael J. Coenen¹, Christopher V. Nagelli¹, Joseph A. Panos¹, Carlos J. Peniche Silva², Johannes Geiger³, Christian Plank³, Christopher H. Evans¹, Elizabeth R. Balmayor^{1,4*}

Injectable Wnt mRNA Accelerates Bone Healing in Mice



Wnt-activating RNA increases bone formation in a **dose-dependent** manner up to 200%



> *Bioact Mater.* 2024 May 23;39:273-286. doi: 10.1016/j.bioactmat.2024.05.020. eCollection 2024 Sep.

β-catenin mRNA encapsulated in SM-102 lipid nanoparticles enhances bone formation in a murine tibia fracture repair model

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