Bone-muscle crosstalk: cancer- and chemotherapy-induced muscle weakness

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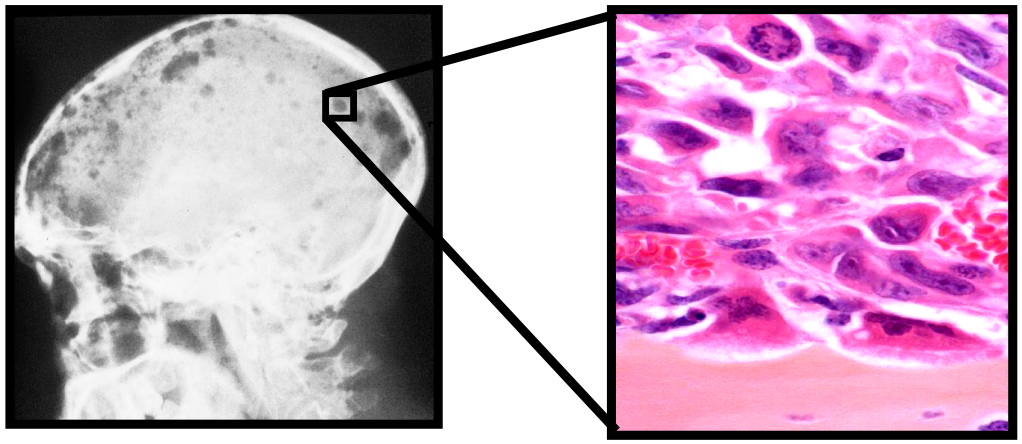
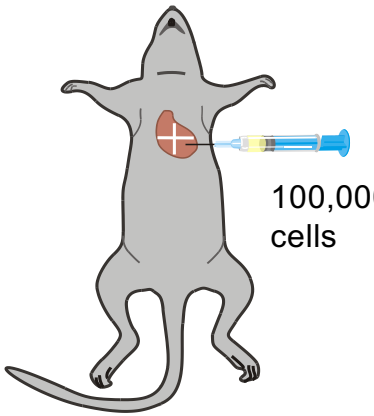
Solid Tumor Metastases

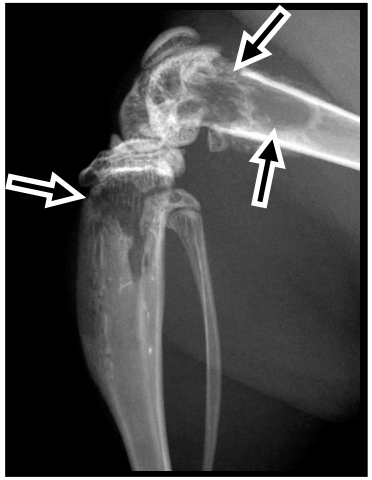


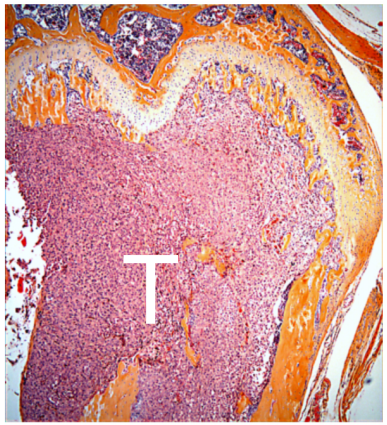
Osteolytic

- Breast & lung
- Bone destruction mediated by osteoclasts

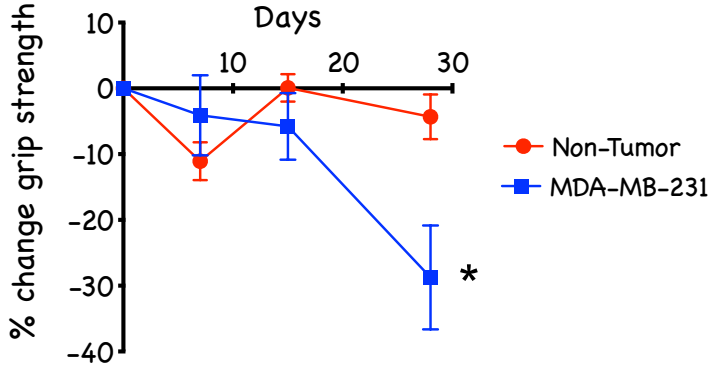
Mouse model: human MDA-MB-231 breast cancer

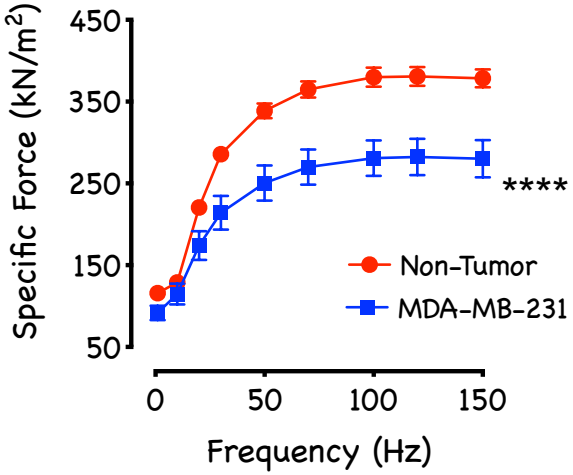


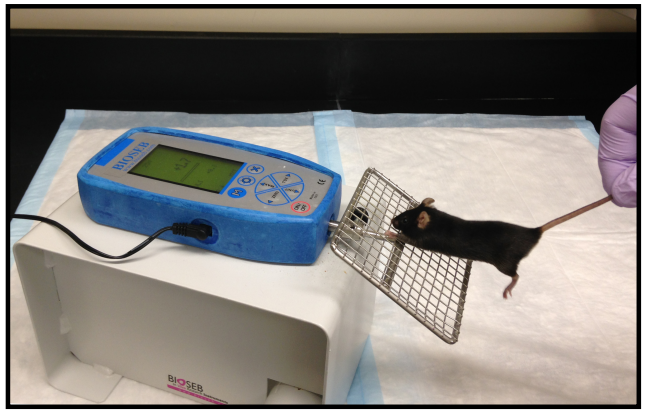


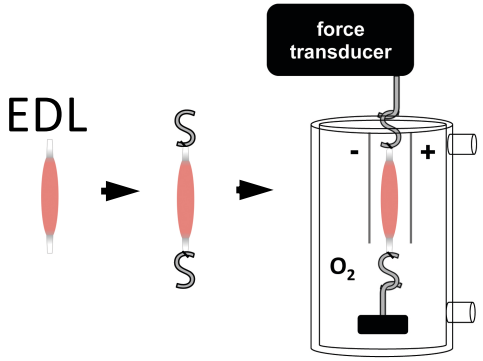


Mice with MDA-MB-231 bone metastases have ⬇ grip strength & ⬇ muscle function





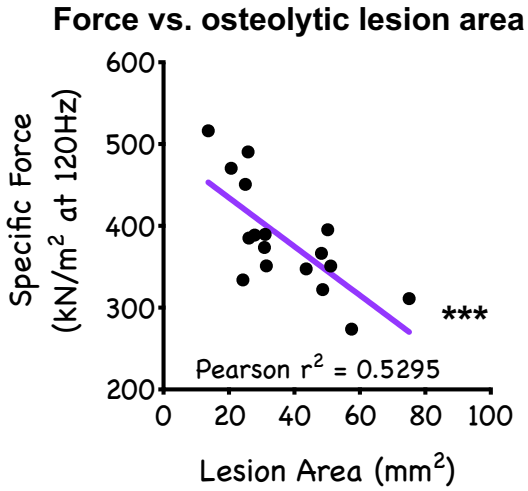




Two-way ANOVA, *p<0.05, ****p<0.0001

Waning DL. et al. (2015) *Nat Medicine*. 21(11):1262.; Bonetto A. et al (2015) *Bonekey Rep*. 4:732.

↑ osteolysis correlates to ↓ muscle function and TGFβ causes muscle weakness



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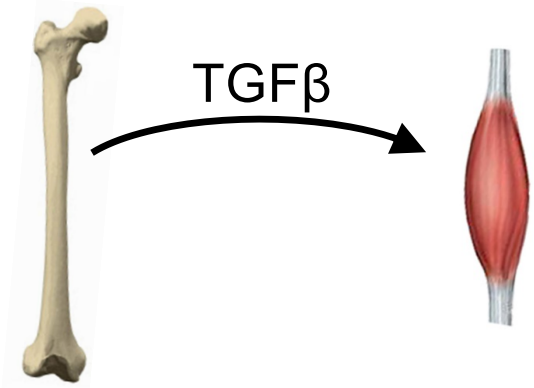


<u>TGFβ signaling in skeletal muscle</u>:

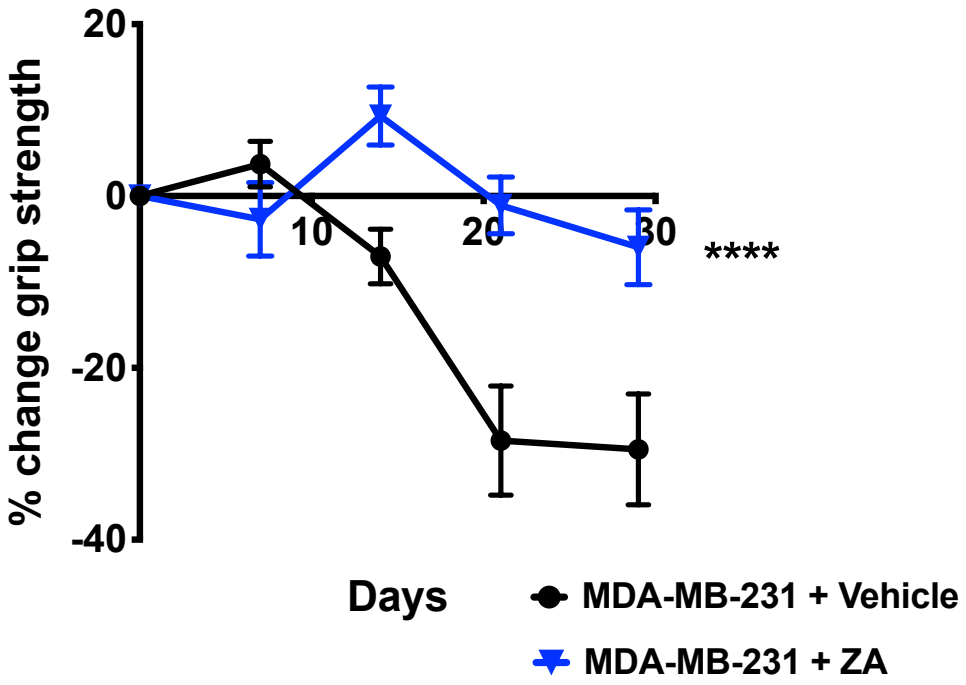
Oxidative stress (NADPH oxidase 4)

Calcium leak (ryanodine receptor 1 oxidation)

Contractile dysfunction

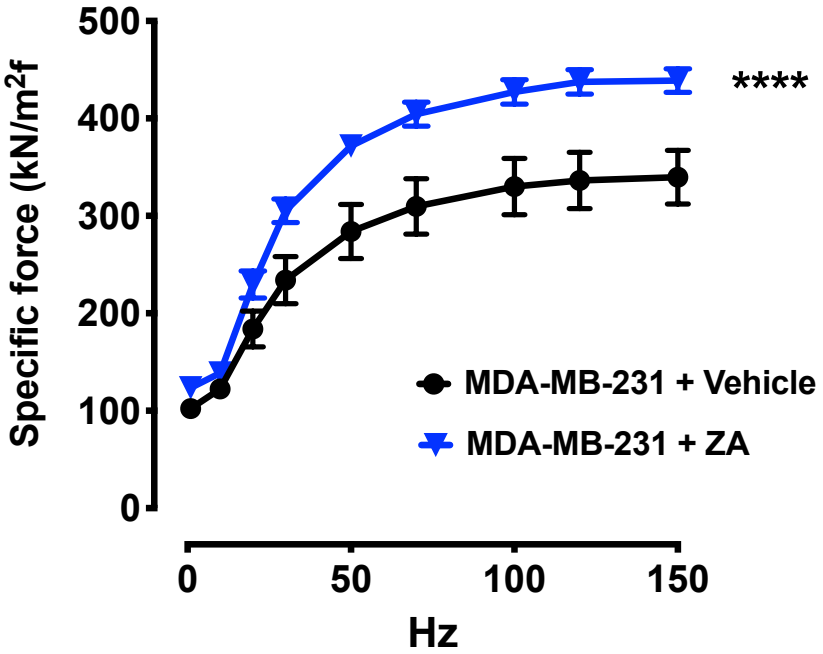
↓ bone resorption with zoledronic acid restores skeletal muscle function

Grip strength



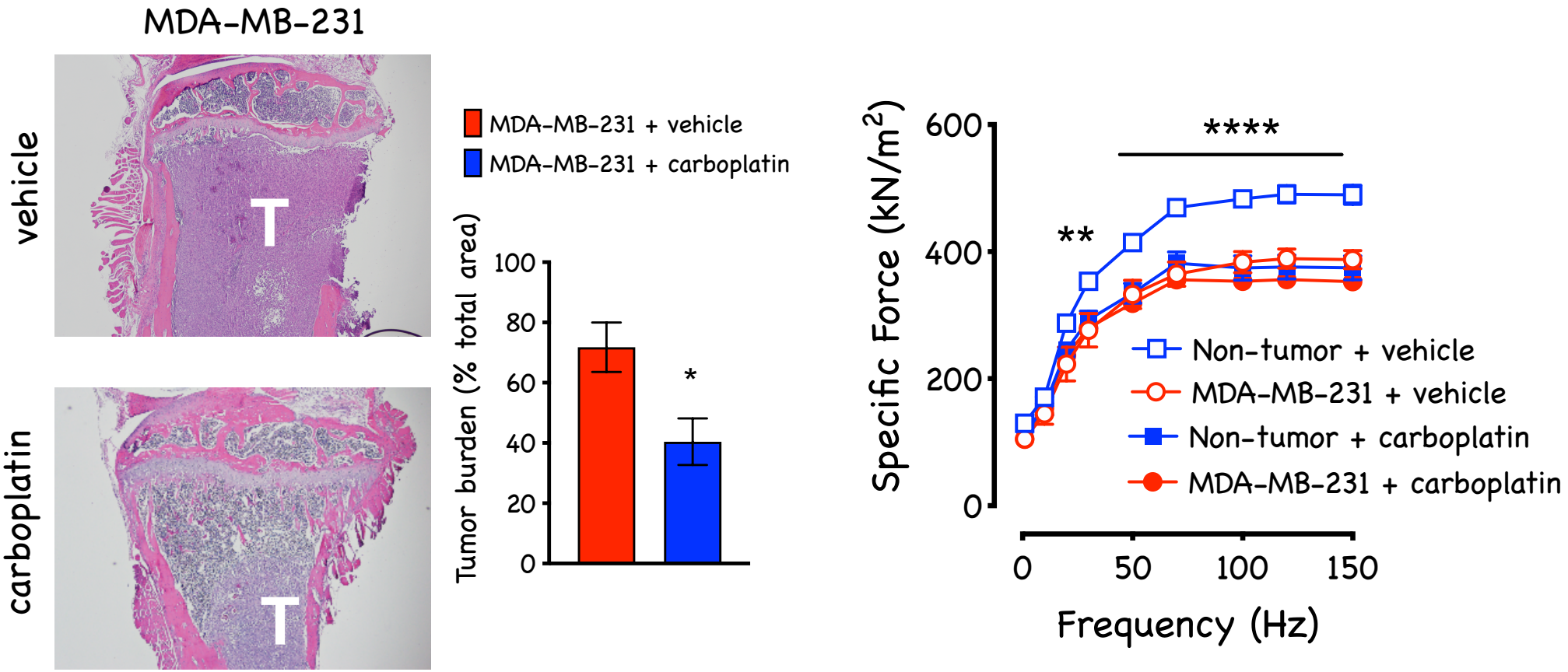
Two-way ANOVA, ****p<0.0001

EDL contractility



Waning DL. et al. (2015) *Nat Medicine.* 21(11):1262.

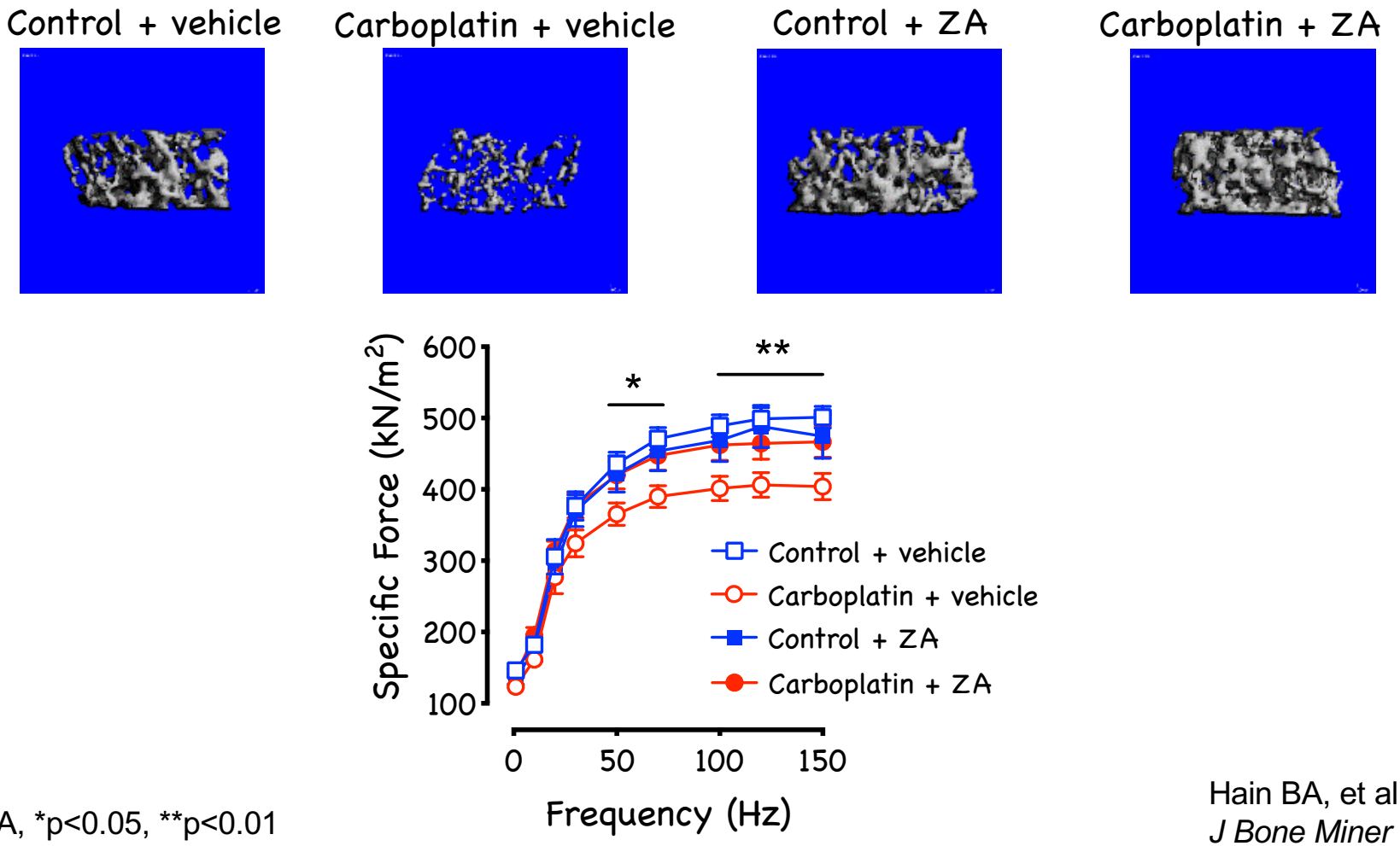
Carboplatin ↓ tumor burden & muscle function



T-test, *p<0.05 Two-way ANOVA, **p<0.01, ****p<0.0001

Hain BA, et al (2019) *JCSM Rapid Comm. 2(1).*

Zoledronic acid prevents carboplatin-induced bone loss and improves muscle function



Two-way ANOVA, *p<0.05, **p<0.01

Hain BA, et al (2020)
J Bone Miner Res. 35(2):368.

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IU School of Medicine
Theresa Guise, MD
Khalid Mohammad, MD PhD

Funding

National Institutes of Health
National Cancer Institute
PA Breast Cancer Coalition
Phi Beta Psi National Project
PennState Cancer Institute
CORTS Center for Orthopaedic Research and Translational Science