

Multimodal Immunoimaging of CCR2-Driven Inflammation in Metabolically Stressed Myocardial Infarction

Katrien Vandoorne
CRS 2025-07-17

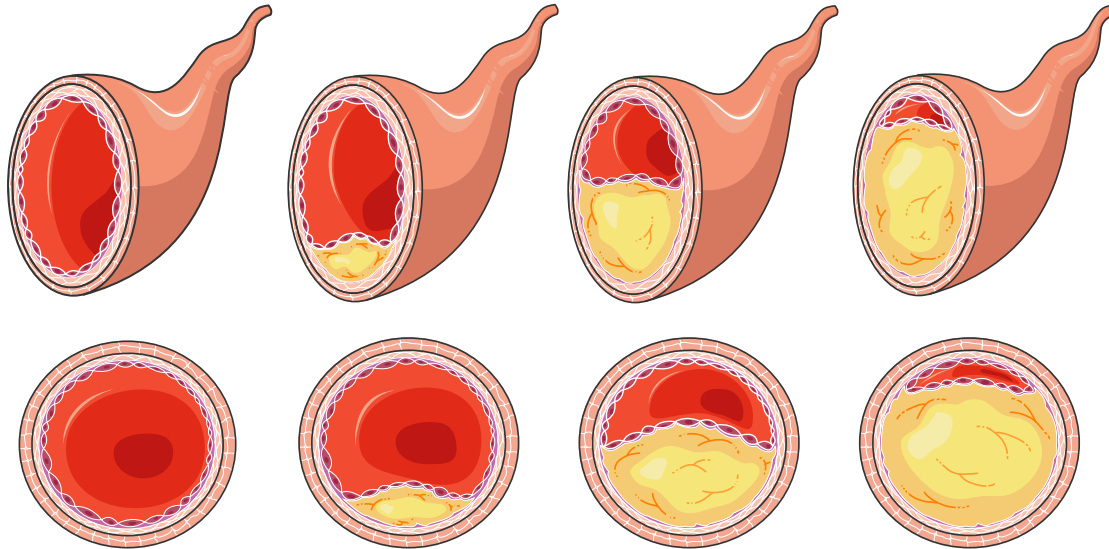


Cardiovascular disease



Stroke, myocardial infarction, heart failure

Cardiovascular Disease



Obstruction : 0 %

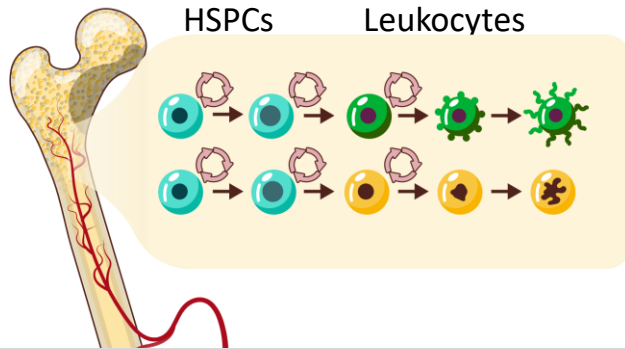
30 %

65 %

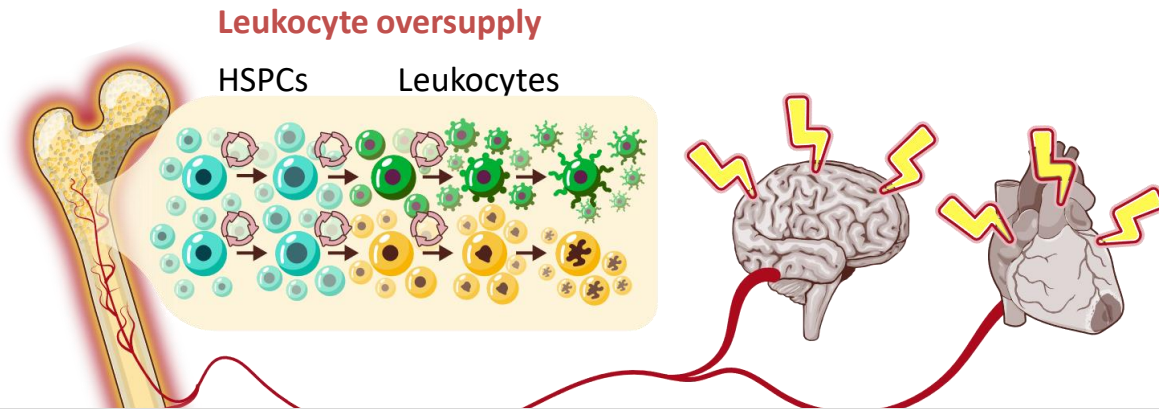
90 %

Obesity-Induced Bone Marrow Vascular Changes

Homeostatic myelopoiesis



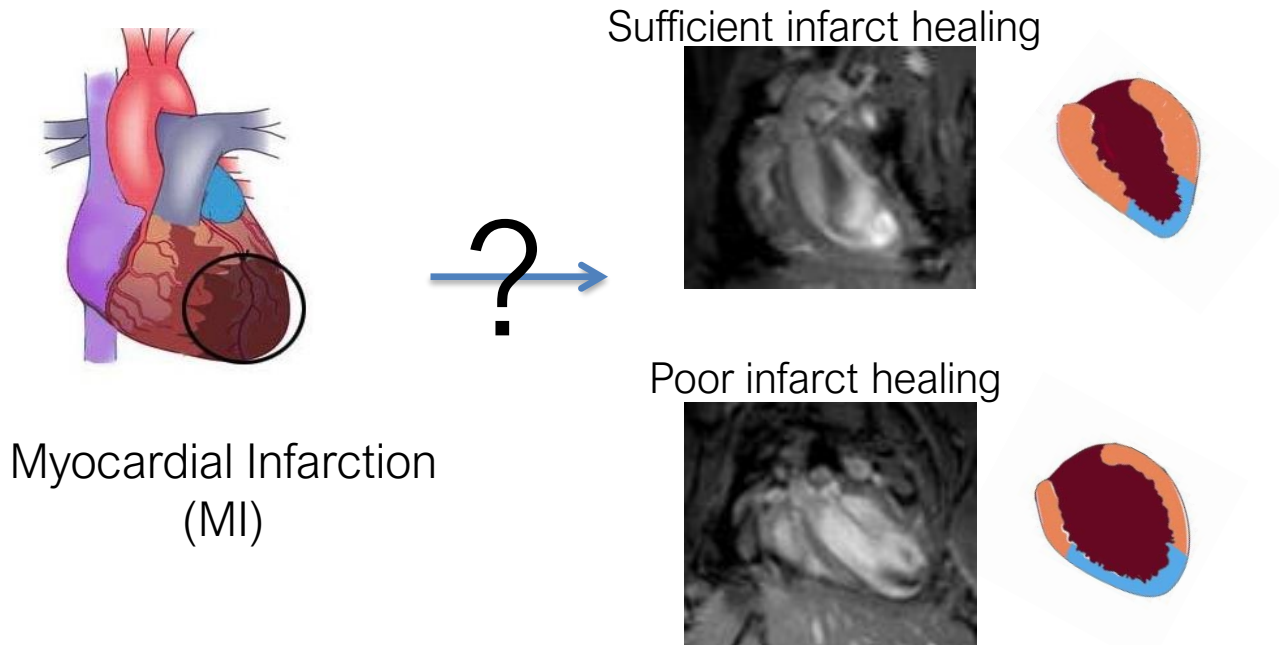
Inflammatory myelopoiesis



How do we trace immune dynamics during diabetic-enhanced myocardial remodeling?

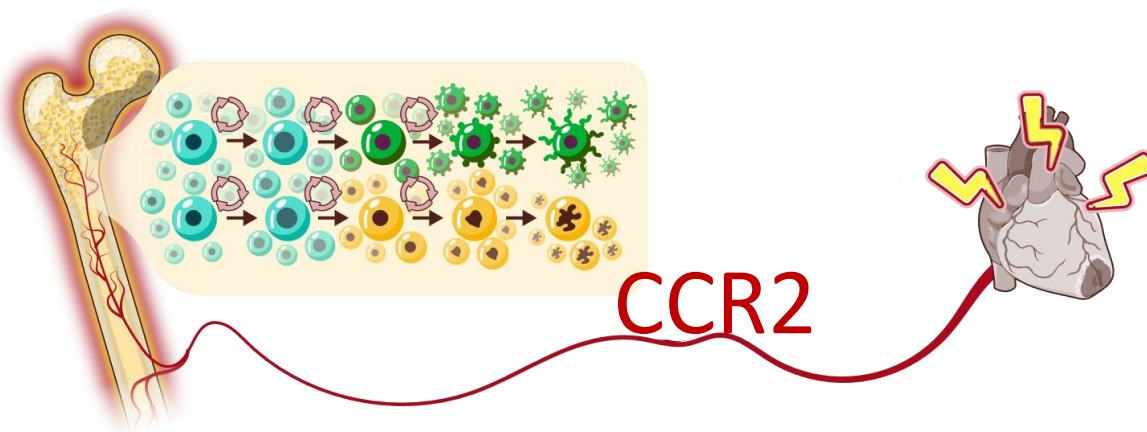
Vandoorne et al, *Circulation Research* 2018
Nahrendorf, Vandoorne, *JACC Imaging* 2019
Rohde & Vandoorne, et al, *Nature Cardiovasc Res* 2022
Haj N.Vandoorne, *ATVB* 2025

Obesity-Enhanced Myocardial Remodeling



Can we noninvasively image biomarkers of immune changes to predict poor infarct healing?

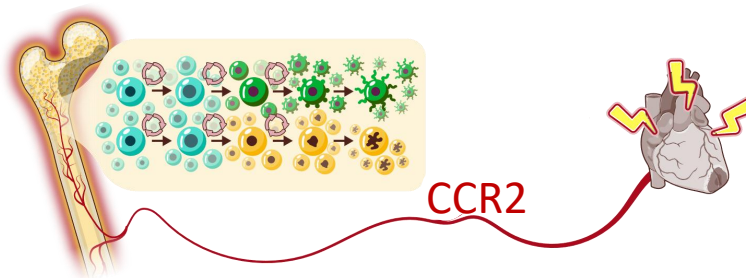
CCR2 - A Key Driver of Post-MI Inflammation



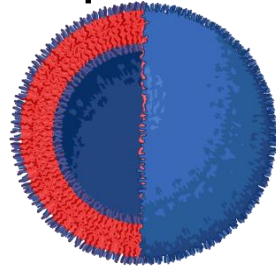
- Binds CCL2 (Monocyte Chemoattractant Protein-1, MCP-1)
- Essential for monocyte recruitment from the bone marrow to inflamed tissues

Hypothesis

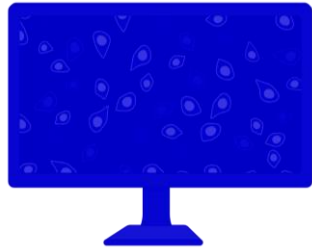
Metabolic stress increases CCR2+ myeloid cell recruitment and hematopoietic activation post-MI, which we can visualize using AF647-cross linked dextran coated iron oxide nanoparticle imaging



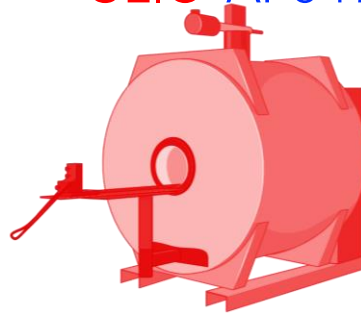
AF647-cross linked dextran coated iron oxide nanoparticles



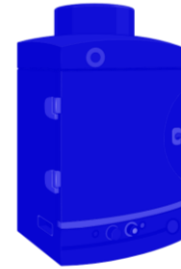
CLIO-AF647



Microscopy

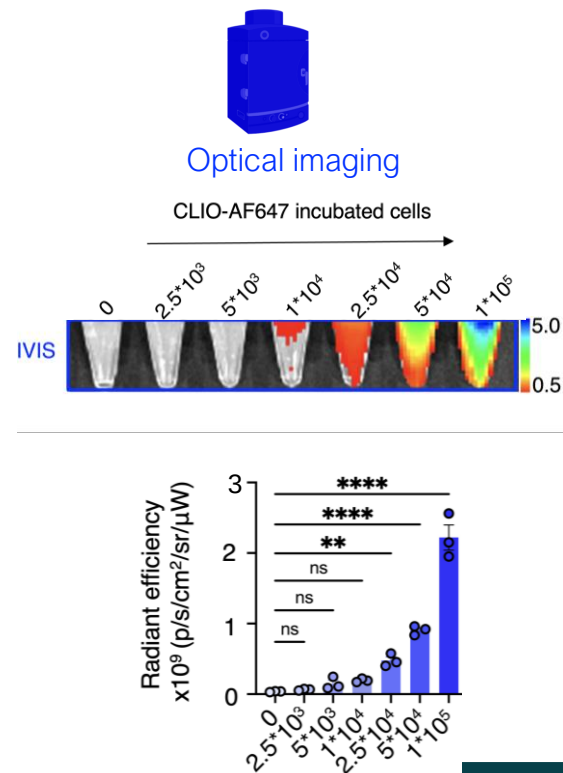
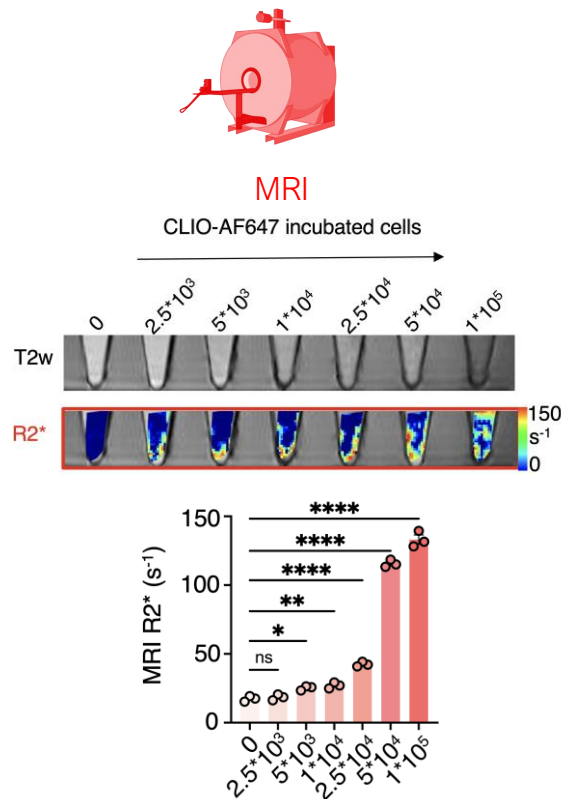
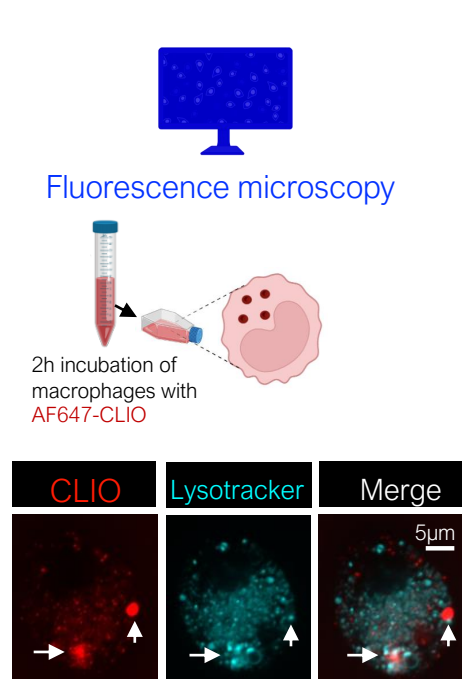


MRI

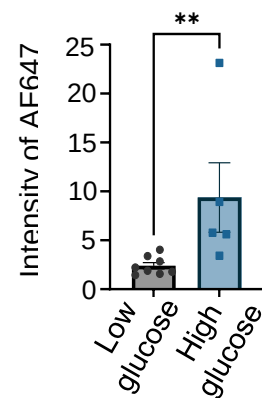
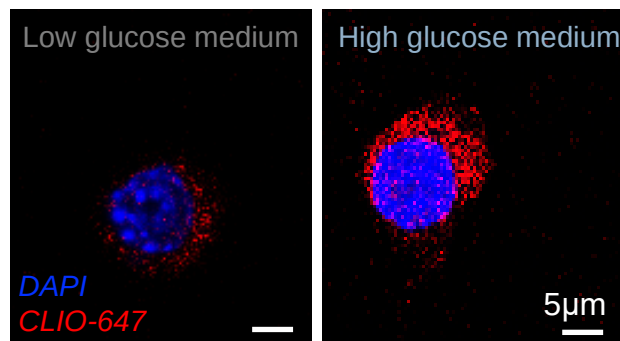
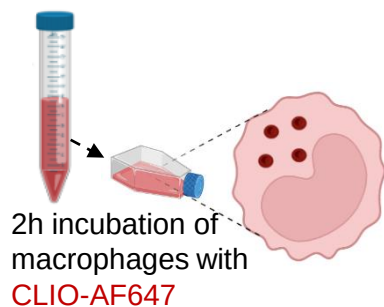


Optical imaging

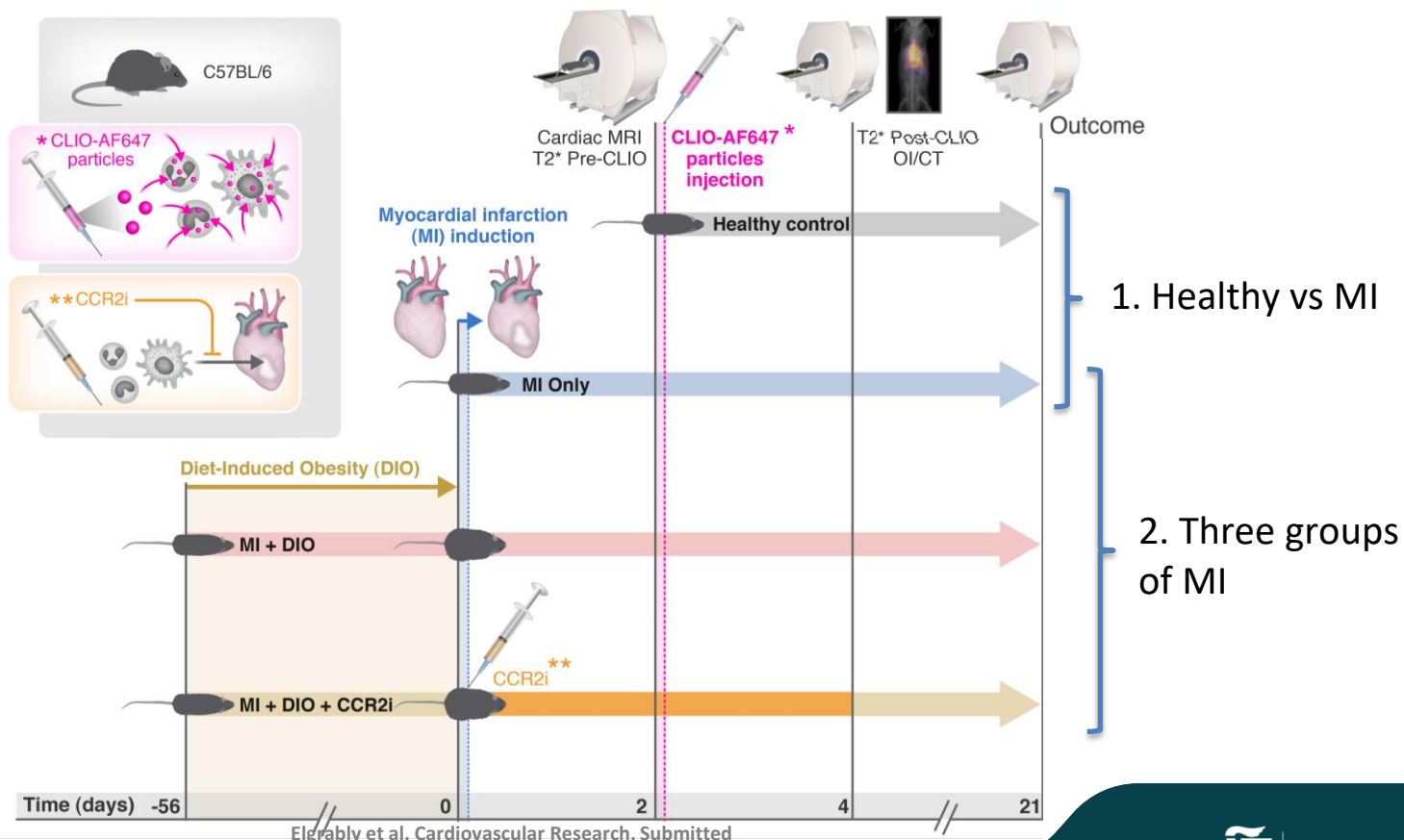
Macrophages phagocytize CLIO nanoparticles in vitro



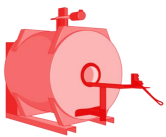
High glucose enhances nanoparticle uptake in vitro



Experimental set-up



Elgrably et al, Cardiovascular Research, Submitted

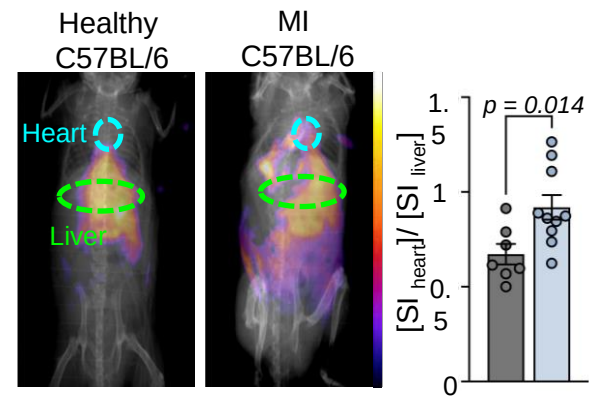
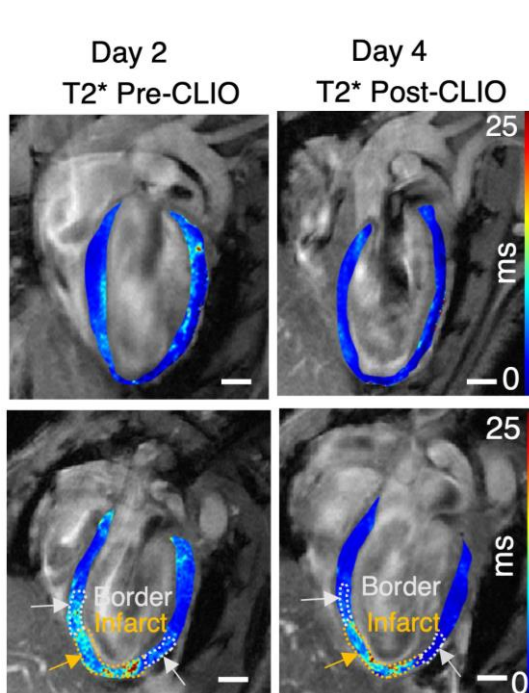
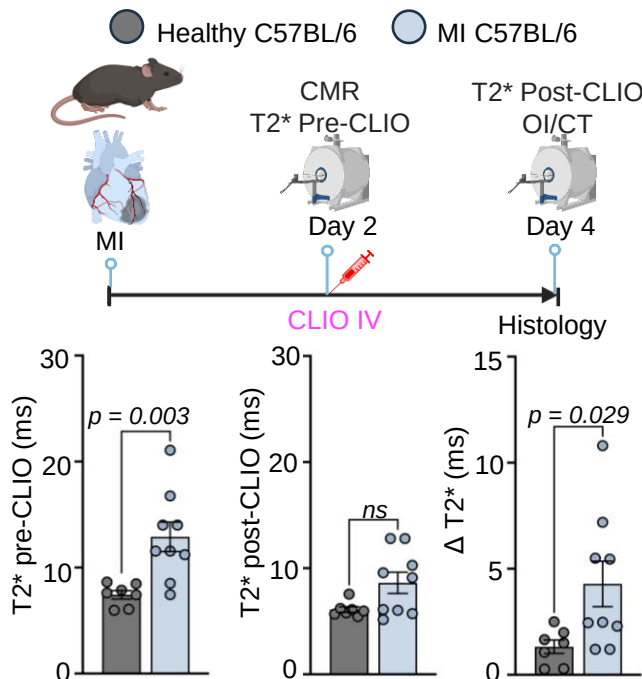


MRI

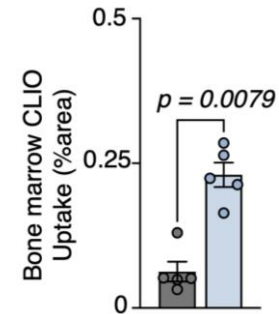
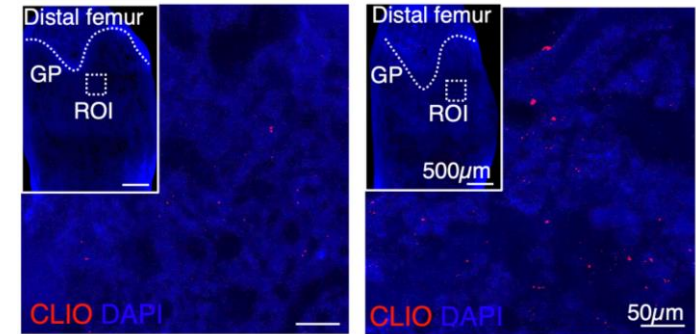
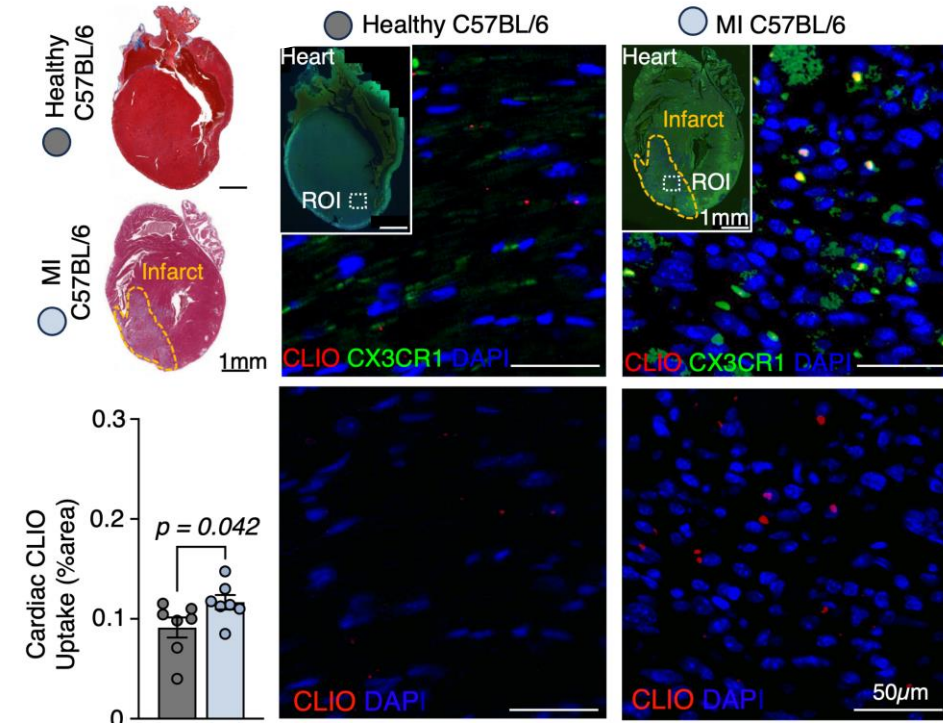
1. MI Enhances Nanoparticle Uptake



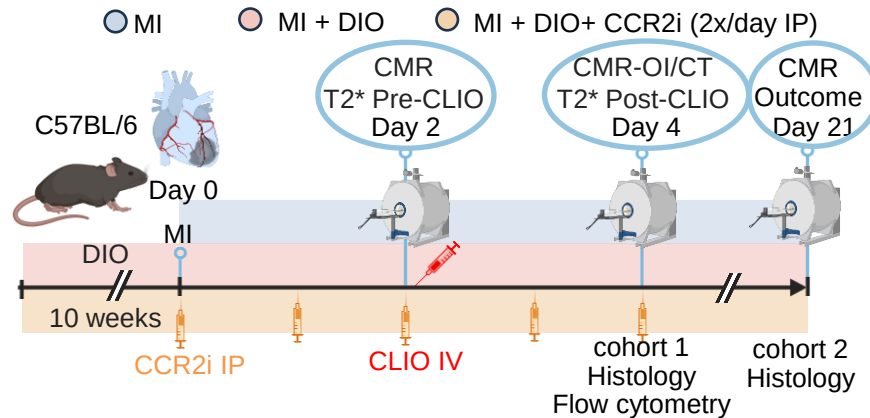
Optical imaging



Elevated uptake of CLIO-AF647 in infarction and hematopoietic bone marrow

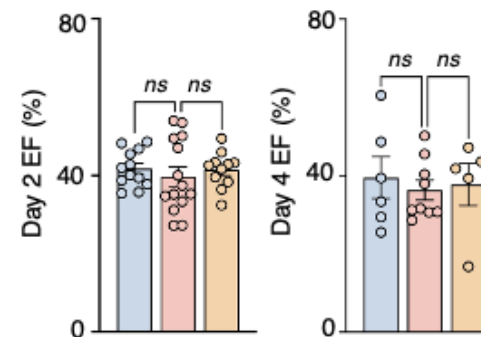
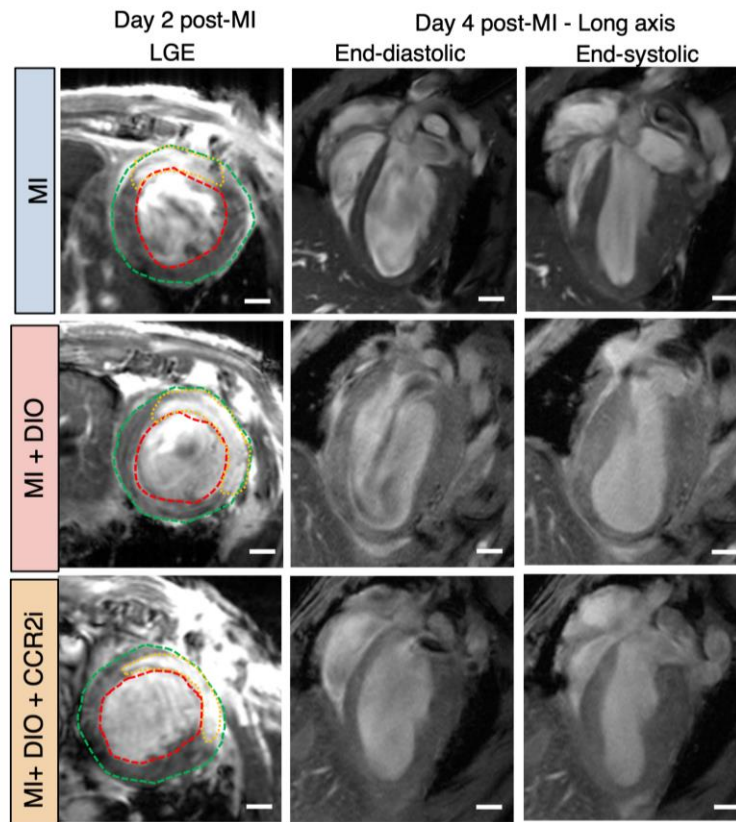


2. Probing CLIO-AF647 uptake after DIO-enhanced myocardial remodeling



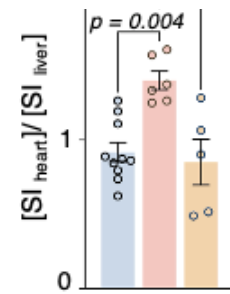
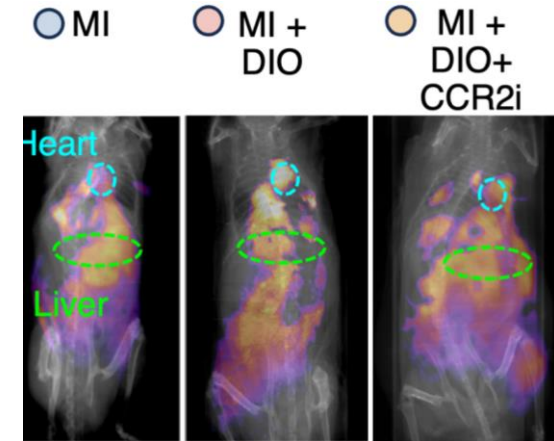
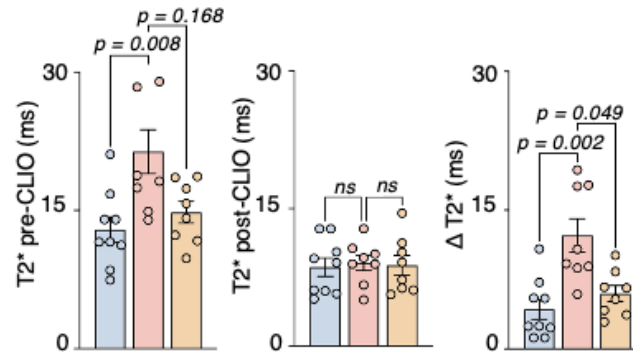
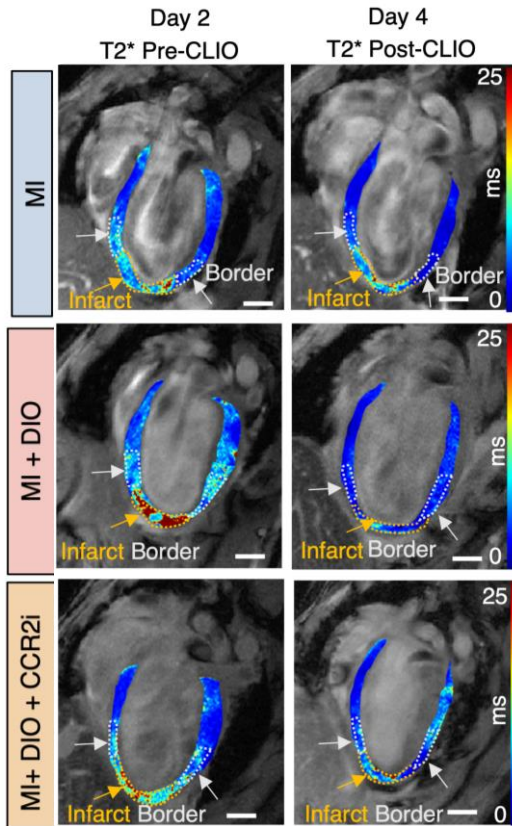
1. Myocardial infarction (MI) in healthy mice
2. MI in mice on Diet Induced Obesity (DIO)
3. MI in mice on DIO with inhibition CCR2 (C-C chemokine receptor type 2)

2. Similar Cardiac Function Early After MI

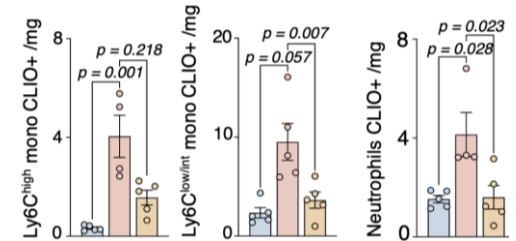
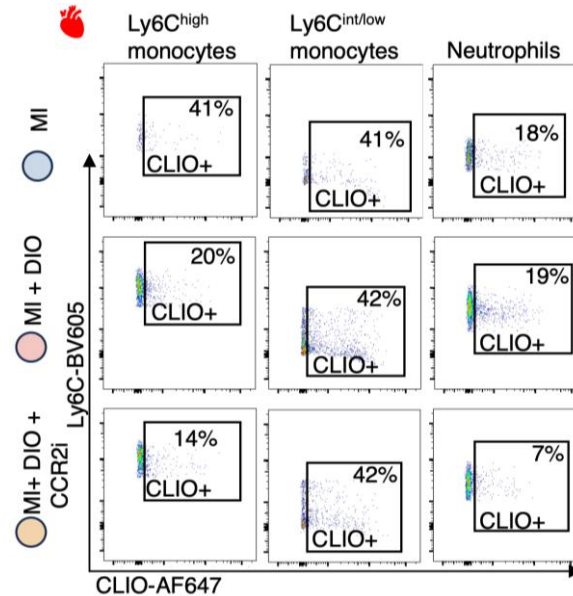
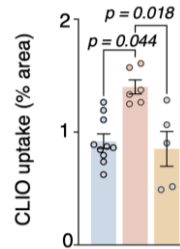
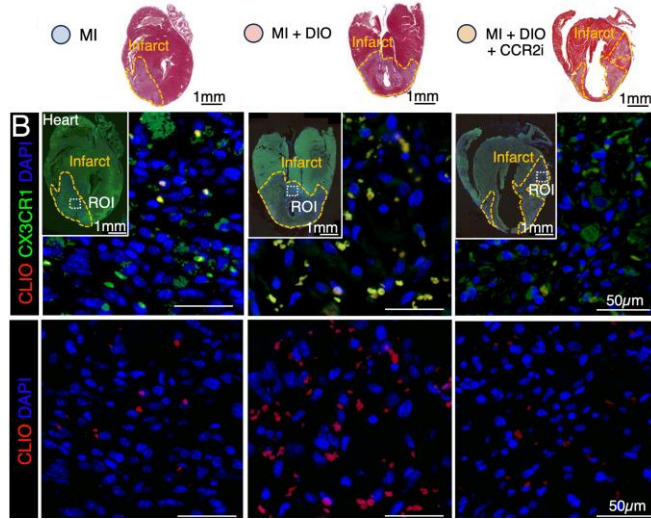


Elgrably et al, Cardiovascular Research, Submitted

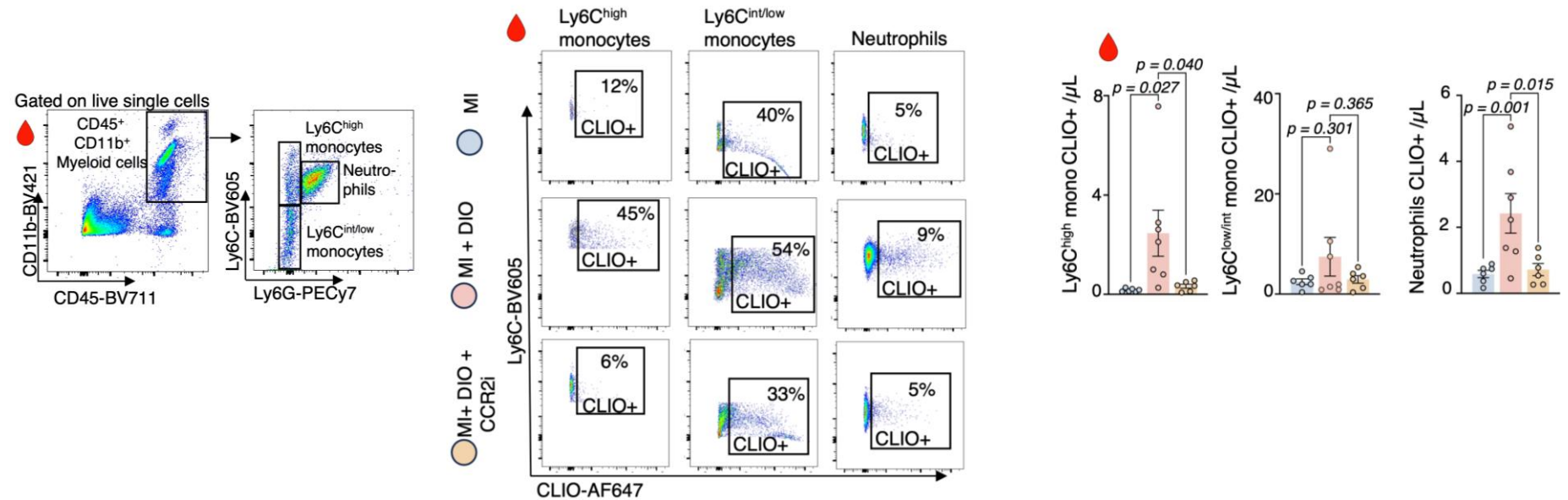
2. Metabolic Stress Amplifies Uptake Through CCR2



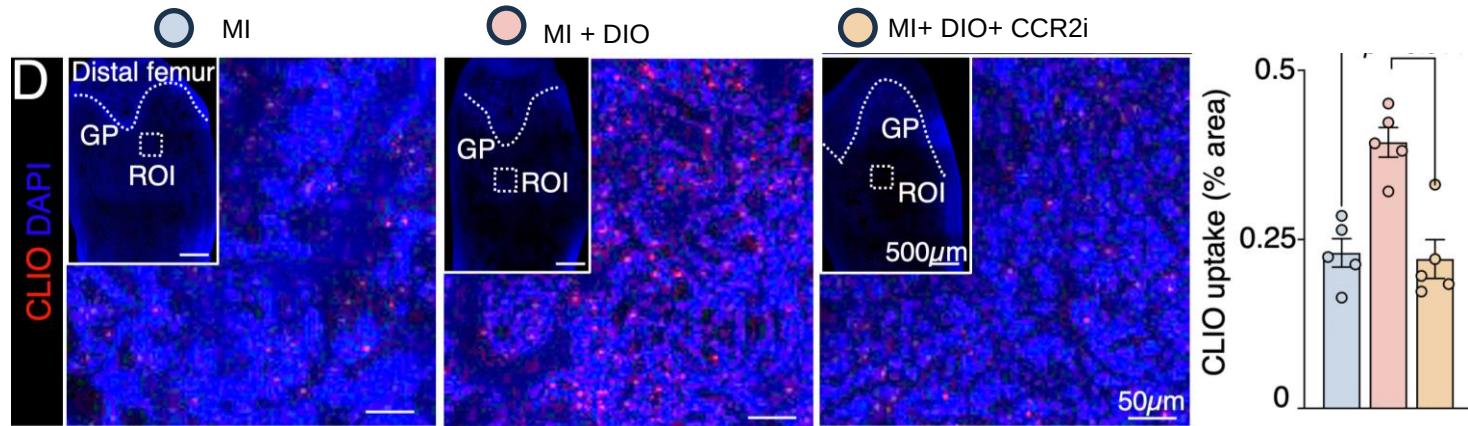
2. Metabolic Stress Amplifies Cardiac Uptake Through CCR2



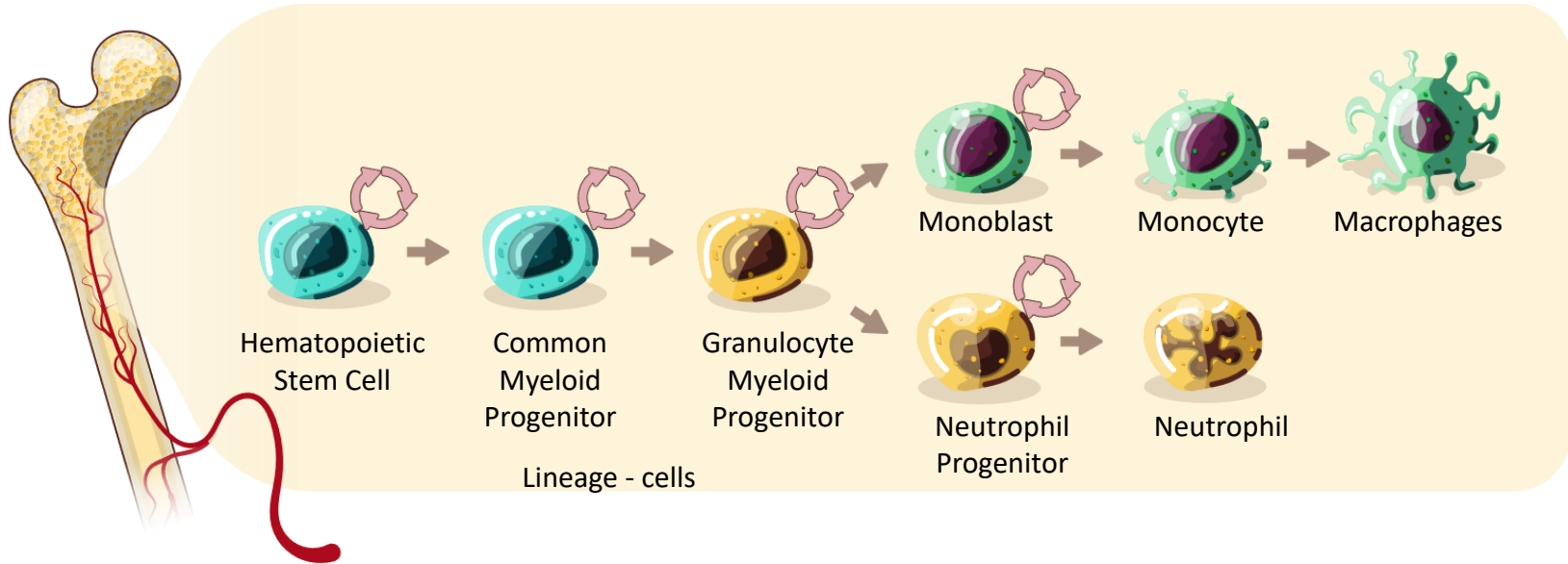
2. Metabolic Stress Amplifies Leukocyte Uptake Through CCR2



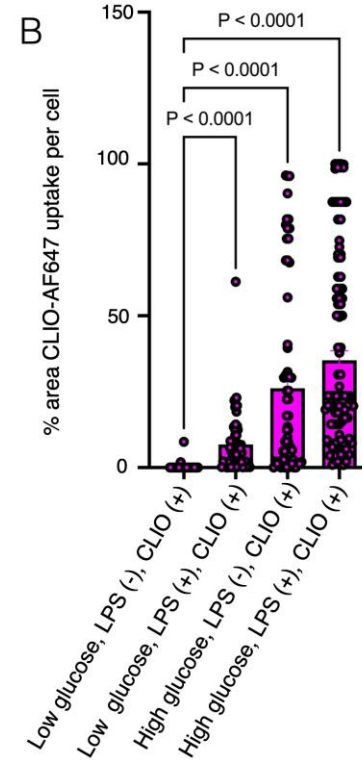
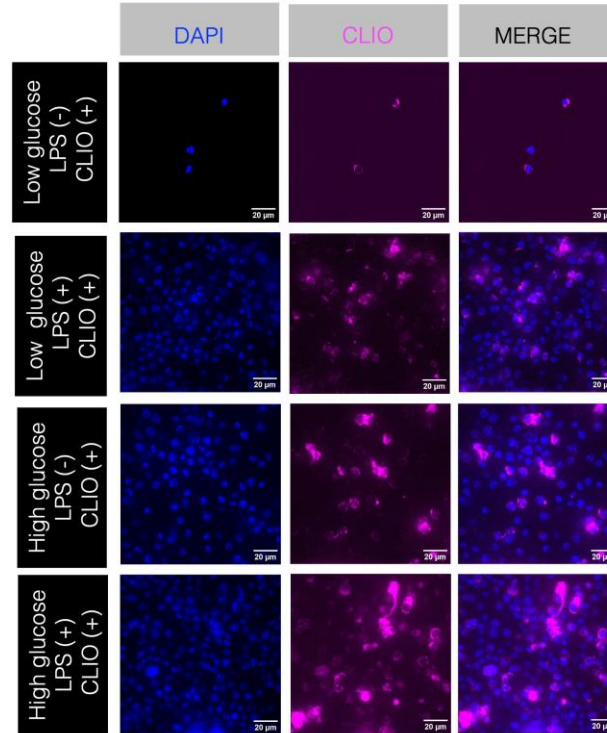
2. Metabolic Stress Amplifies Bone Marrow Uptake Through CCR2



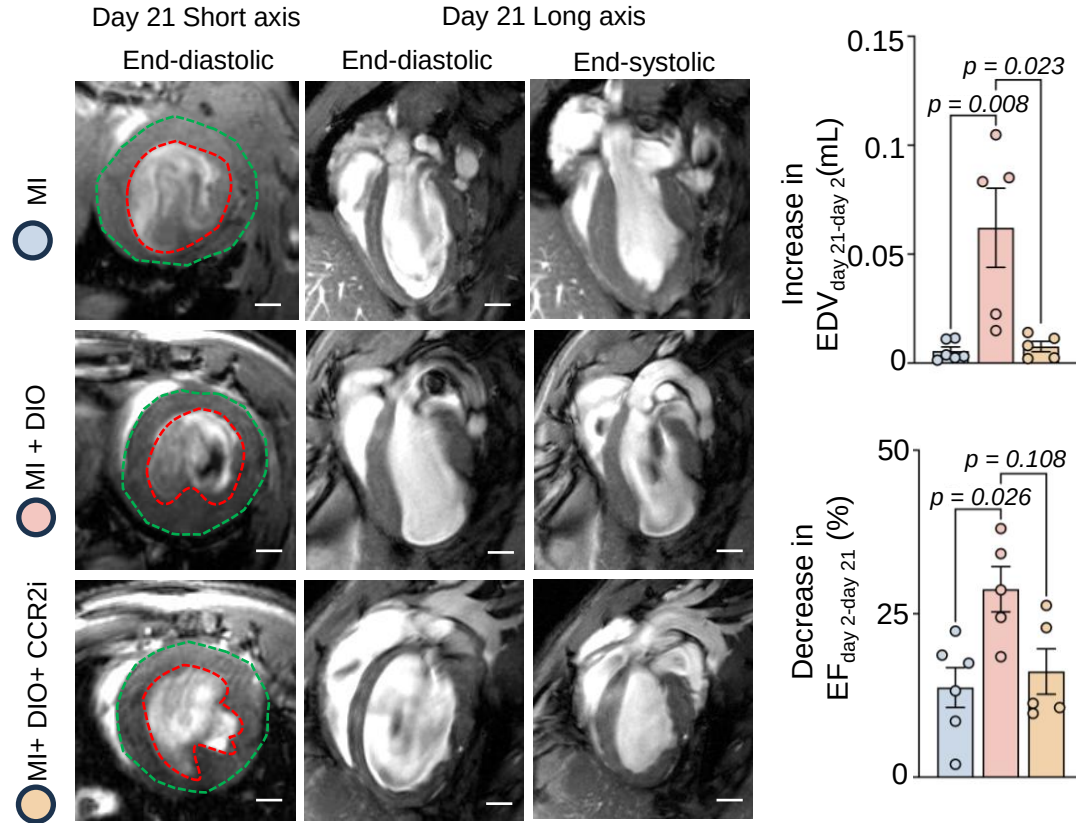
Myelopoiesis



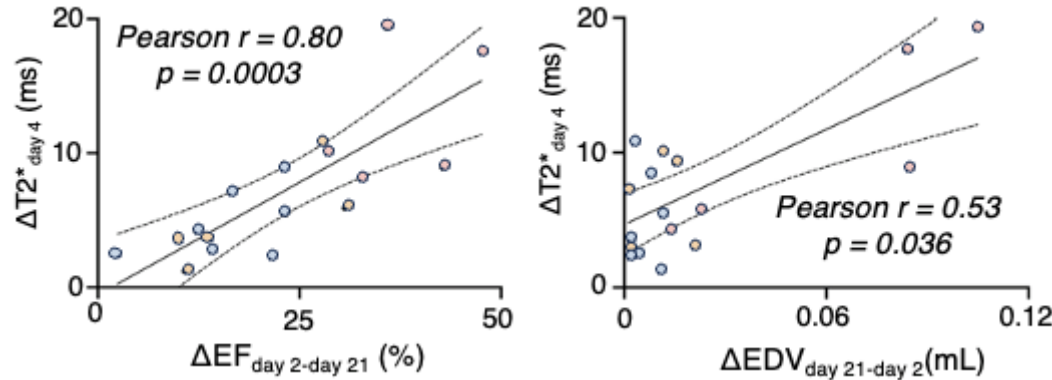
Metabolic and Inflammatory Stimuli Synergistically Enhance Nanoparticle Uptake by Hematopoietic Progenitors



DOI Enhances Cardiac Remodeling Through CCR2



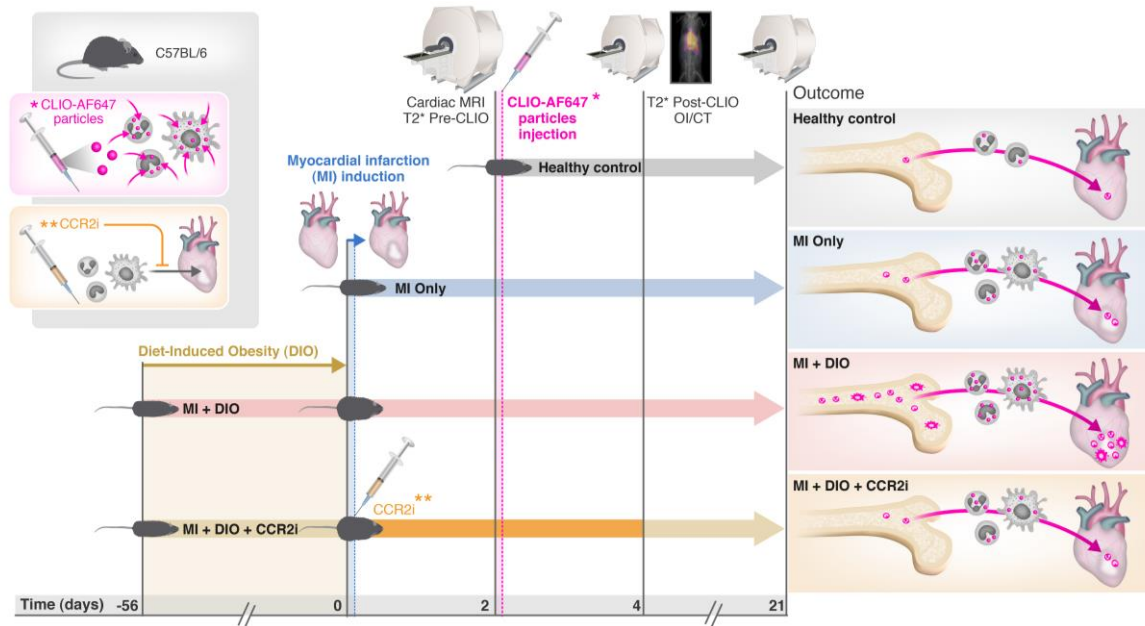
CLIO-AF647 Uptake Predicts Outcome



ΔT_2^* at Day 4 – A Predictor of Cardiac Remodeling

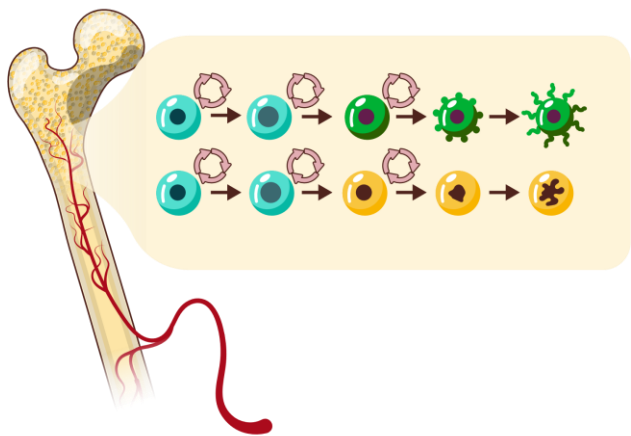
- Quantifies CLIO-AF647 Uptake
- Correlates with day 21:
 - ✓ Decline in Ejection Fraction (EF)
 - ✓ Ventricular Dilation (End-Diastolic Volume, EDV)

Conclusion: Nanoparticle Immunoimaging Reveals Metabolic Dysfunction Fueling CCR2-Dependent Inflammation in Infarcted Hearts

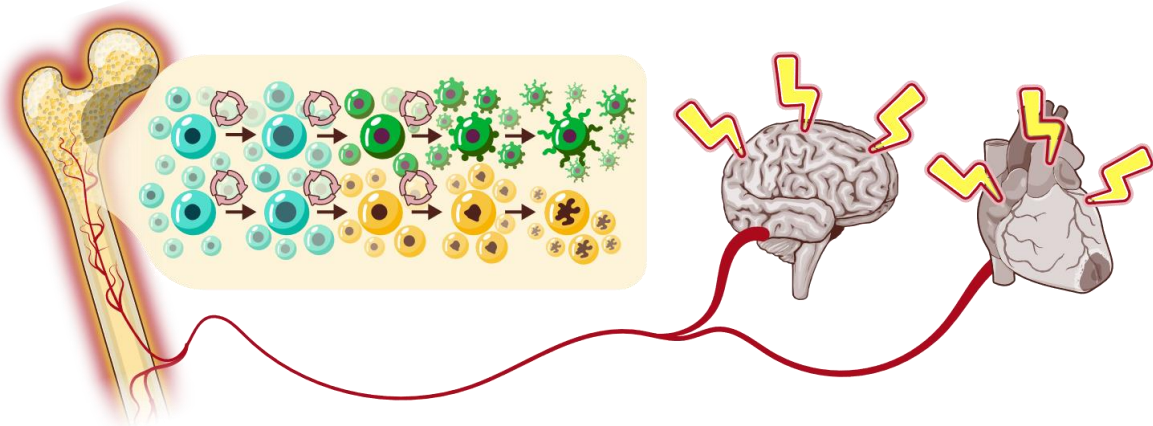


Inflammation-Driven Enhanced Labeling in Bone Marrow

How does CLIO nanoparticle uptake occur at the bone marrow during increasing levels of inflammation?

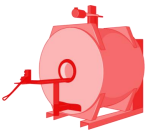


Homeostatic myelopoiesis

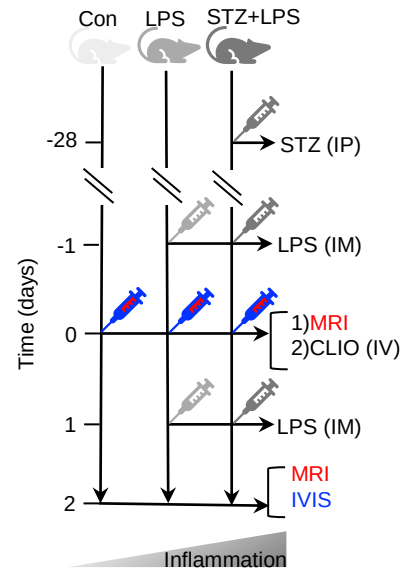


Inflammatory myelopoiesis

Elevated uptake of CLIO-AF647 in inflamed muscle and hematopoietic bone marrow

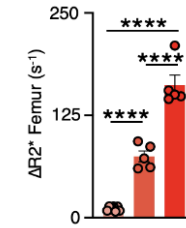
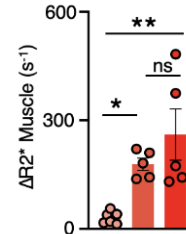
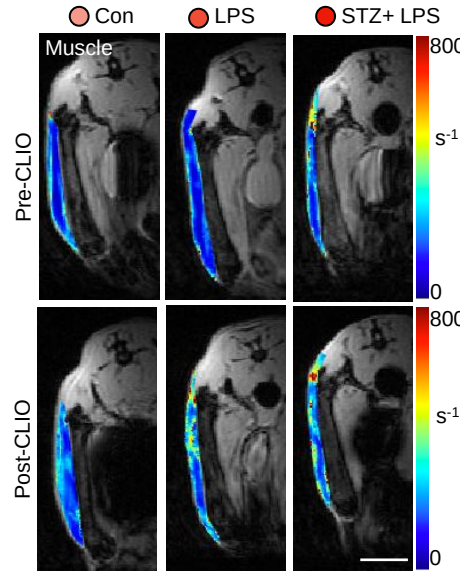


MRI

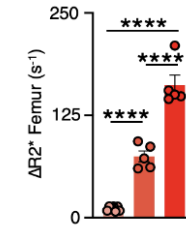
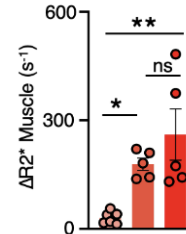
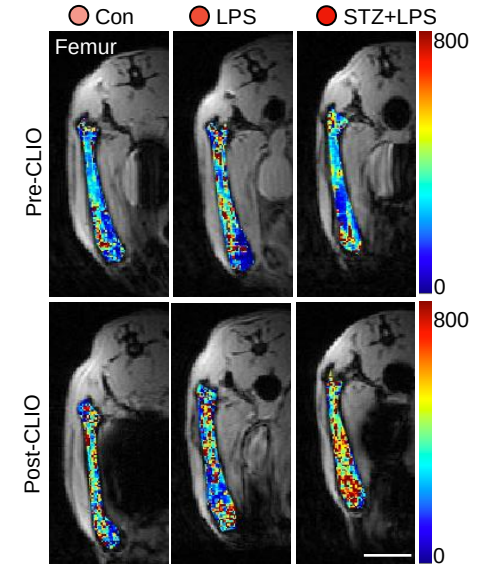


Con = Control
LPS = Lipopolysaccharide 2 injections IM
STZ+LPS = Streptozotocin (STZ)-induced diabetes and Lipopolysaccharide 2 injections IM

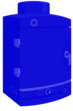
Muscle



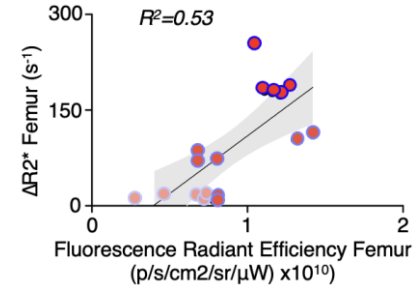
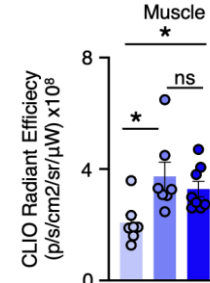
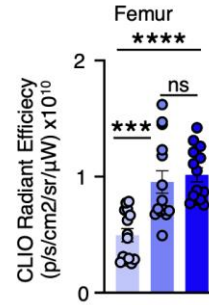
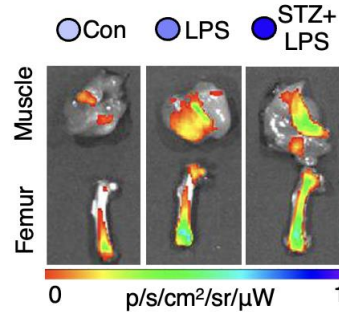
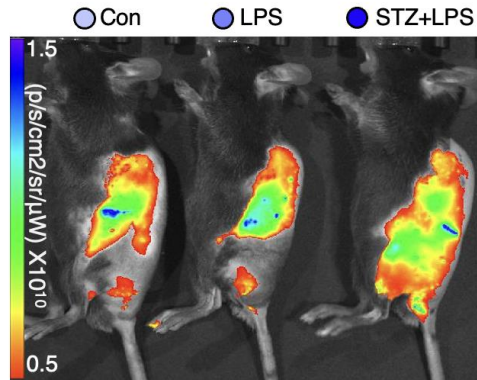
Bone Marrow



Elevated uptake of CLIO-AF647 in inflamed muscle and hematopoietic bone marrow

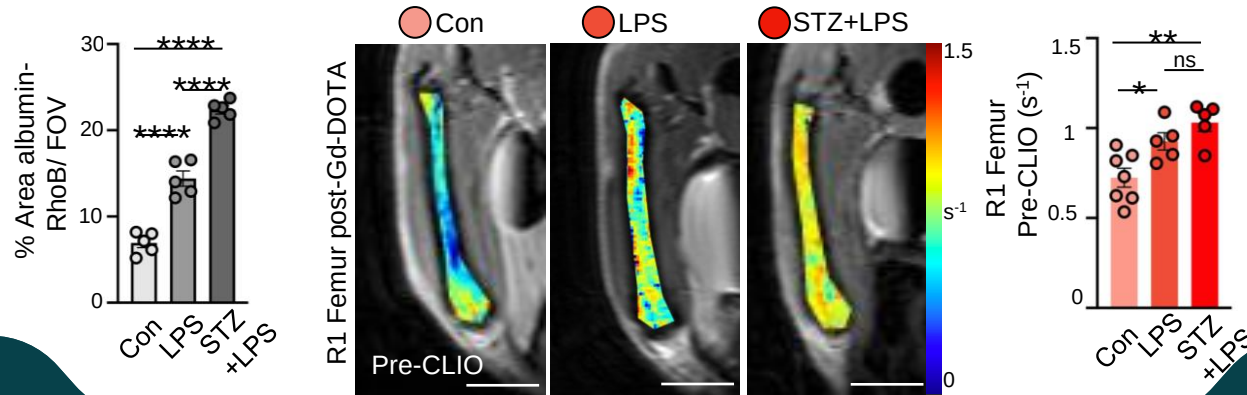
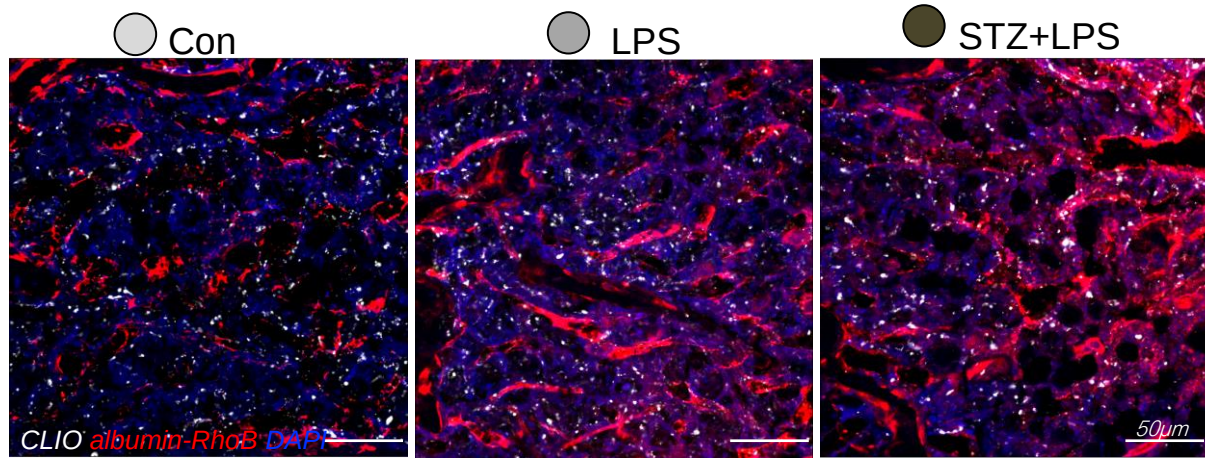


Optical imaging

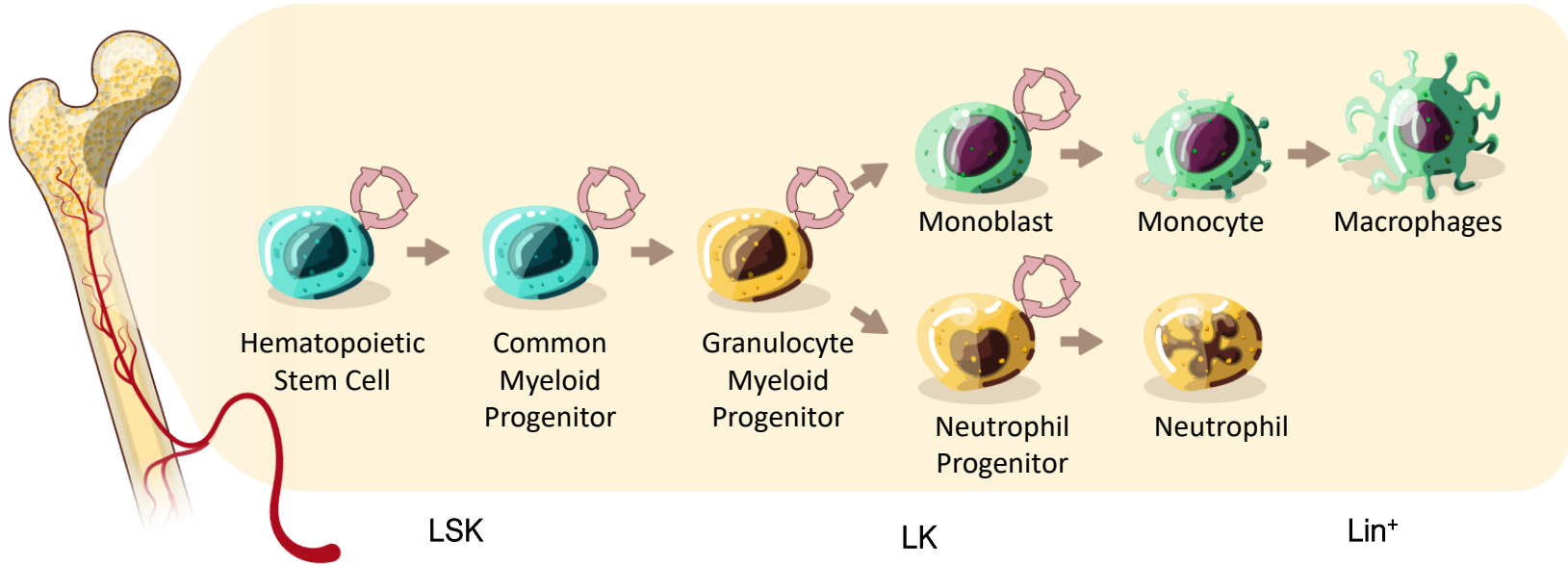


Con = Control
 LPS = Lipopolysaccharide 2 injections IM
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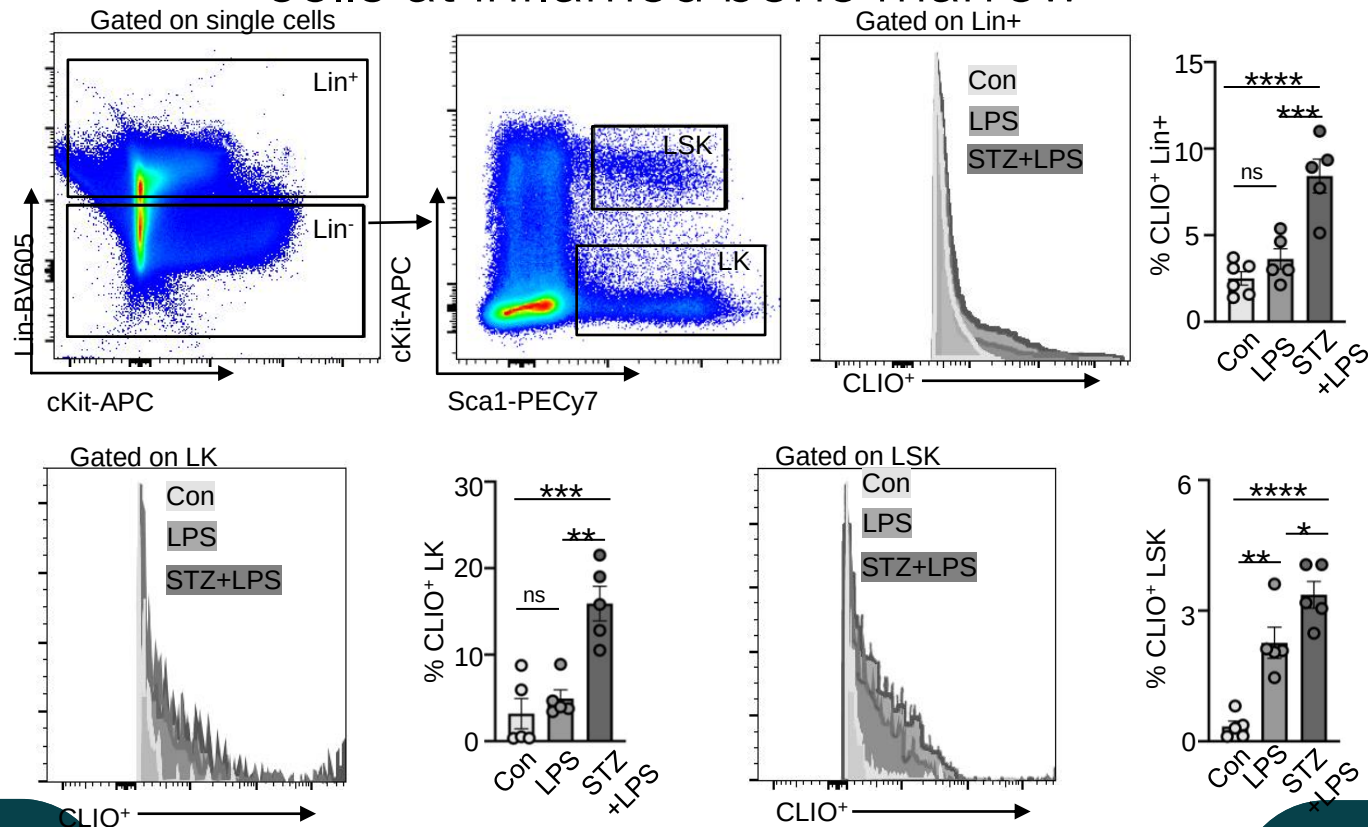
Enhanced permeability at inflamed bone marrow



Myelopoiesis



Elevated CLIO-AF647 uptake in hematopoietic stem and progenitor cells at inflamed bone marrow



Enhanced trafficking of CLIO-AF647 nanoparticles at the bone marrow under cumulative inflammatory conditions



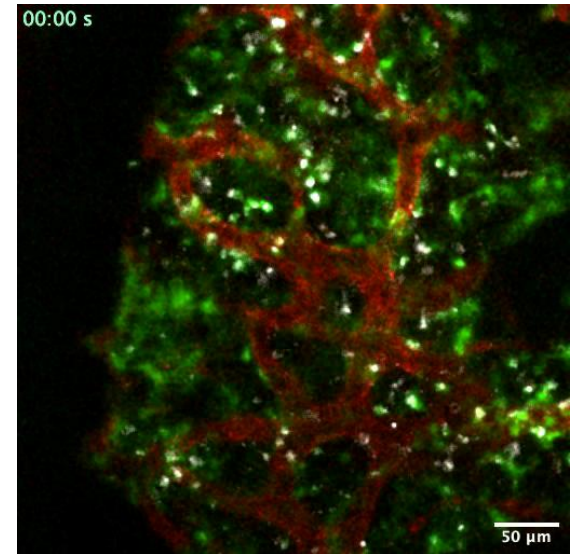
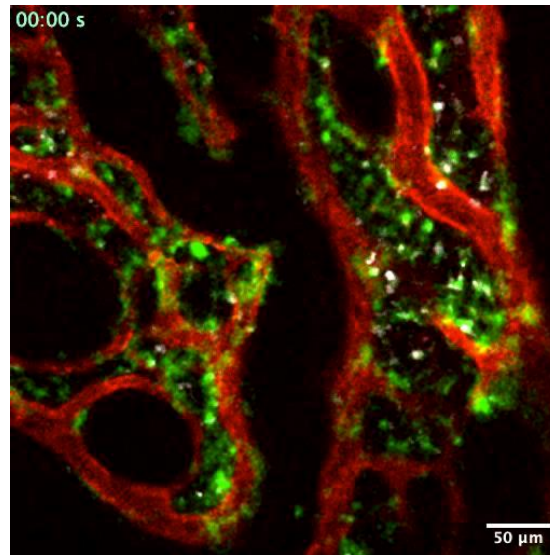
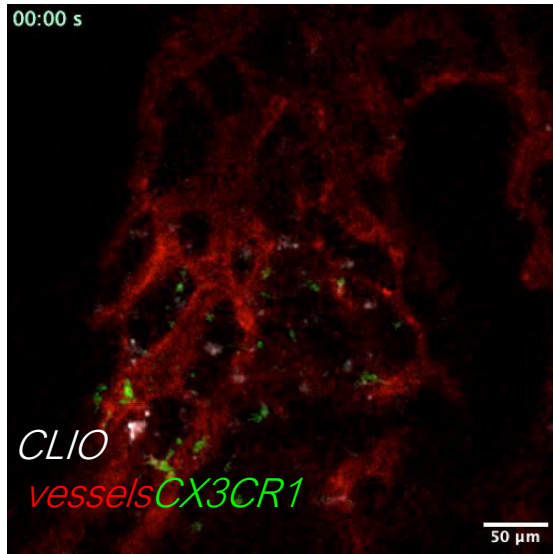
Intravital
microscopy

○ Con

○ LPS

● STZ+LPS

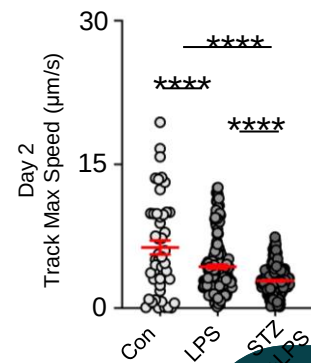
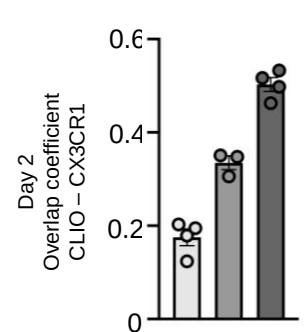
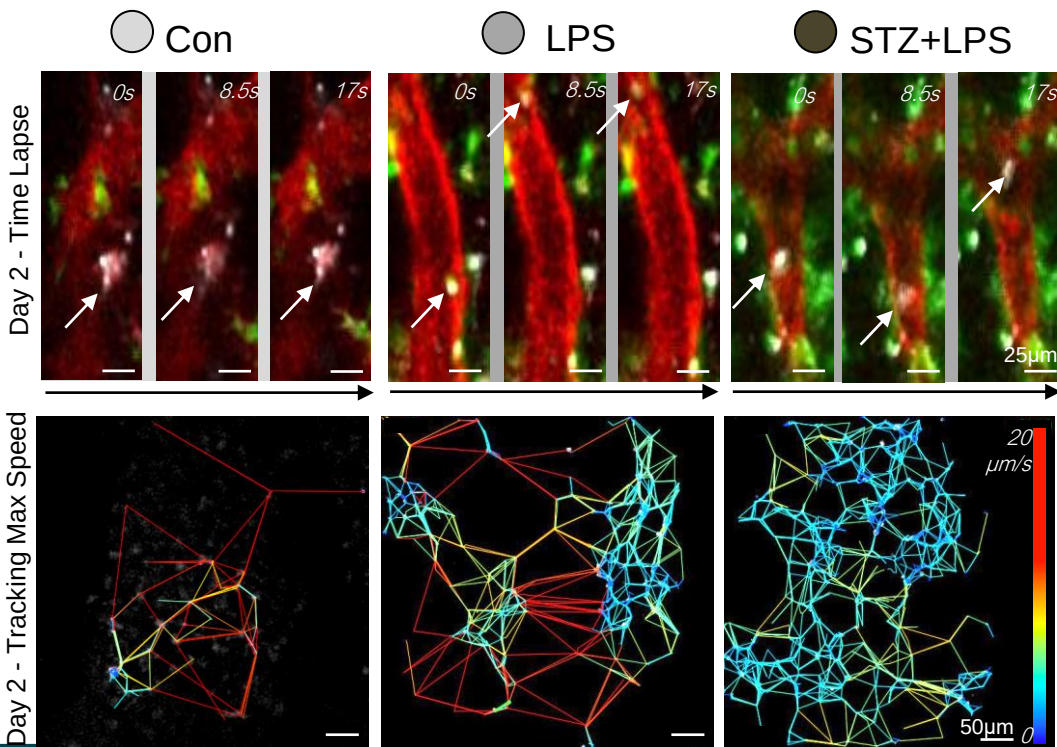
IVM 2 days after CLIO



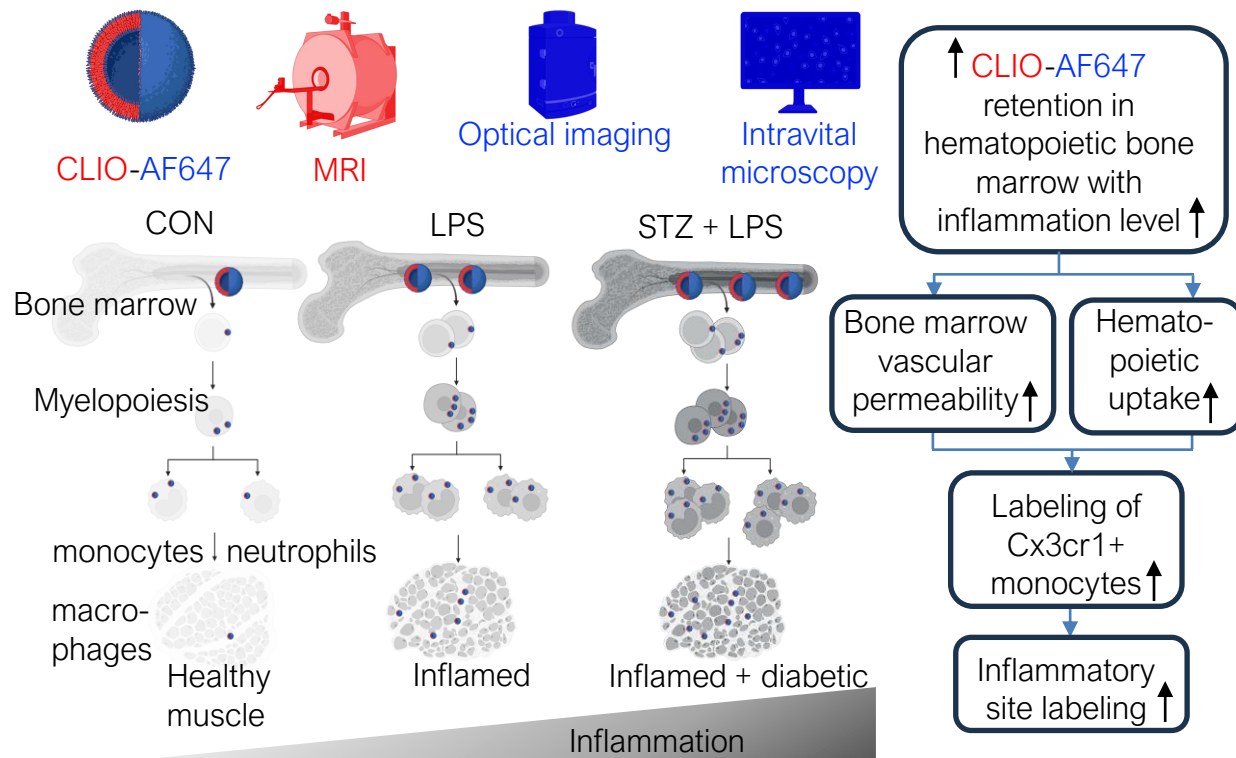
Enhanced trafficking of CLIO-AF647 nanoparticles 2 days after injection



Intravital
microscopy



Cross-Modal Imaging Reveals Nanoparticle Uptake Dynamics in the Hematopoietic Bone Marrow during Inflammation



Acknowledgement

Team & Funds

Biomedical Engineering

@Technion:

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Noga Kalish Achrai

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Dareen Saab

Tehila Alter

Maya Sharoni

BCF @Technion:

Galit Saar

Maya Holdengreber



The Wolfson*
Foundation

BIRAX Ageing



TECHNION



Human Health Initiative

The Vandoorne Lab



Advancing In vivo Imaging



First-in-country
VECTor7, MILabs
PET/SPECT/CT/OI



9.4T Bruker MRI



Intravital confocal
microscope

Collaborators

Moti Freiman – Technion

Ramez Daniel – Technion

Yosi Shamay – Technion

Assaf Gilad – MSU

Daniel Stuckey – UCL



Technion
Israel Institute of Technology