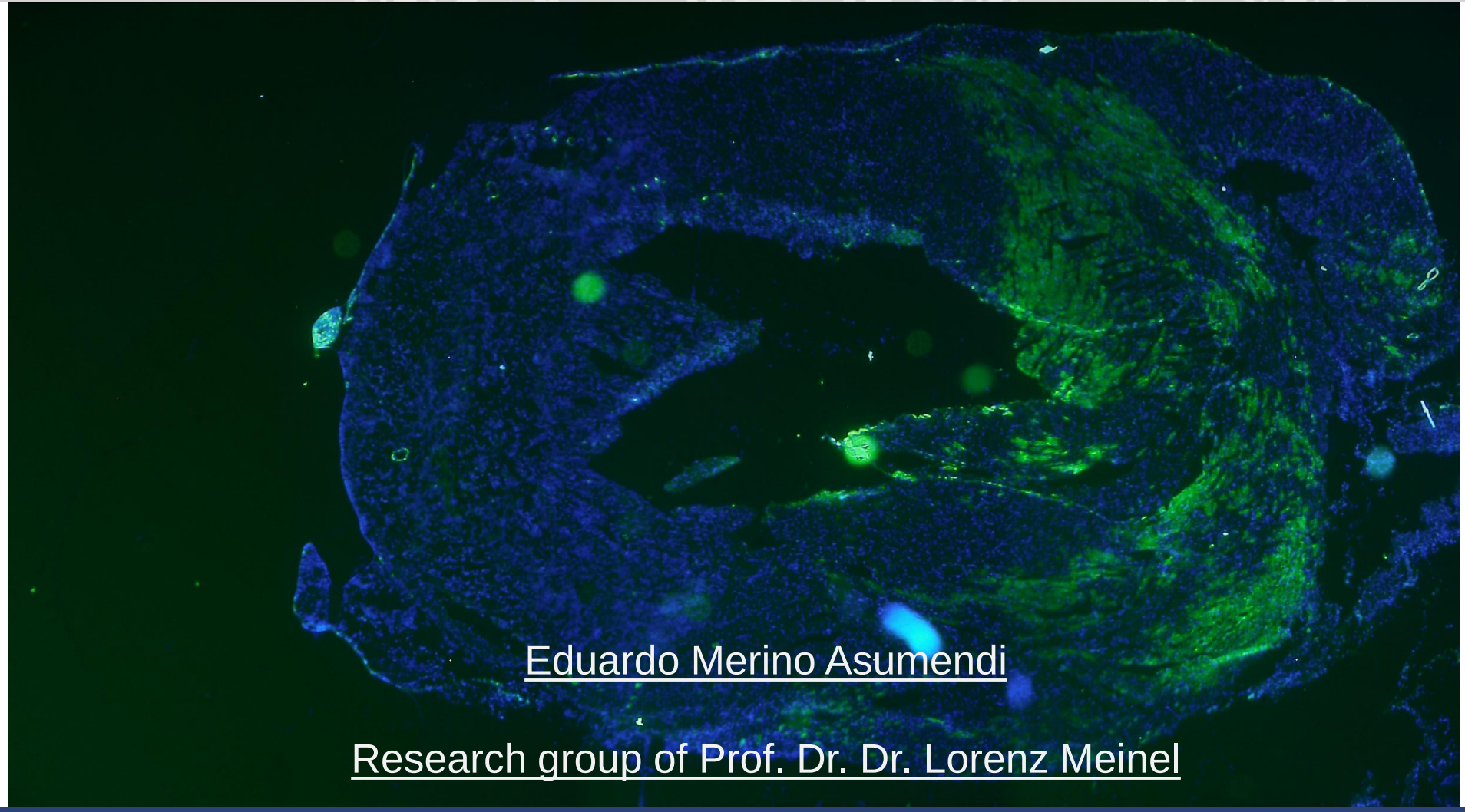
Julius-Maximilians-
UNIVERSITÄT
WÜRZBURG

Building drug depots within the heart

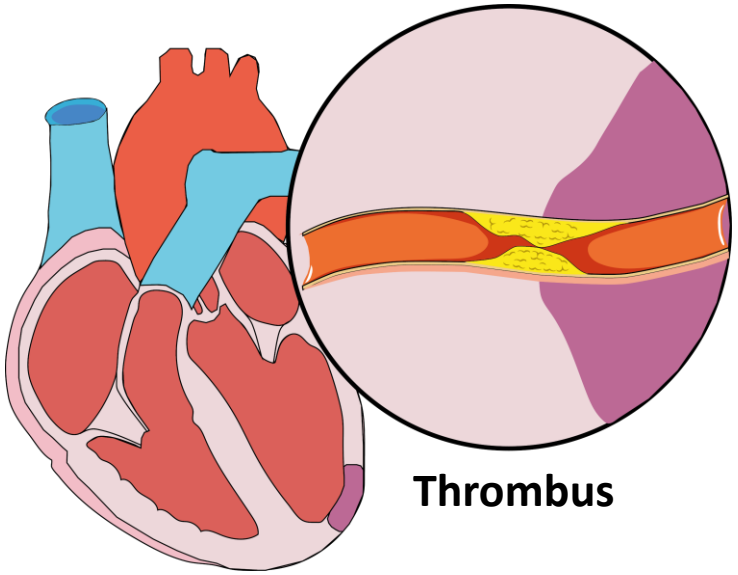


Eduardo Merino Asumendi

Research group of Prof. Dr. Dr. Lorenz Meinel

Myocardial Infarction and Heart Failure

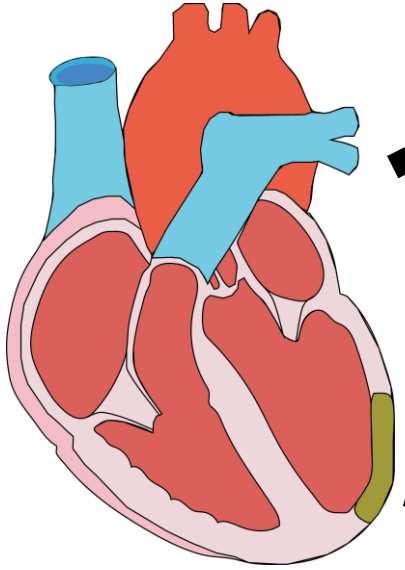
Myocardial Infarction

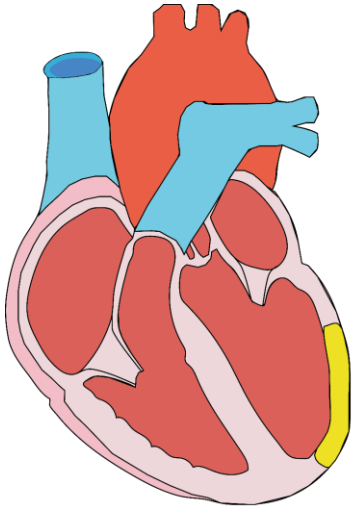


Intervention

P-PCI
FT

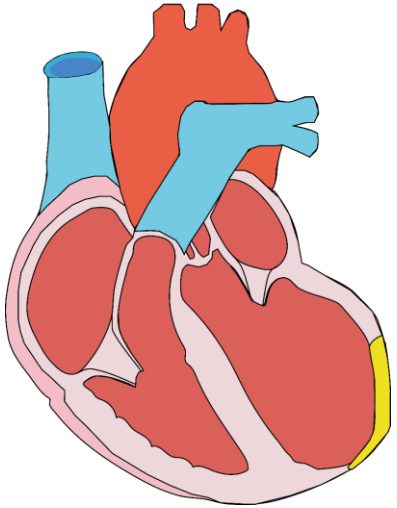
Fibrotic answer and Scar Formation





Left ventricular Hypertrophy

Heart Failure

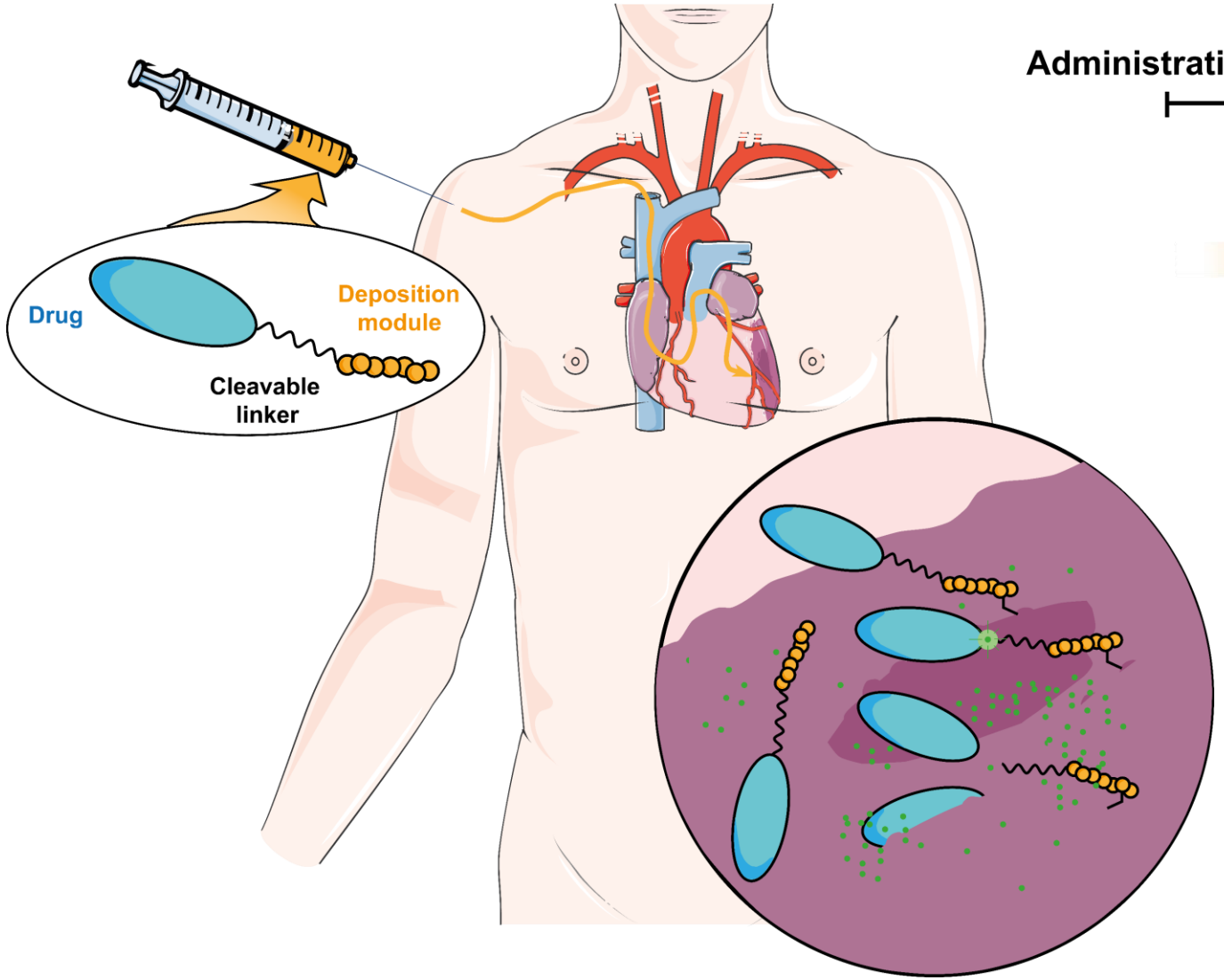


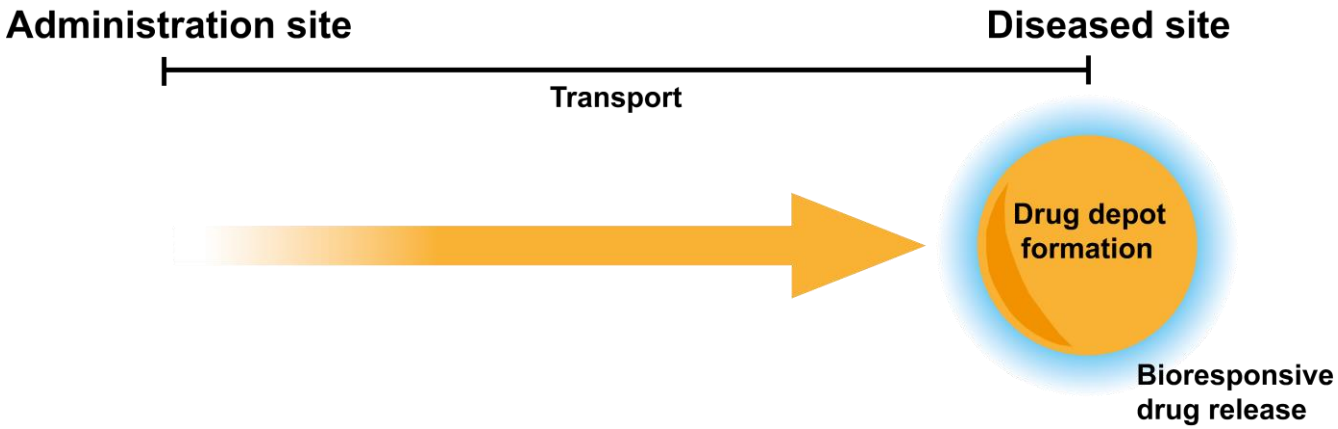
Left ventricular Dysfunction

Fibrinolitic therapy **(FT)**

Primary percutaneous coronary intervention **(P-PCI)**

Modular drug depots





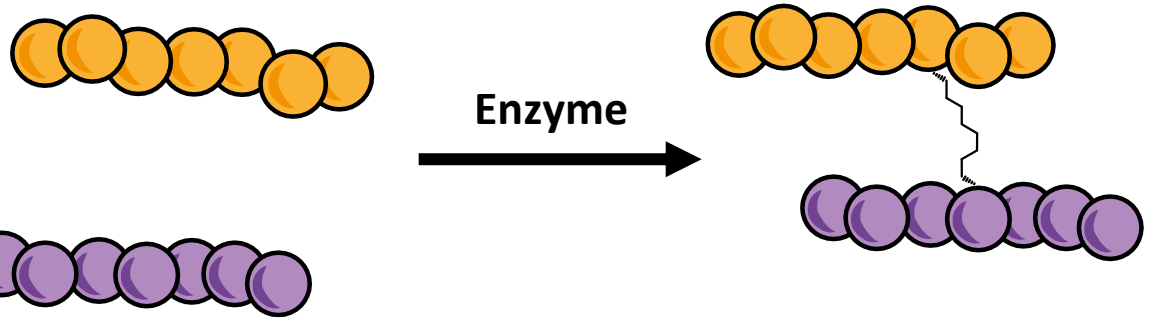
Targeted Accumulation and **Controlled Release**

Modified from smart.servier.com

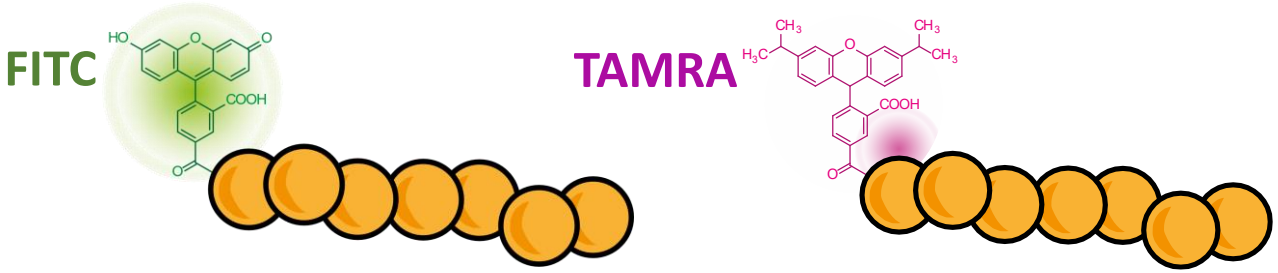
Targeting infarcted heart

A natural cross-linking reaction:

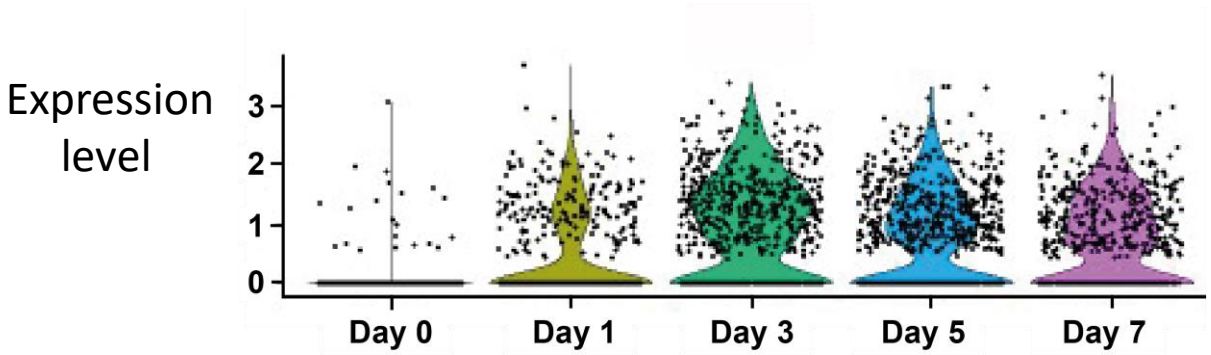
Peptide



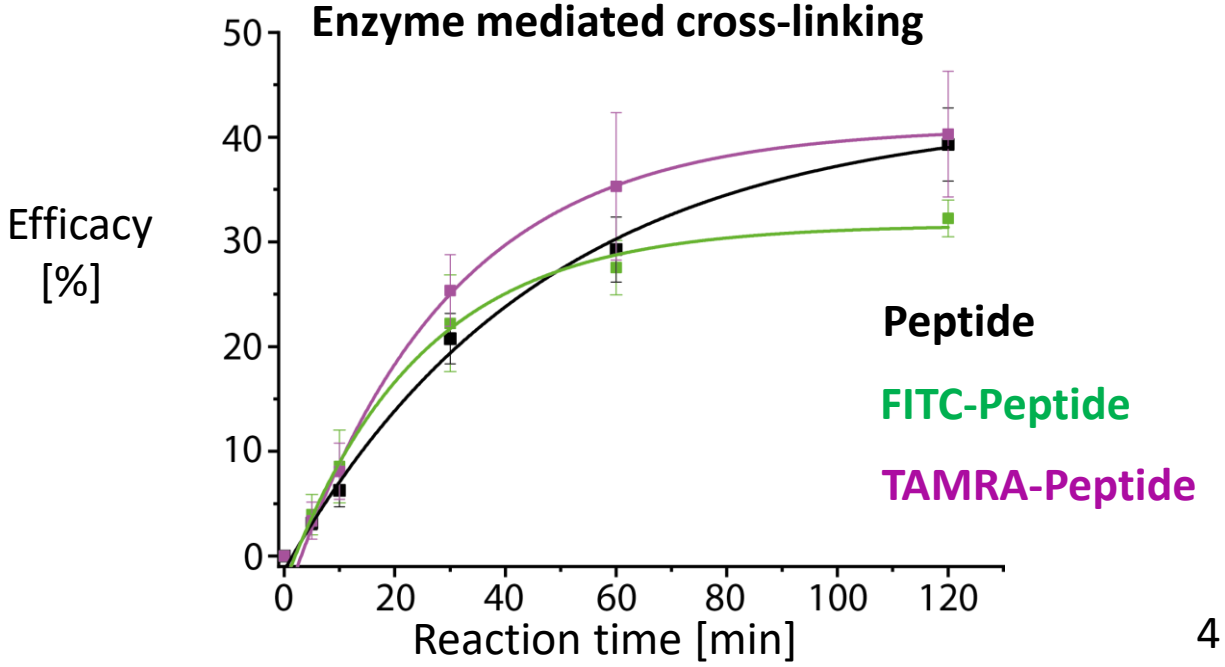
Extracellular matrix (ECM)



Enzyme expression in myeloid cells



Enzyme mediated cross-linking

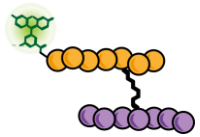


Targeting infarcted heart

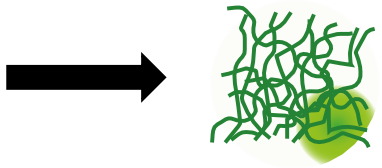
Immobilization onto the extracellular matrix (ECM)

Fibroblast

Isolated ECM



Enzymatic cross-linking

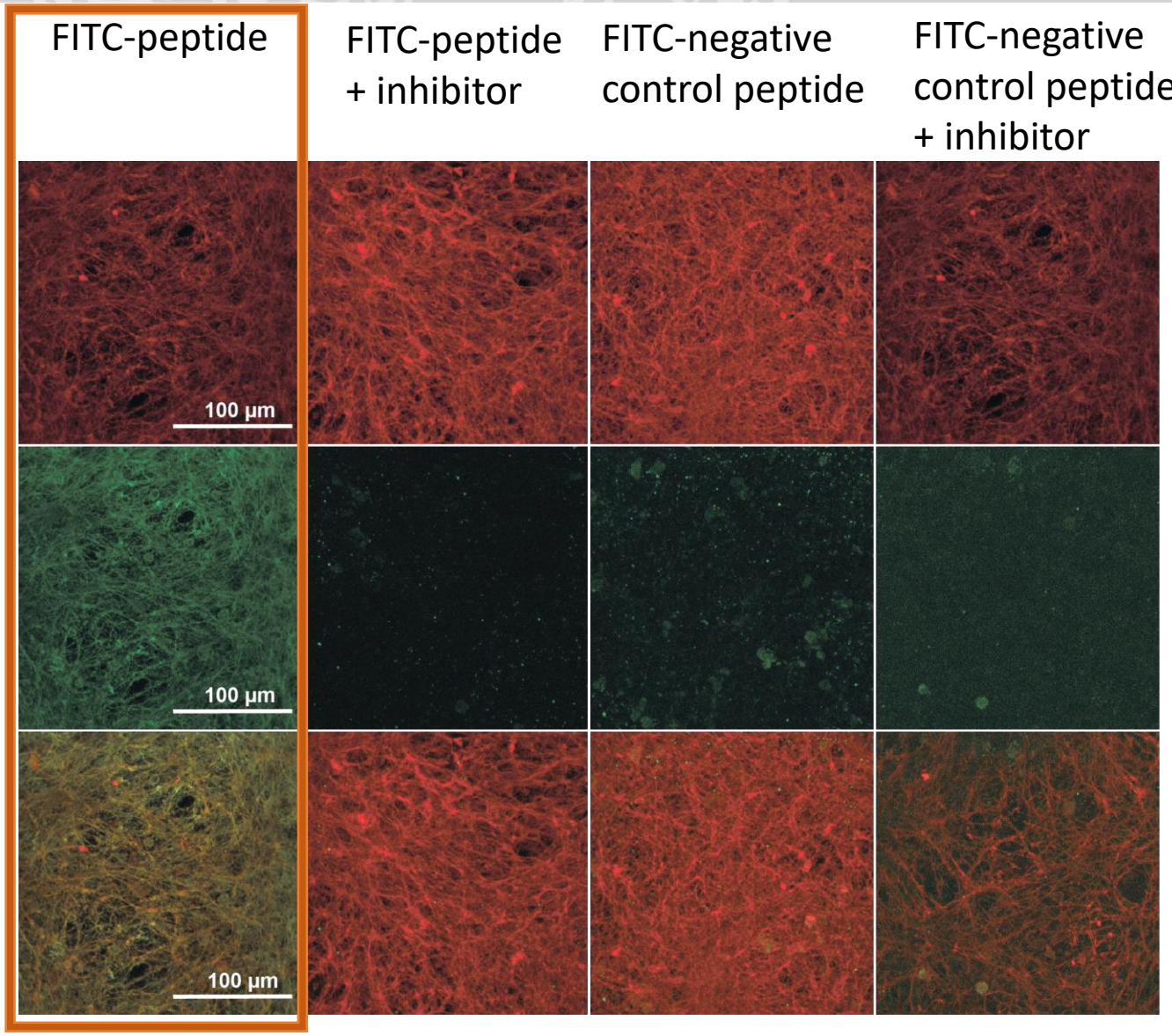


Functionalized ECM

Fibronectin Alexa633

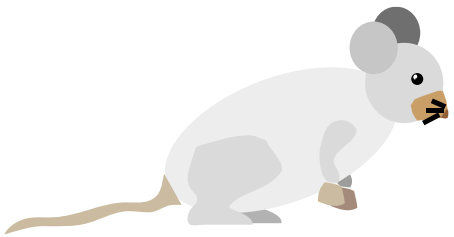
FITC

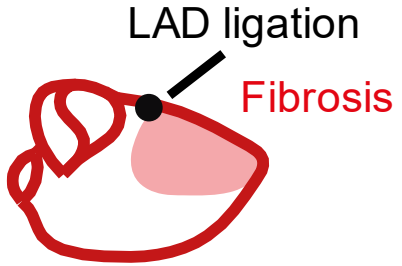
Overlay



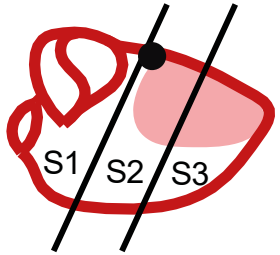
Targeting infarcted heart

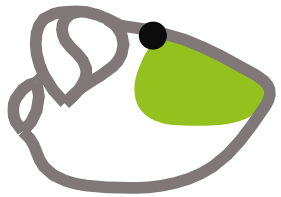
Immobilization onto infarcted mice hearts





Sectioning and
fluorescence imaging





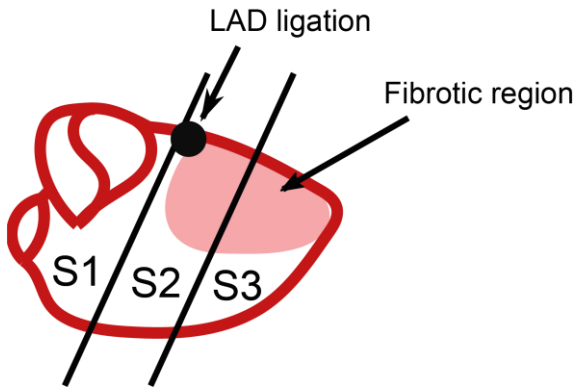
Left anterior descending artery (LAD) ligation is perfomed to simulate a myocardial infarction

Extraction of the hearts 7 days after LAD-ligation and perfusion with the peptide

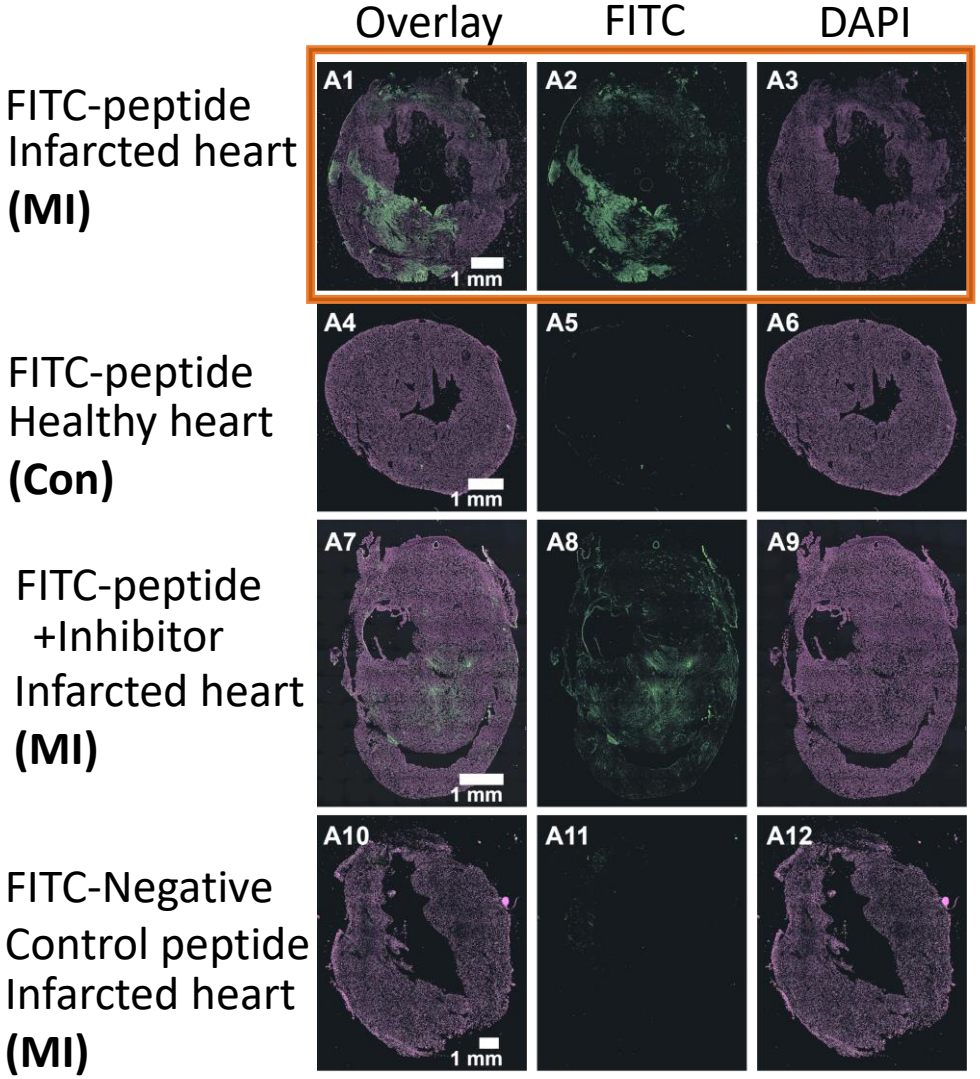
Clearing and 3D-imaging with light sheet fluorescence microscopy (LSFM)

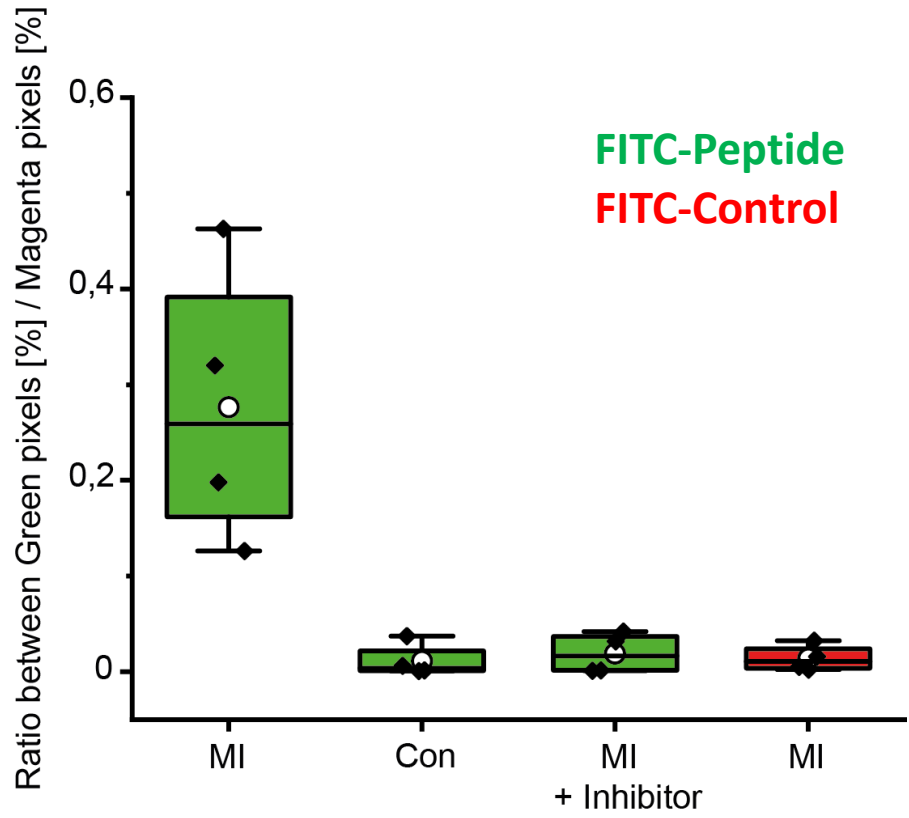
Targeting infarcted heart

Immobilization onto infarcted mice hearts



Sectioning and fluorescence imaging

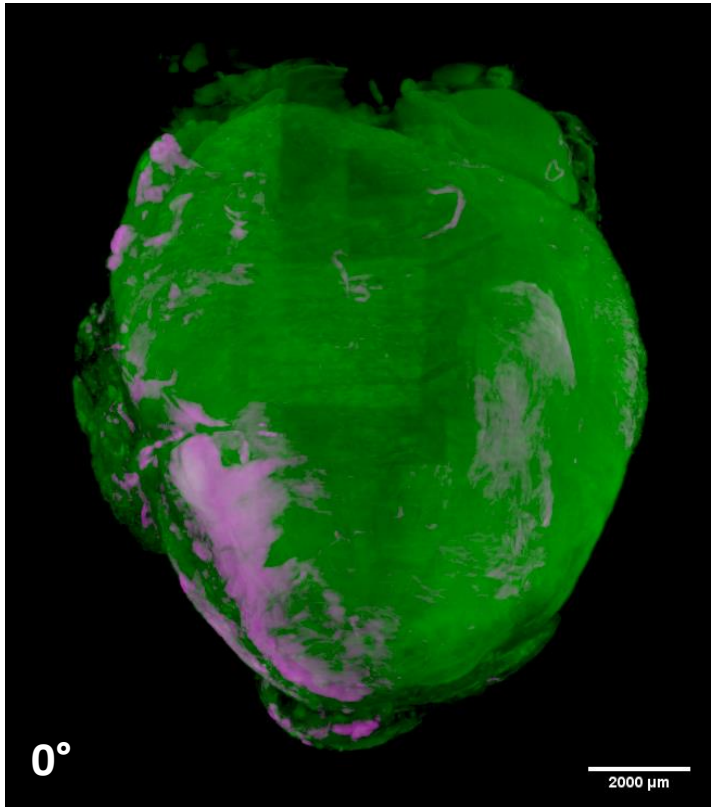


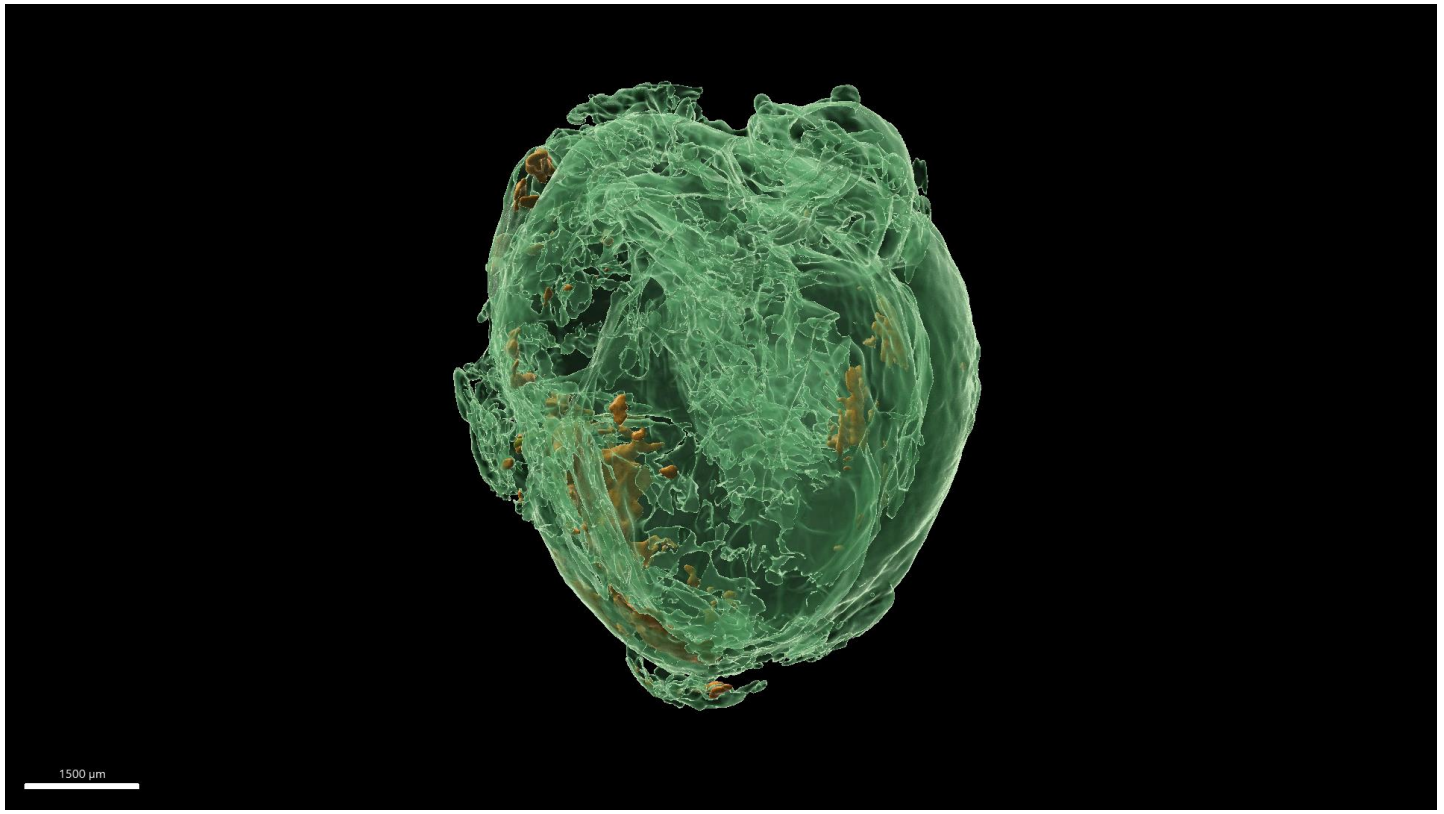


Targeting infarcted heart

Immobilization onto infarcted mice hearts

Infarcted mouse heart, perfused with TAMRA-peptide





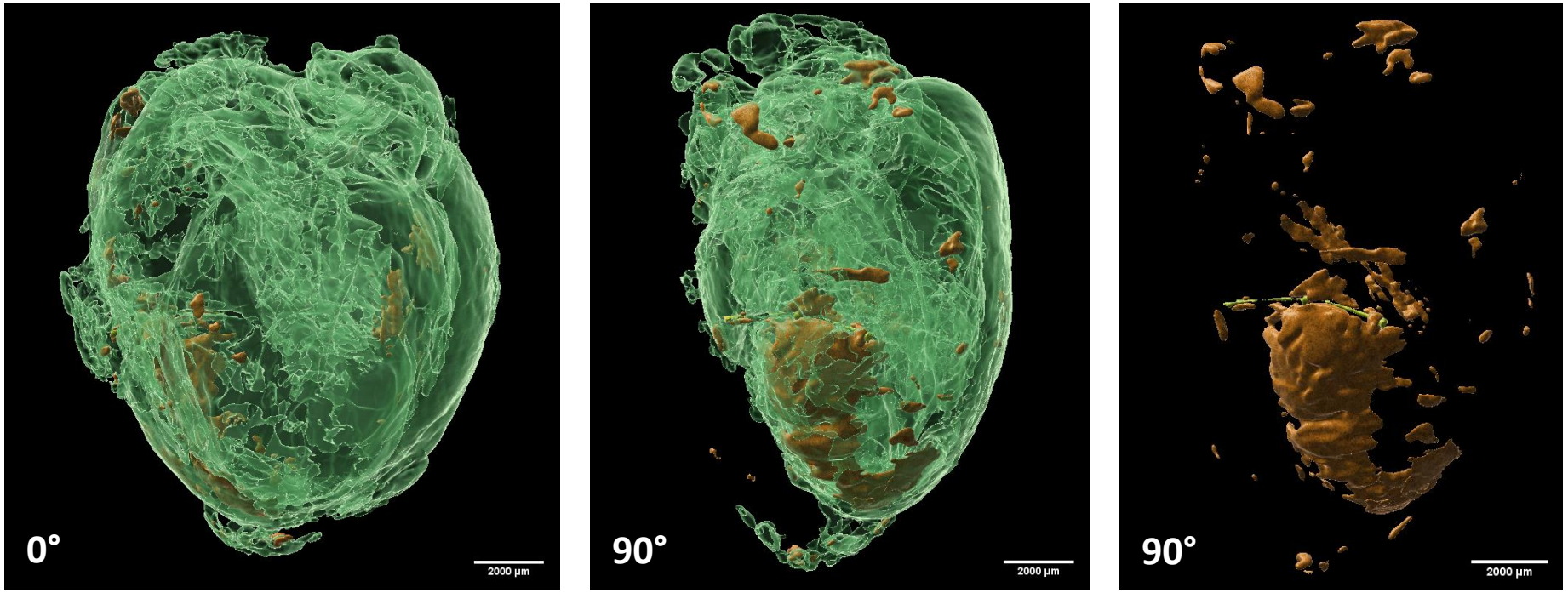
Tissue autofluorescence

TAMRA fluorescence

Targeting infarcted heart

Immobilization onto infarcted mice hearts

Infarcted mouse heart, perfused with TAMRA-peptide



Surface calculated from the autofluorescence

Surface calculated from the TAMRA fluorescence

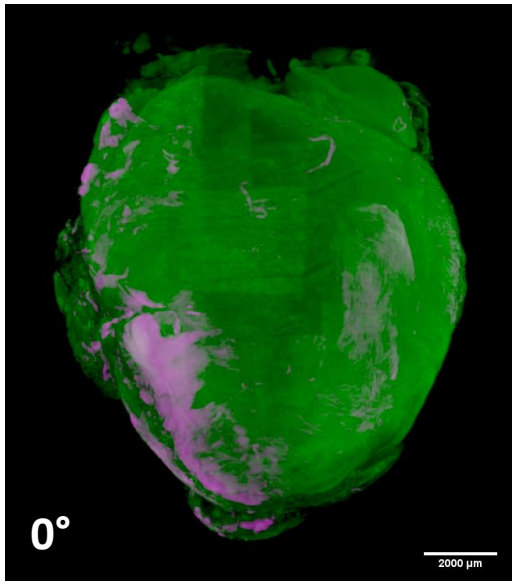
Surface calculated from the shadow formed by LAD-ligation knot

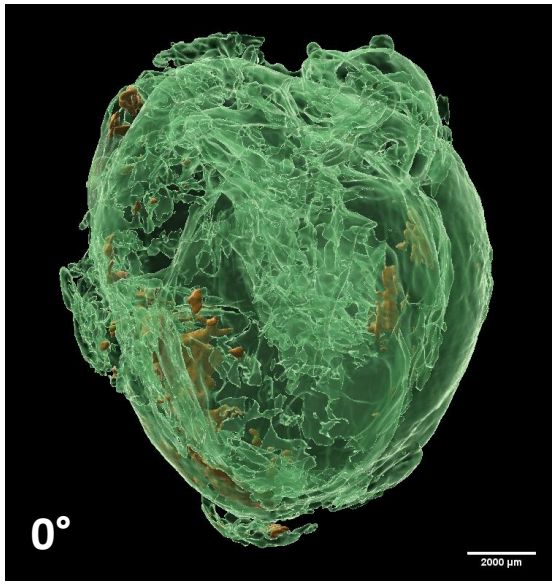
Unpublished data

Targeting infarcted heart

Immobilization onto infarcted mice hearts

Infarcted mouse heart, perfused with CTAMRA-peptide

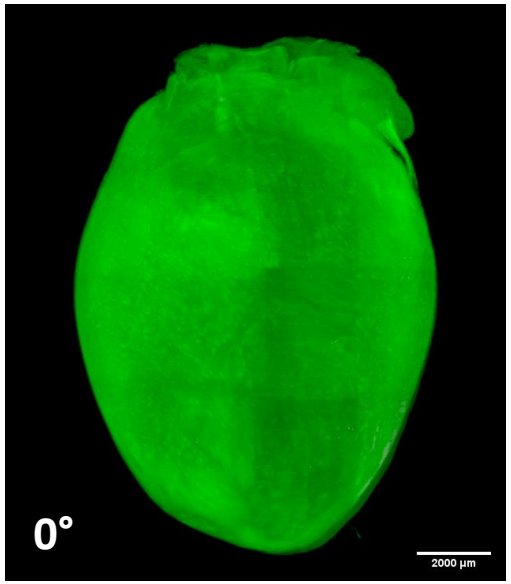


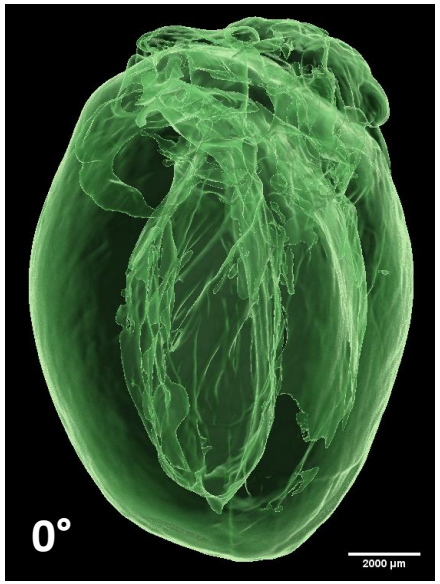


Tissue autofluorescence

TAMRA fluorescence

perfused **healthy mouse heart**





Conclusion and Outlook

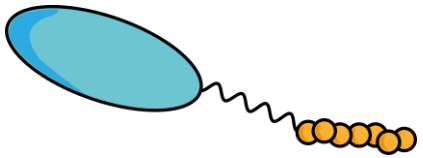
Conclusion

Specific accumulation onto fibrotic tissue

Outlook

In vivo characterization

Expansion of the peptide with a linker module and drug



End

„Receptor Dynamics“
Doktorandenkolleg

Elitenetzwerk Bayern

Institute for Pharmacy and Food Chemistry

Prof. Dr. Dr. Lorenz Meinel
Prof. Dr. Tessa Lühmann
Prof. Dr. Michael Decker
Prof. Dr. Alma Zernecke-Madsen
Sarah Schäfer

AK Meinel

CRS Germany Local Chapter

CRS BeNeLux & France Local Chapter

Thank you for your attention!