An Experimental Suite for RNA-based EMT Targeting in Breast Cancer

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CONTROLLED RELEASE SOCIETY
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INTEGRATING
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ACROSS DISCIPLINES

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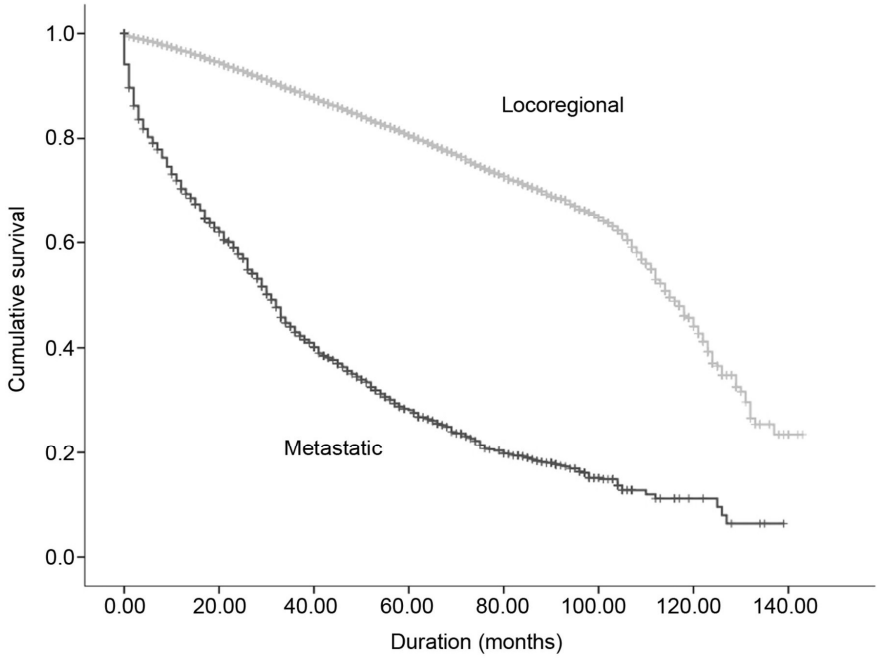
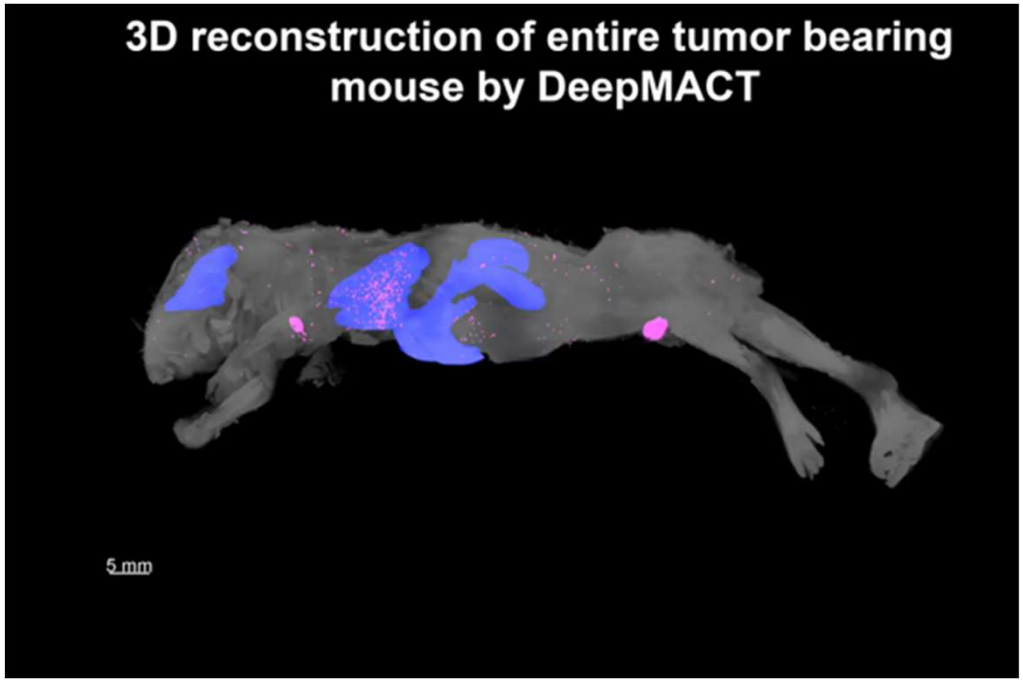
Metastasis in Breast Cancer



Gomes I et al. - Overall Survival of Patients With Locoregional and Metastatic Breast Cancer: Is the Influence of Baseline Characteristics the Same? *Anticancer Res. 2019*



Pan C et al. - Deep Learning Reveals Cancer Metastasis and Therapeutic Antibody Targeting in the Entire Body. *Cell. 2019*

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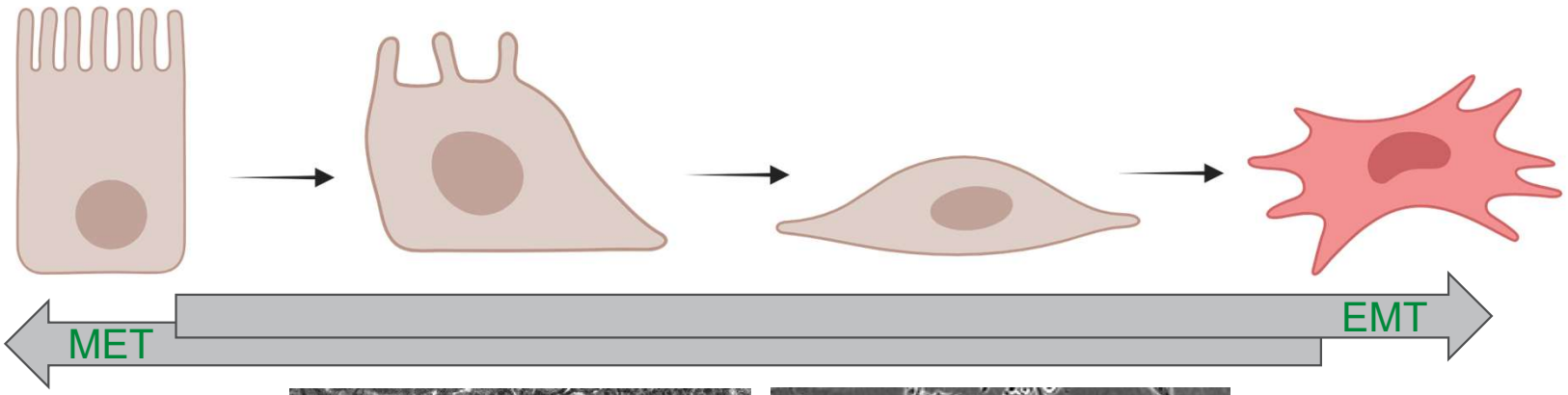
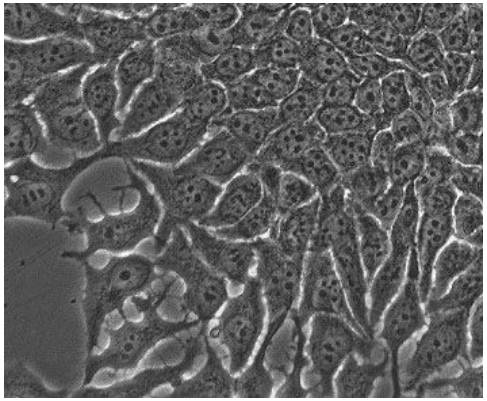
Epithelial-Mesenchymal Transition (EMT)

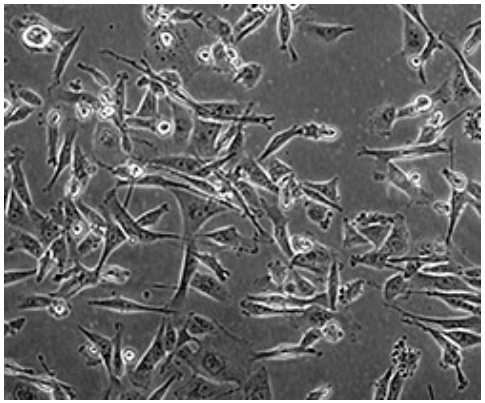


Epithelial phenotype
- apico-basal polarity
- organisation of cell-cell junctions/cytoskeleton

→ **poor migrative/invasive potential**



MCF7 cells (from DSMZ)



MDA-MB-231 cells (from ATCC)

Mesenchymal phenotype
- front-back polarity
- absence of tight-junctions + less adherence junctions
- resistance against anoikis

→ **highly invasive/migrative**

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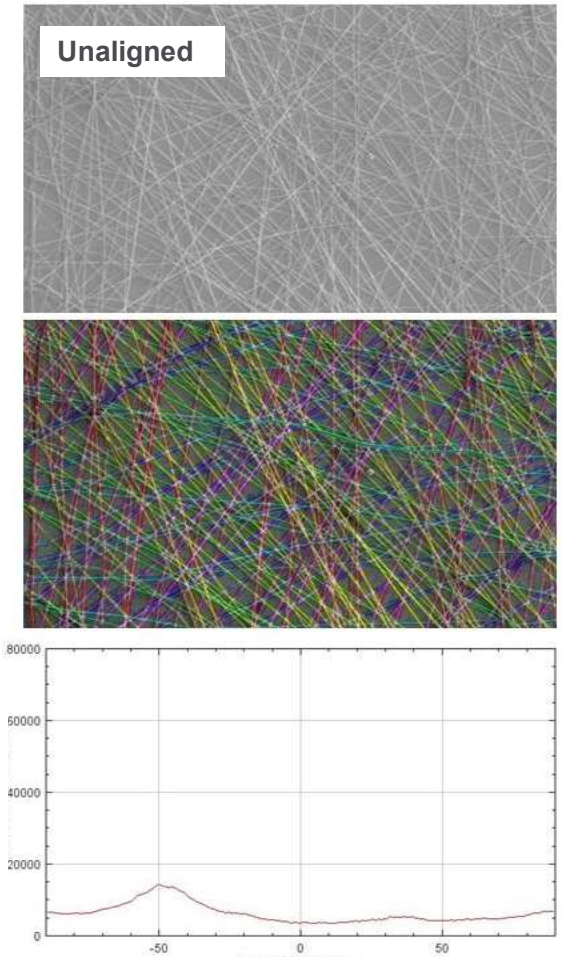
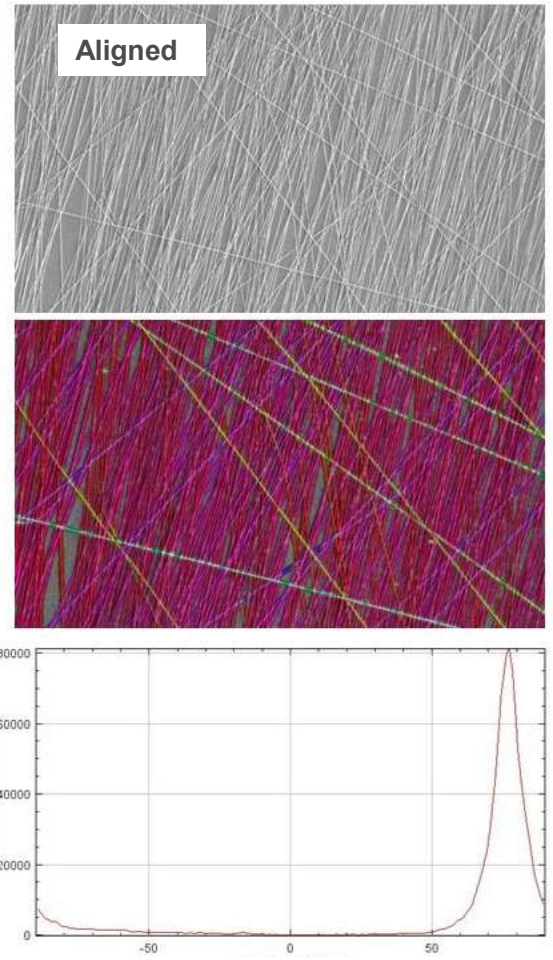
Our EMT model: electrospinning fibers

Coverslips with aligned fibers production



Orientation frequency plot



Orientation frequency plot

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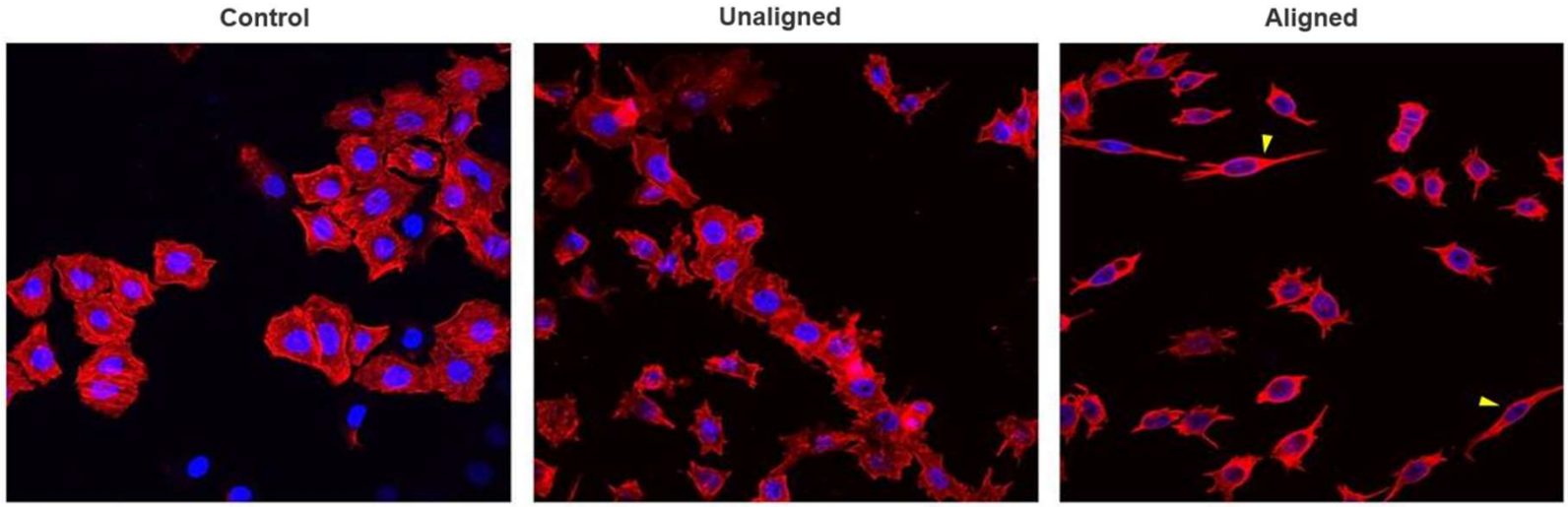
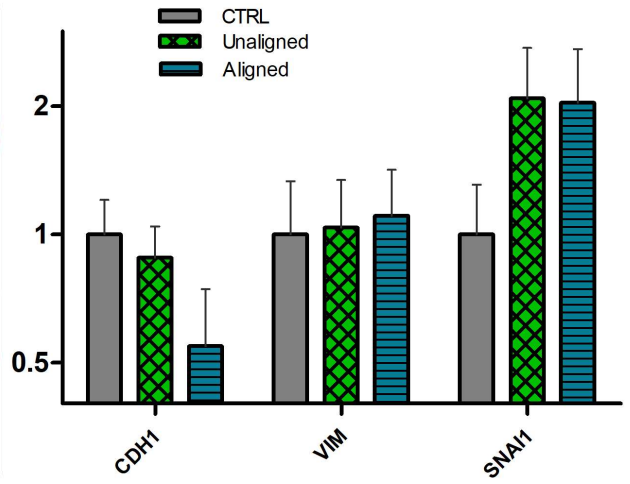
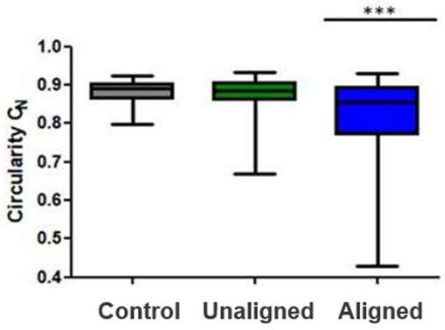
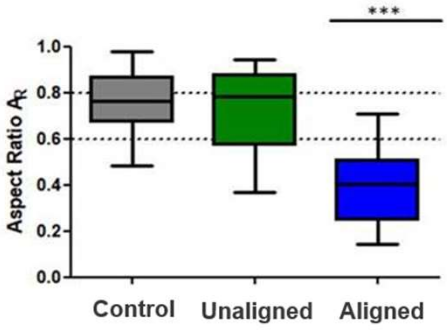
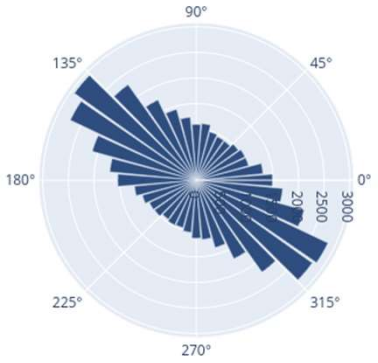
Contact guidance EMT on MDA-MB-468



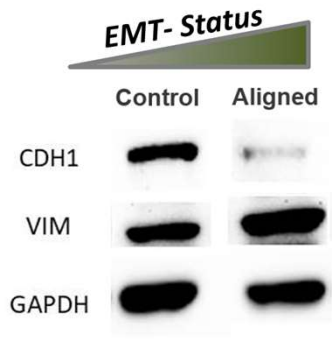




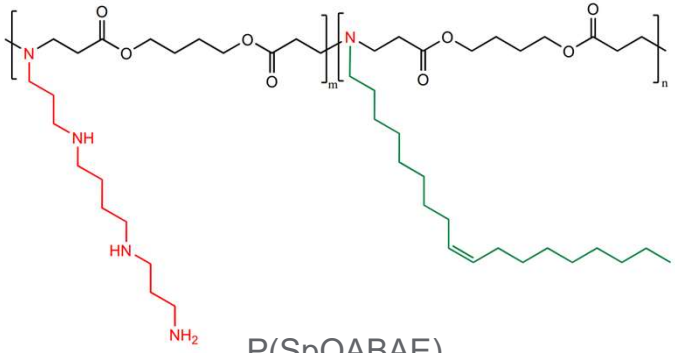




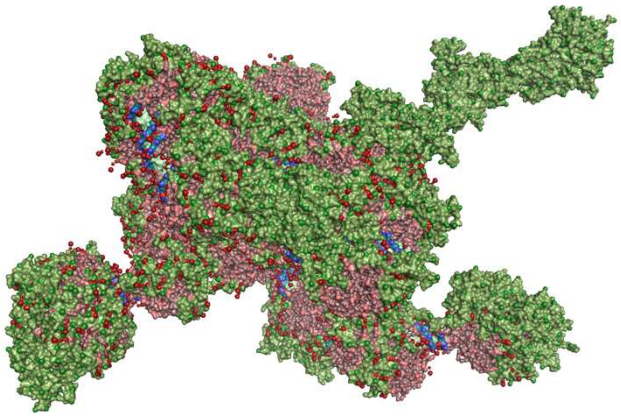
Cell movement speed plot



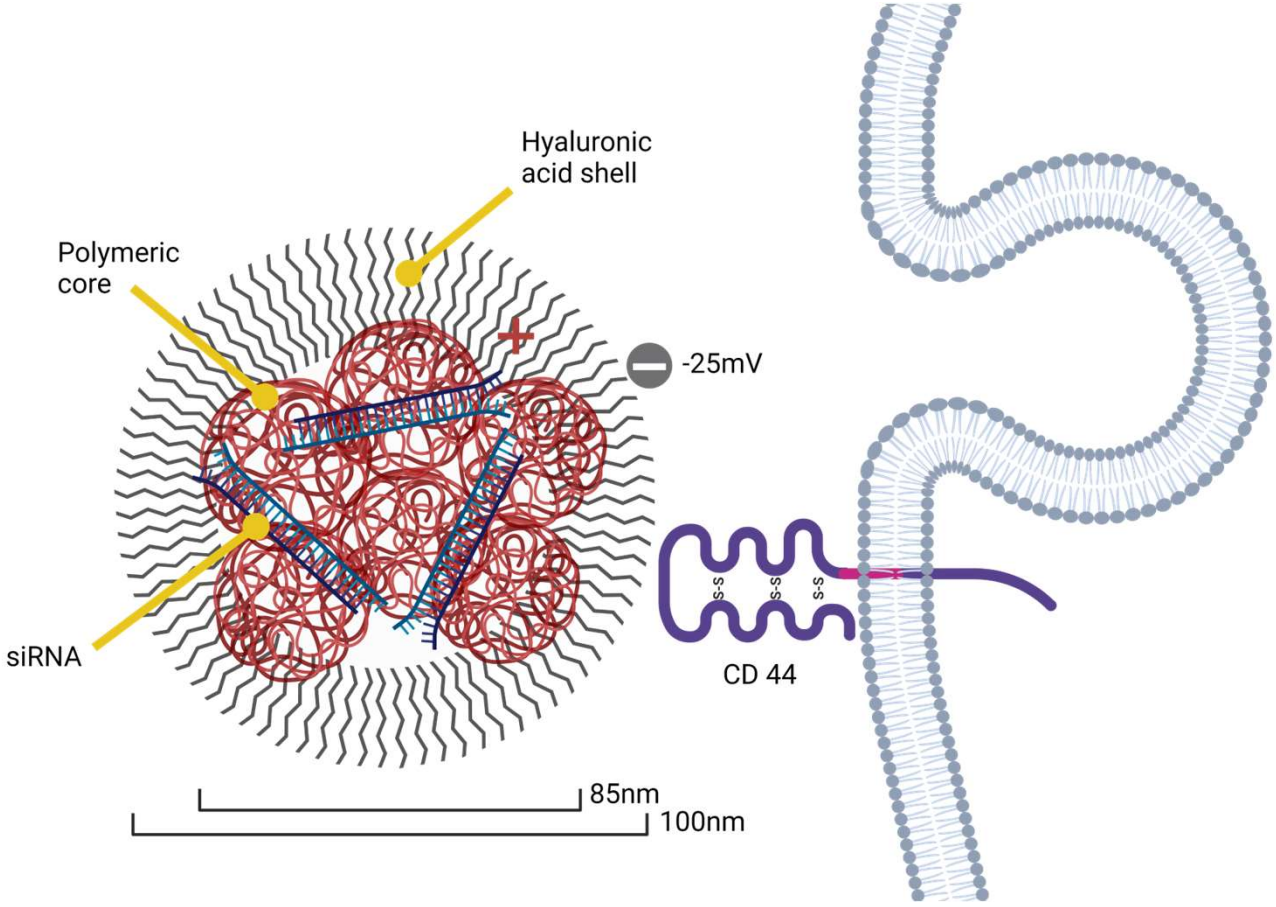
Hyaluronic Acid coated PBAE Polyplexes (HAPy) to enable EMT targeting



P(SpOABAE)



Molecular Dynamics simulation of HAPy



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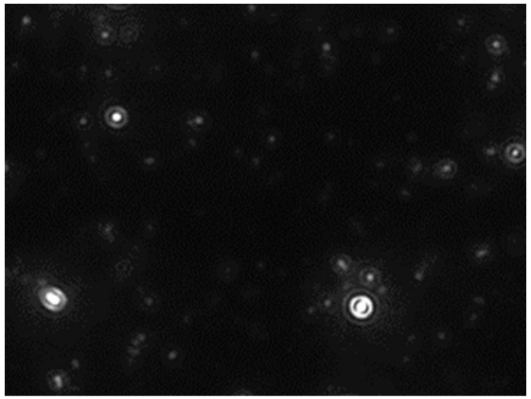
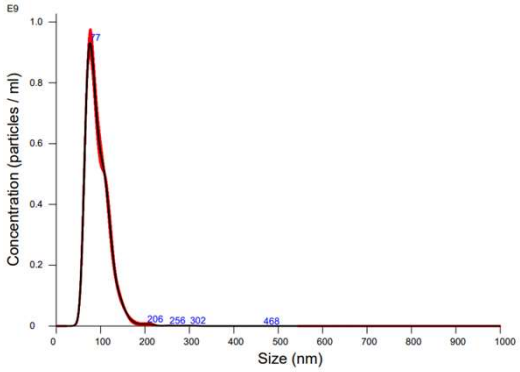
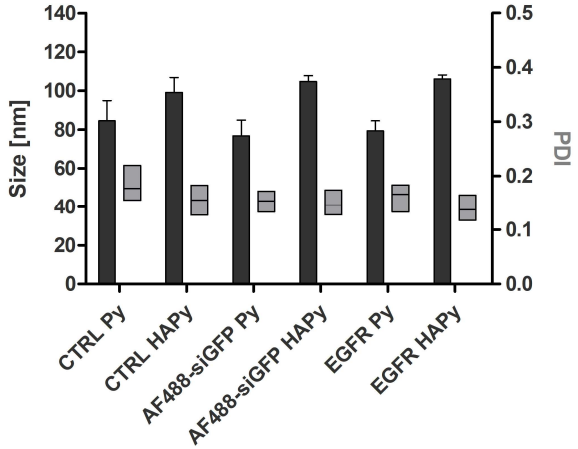
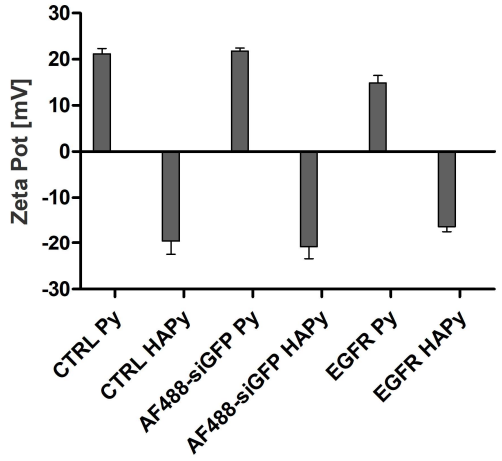
HAPy characterization

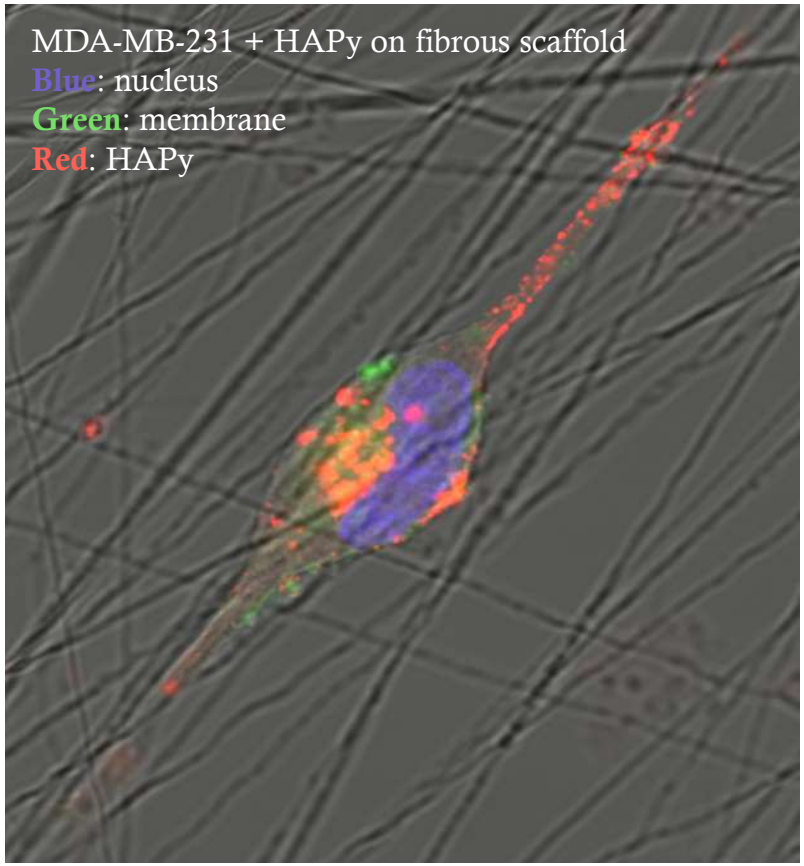


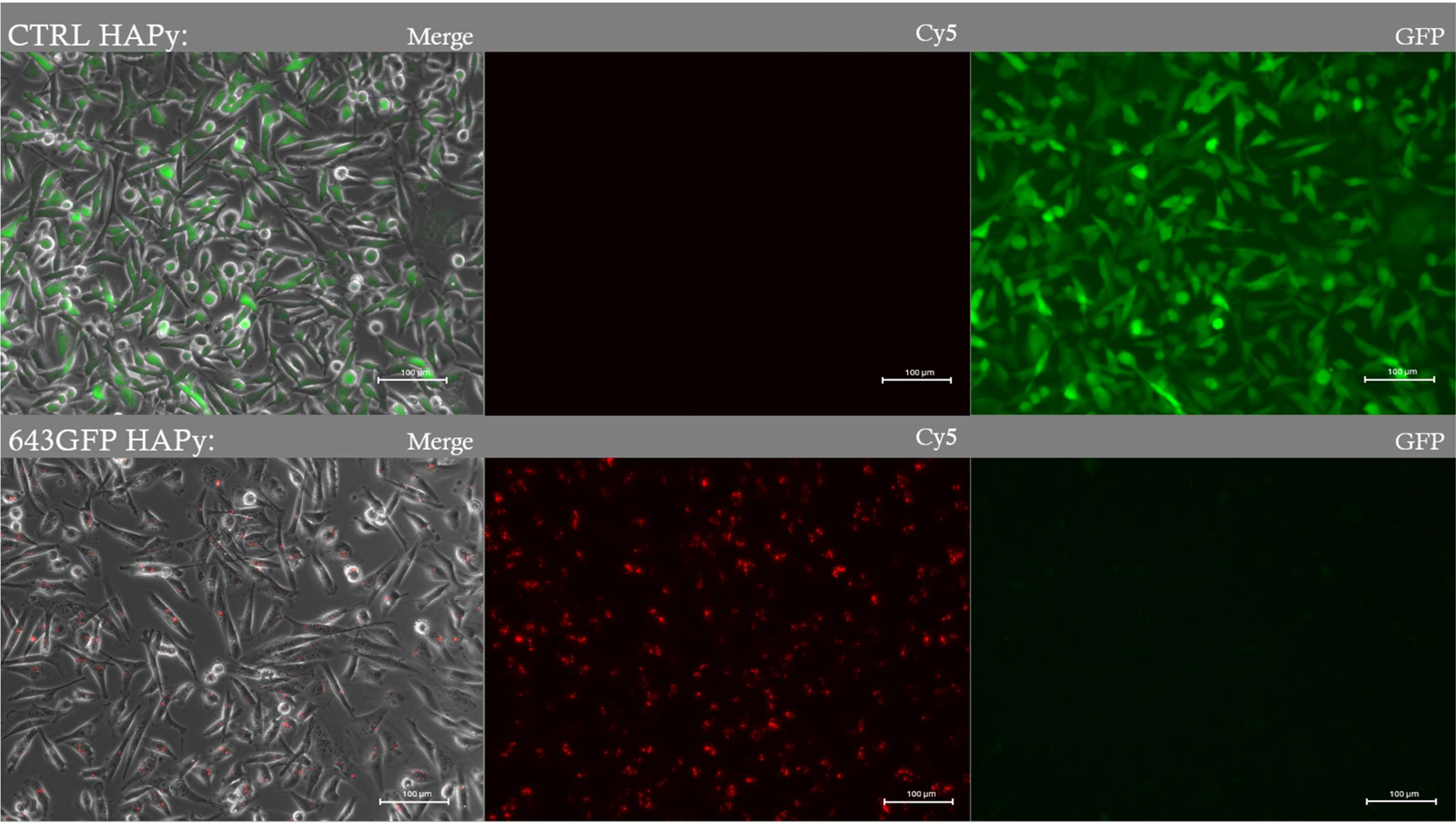


CTRL HAPy population, NTA data








CTRL HAPy:
Merge
Cy5
GFP
643GFP HAPy:
Merge
Cy5
GFP
100 µm

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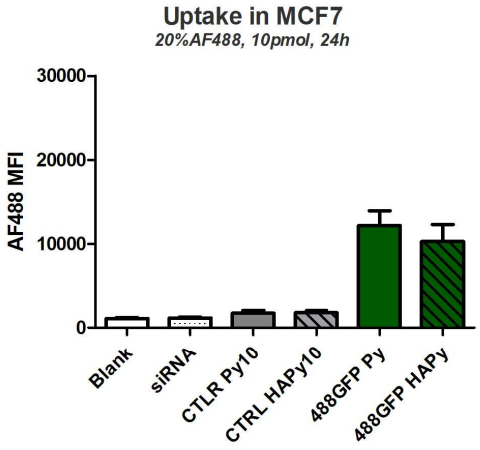
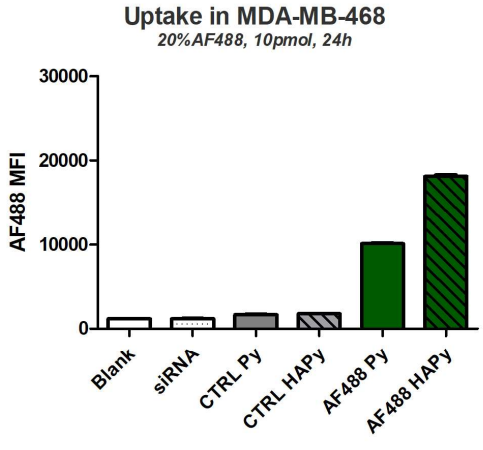
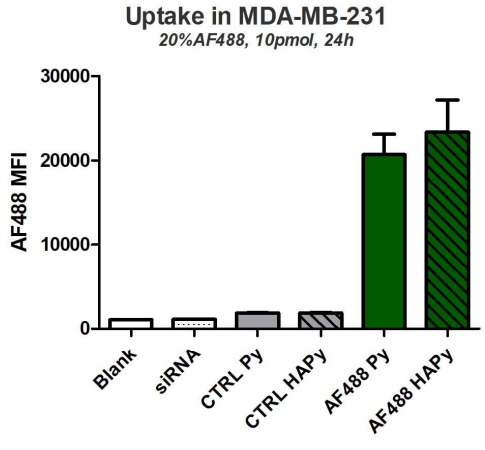
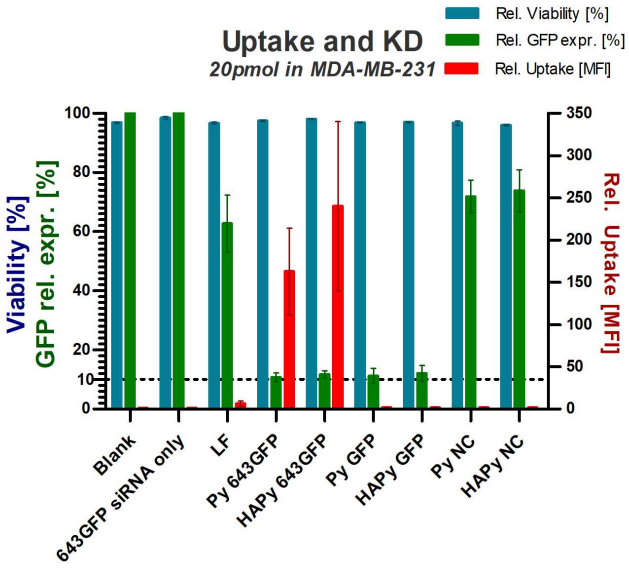
HAPy *in vitro*

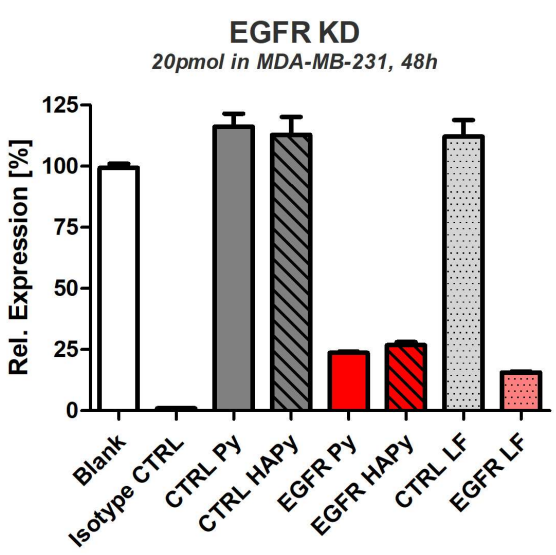
- Uptake is favoured for mesenchymal cells in our panel.
- Potent knockdown was achieved for reporter and therapeutically relevant genes at low, nontoxic dosage











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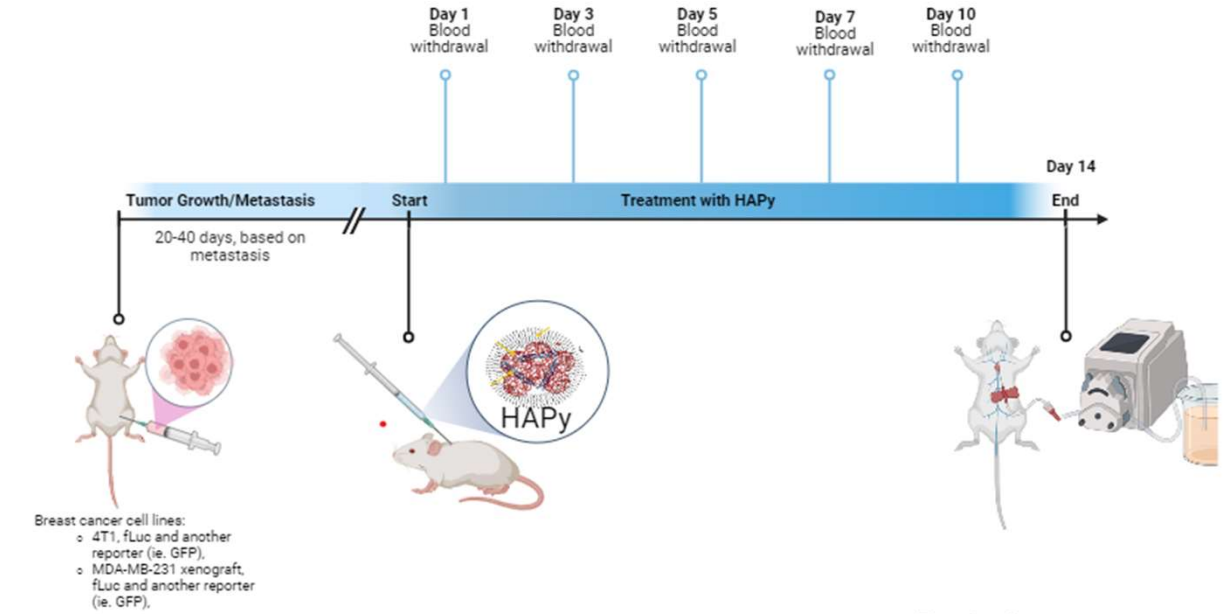
In vivo Proof of Concept ongoing



Translation objectives

- ➔ HAPy distribution, efficacy
- ➔ Expansion of proteomics fingerprinting after HAPy treatment on fibrous scaffold
- ➔ RNA expression profile
- ➔ Comparison of *ex vivo* results with fibrous scaffold model results

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Thank you for your attention!

Acknowledgments:

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Munich Multiscale Biofabrication Network

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