Polymer-based nanoparticles

for active and passive targeted drug delivery to cancer cells

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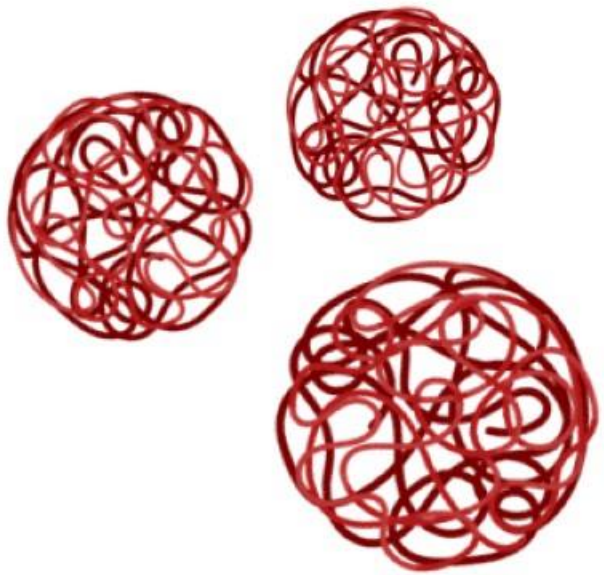
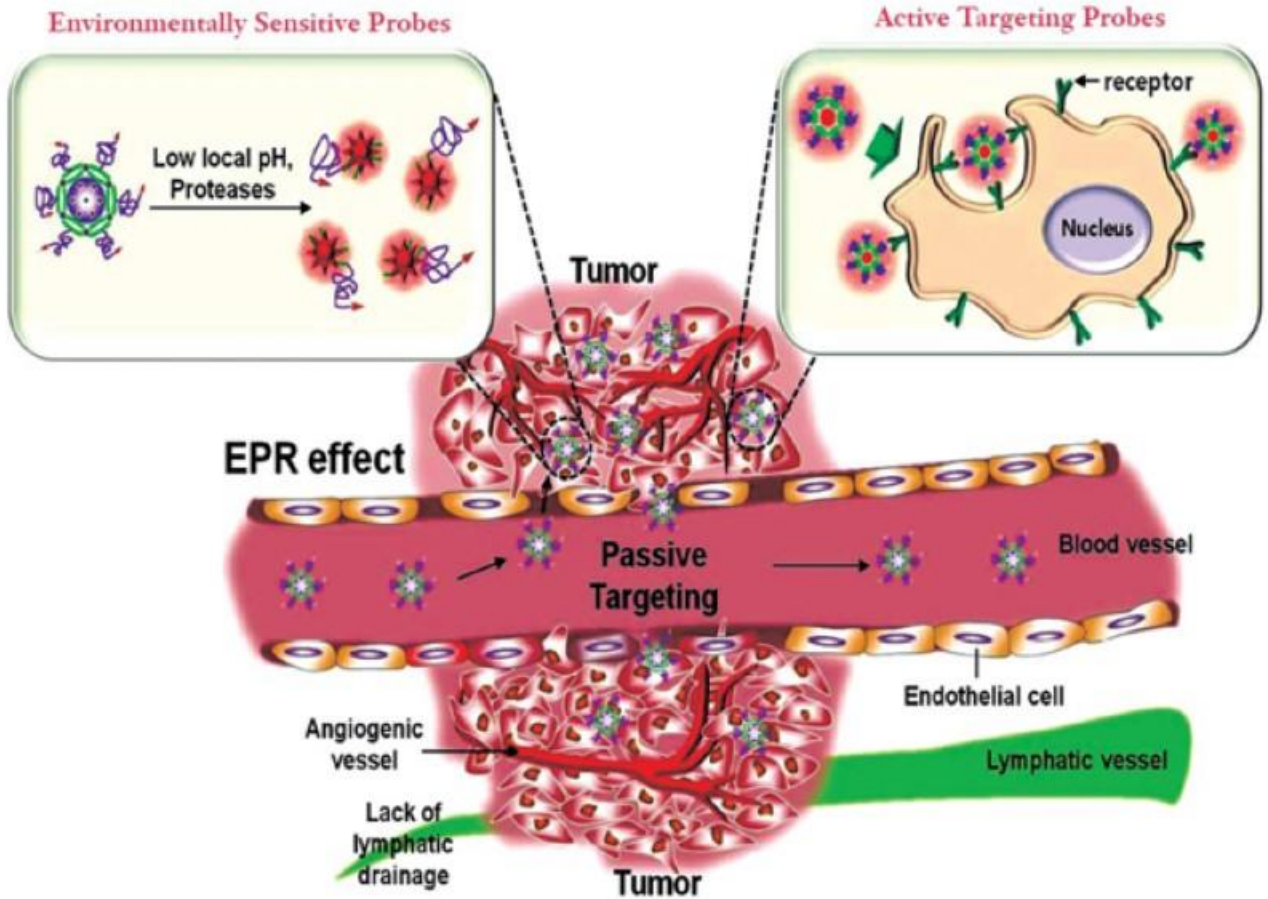
- Polymer-based nanoparticles and strategies for drug targeting
- Passive targeting to cancer cells by doxorubicin-loaded MIL-101 (Fe) MOFs
- Active targeting by EGFR-targeted MIPs

Polymer-based nanoparticles



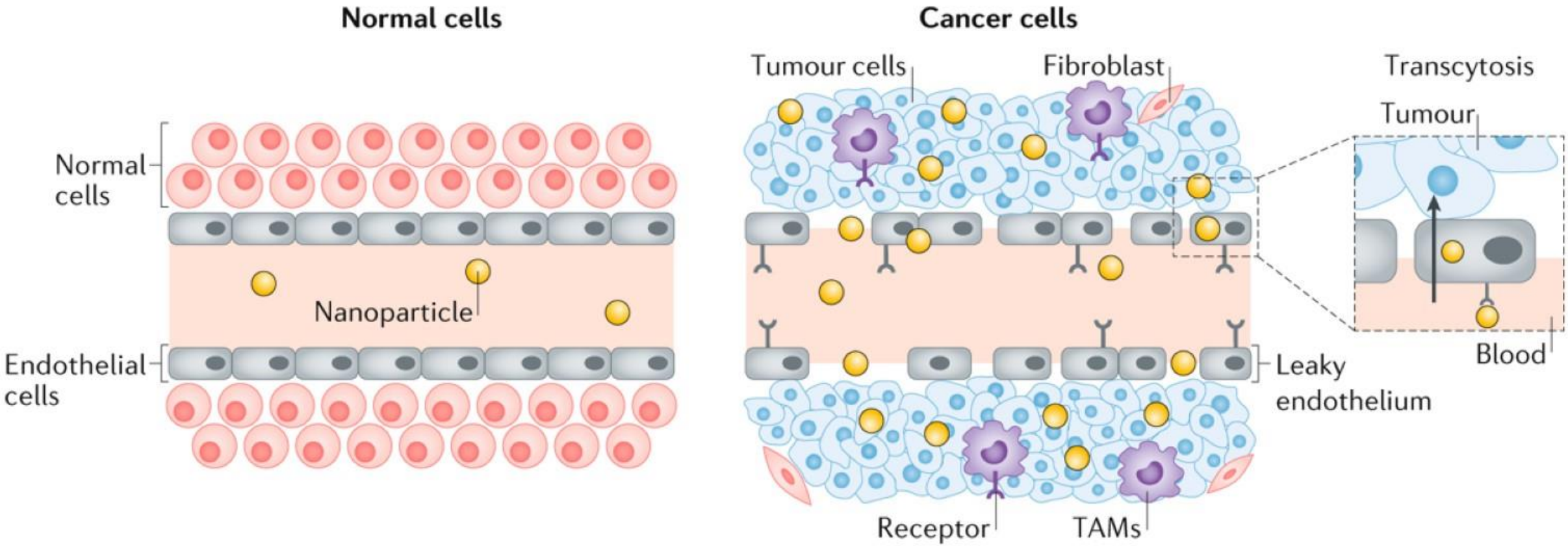
- Biocompatibility
- Blood circulation time
- Bioconjugation
- Drug loading
- Sustained release
- Intricate architecture

Cell surface markers, EPR effect and localised release

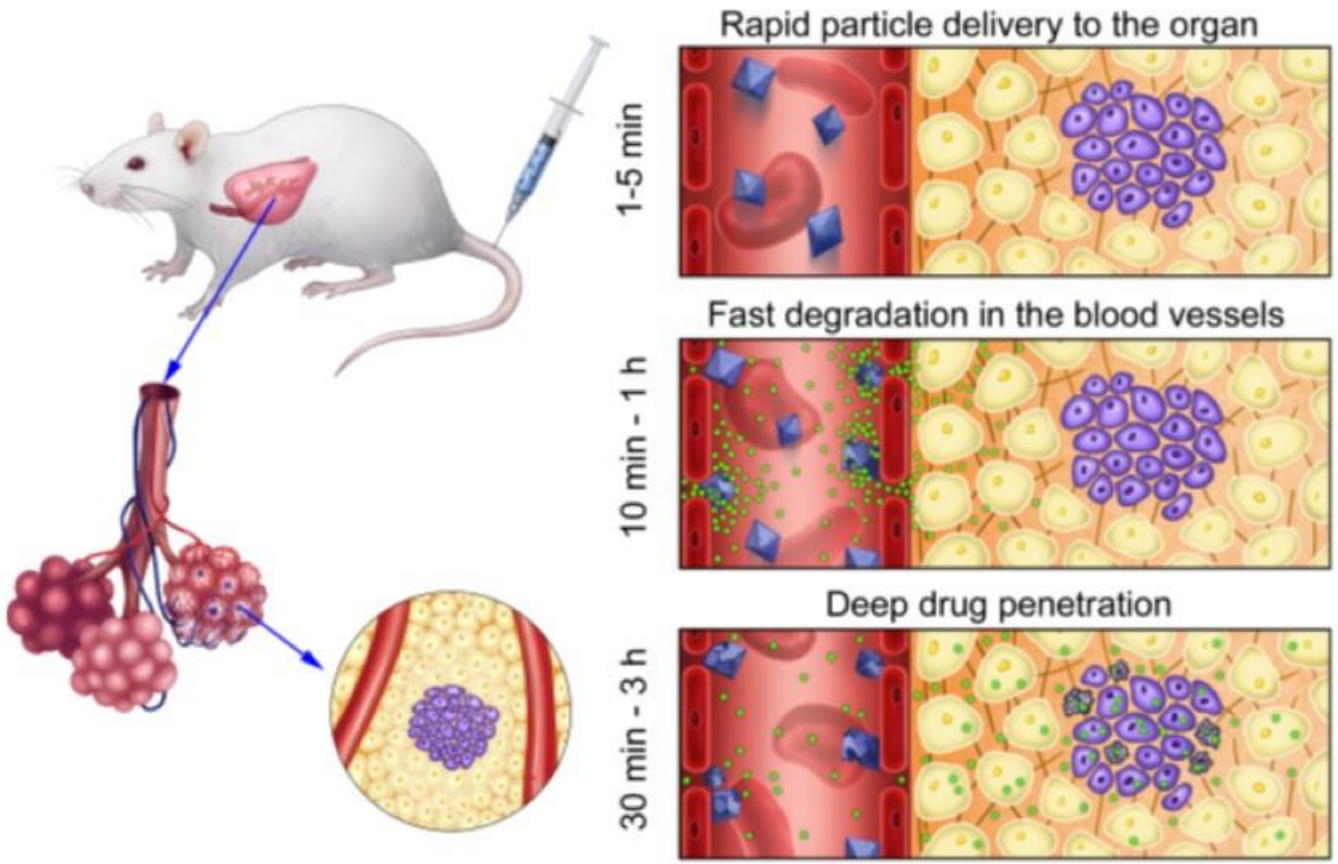


Park K. Polysaccharide-based near-infrared fluorescence nanoprobes for cancer diagnosis. Quant Imaging Med Surg 2012;2(2):106-113.
DOI: 10.3978/j.issn.2223-4292.2012.05.01

Not so enhanced EPR effect



Manzari, M.T., Shamay, Y., Kiguchi, H. *et al.* Targeted drug delivery strategies for precision medicines. *Nat Rev Mater* **6**, 351–370 (2021). https://doi.org/10.1038/s41578-020-00269-6



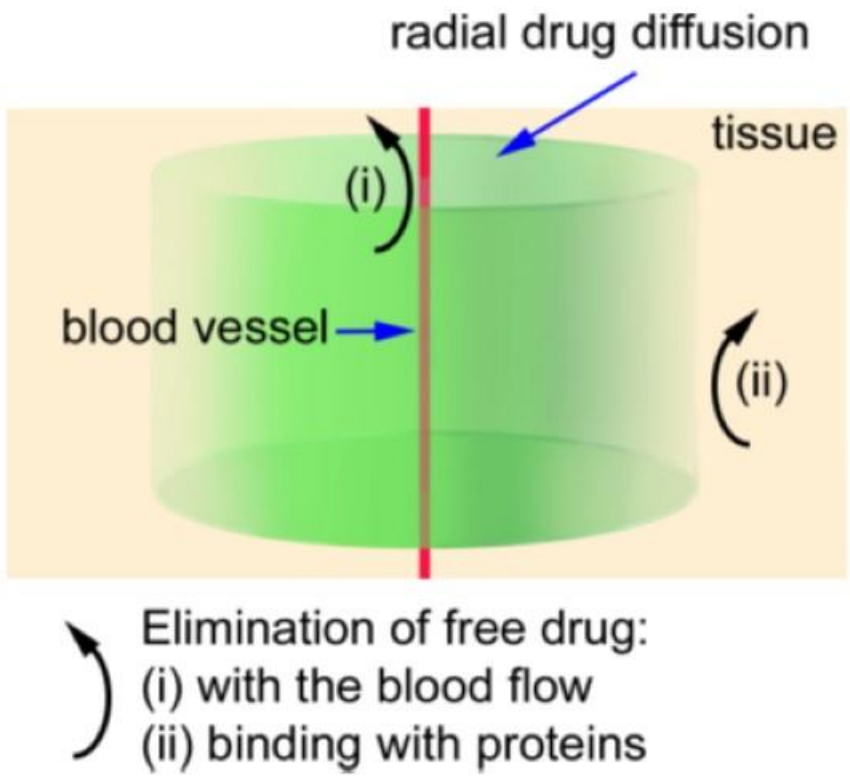
Flash release (FLARE)

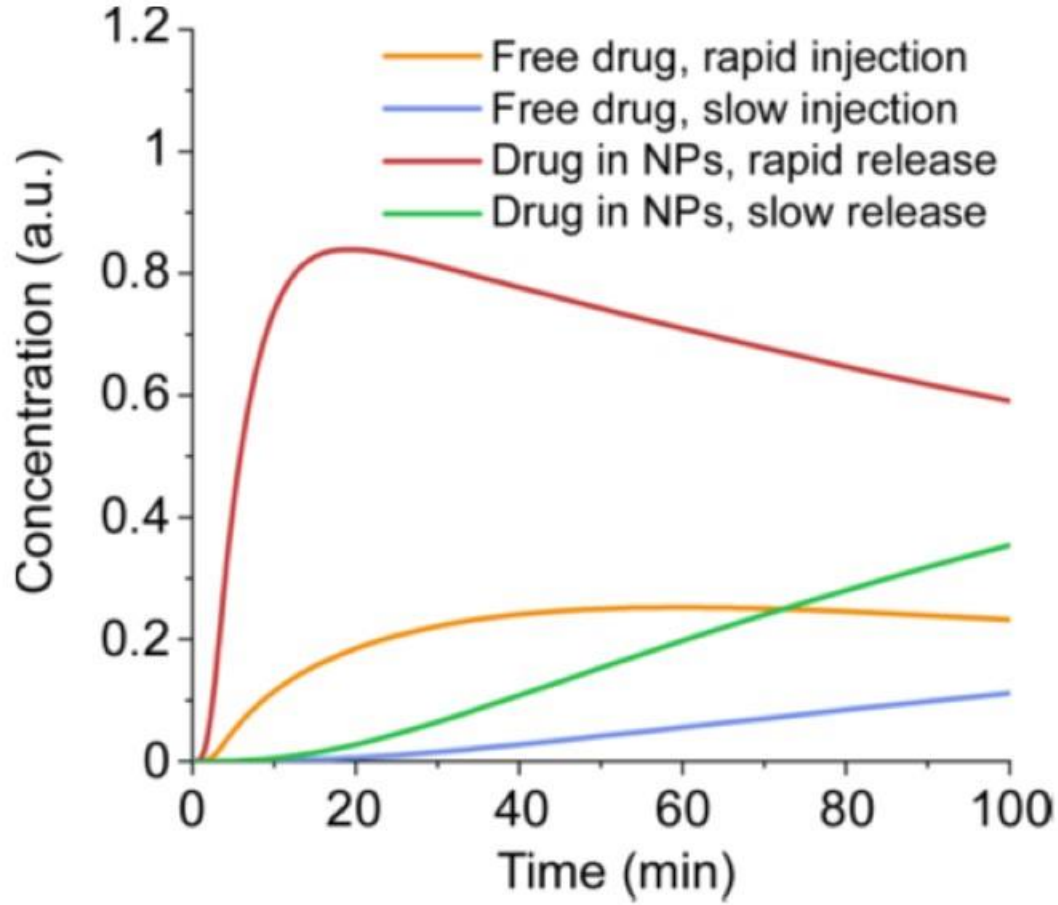
Higher chances for acute toxicity

Waste of drug due to the fast blood clearance

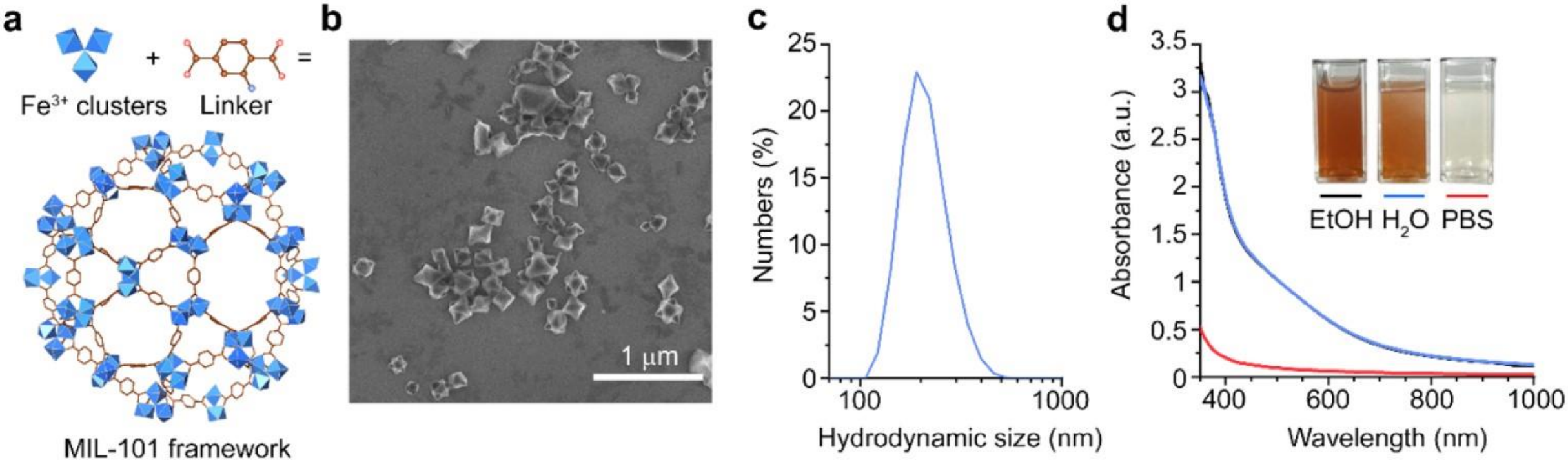
BUT

Better delivery and higher efficacy?


radial drug diffusion
tissue
(i)
blood vessel
(ii)
Elimination of free drug:
(i) with the blood flow
(ii) binding with proteins


Free drug, rapid injection
Free drug, slow injection
Drug in NPs, rapid release
Drug in NPs, slow release
Concentration (a.u.)
Time (min)
0
0.2
0.4
0.6
0.8
1
1.2
0
20
40
60
80
100

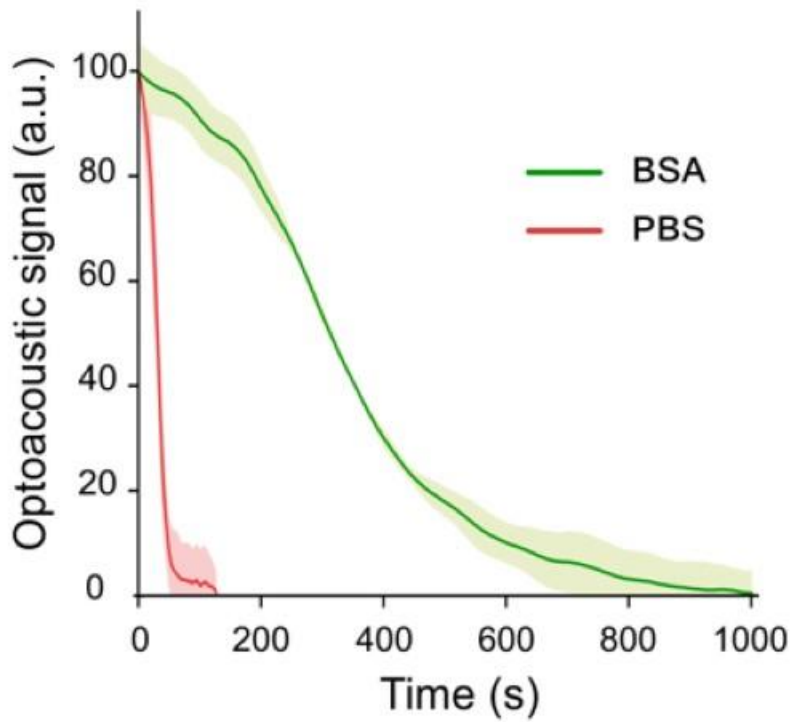
MIL-101 (Fe) as a prospective carrier

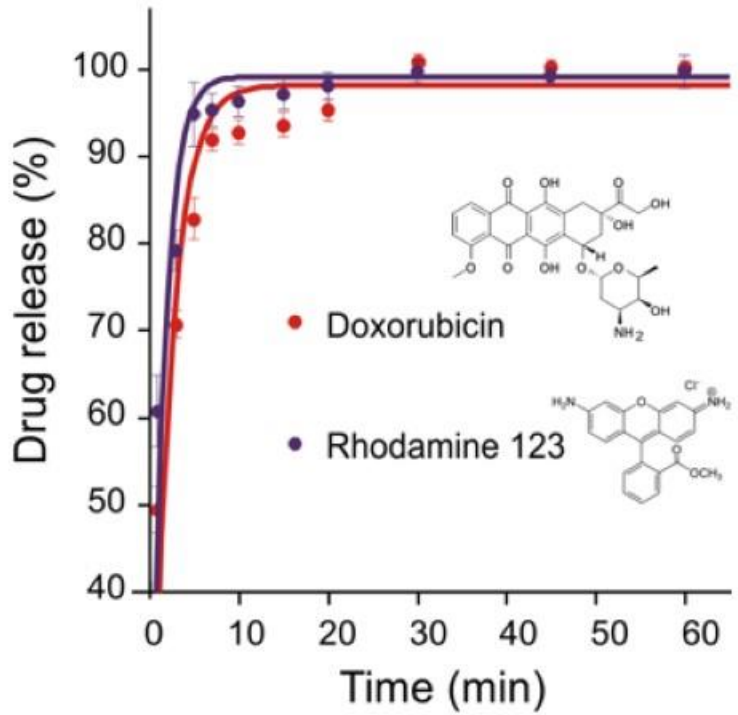


BET surface area >1000 m^2/g

Degradation time in phosphate-rich media 44 ± 7 s

Particle degradation kinetics matches flash drug release

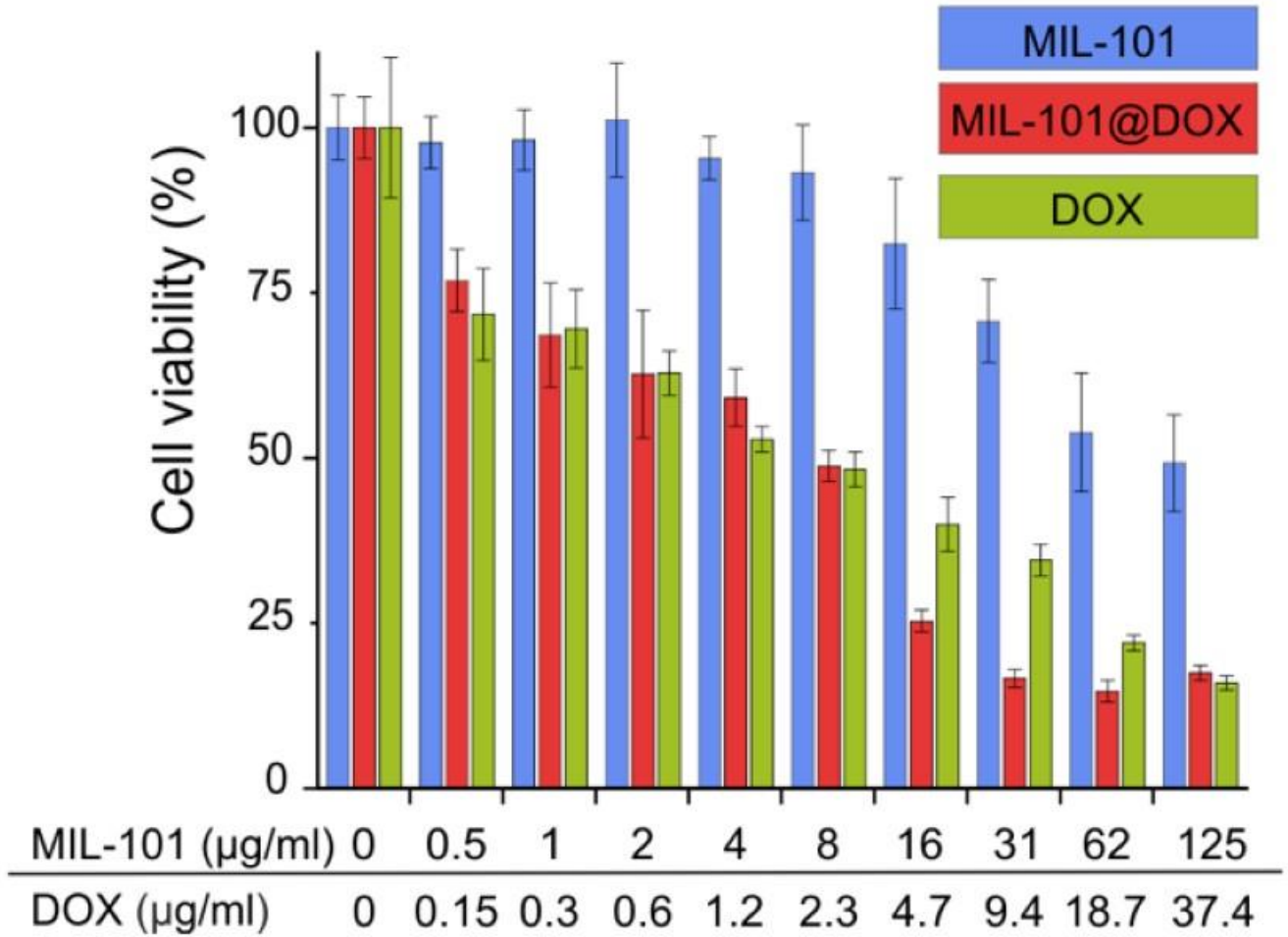




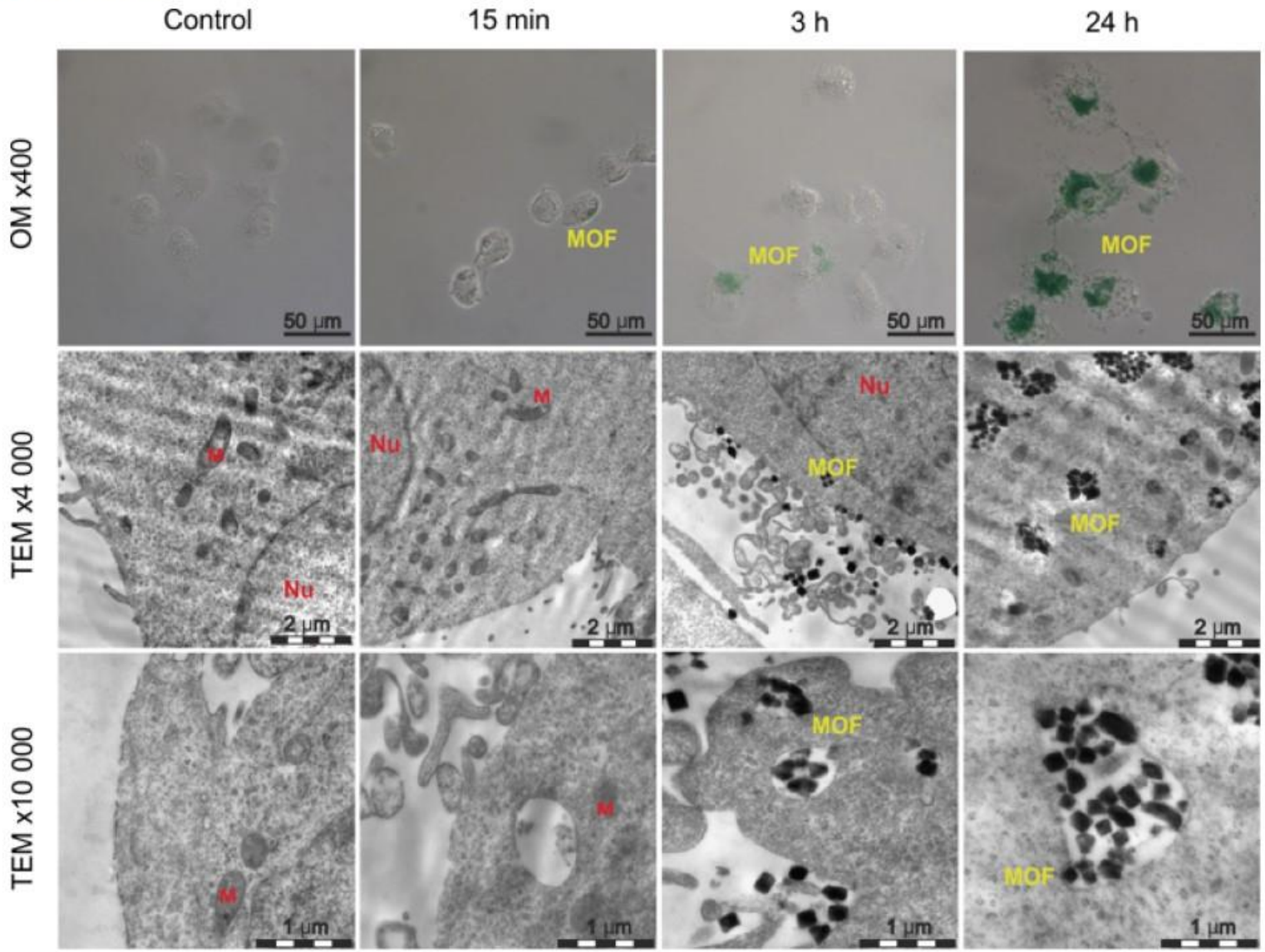
BET surface area >1000 m^2/g

Degradation time in phosphate and protein rich media ~ 15 min

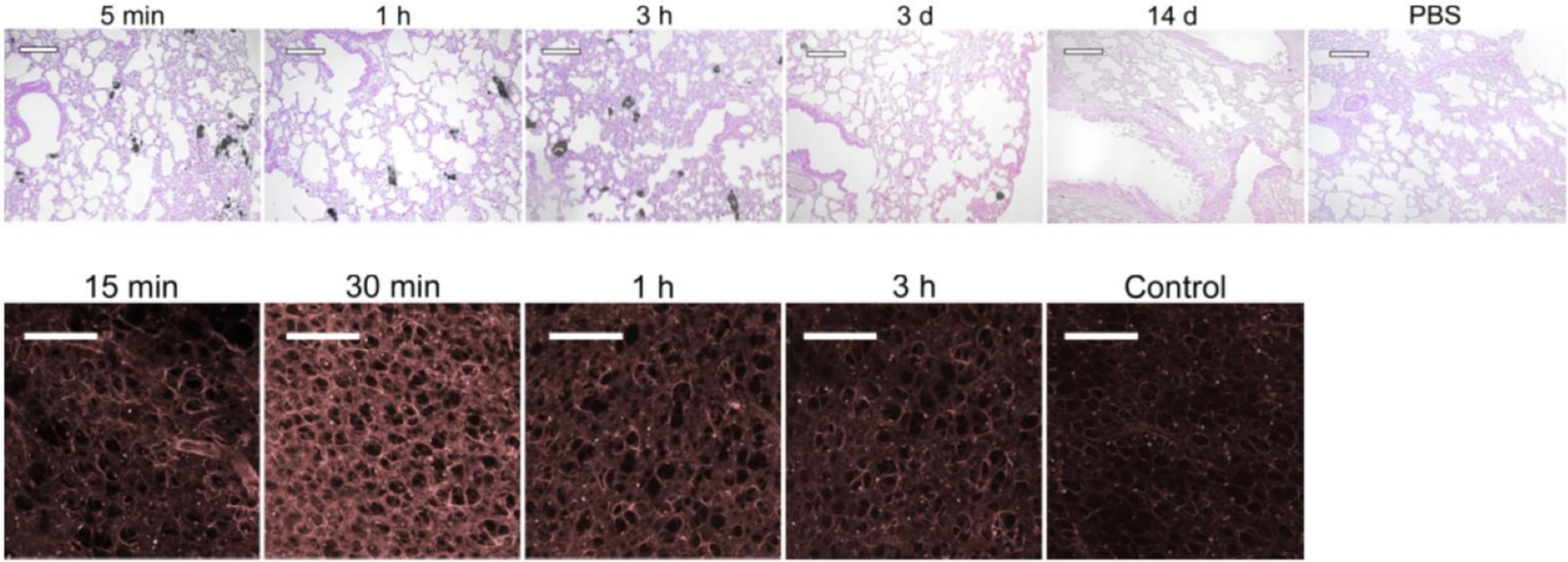
MIL-101 (Fe) doesn't add up to the formulation toxicity



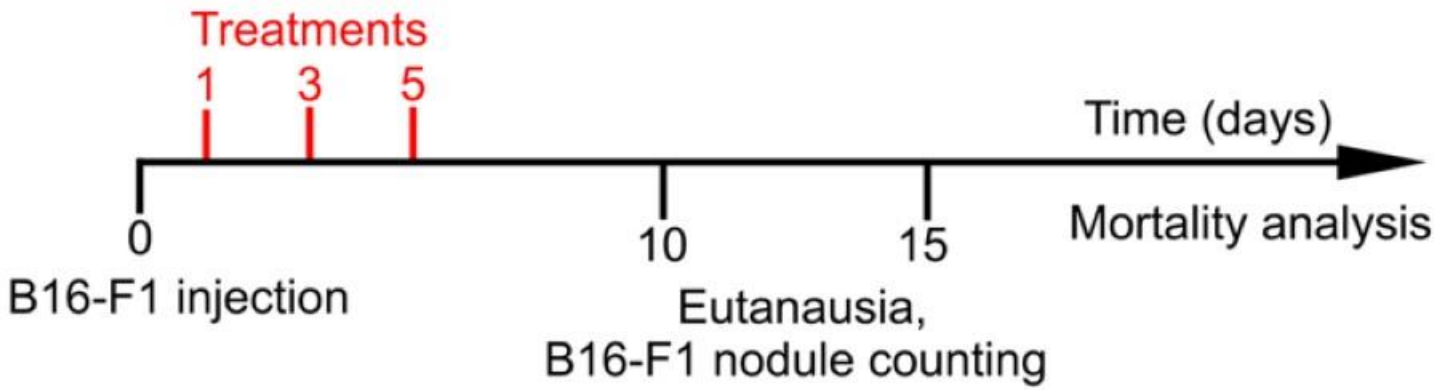
The drug release occurs prior to the particle uptake

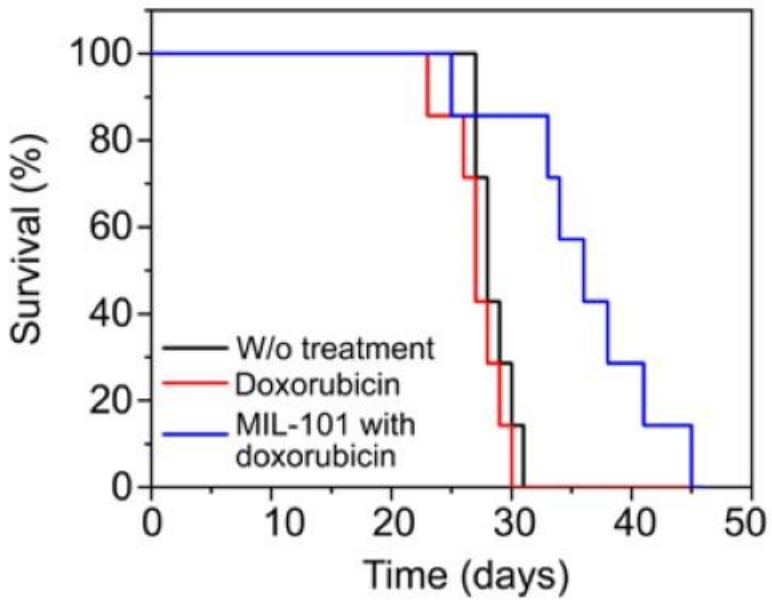


MIL-101 (Fe) MOFs accumulate in lungs and liver

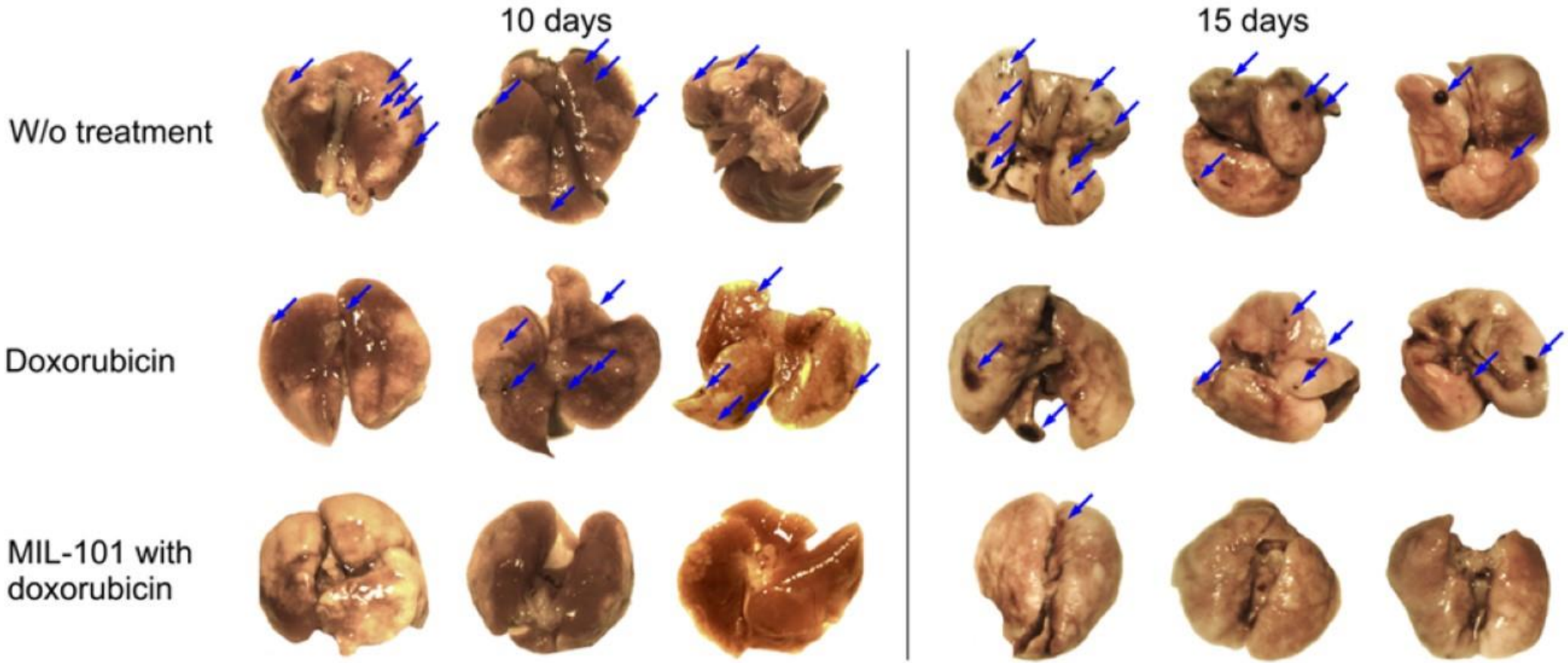


Doxorubicin-loaded MIL-101 NPs are more beneficial therapeutic option for the treatment of lung metastasis melanoma model





Doxorubicin-loaded MIL-101 NPs decrease size and number of metastatic nodules



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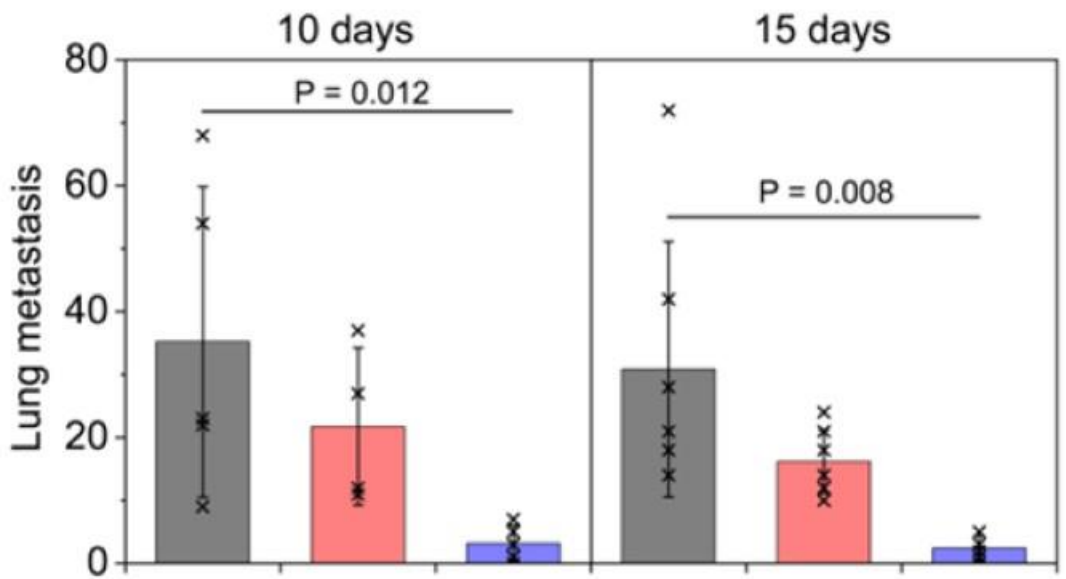
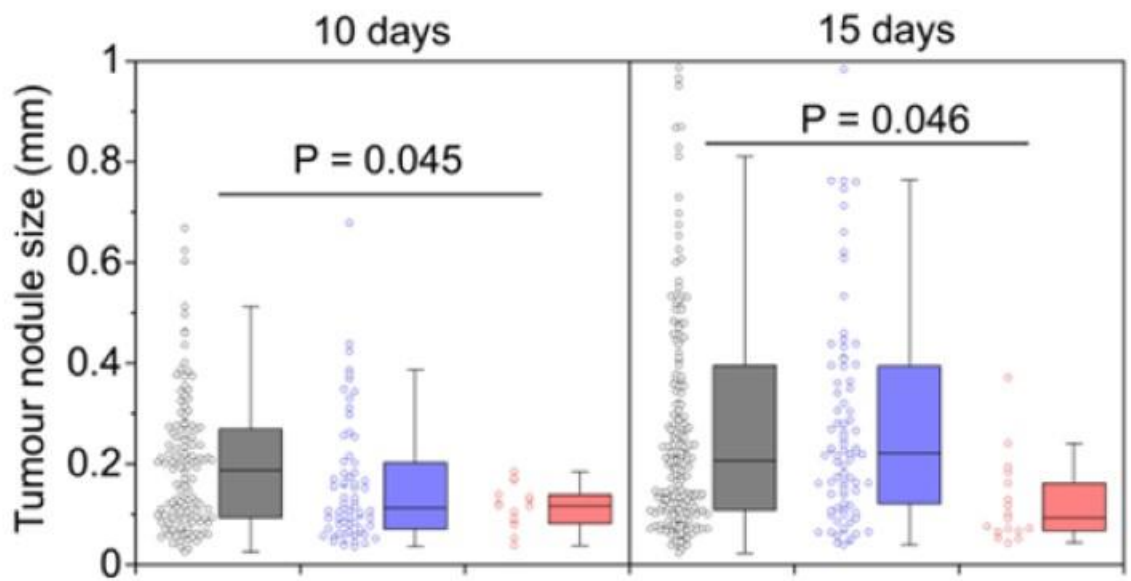




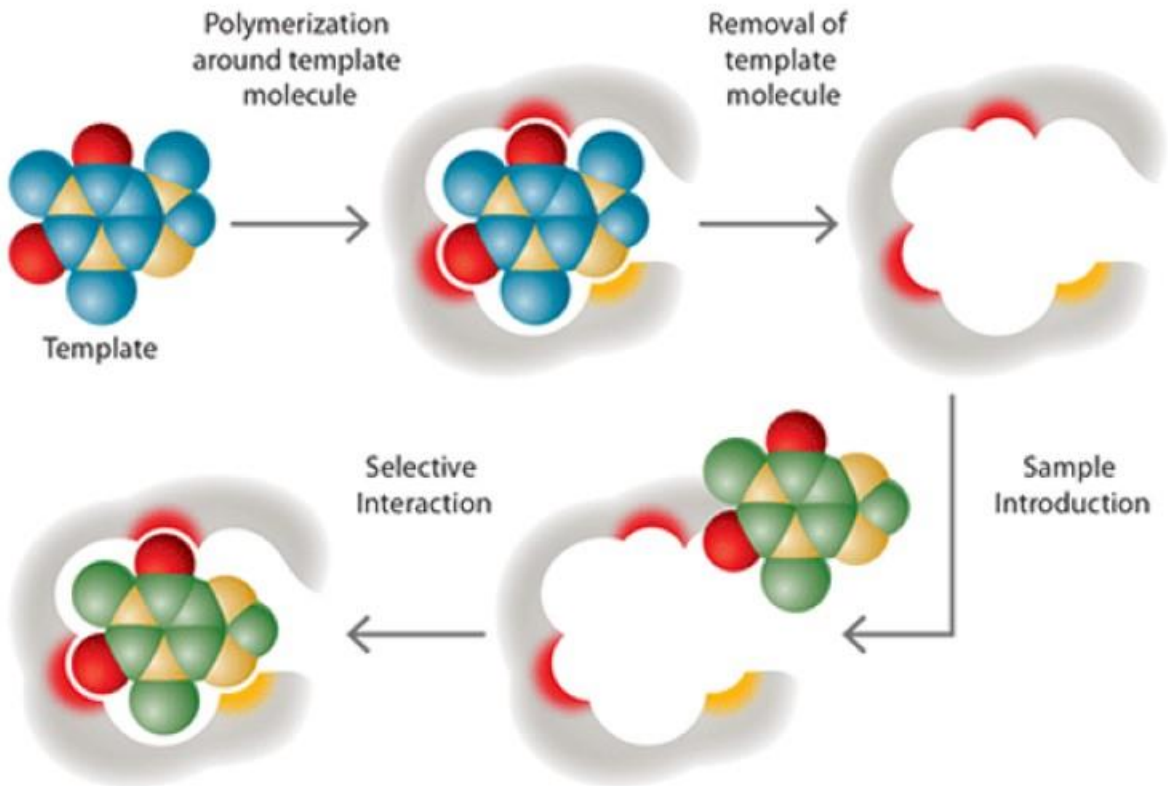
W/o treatment Doxorubicin MIL-101 with doxorubicin

12.7-fold decrease in nodule number

Prevention of nodule growth

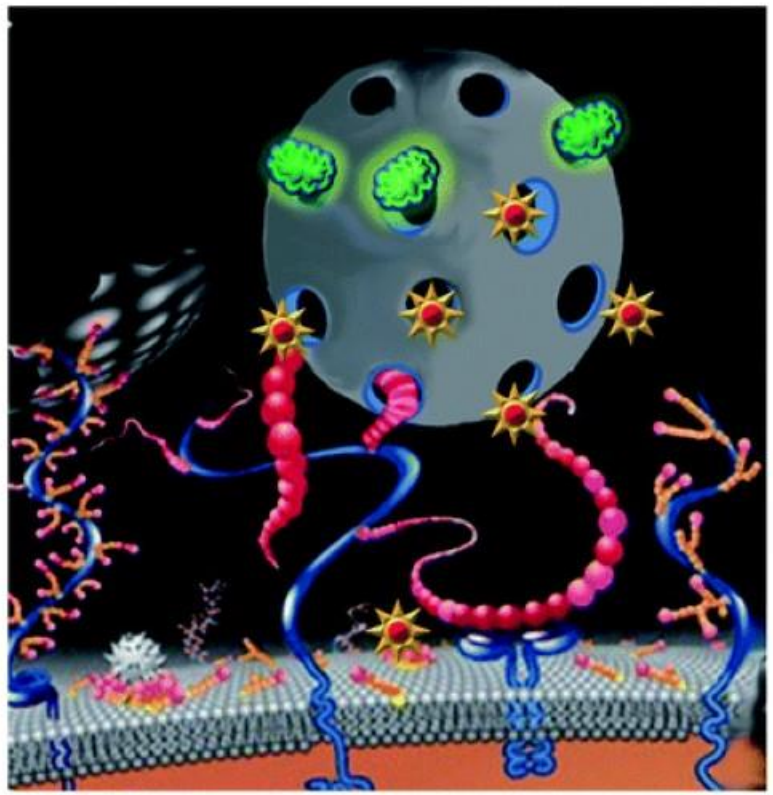
- FlaRE delivery strategy relies on the minutes-scale degradation of drug-loaded nanocarriers in the tumour-surrounding blood vessels.
- Therapeutic potential of the FlaRE delivery is demonstrated by the treatment of melanoma pulmonary metastases in mice using doxorubicin loaded MIL-101 NPs.
- Strategy expands the repertoire of potential drug carriers by redefining their advantageous properties to prioritise rapid drug release kinetics.

Molecularly imprinted polymers (MIPs)



E. Barrey, Aminoglycoside analysis in honey using MIP cleanup and LC/MS/MS detection, Sigma Aldrich application note, Reporter 33.1.

MIPs – the swiss-knife particles



- fluorescent label

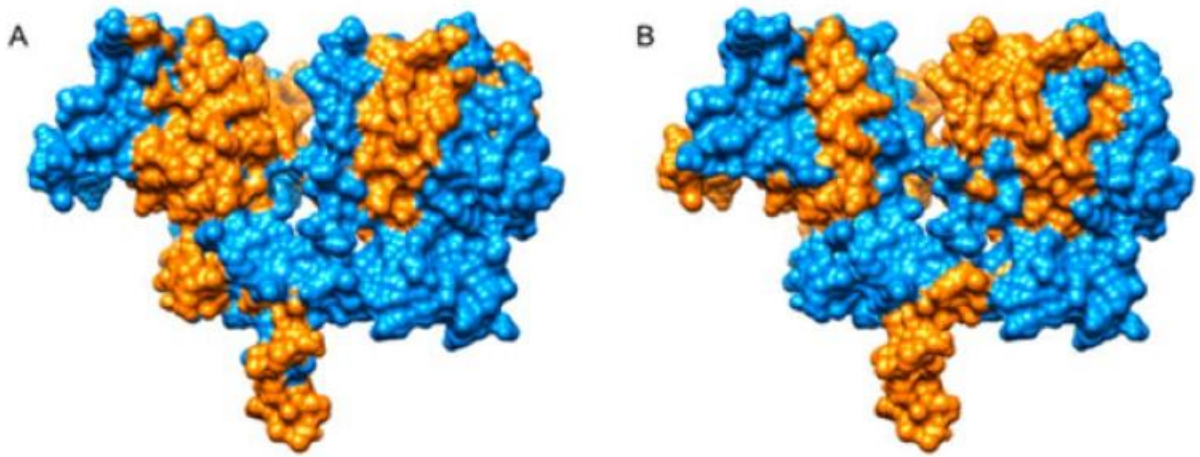
-drug molecule payload

- Drug release
- Cell targeting
- Epitope tagging

in one particle

Shevchenko et al., Nano-molecularly imprinted polymers (nanoMIPs) as a novel approach to targeted drug delivery in nanomedicine, RSC Adv., 2022,12, 3957-3968

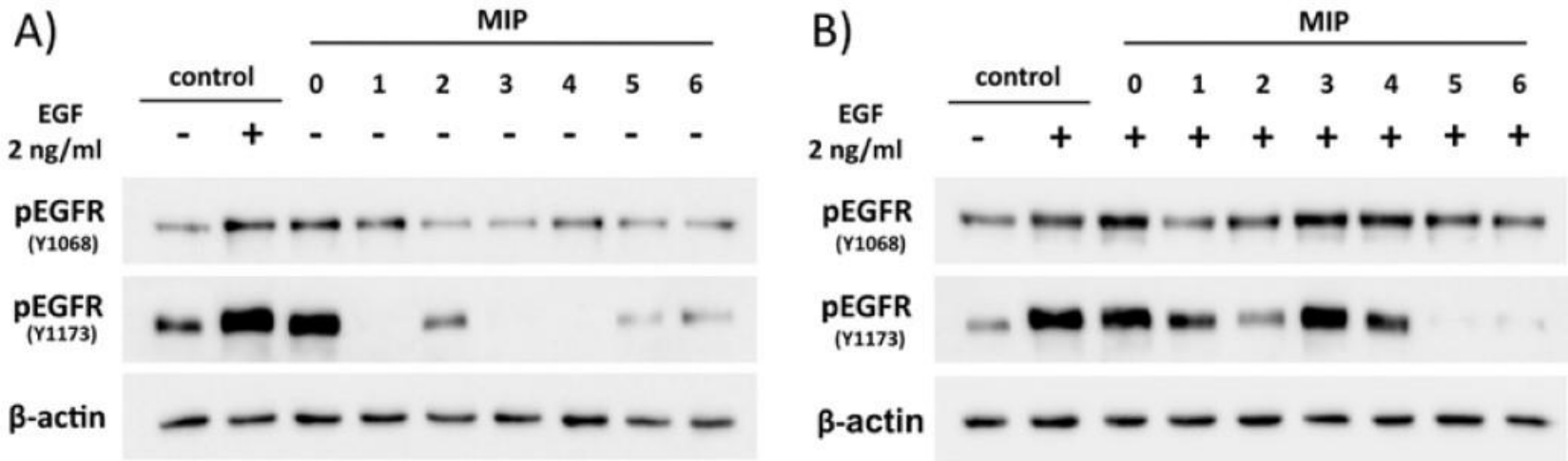
EGFR-binding nanoMIPs

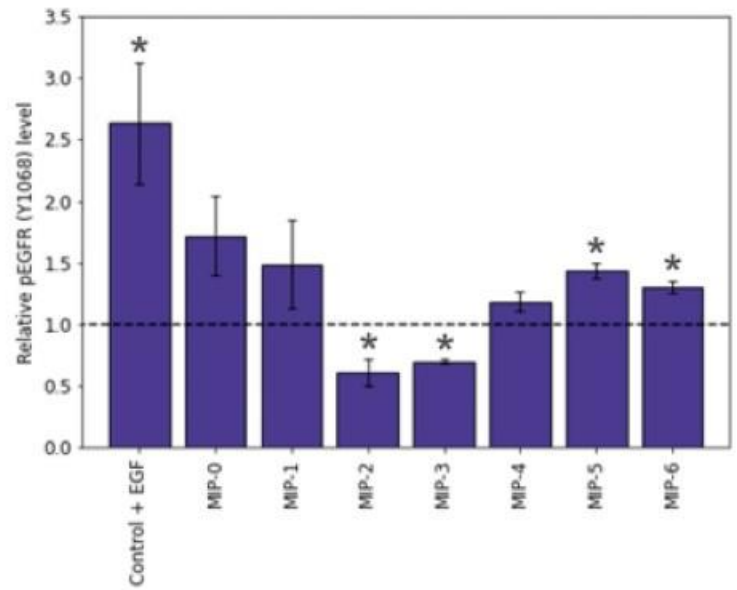


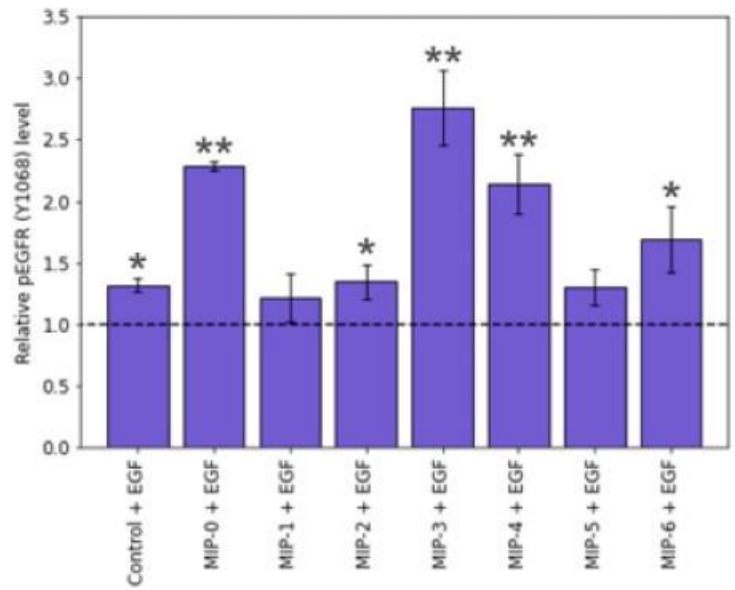
MIP-0	(CG)TKGKLQSGF	N/A (scrambled sequence)
MIP-1	(CG)KLFGTSGQK	extracellular
MIP-2	(CG)GMNYLEDR	intracellular (kinase domain edge)
MIP-3	(CG)GVLGSGAFGTVYK	intracellular (kinase domain centre)
MIP-4	(CG)NLQEILHGAVR	extracellular
MIP-5	(CG)MHLPSPTDSNFYR	intracellular
MIP-6	(CG)LTQLGTFEDHFLSLQR	extracellular (EGF binding domain)

Piletsky et al., Modulation of EGFR Activity by Molecularly Imprinted Polymer Nanoparticles Targeting Intracellular Epitopes, Nano Lett. 2023, 23, 21, 9677–9682

nanoMIPs modulate EGFR phosphorylation in MDA-MB-468 cells







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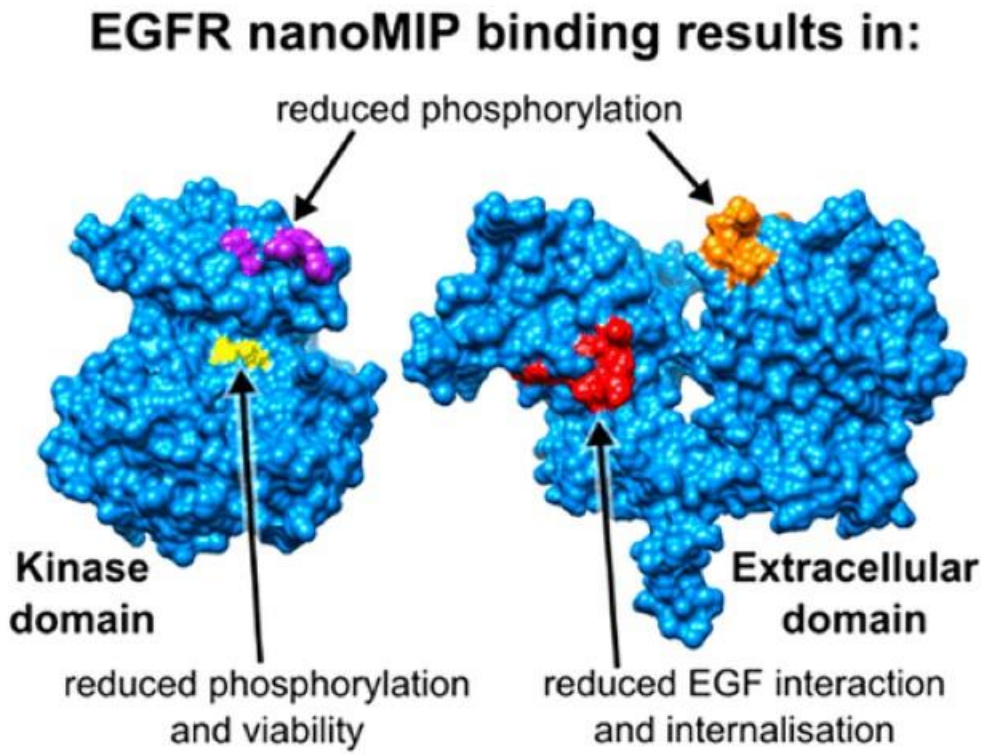

- nanoMIPs selectively modify EGFR phosphorylation
- nanoMIPs modulate interaction EGFR with its specific ligand
- nanoMIPs is a promising platform for targeted co-delivery of small molecules

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Picasso