Biomodulating Porous Nanomaterials for Oral Drug Delivery


Source: Sailor Lab-UCSD

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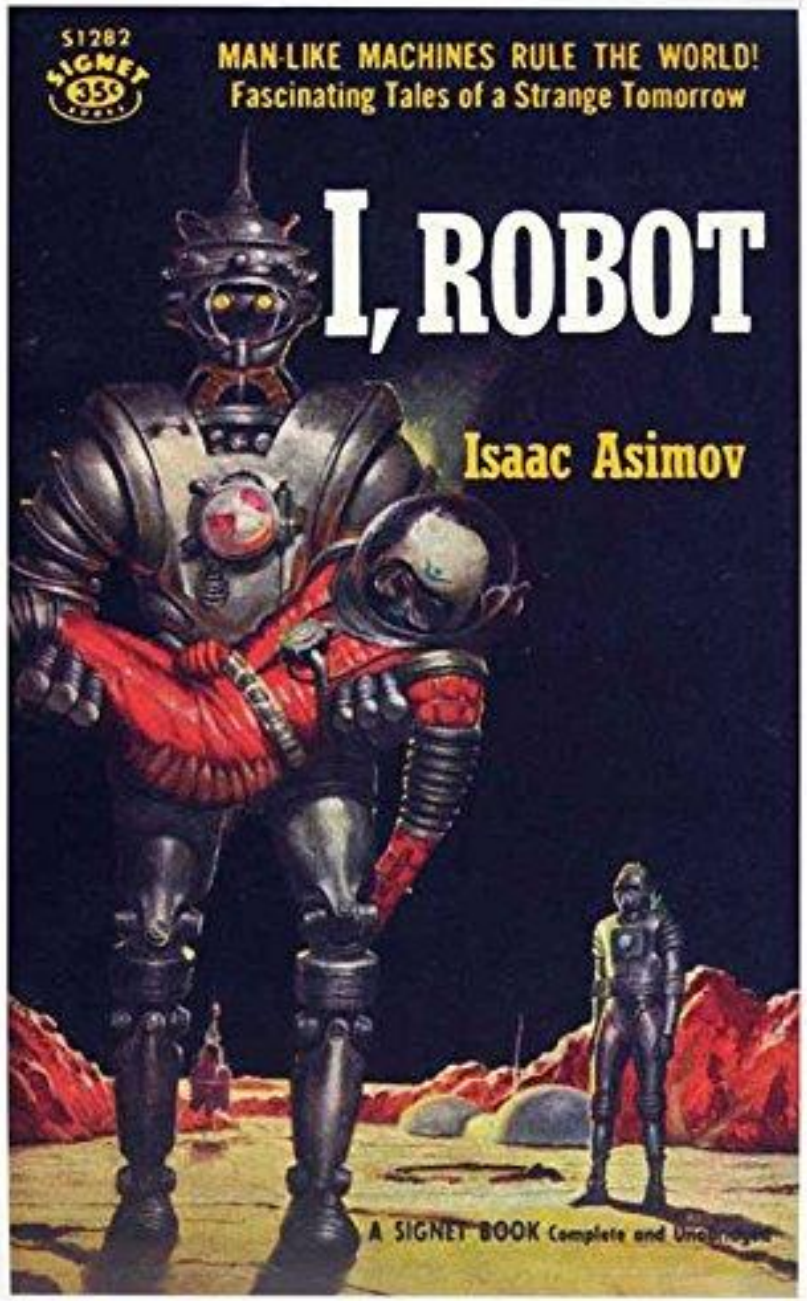
School of Materials Science and Engineering

Australian Centre for NanoMedicine

University of New South Wales-Sydney, Australia

3 Laws of Robotics



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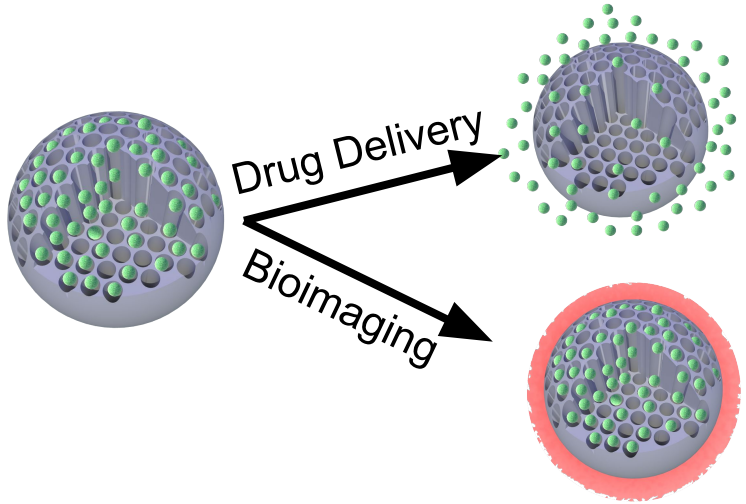
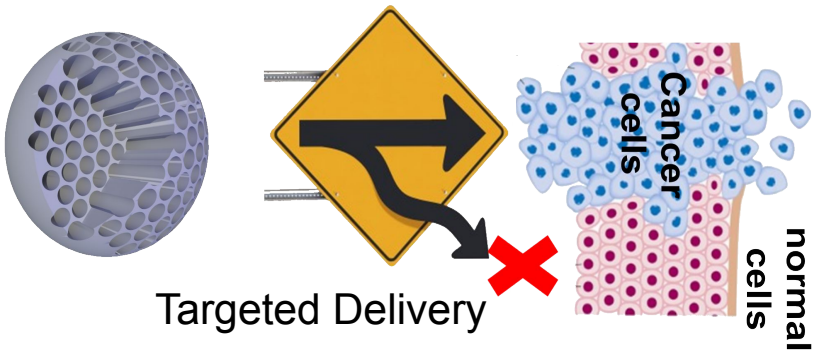
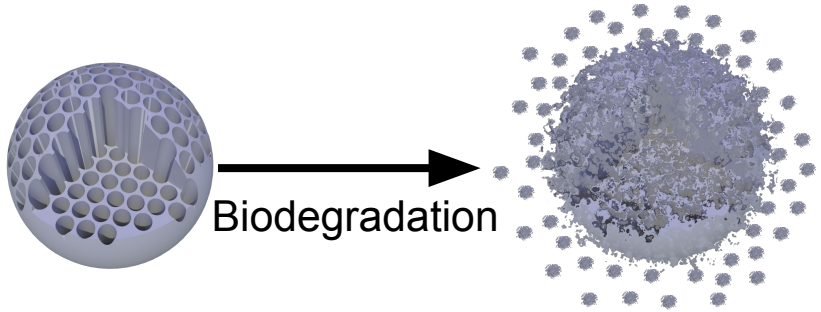
3 Laws of Nanomedicine



Nanomedicine, must achieve its intended function; i.e. diagnosis or therapeutic delivery or both.



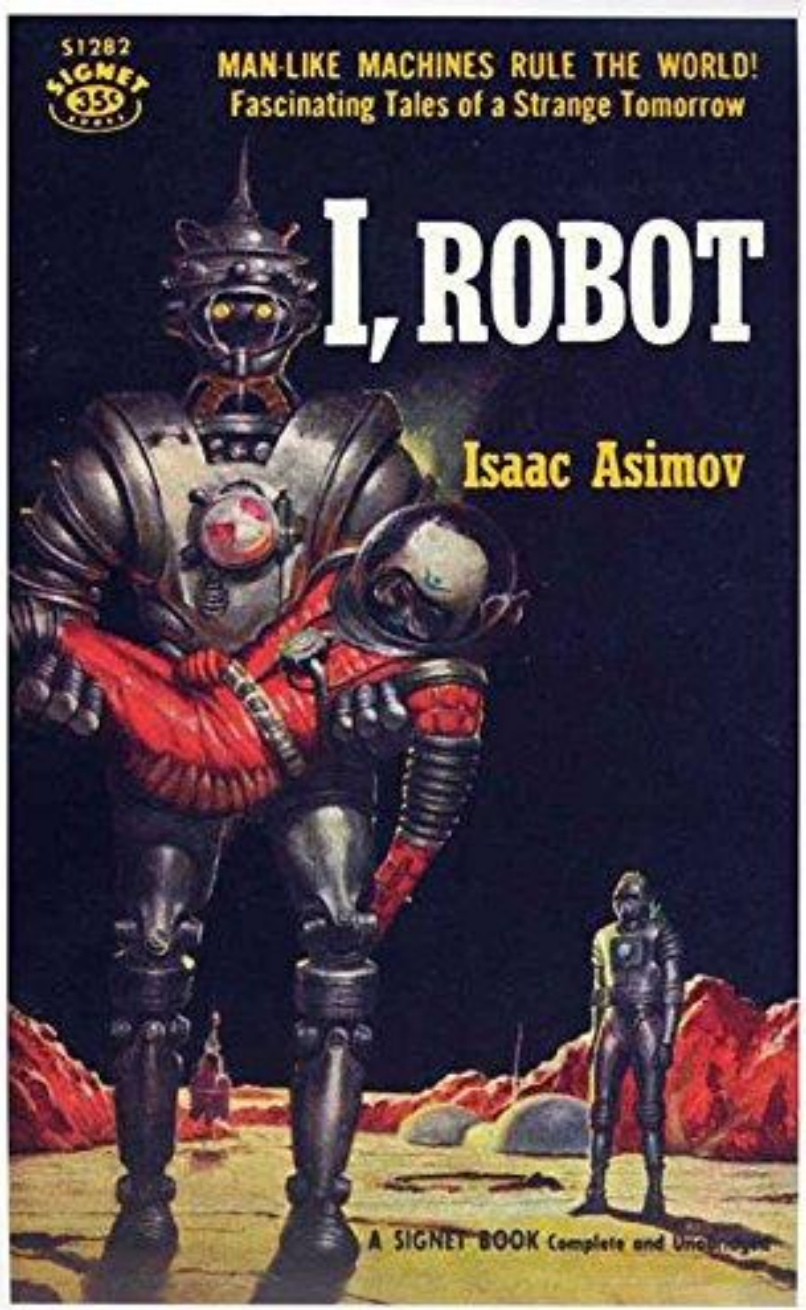
Nanomedicine, must only target the diseased/desired organ and not show any off-target effects.



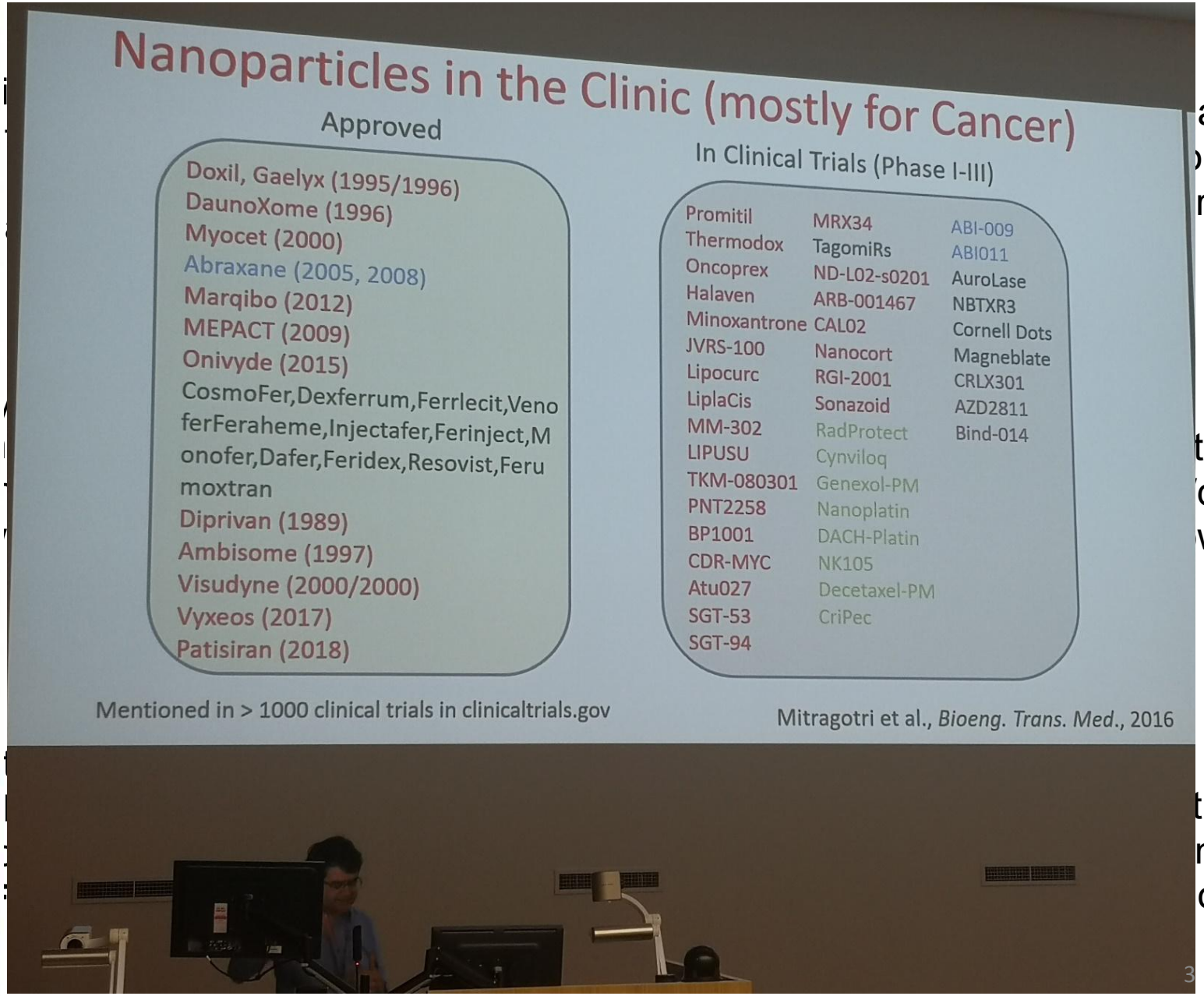
Nanomedicine, must clear out after performing its intended function as non-toxic entities.

Inspiration: Prof. M. J. Sailor, UCSD

3 Laws of Robotics



3 Laws of Nanomedicine



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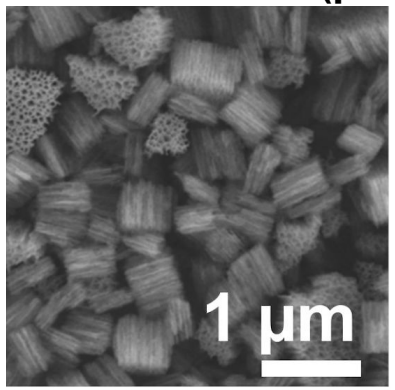
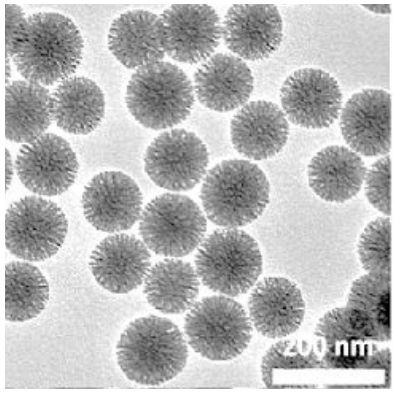
Porous Silicon (pSi)



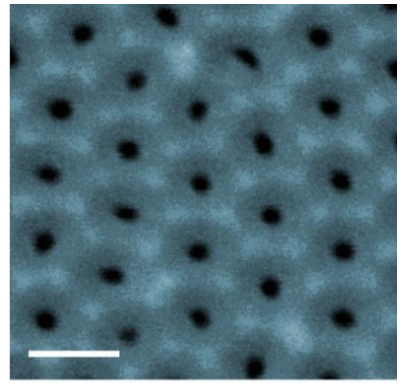
Kokil et al **2023**
Raza et al Mater Today Adv **2022**
Kumeria et al Sensors **2018 & 2022**
Marini et al Adv Funct Mater **2020**
Wang et al ACS APMI **2018**

Mesoporous Silica (MSN)



Cao et al Biomater Sci **2023**
Raza et al Acta Biomater **2022**
Altalhi et al Anal Chimica Acta **2021**
Raza et al ACS Biomater Sci Eng **2021**

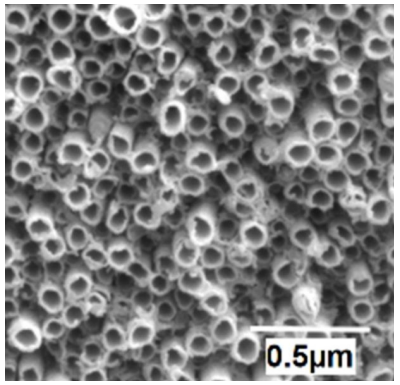
Nanoporous Alumina (NAA)



Law et al Sens Actuate B **2022**
Kaur et al Anal Chem **2019**
Eckstein et al JMC C **2019**
Bindra et al Nanotechnology **2018**

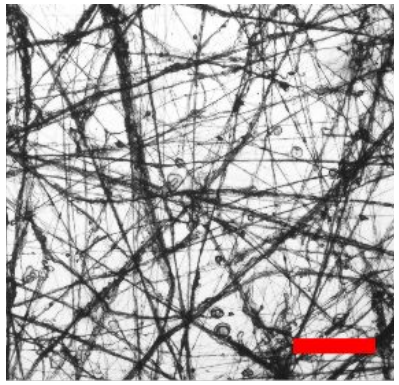
Porous Nanomaterials in Kumeria Lab

Titania Nanotubes (TiNTs)



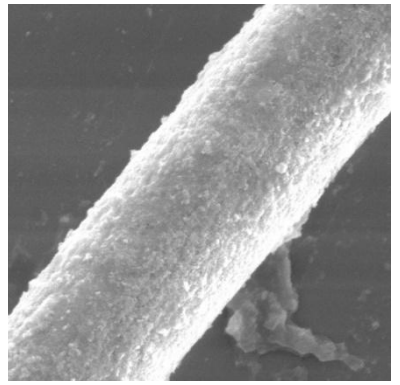
Ali et al **2023 (under Revision)**
Kumeria et al JMC B **2015**

Composite Nanofibers



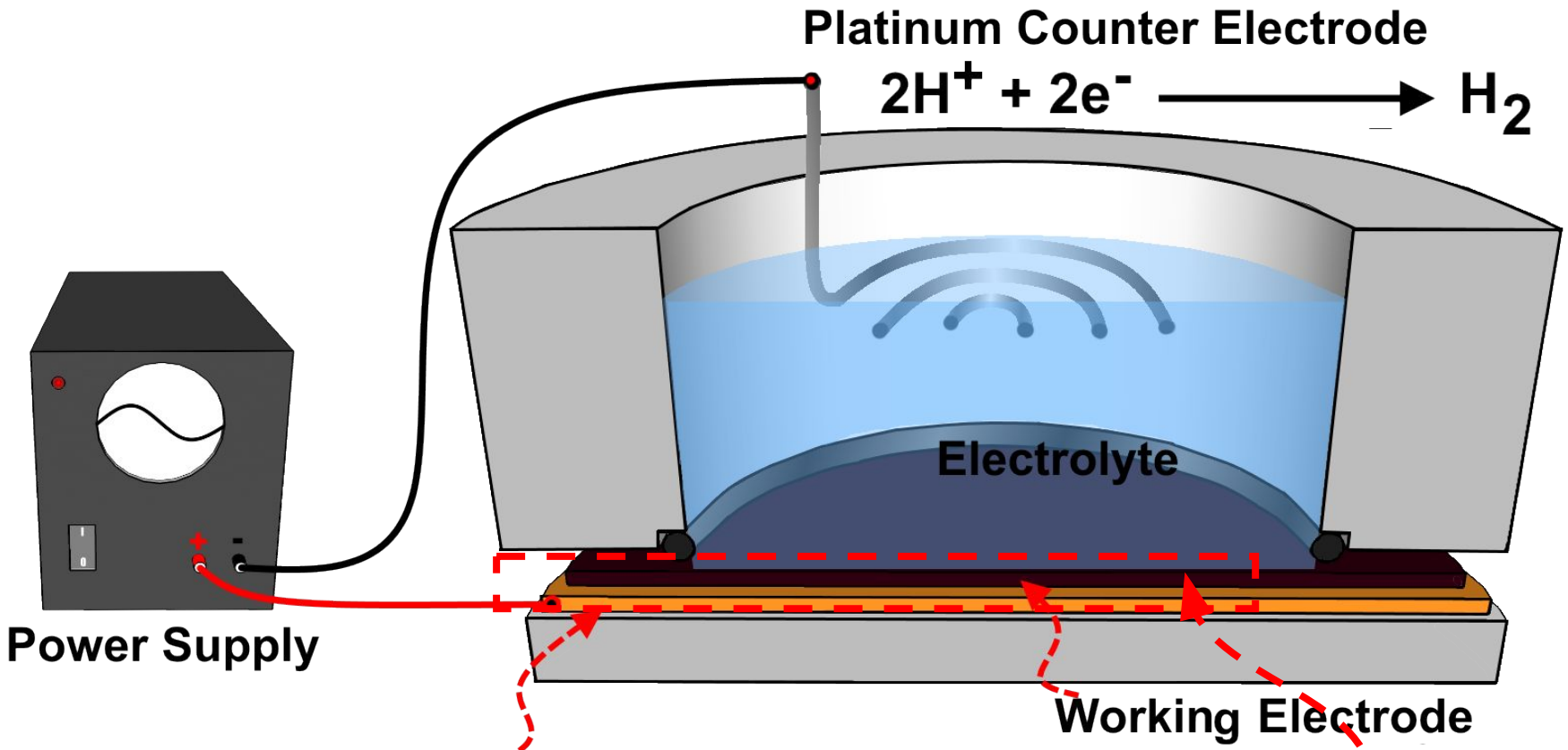
McKeena et al Biofab **2023**
Bakshi et al Adv Funct Mater **2022**
Zuidema et al Adv Mater **2018**

Porous Silicon Microrods (pSi-MR)



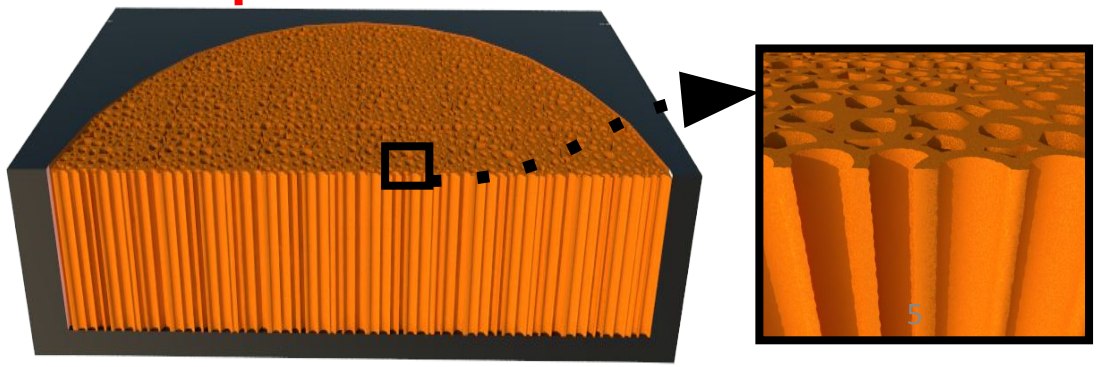
Coming Soon…

Fabrication: Electrochemical Anodization

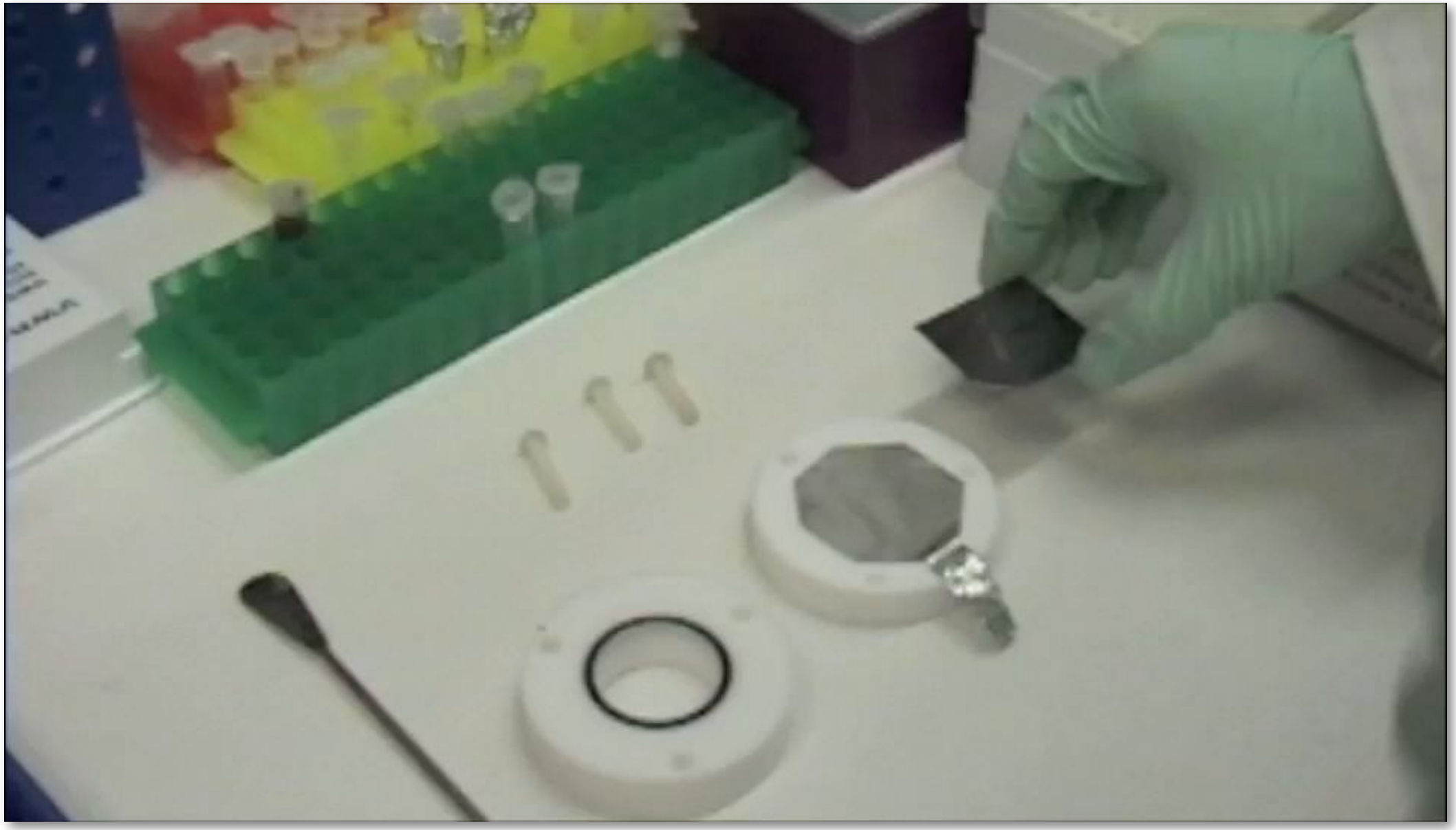


$2Al + 3H_2O \rightarrow Al_2O_3 + 6H^+ + 6e^-$

$Si + 2h^+ + 6HF \rightarrow SiF_6^{2-} + H_2 + 4H^+$



Fabrication: Porous Silicon



Source: Sailor Lab-UCSD

Porous Silicon

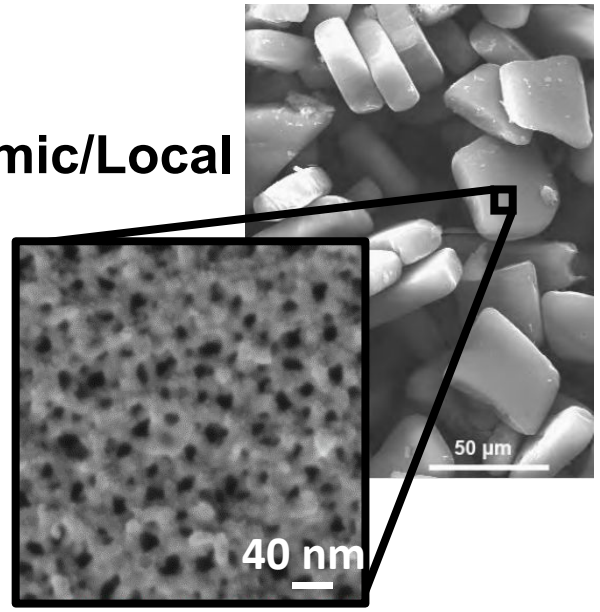
Drug Delivery

- **Oral Delivery/Systemic/Local Delivery**
- Protein
- Small Molecules
- Genes

Tissue Engineering

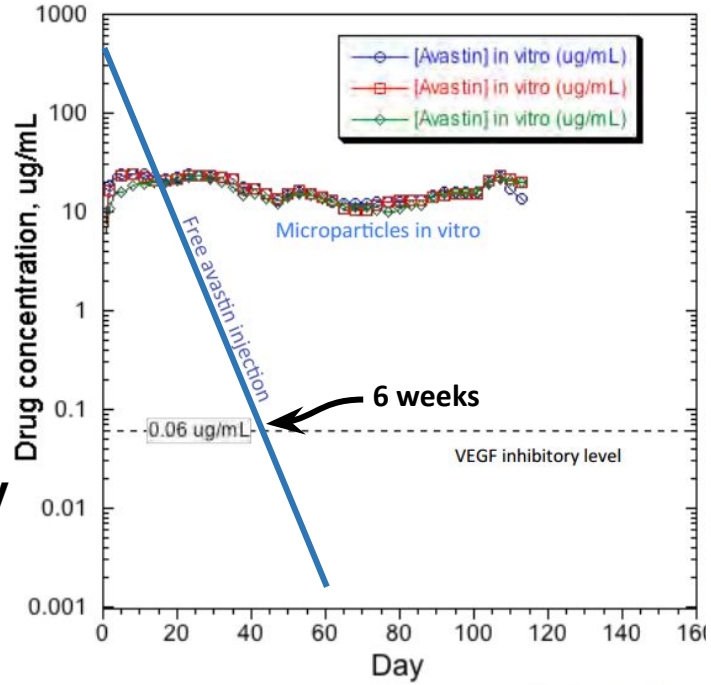
Bioimaging

Sensing

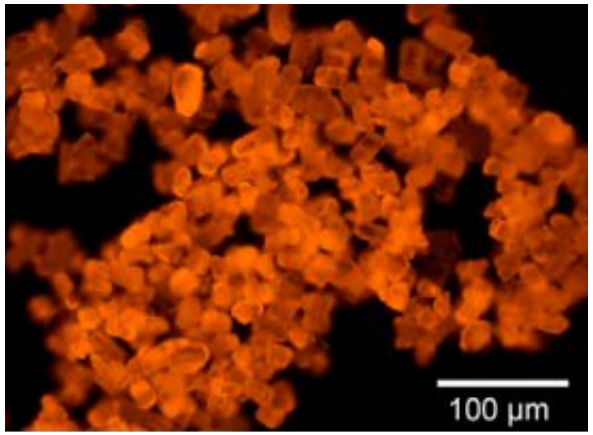


- Cytocompatibility
- High loading capacity
- Tunable release profiles
- Biodegradability

- **Tunable pore structure**
- **Tunable surface chemistry**

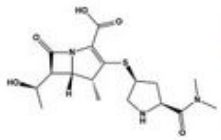


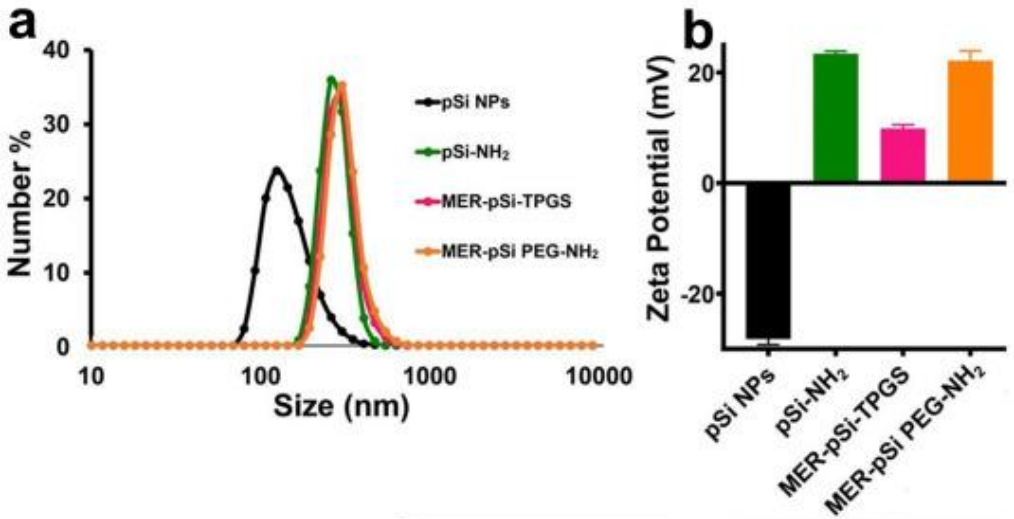
- **Tunable photoluminescence**

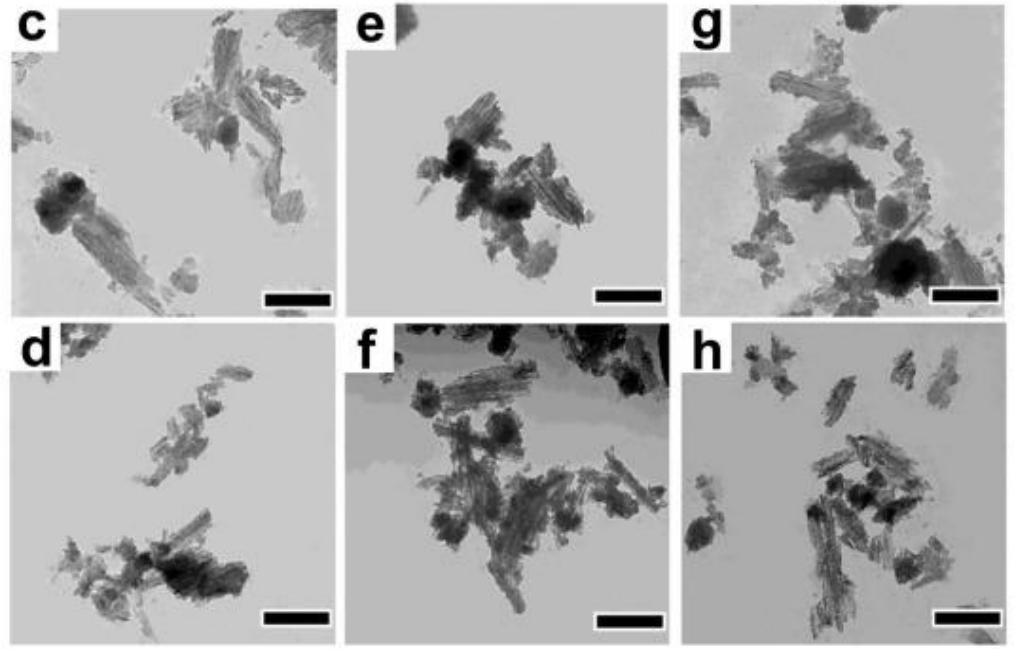


Kumeria, Expert Opinion in Drug Delivery, 2017
Spinnaker BioSciences

1. Orl Meropenem Delivery Using pSi-PEG

Name	Structure	Molecular formula	Production	Half-life (hour)	water solubility
Meropenem		C_{17}-H_{25}-N_3-O_5-S-H_2-O	Synthetic	1.0	5.63 mg/mL





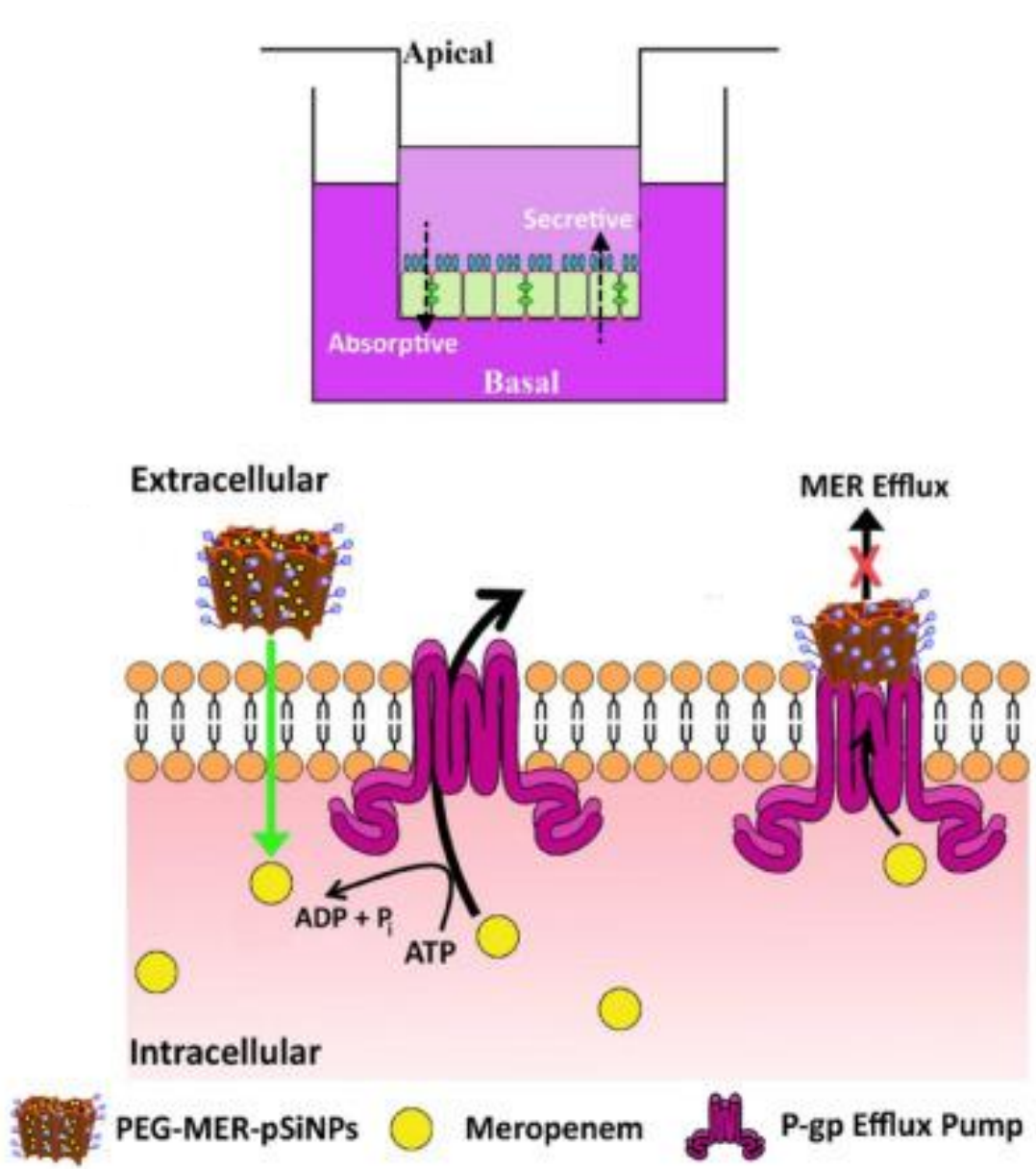
Intestinal Efflux

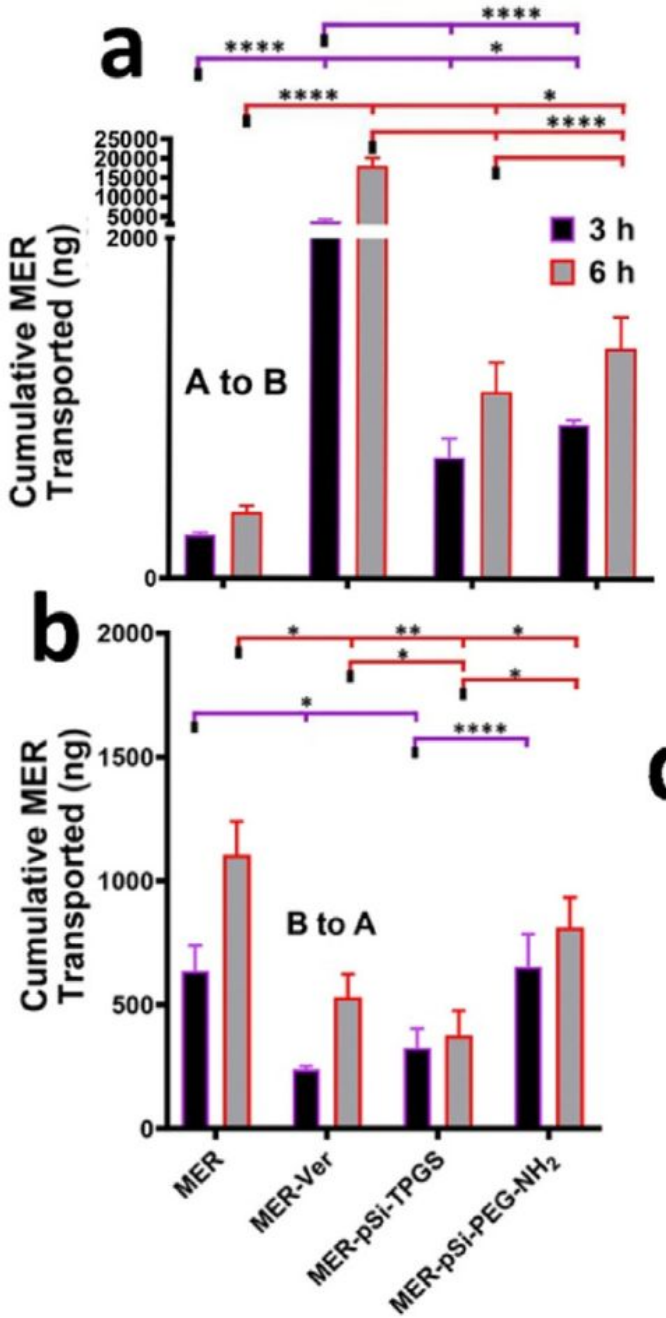
Degradation

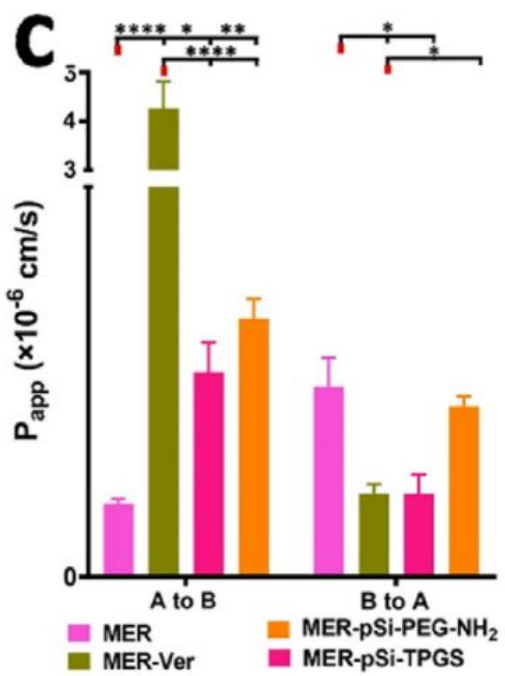
Controlled release

Raza…Kumeria, Materials Today Advances, 2022

pSi-PEG for Efflux Regulation





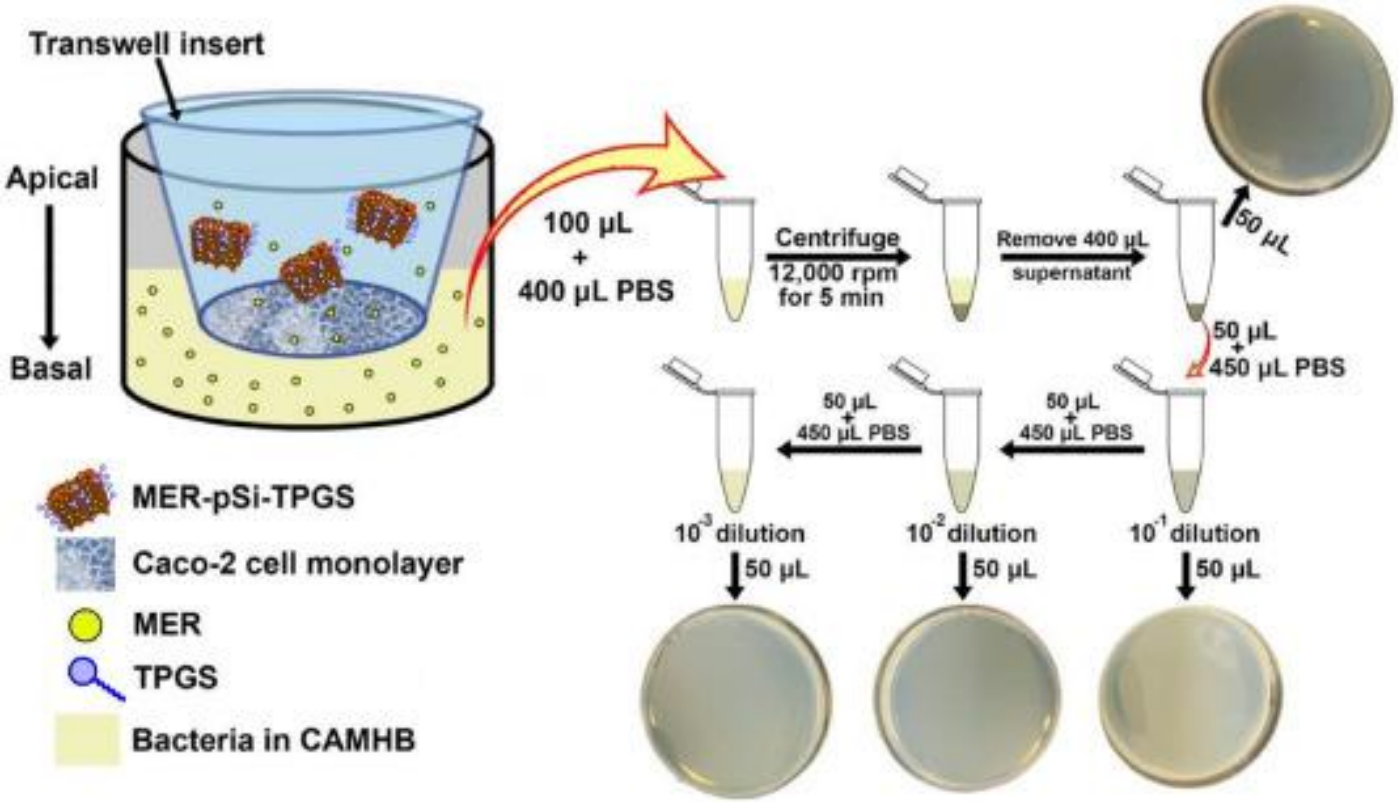


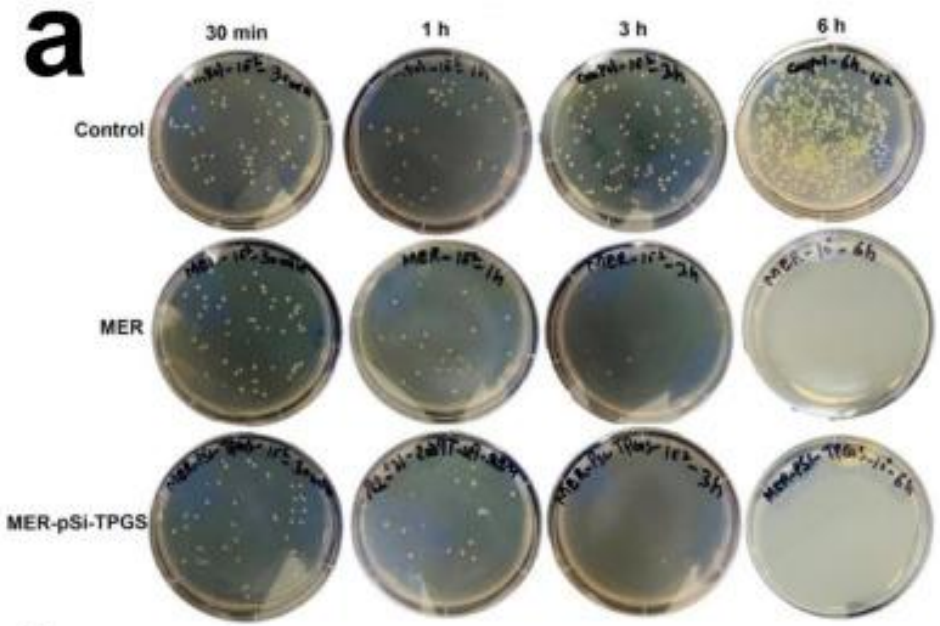
d

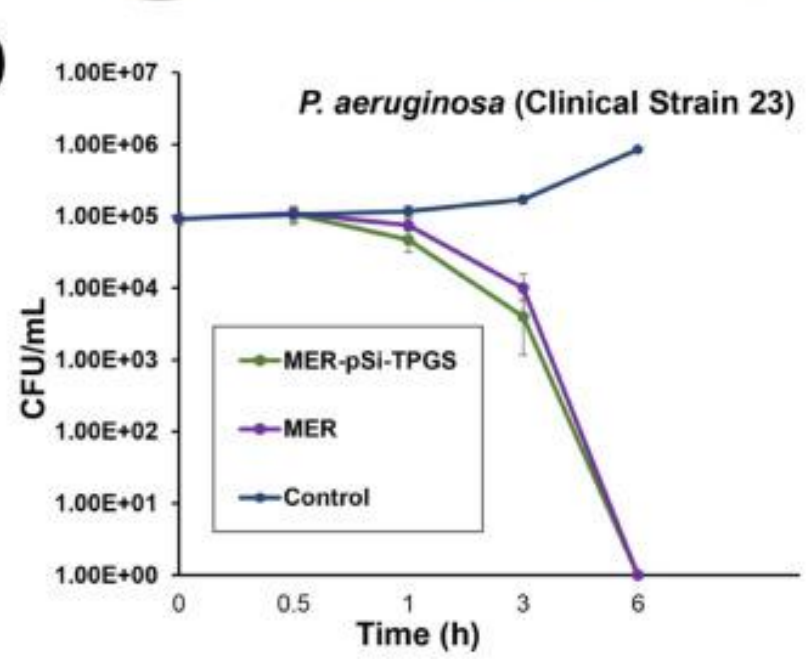
Formulations	Efflux ratio
MER	2.62
MER-Ver	0.03
MER-pSi-TPGS	0.40
MER-pSi-PEG-NH_2	0.66

Raza…Kumeria, Materials Today Advances, 2022

MER activity retention





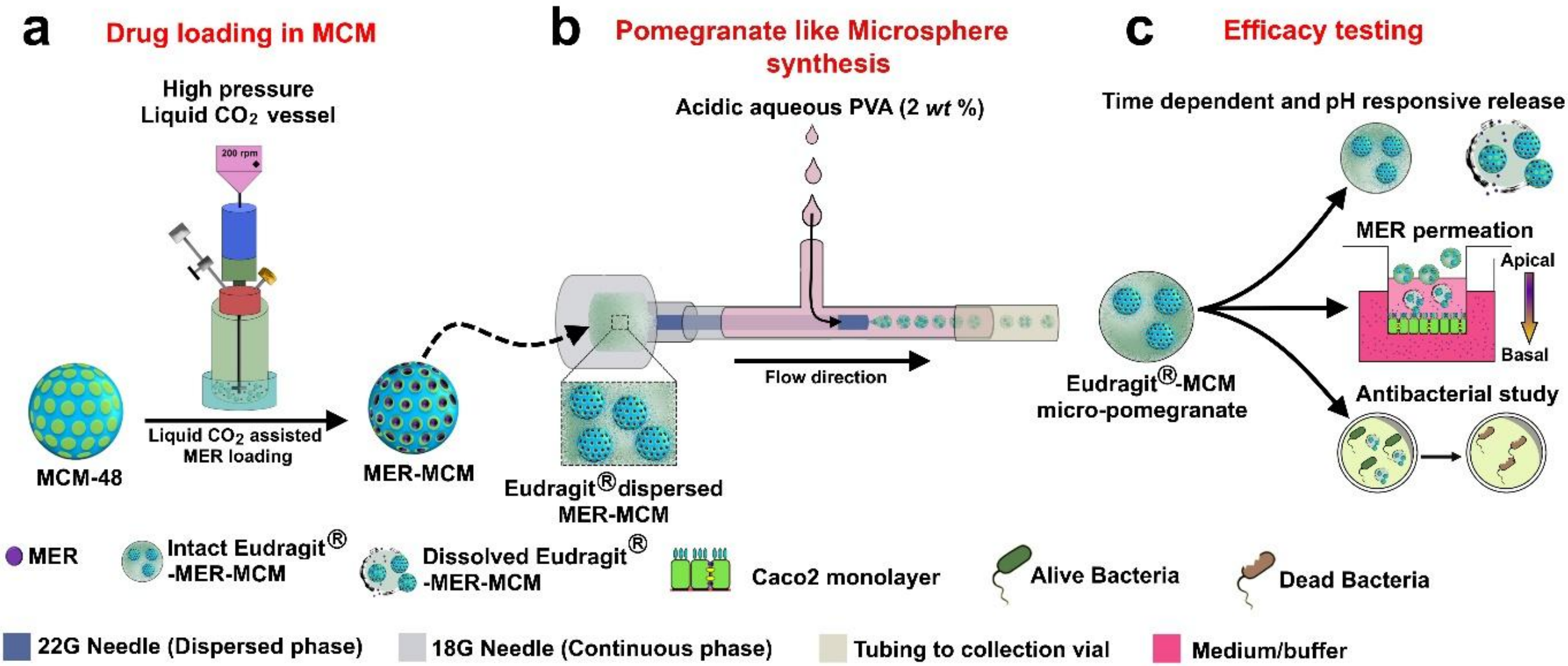


Intestinal Efflux ✓

Controlled release ✗

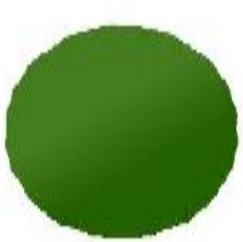
Raza, Materials Today Advances

2. Biomodulating Microspheres for oral Meropenem



Raza…Kumeria, Acta Biomaterialia, 2021

Mesoporous Silica Nanoparticles (MSN)

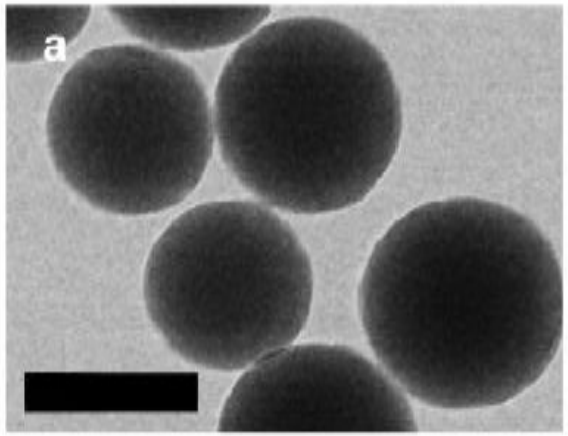


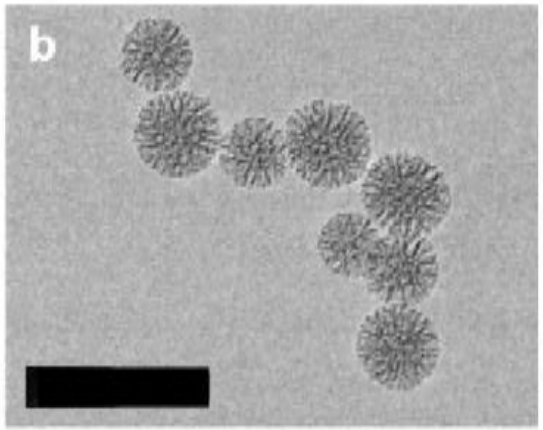
Solids
(S)

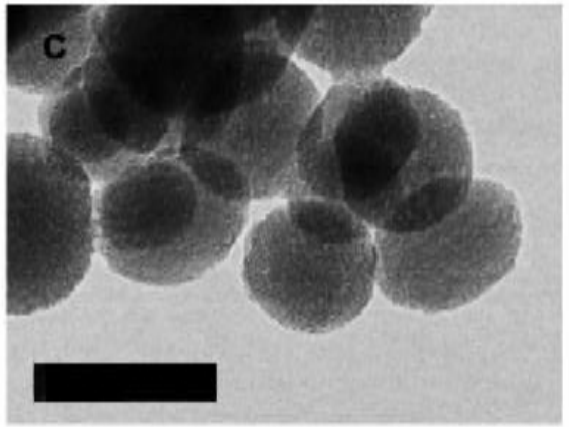
Dendritics
(D)

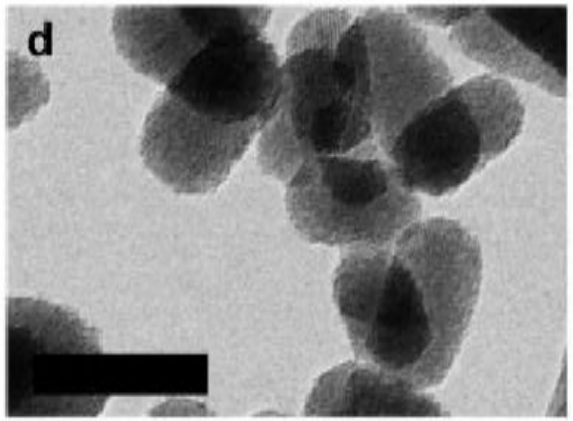
MCM-41
(M)

Rods
(R)







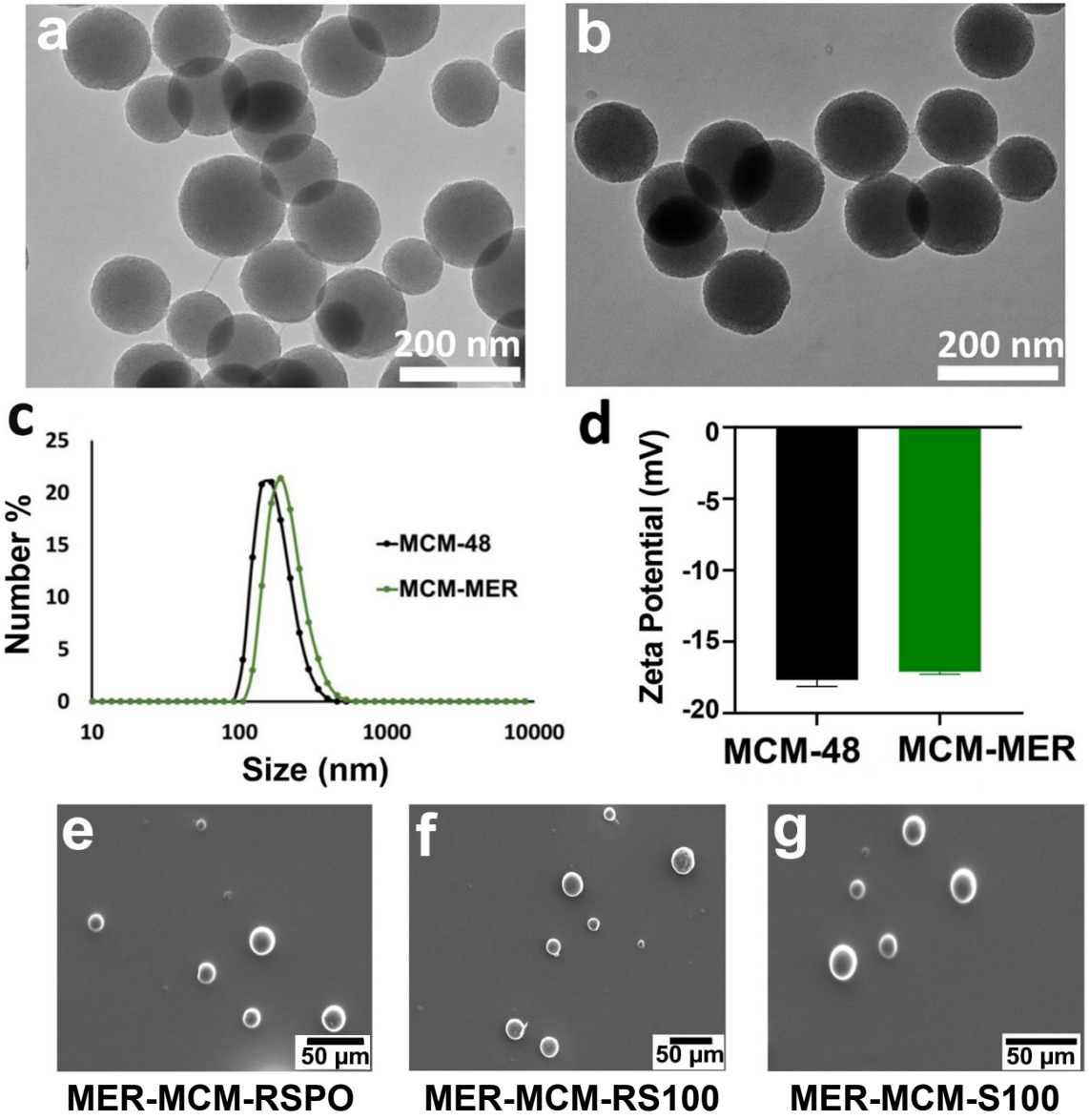


Structure and Morphology

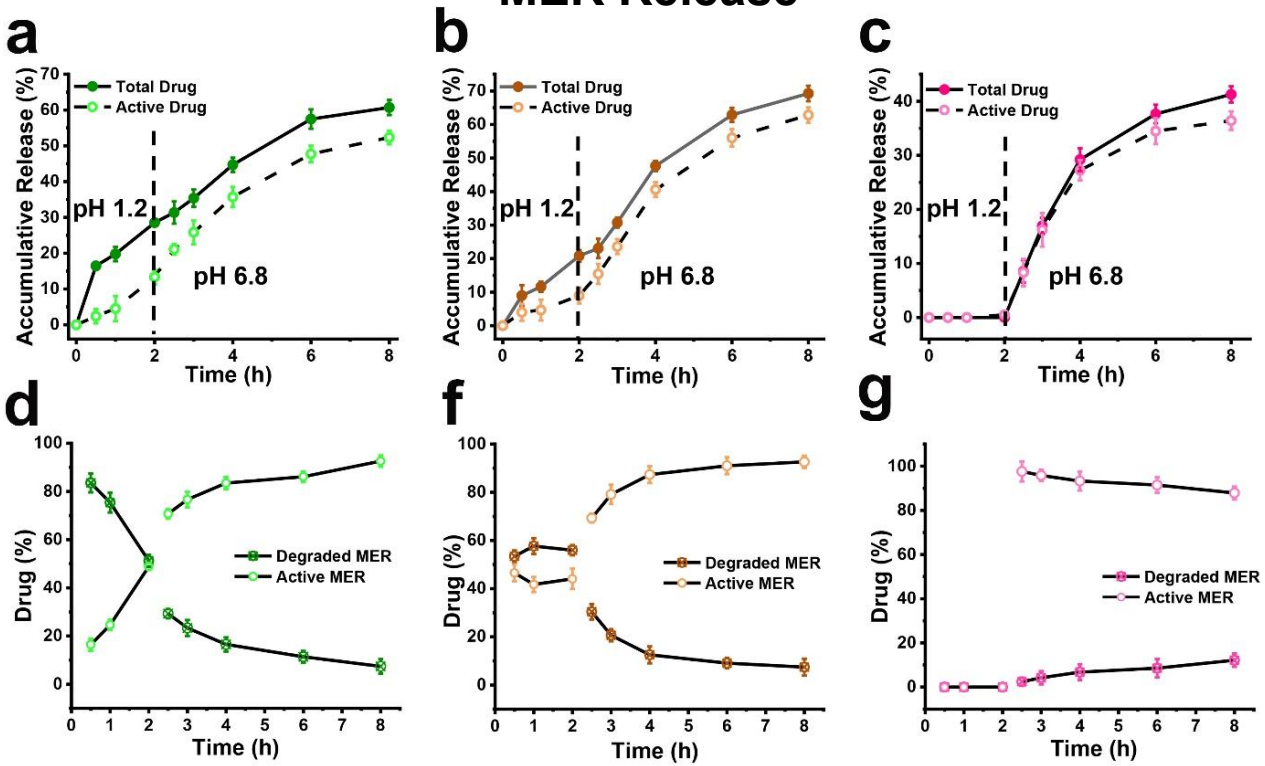
Large scale production

MCM-48/Eudragit® Microspheres

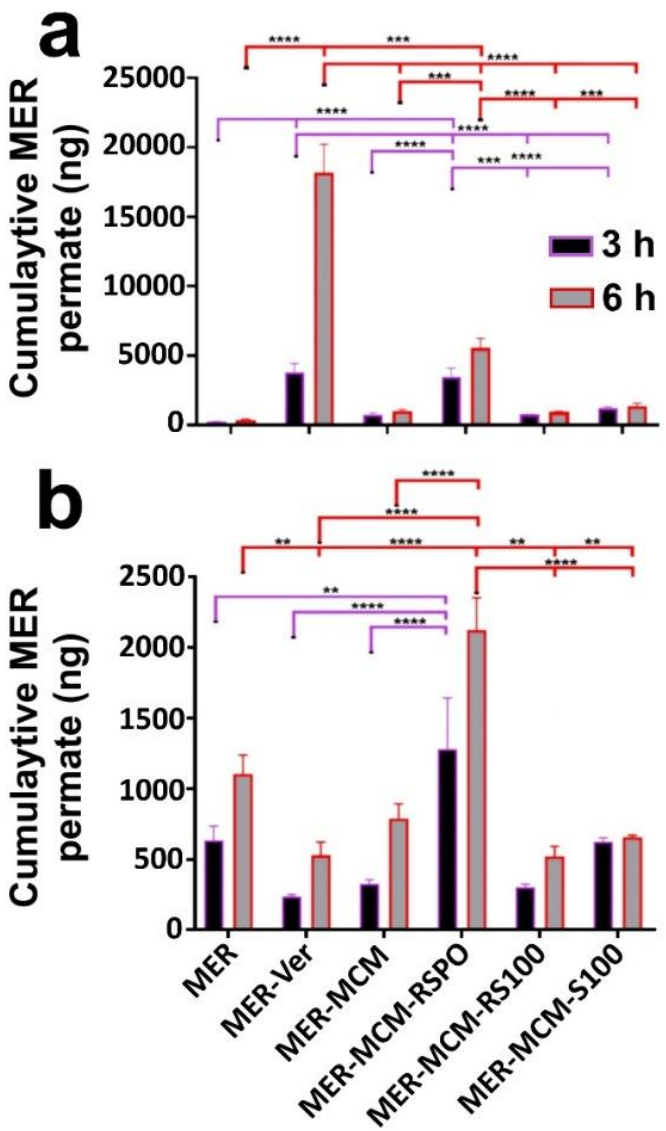
Particle size and surface charge

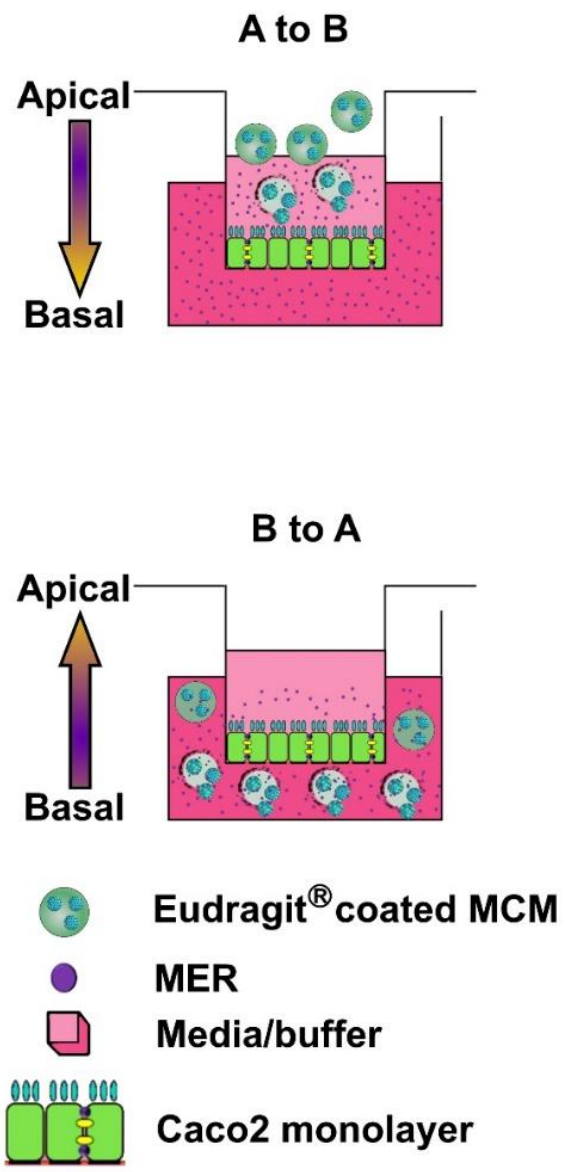


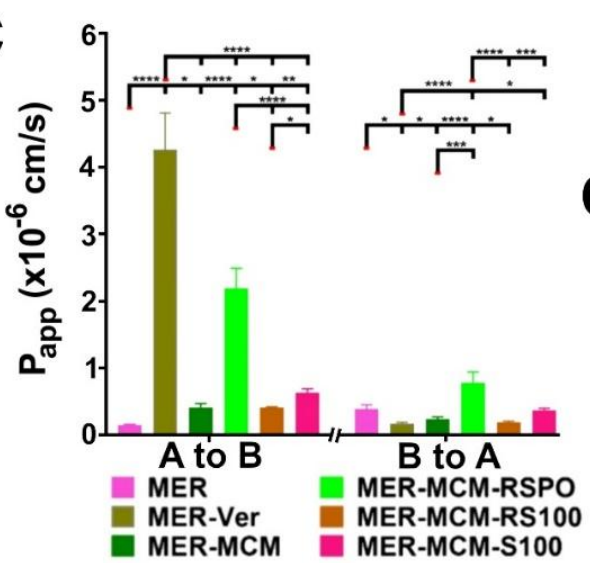
MER Release



MCM-48/Eudragit® Microspheres







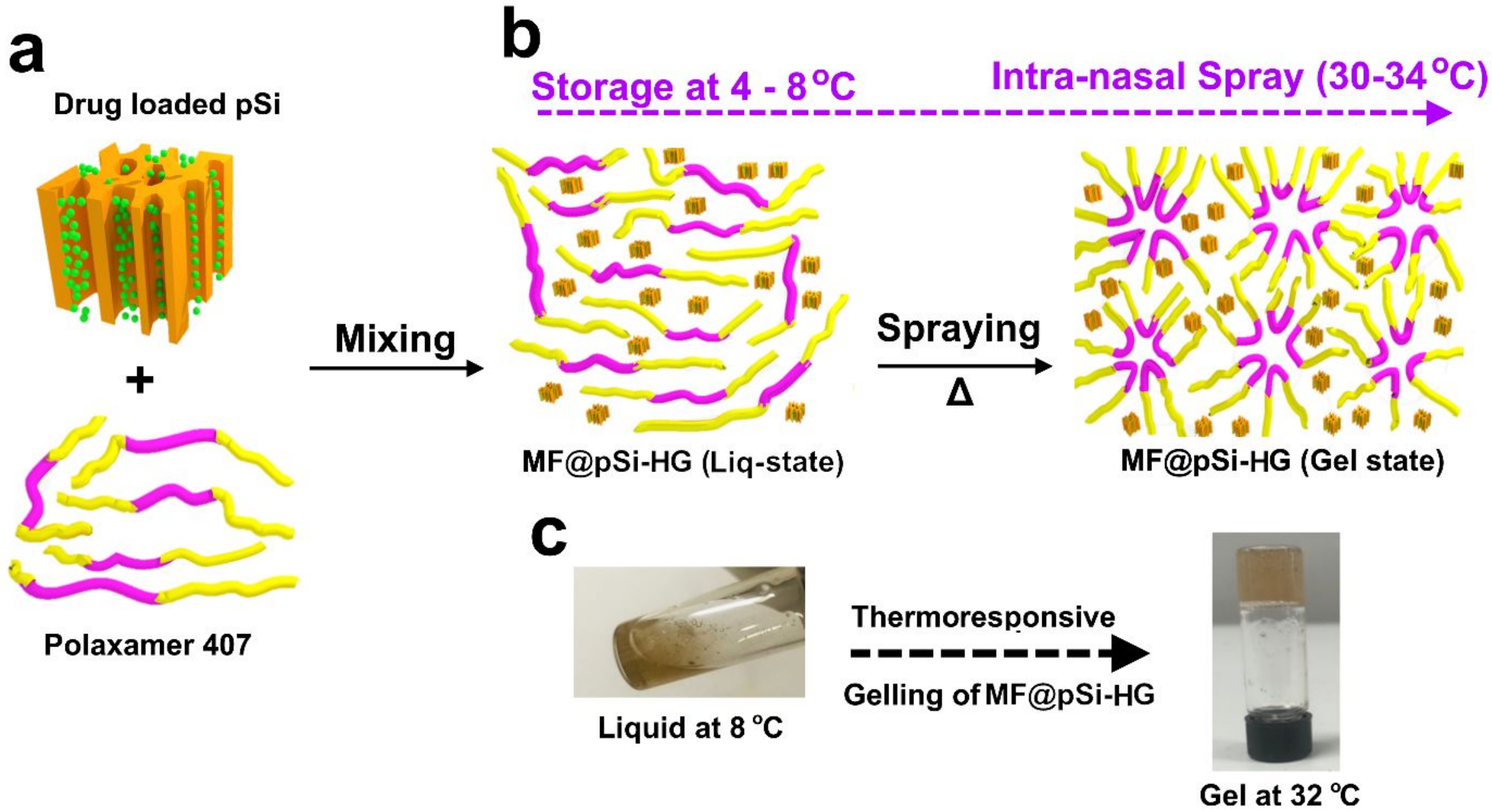
d

Formulations	Efflux ratio
MER	5.31
MER-Ver	0.09
MER-MCM	1.23
MER-RSPO	0.71
MER-RS100	0.96
MER-S100	0.99

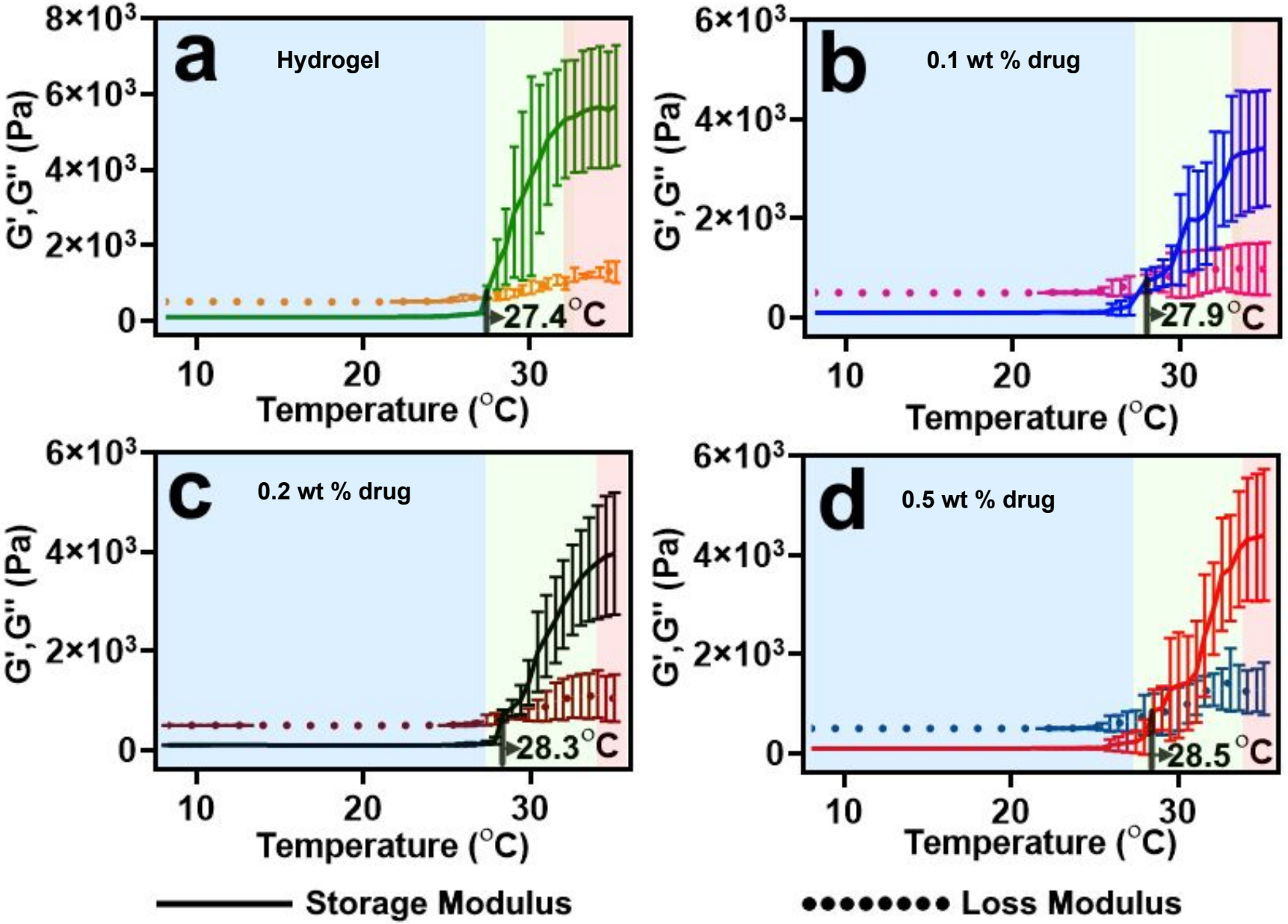
Intestinal Efflux ✓

Controlled release ✓

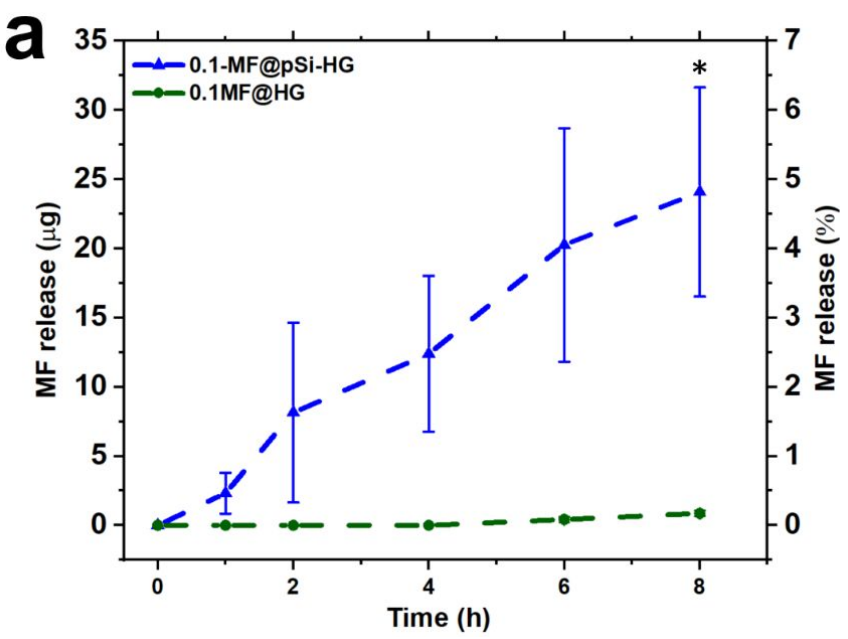
pSi/Hydrogel Composite

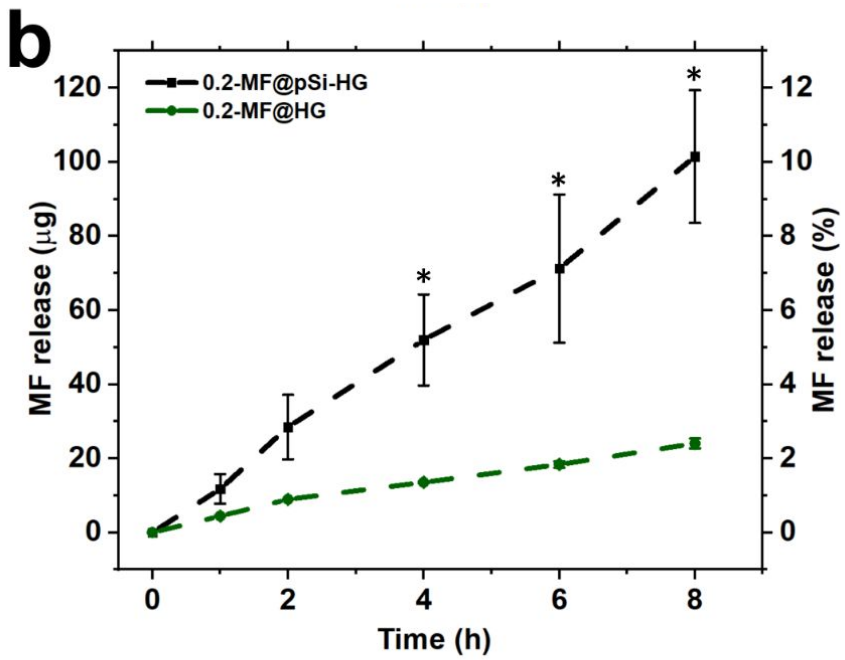


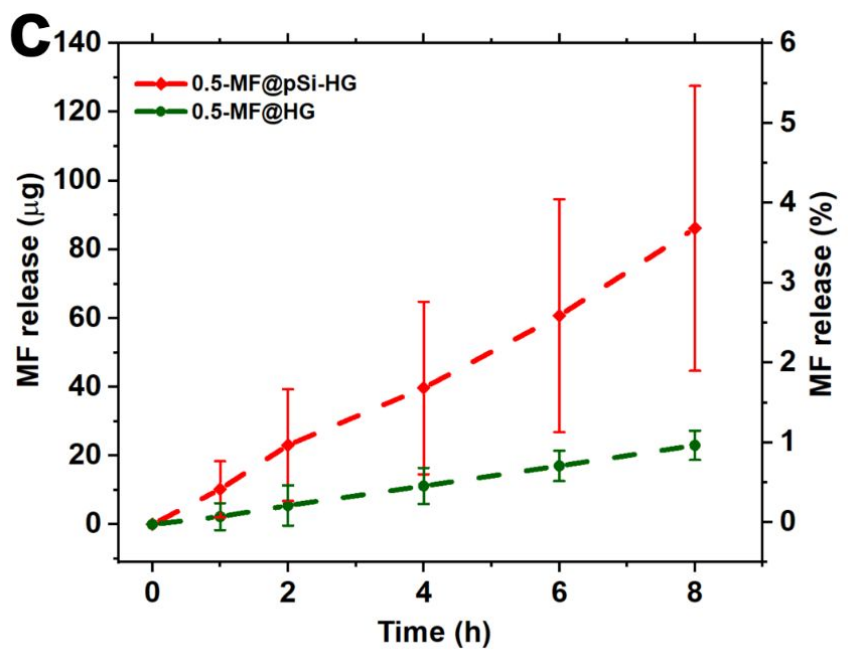
pSi/hydrogel Composite

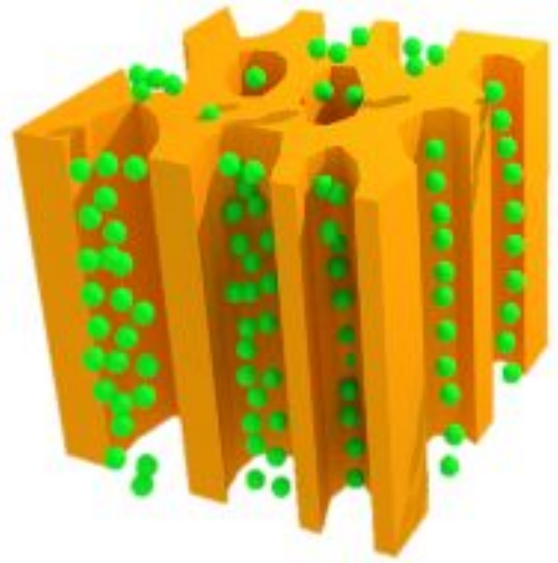


MF release in SNF

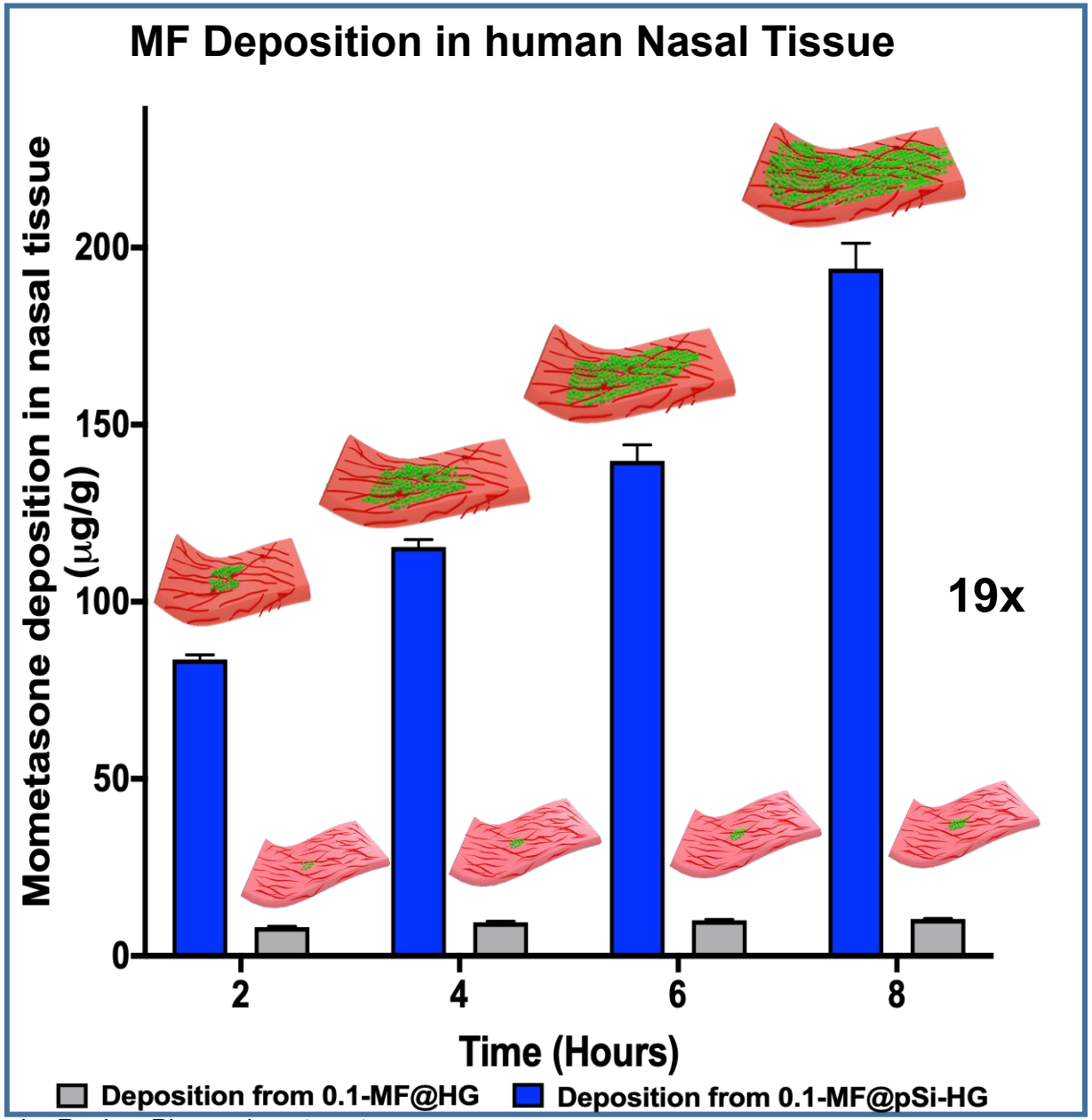


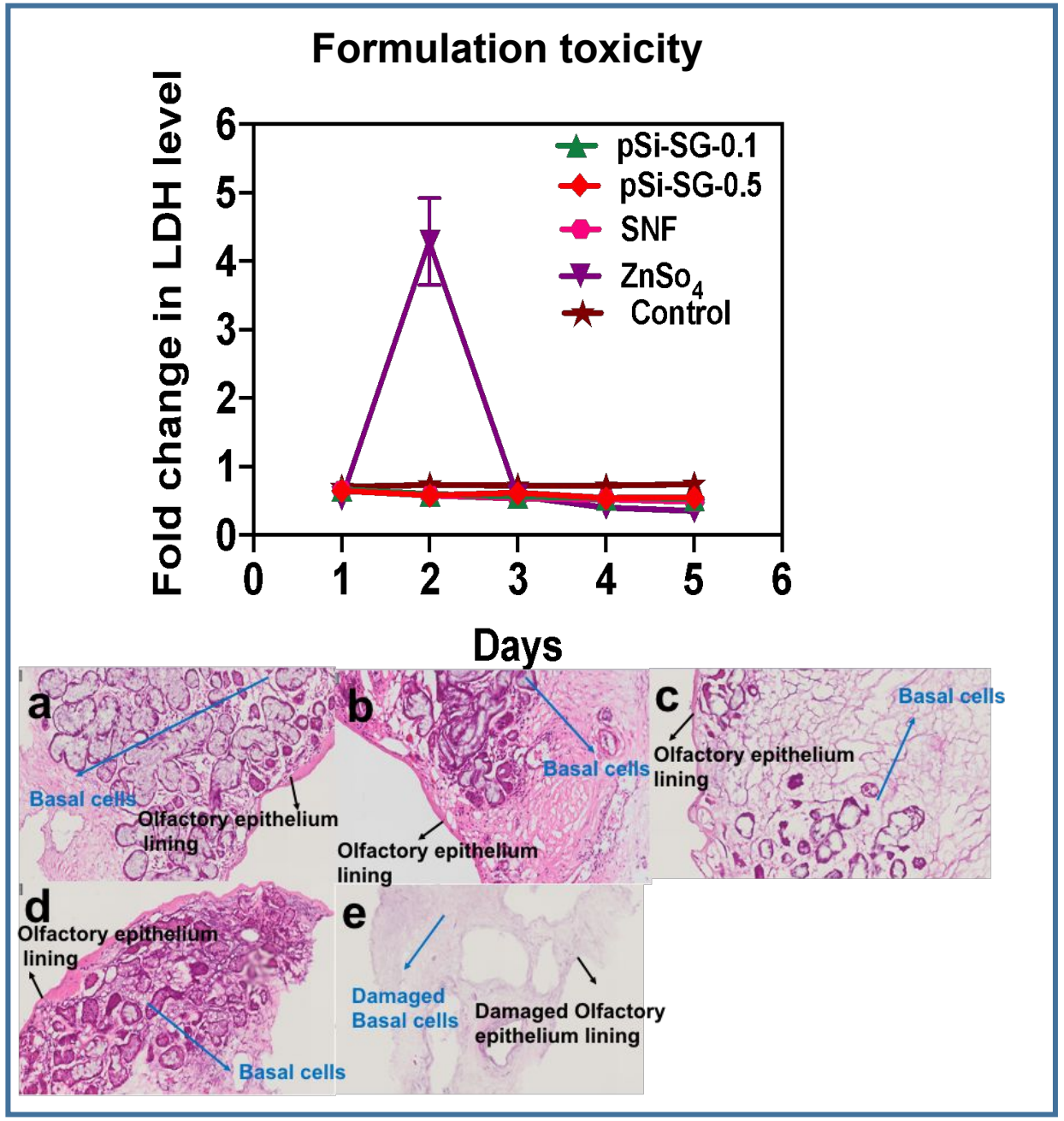




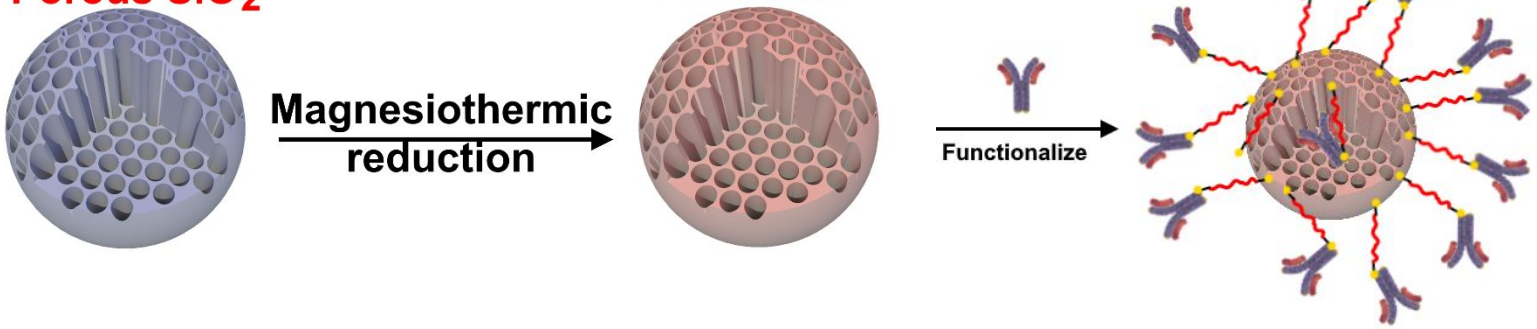


pSi/Hydrogel Composite





pSiNPs for Photoacoustic (PA) Bioimaging



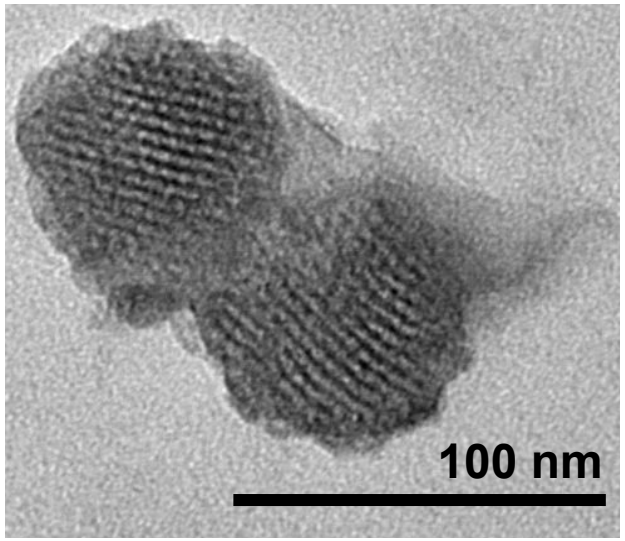
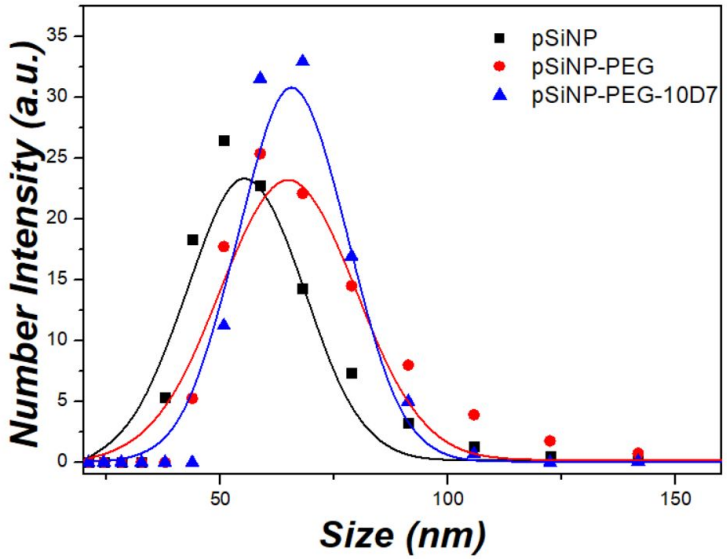
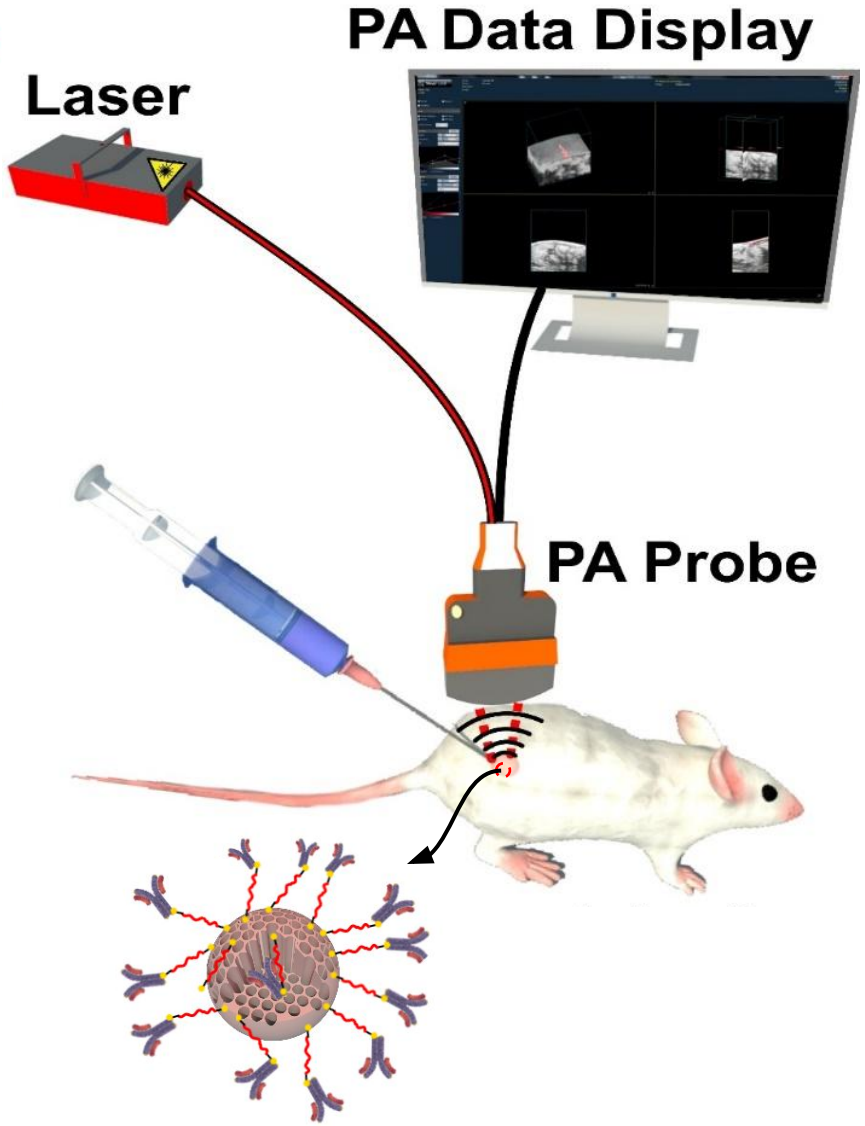


Figure. TEM images of pSiNPs





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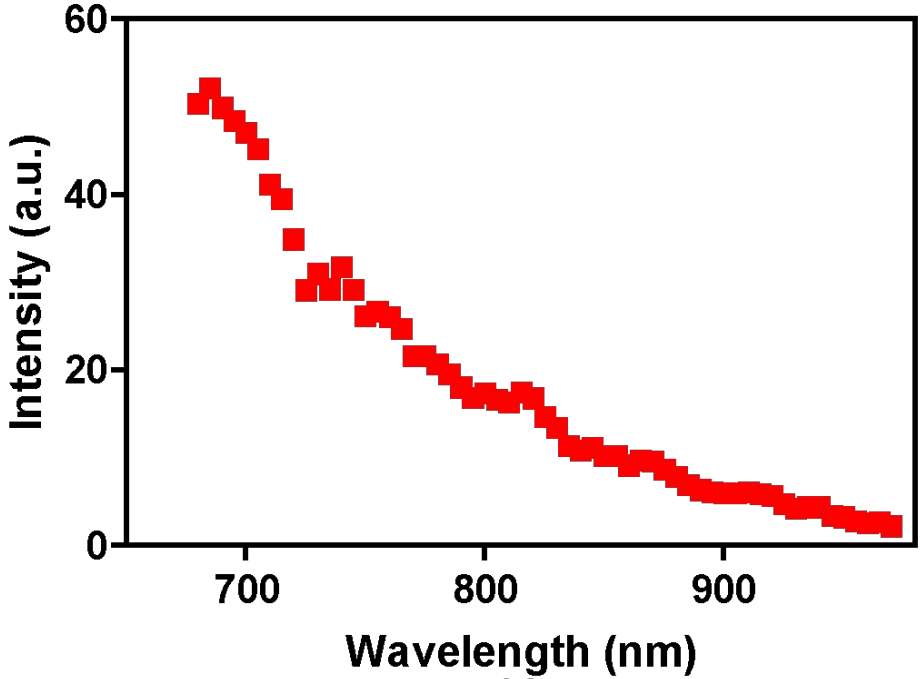
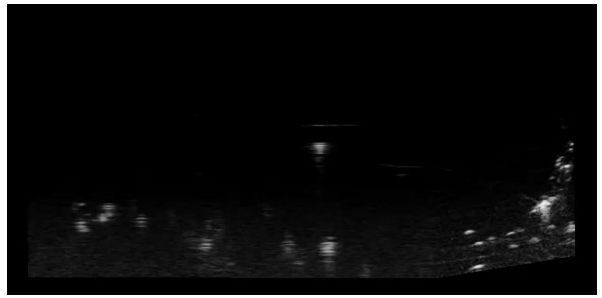
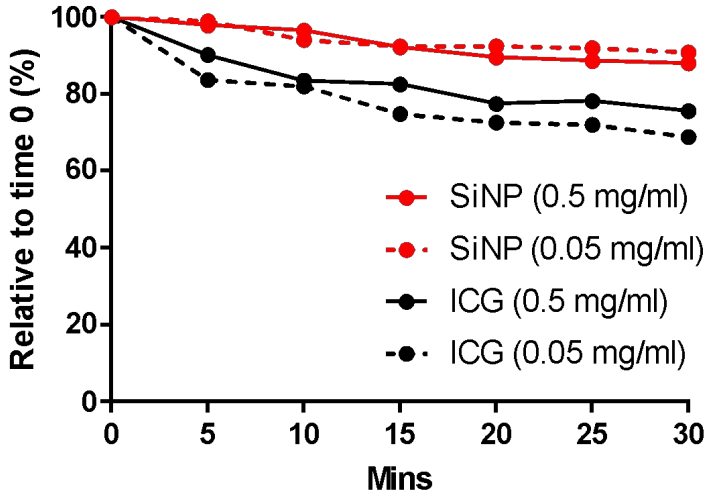
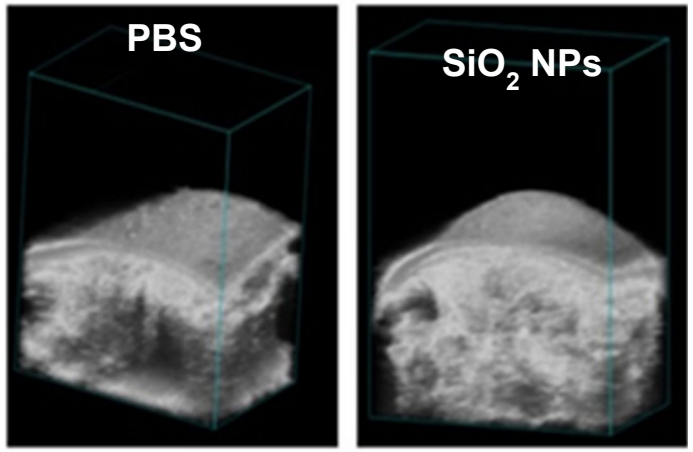


Figure. PA imaging intensity of SiNPs in-vitro

	SiO_2 NPs	ICG
PA Enhancement	81.2	6.2







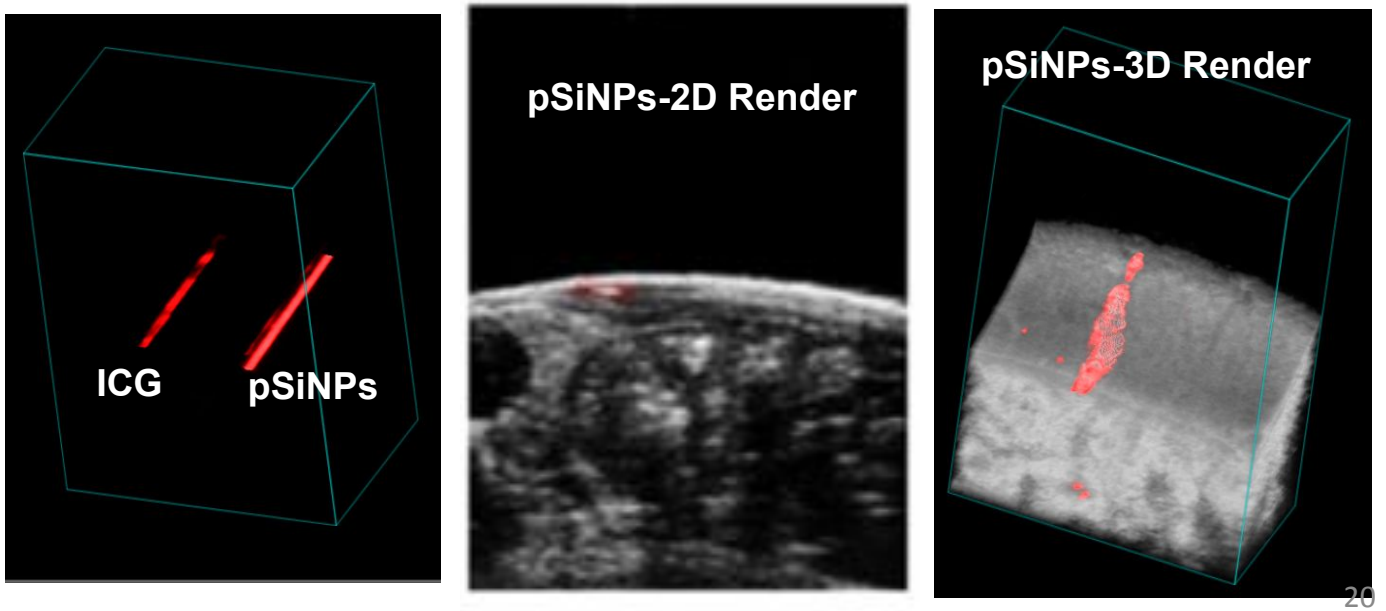
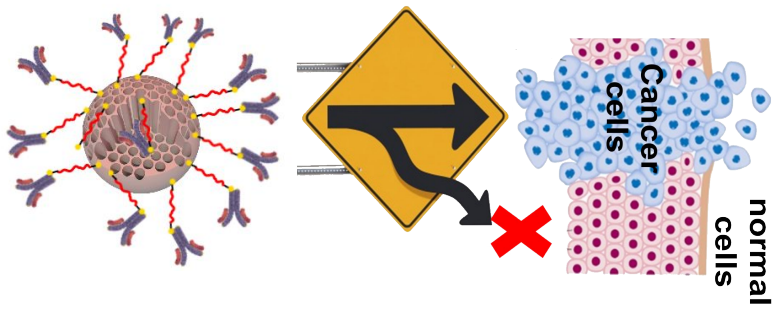
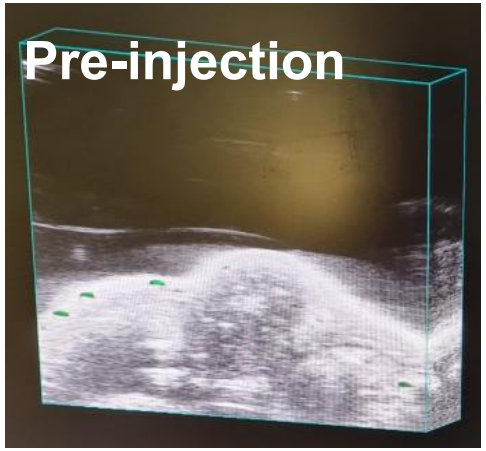
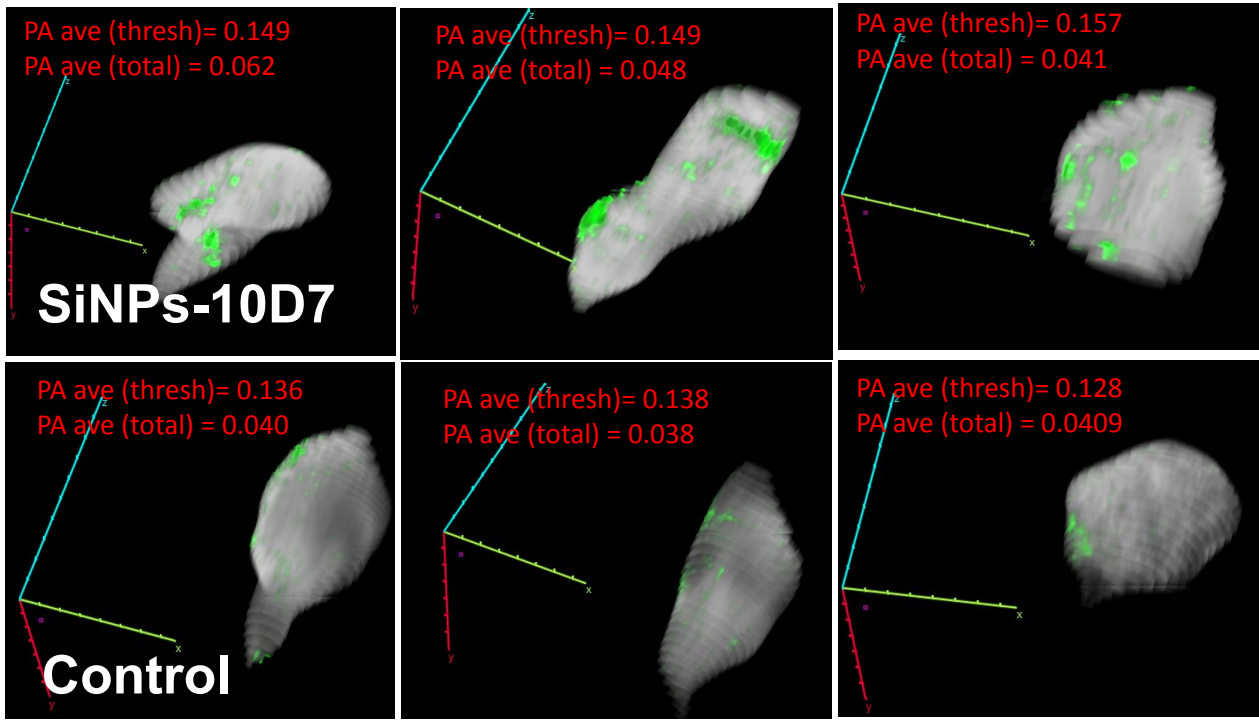


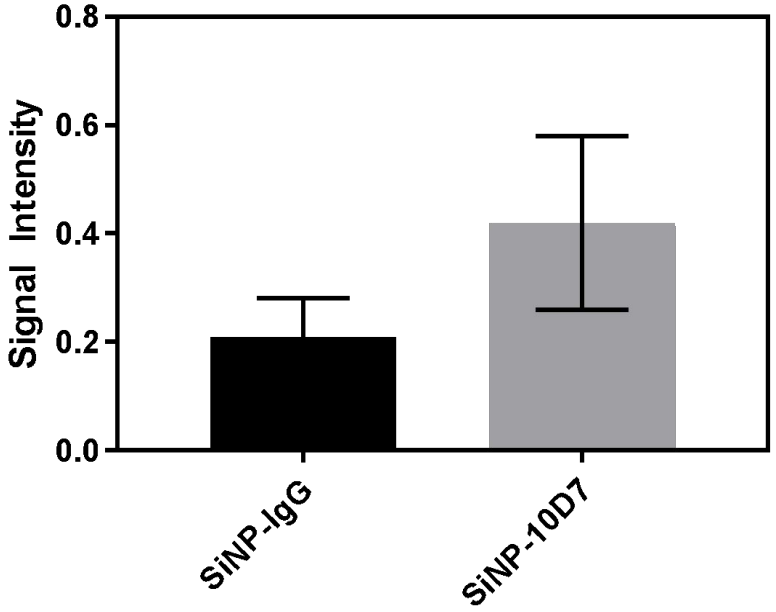
Figure. In-vitro and Ex-vivo PA imaging using pSiNPs

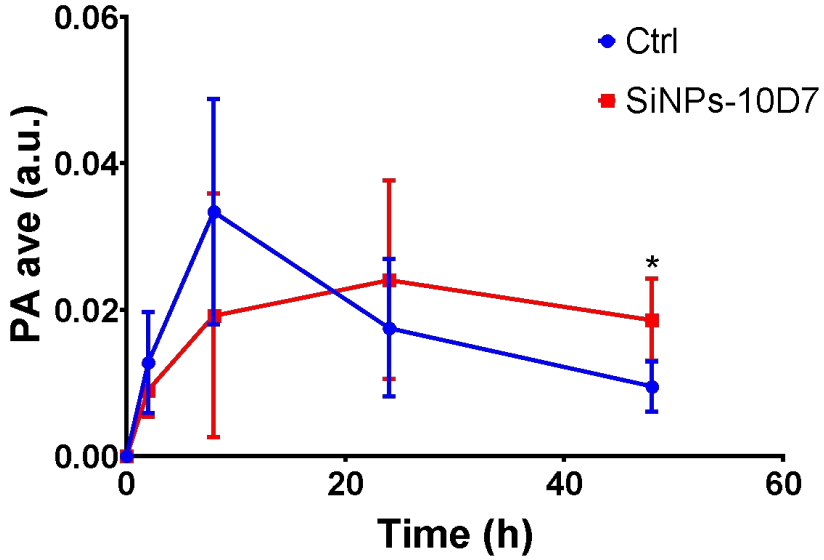
Targeting and Degradation of pSiNPs

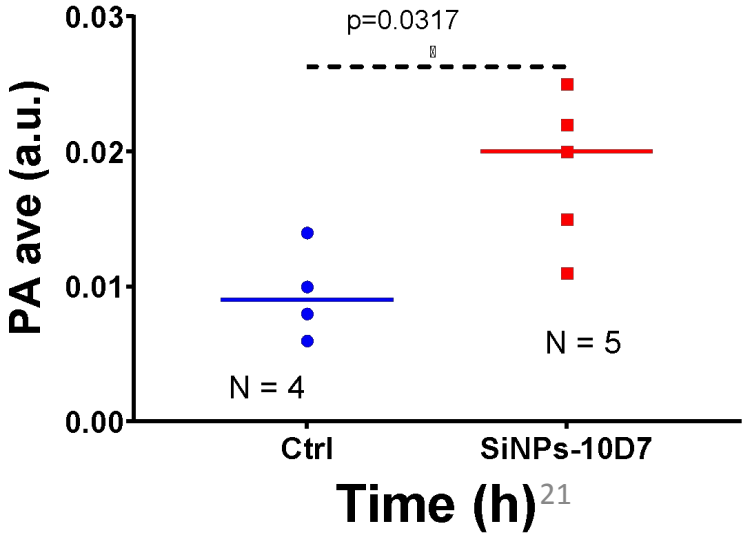












pSiNPs for Photoacoustic (PA) Bioimaging

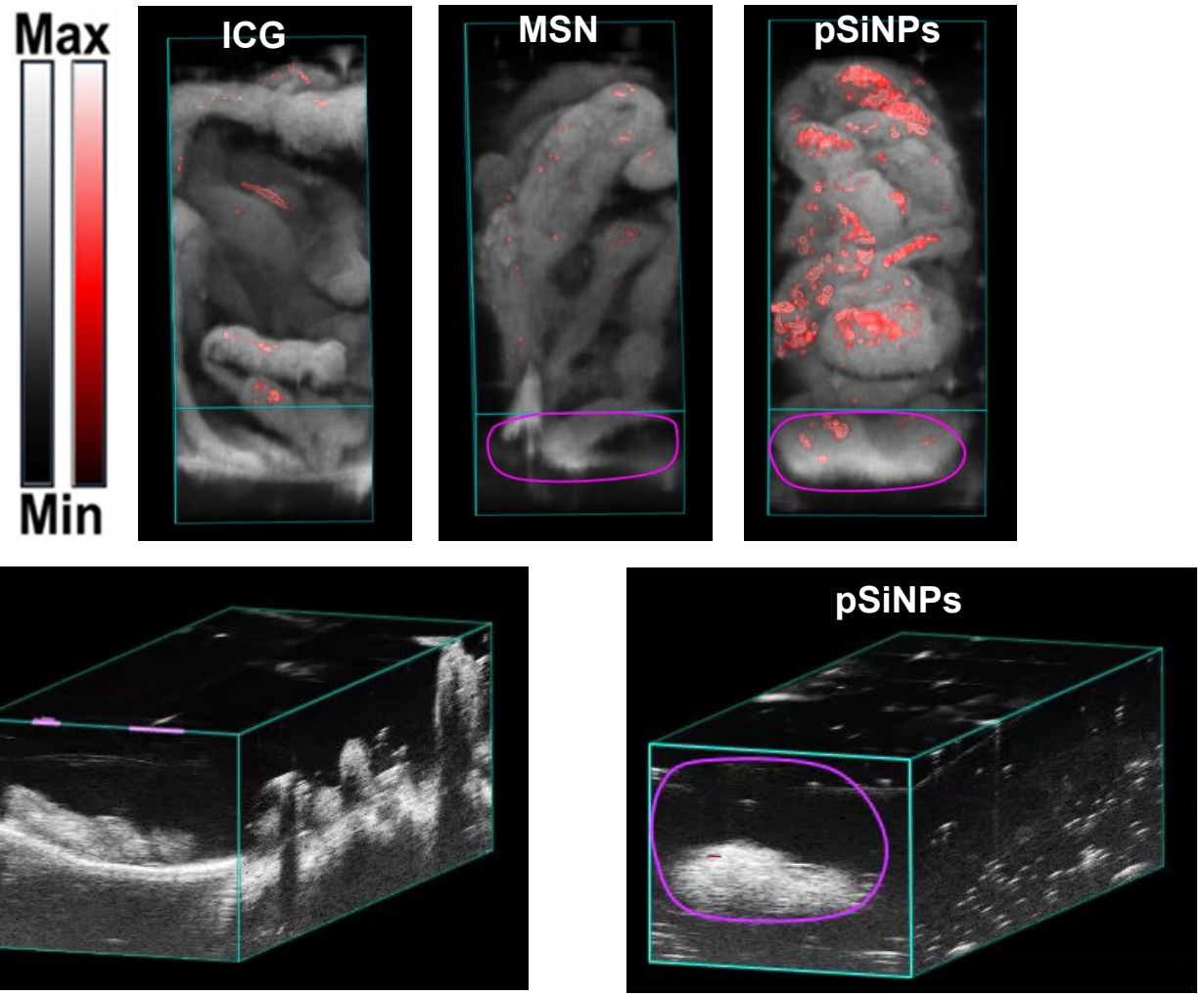


Figure. PA imaging using of orally injected ICG, SiO_2, and pSiNPs

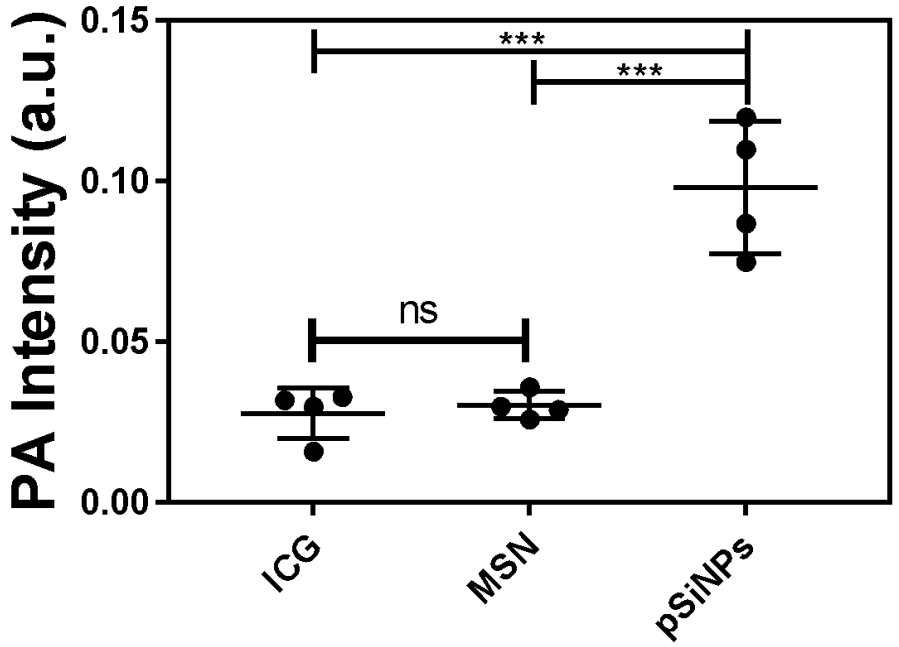


Figure. PA imaging intensity of pSiNPs in the GI Tract
N = 4

	SiO_2 NPs	ICG
PA Enhancement	3.2 ± 0.35	3.7 ± 0.76

Acknowledgements

Institutions

UNSW SYDNEY

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- Yuxue Cao
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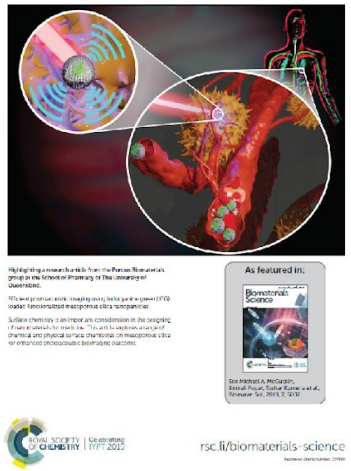
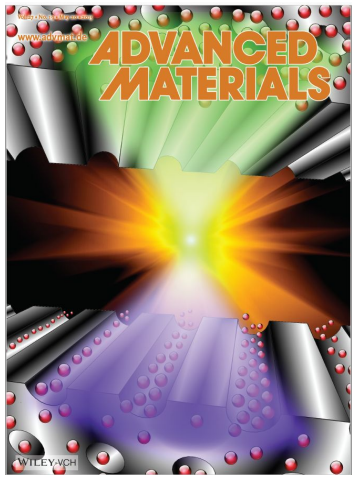
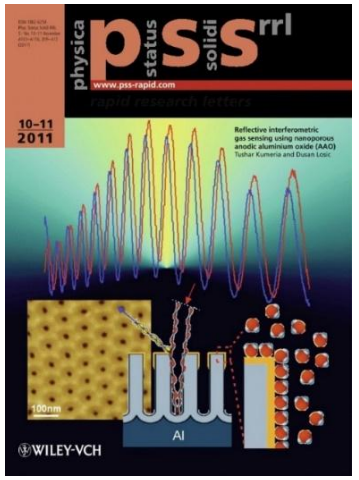
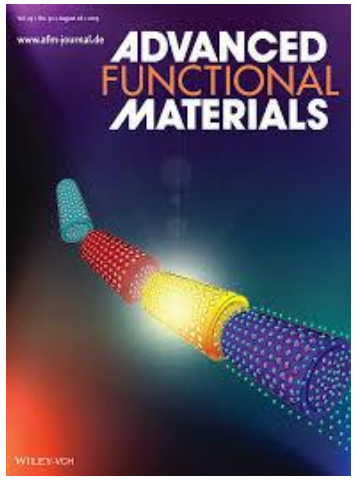
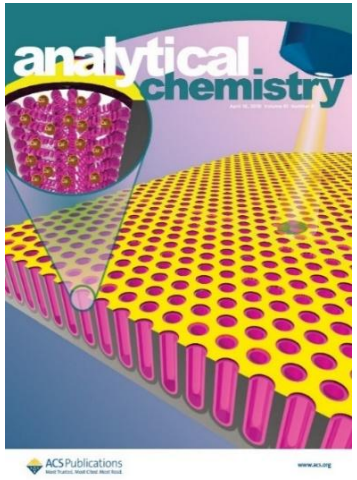
Thank You!!

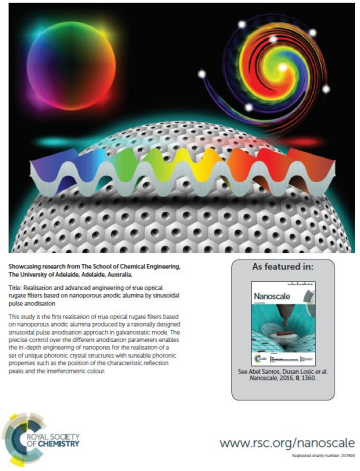


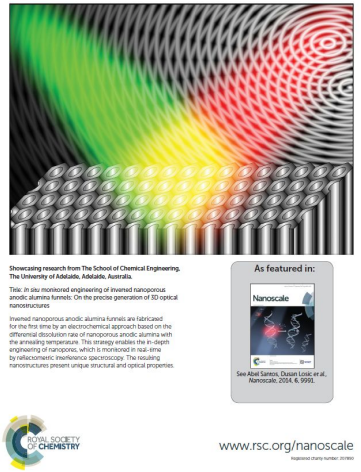


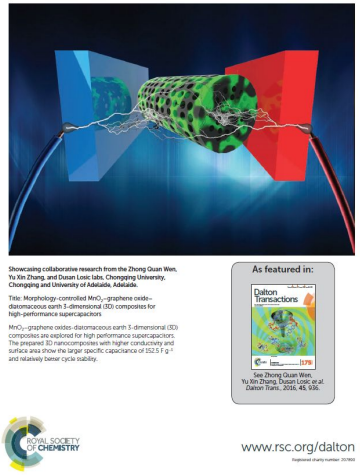












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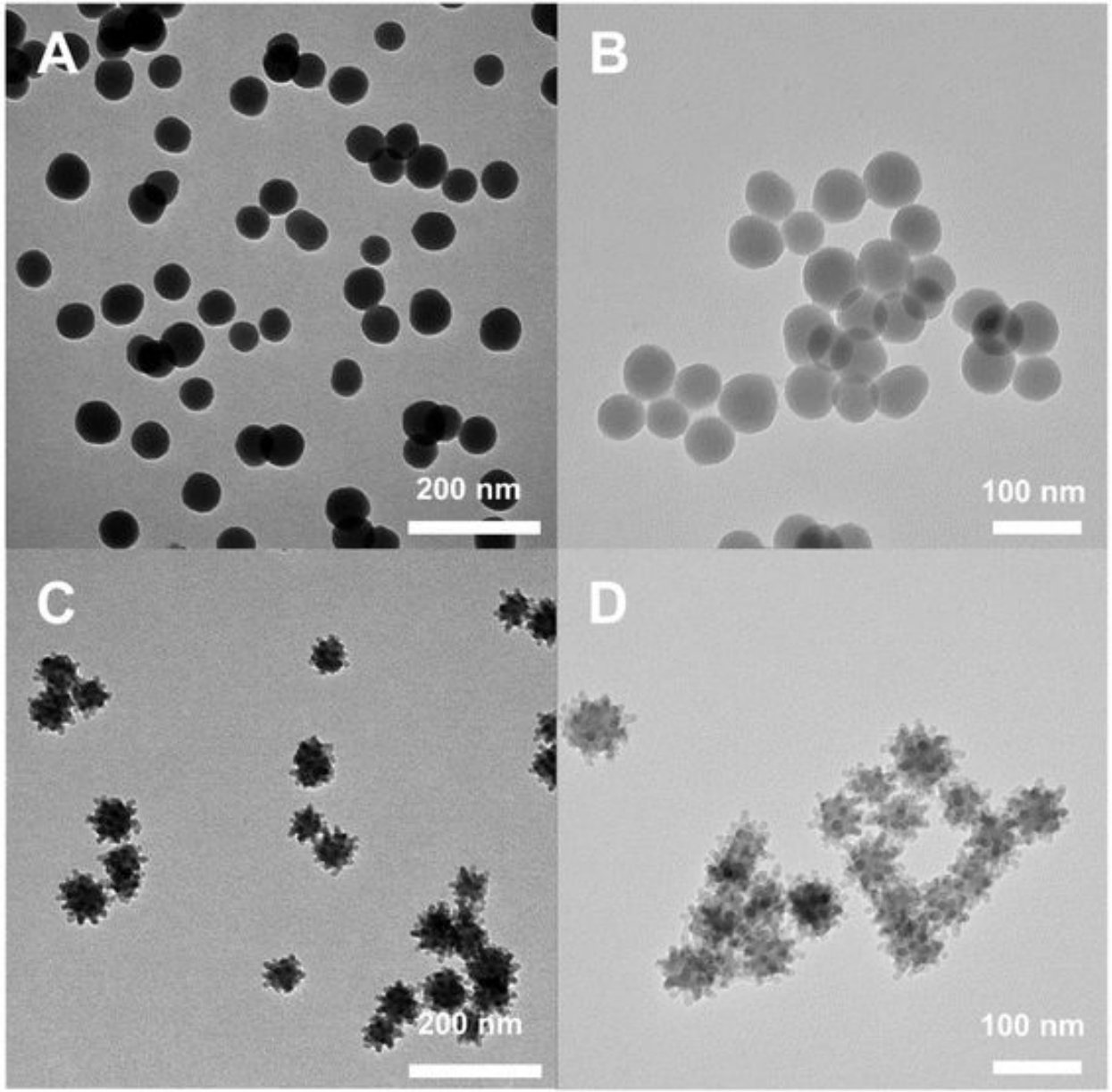
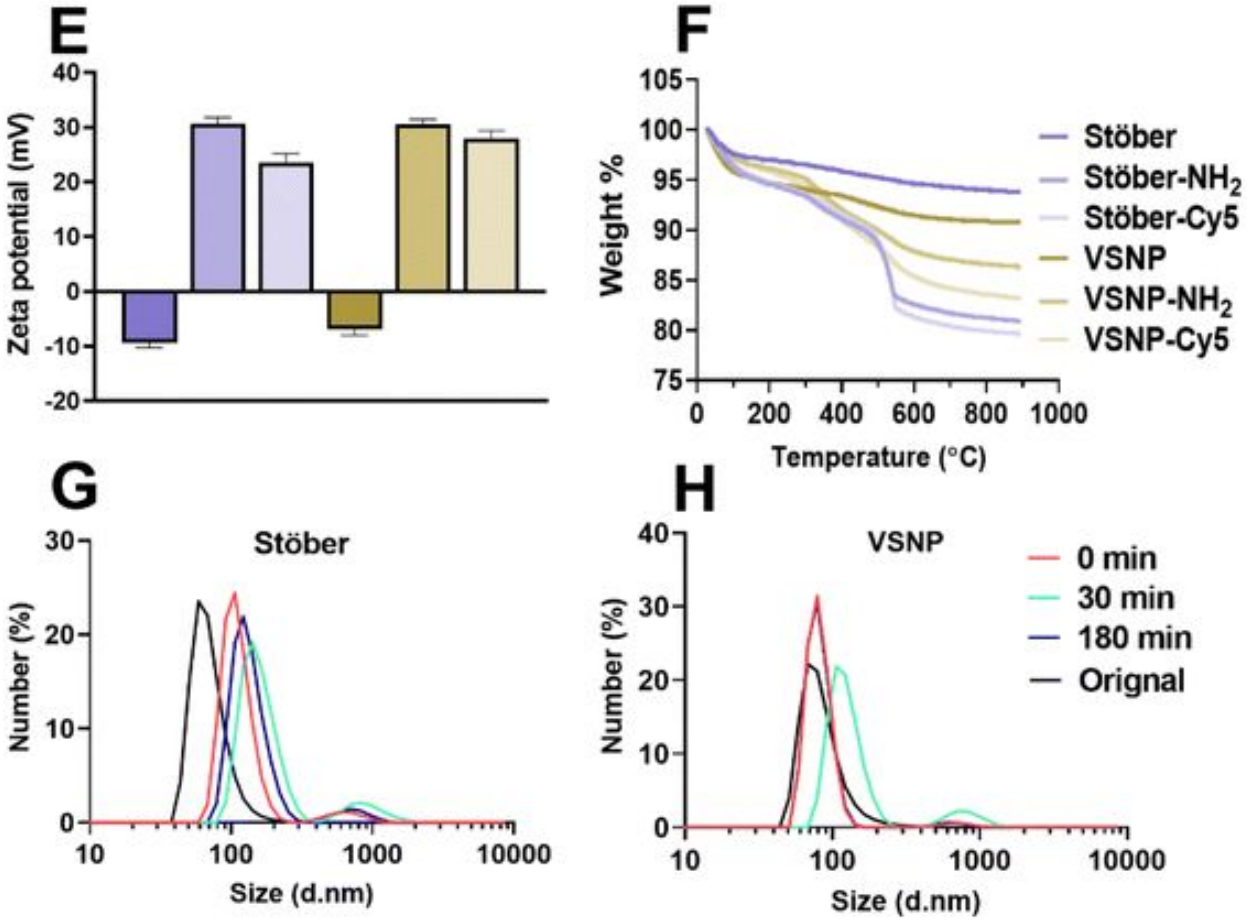
Tushar Kumeria

Backup Charts!

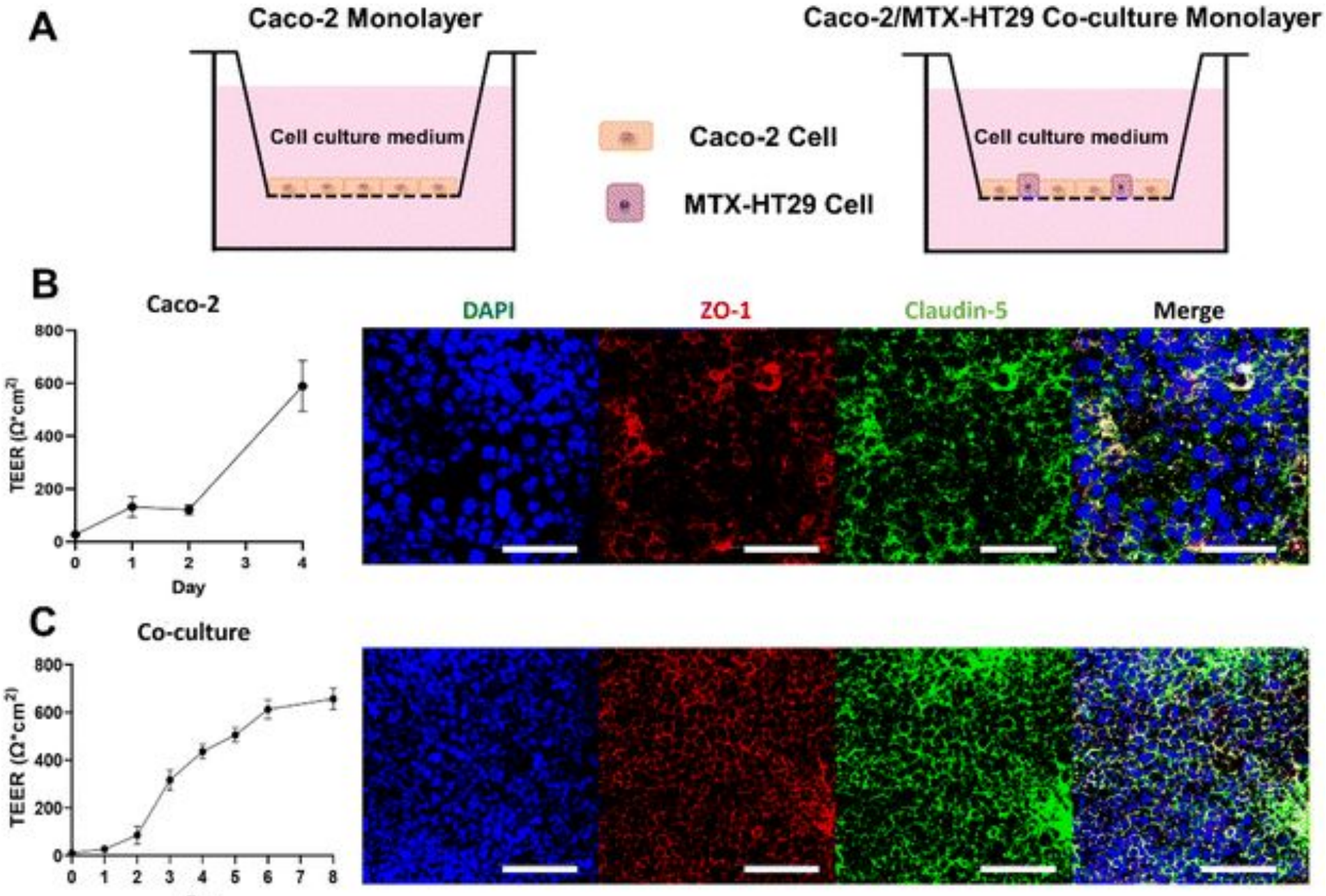
3. Biomodulating Spikey Virus-like MSN



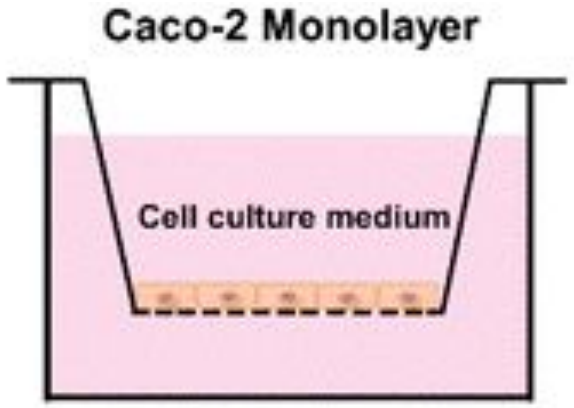


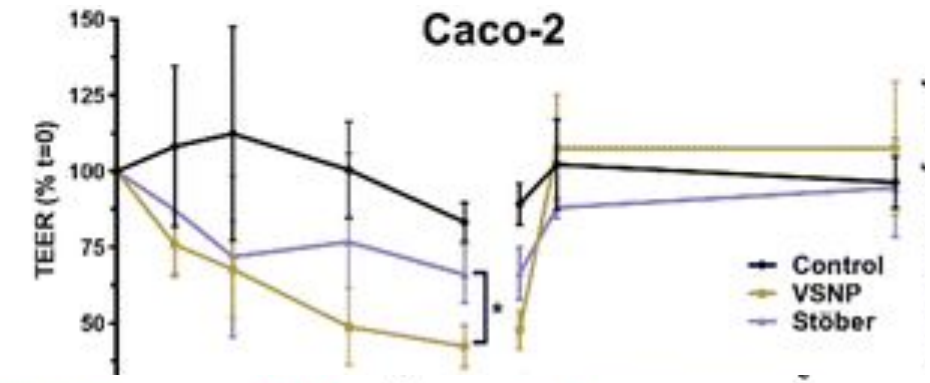
Cao, Biomaters Science, 2023

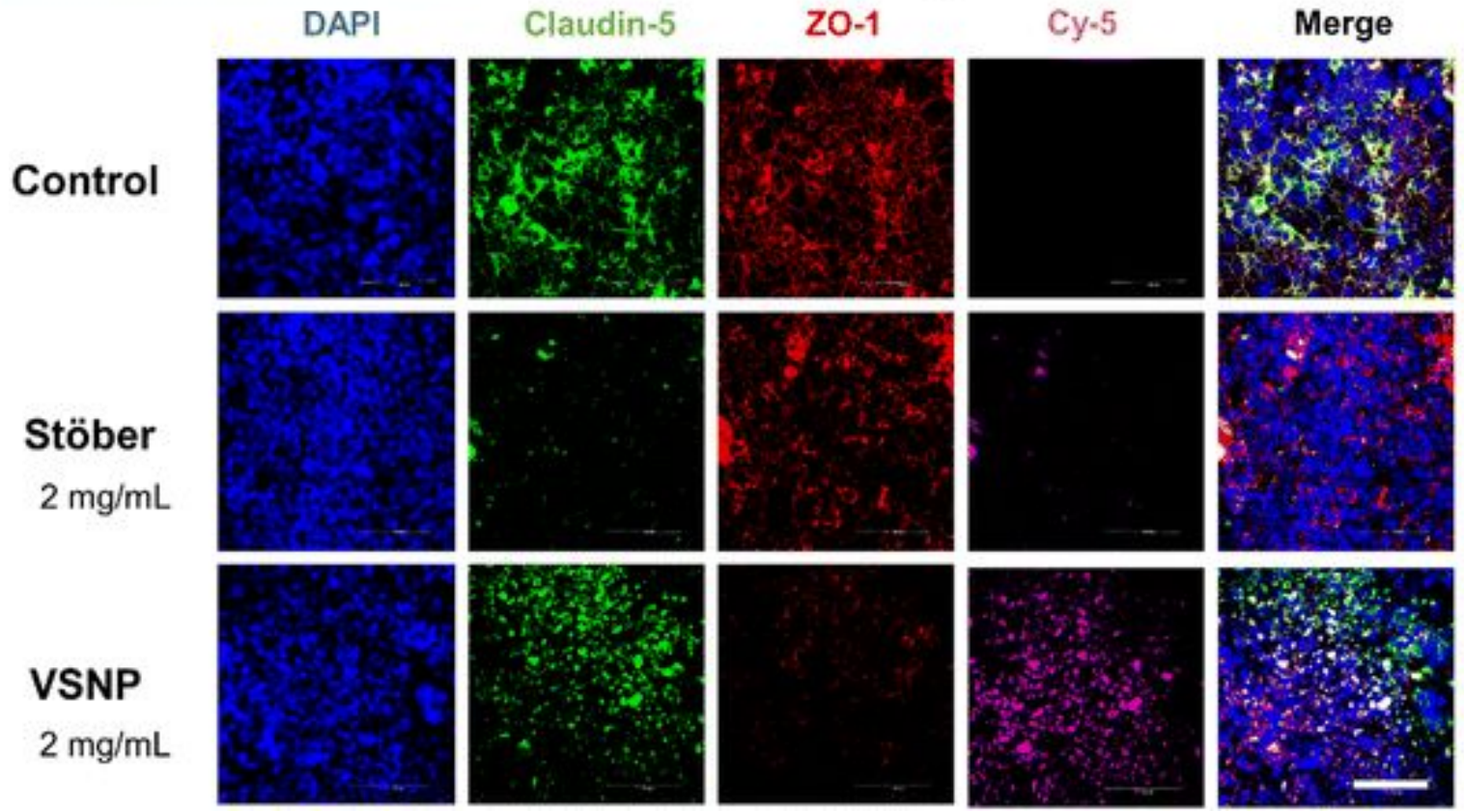
In-vitro Permeation Model Development

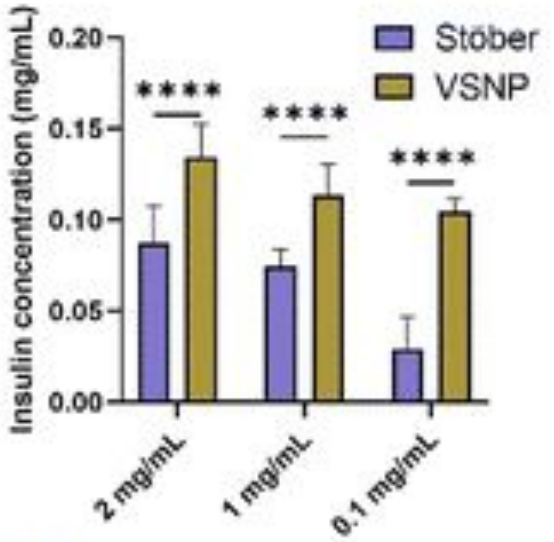


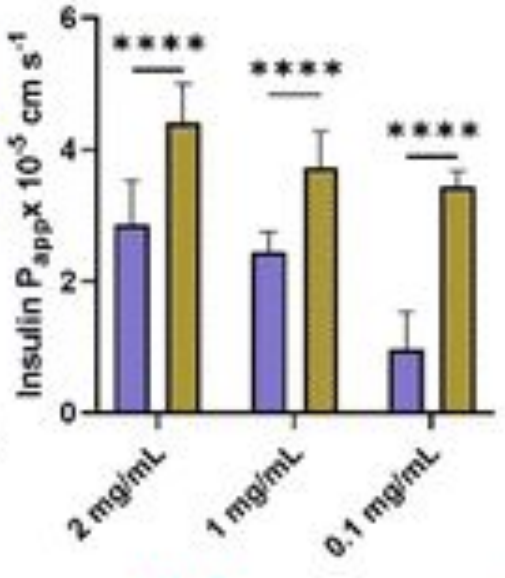
VSNPs Mediated Permeation











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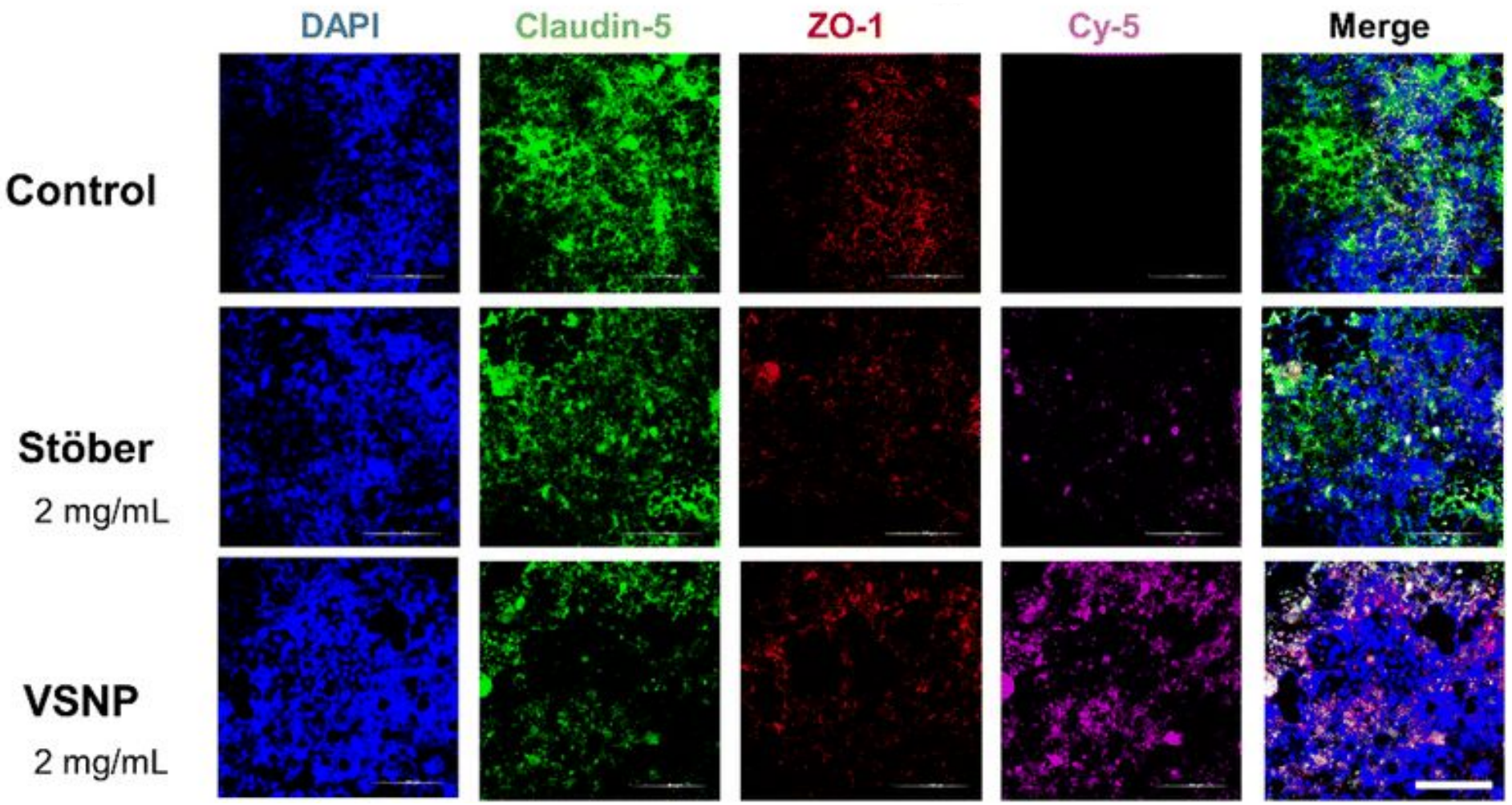
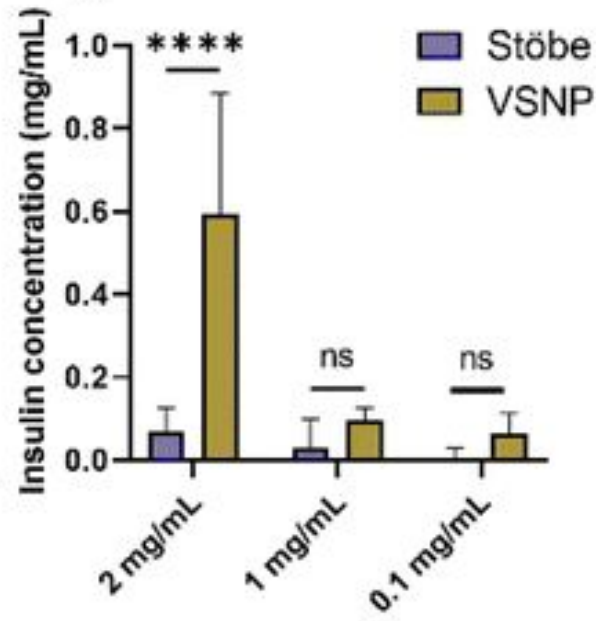
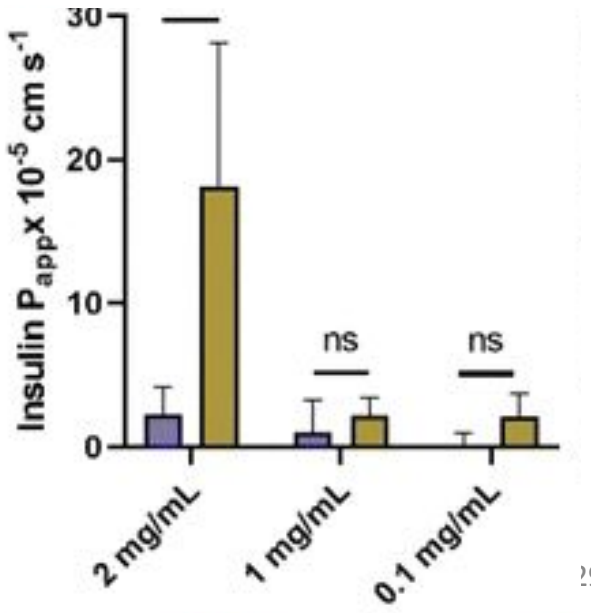
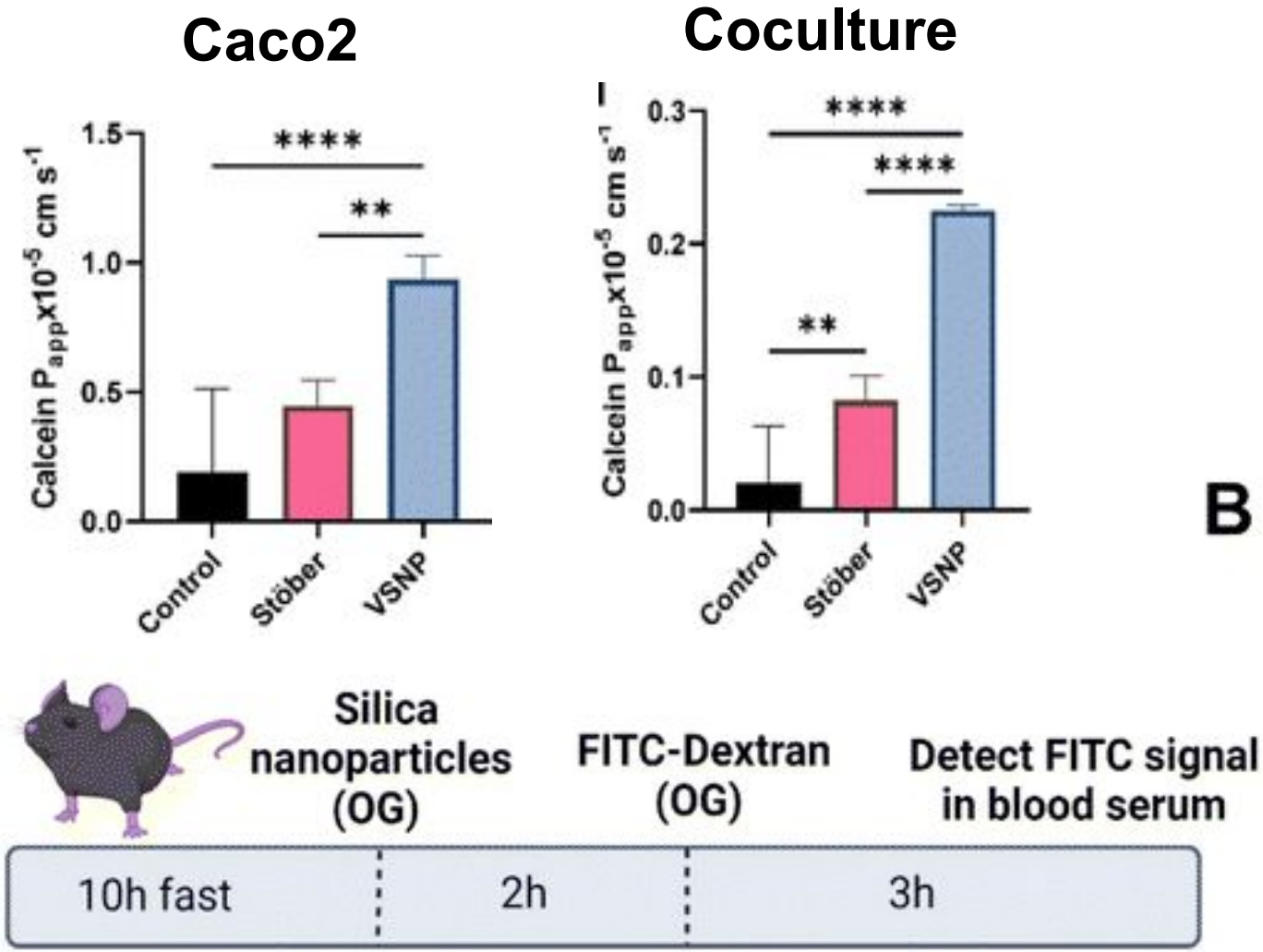
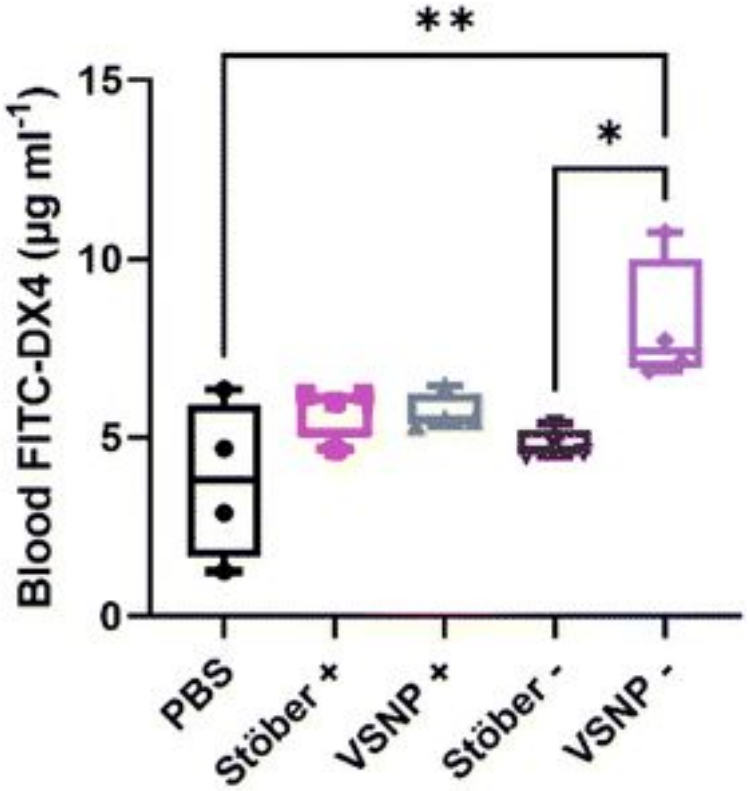




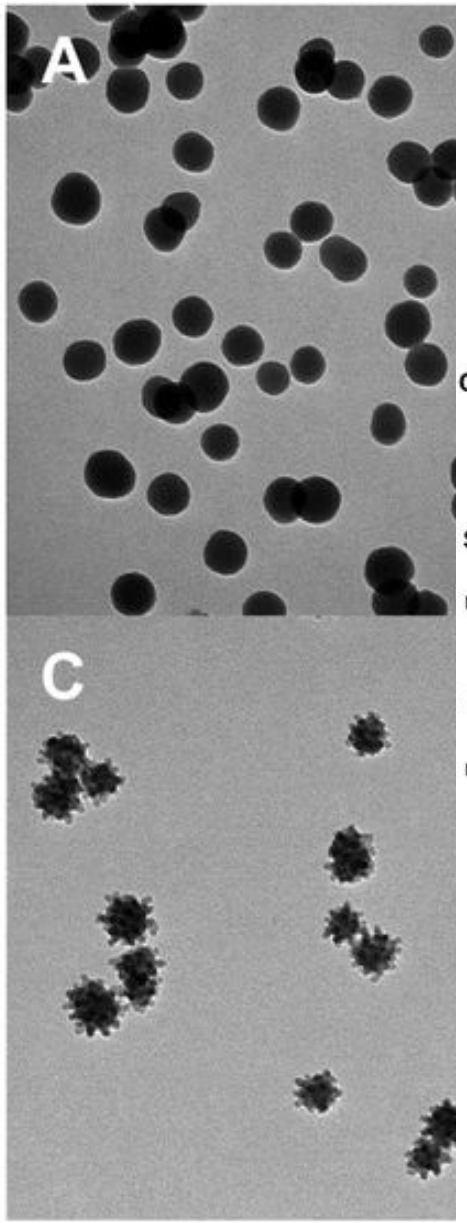


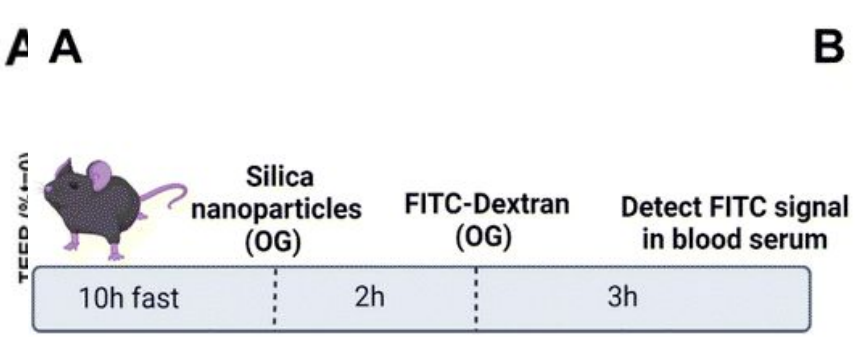
VSNPs Mediated Oral Uptake

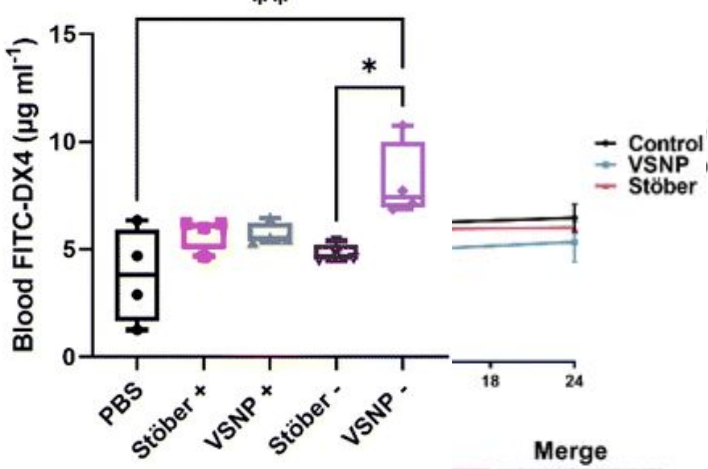


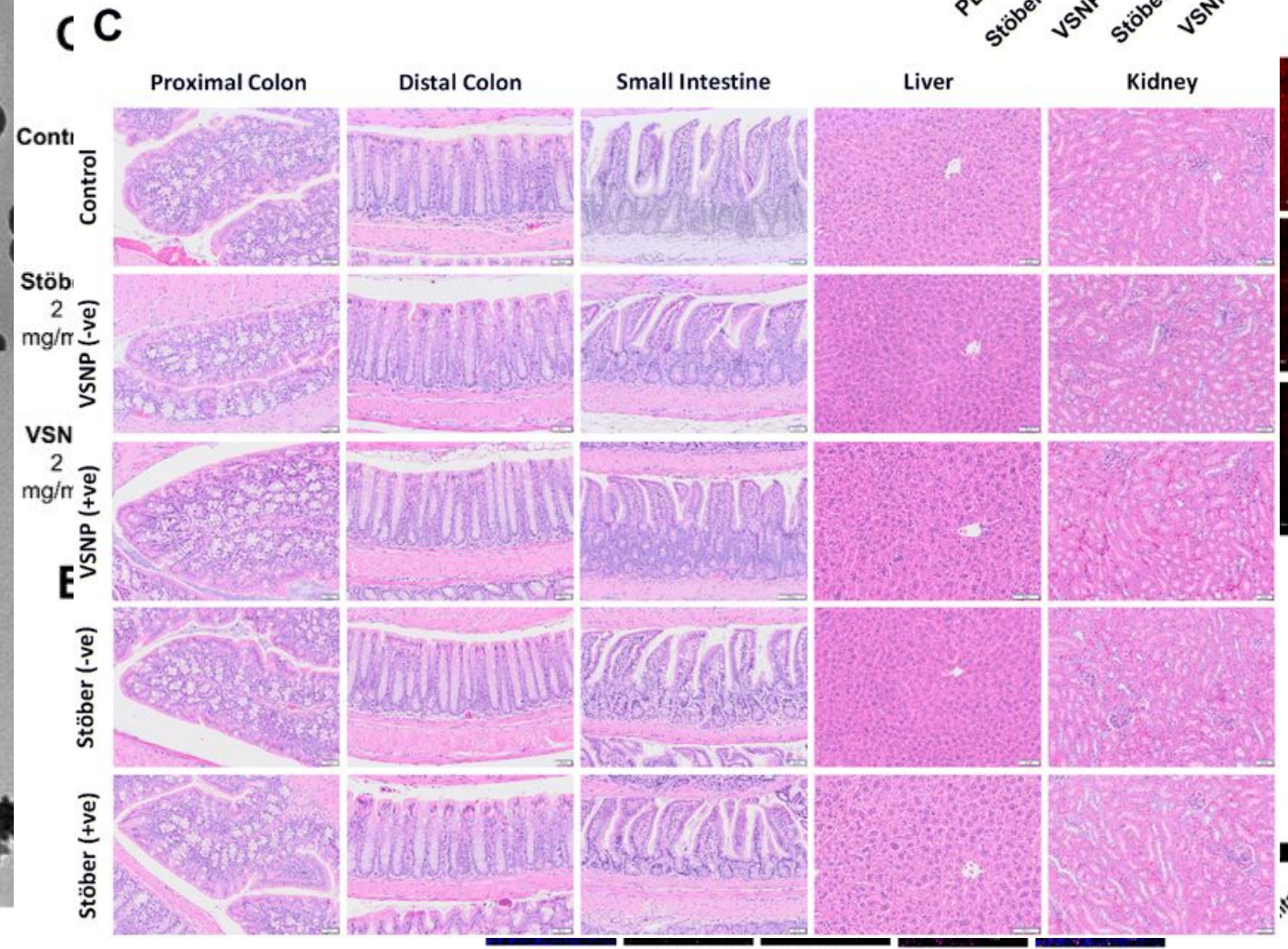


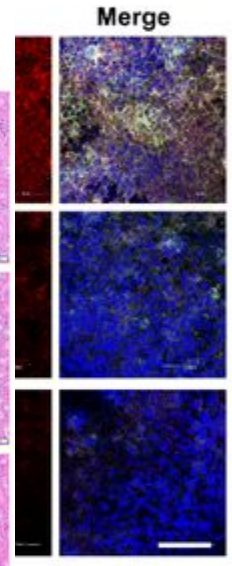
Biomodul

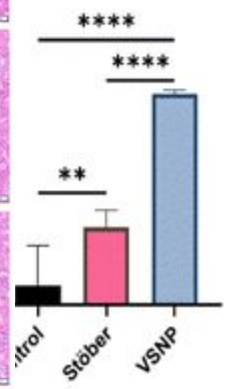

A
C

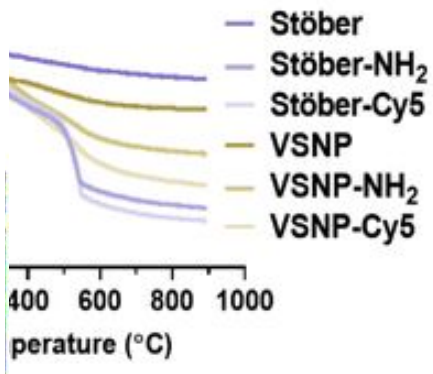

A
Silica nanoparticles (OG)
FITC-Dextran (OG)
Detect FITC signal in blood serum
10h fast
2h
3h

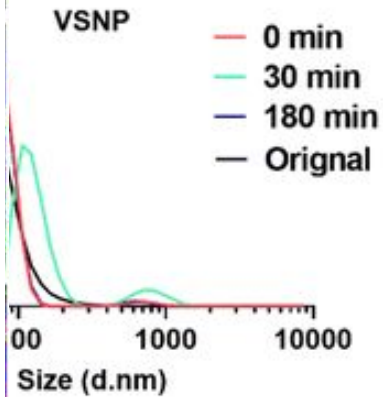

B
Blood FITC-DX4 (μg ml⁻¹)
15
10
5
0
**
*
PBS
Stöber +
VSNP +
Stöber -
VSNP -
Control
VSNP
Stöber
18
24


C
Proximal Colon
Distal Colon
Small Intestine
Liver
Kidney
Control
VSNP (-ve)
VSNP (+ve)
Stöber (-ve)
Stöber (+ve)


Merge


****
****
**
Stöber
VSNP


Stöber
Stöber-NH2
Stöber-Cy5
VSNP
VSNP-NH2
VSNP-Cy5
400
600
800
1000
perature (°C)


VSNP
0 min
30 min
180 min
Orignal
00
1000
10000
Size (d.nm)

pSi based Oral Protein Delivery

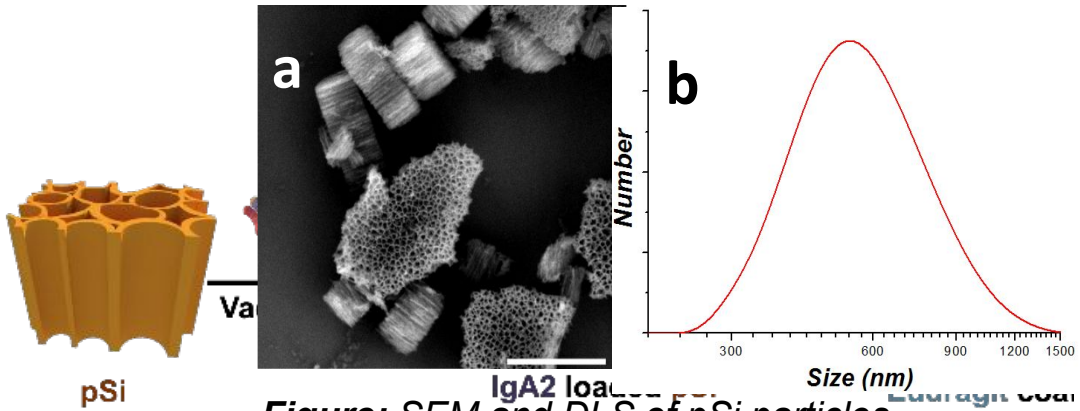


Figure: *SEM and DLS of pSi particles*

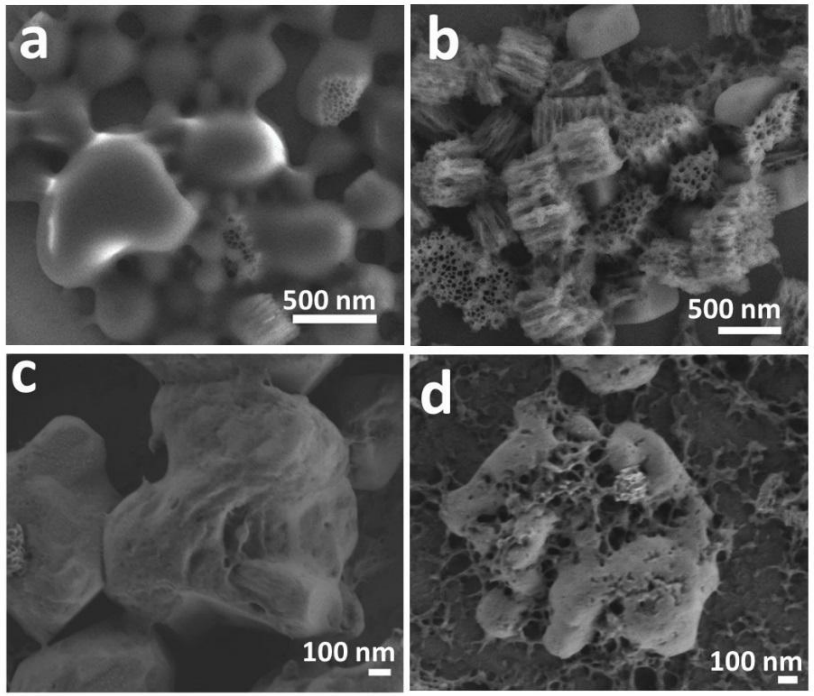


Figure: *SEM images of Eudragit coated pSi formulations*

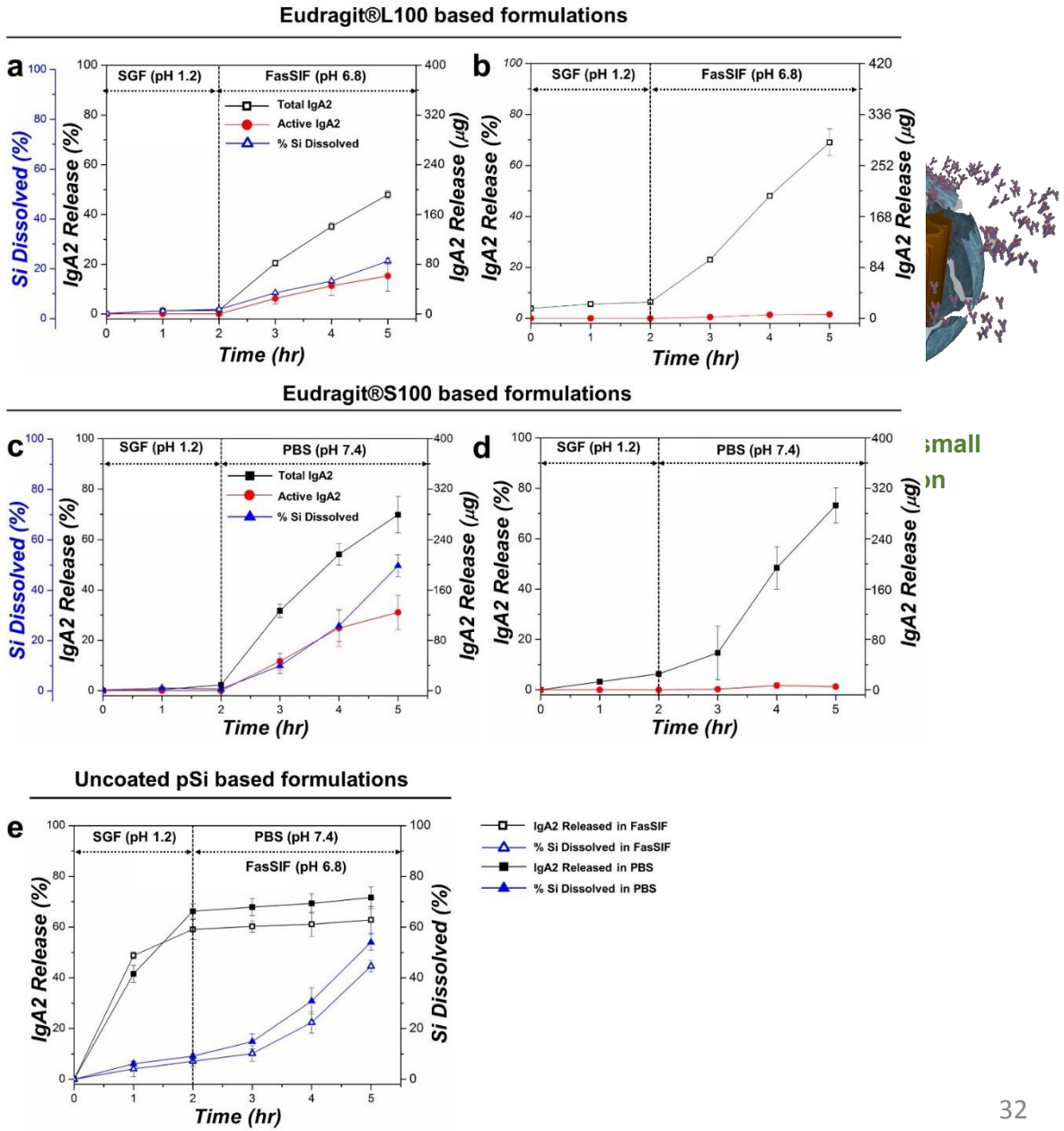
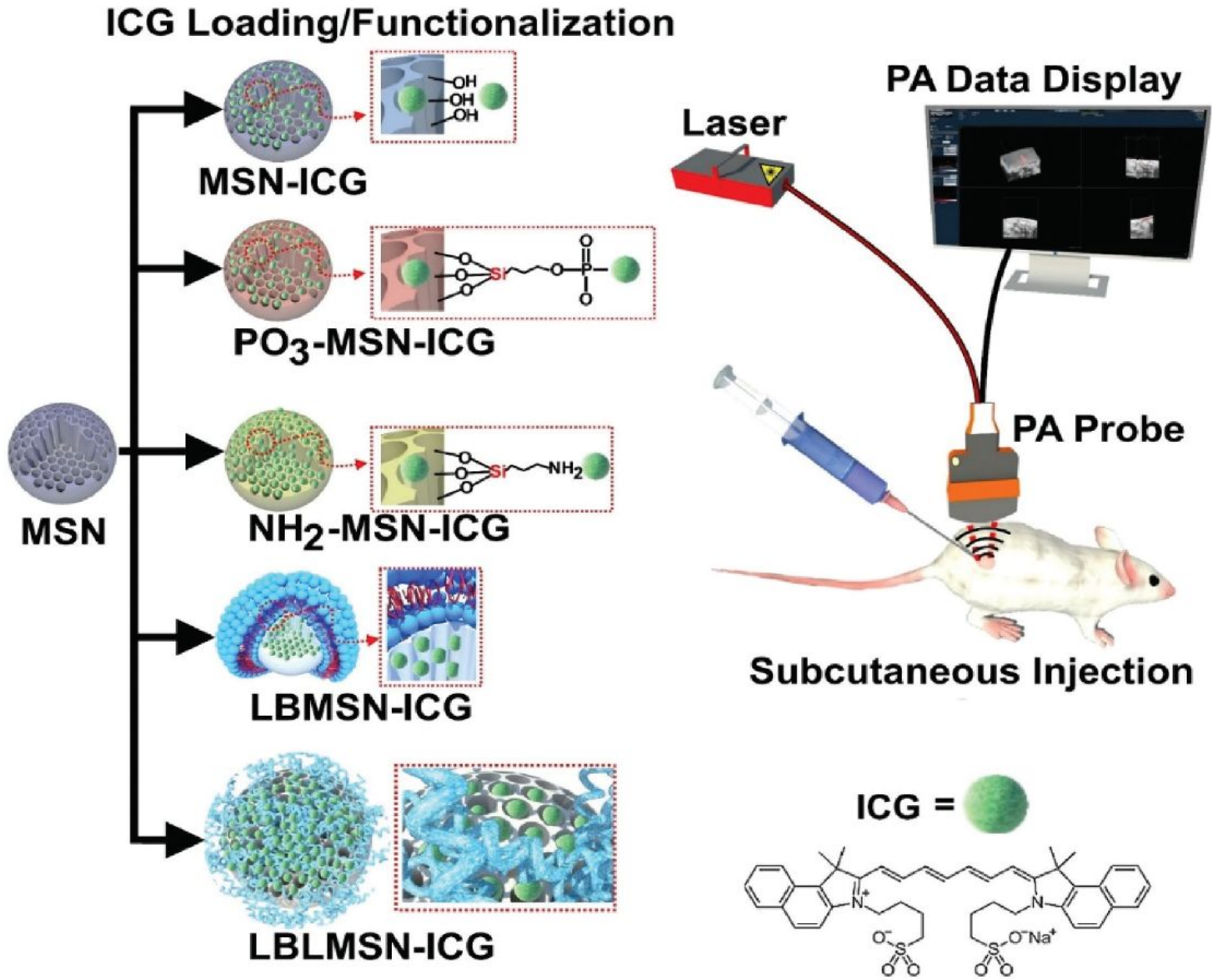
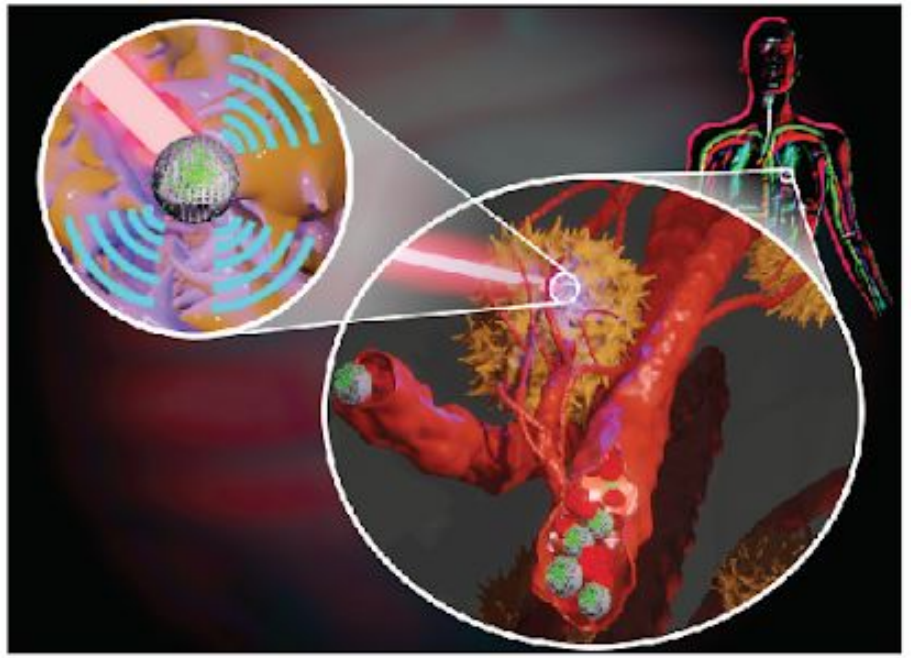


Figure: *In-vitro release of IgA2 from pSi-Eudragit formulations*

Kumeria, 2020, ACS Biomaterials Science and Engineering

ICG/Functionalized MSN for PA imaging





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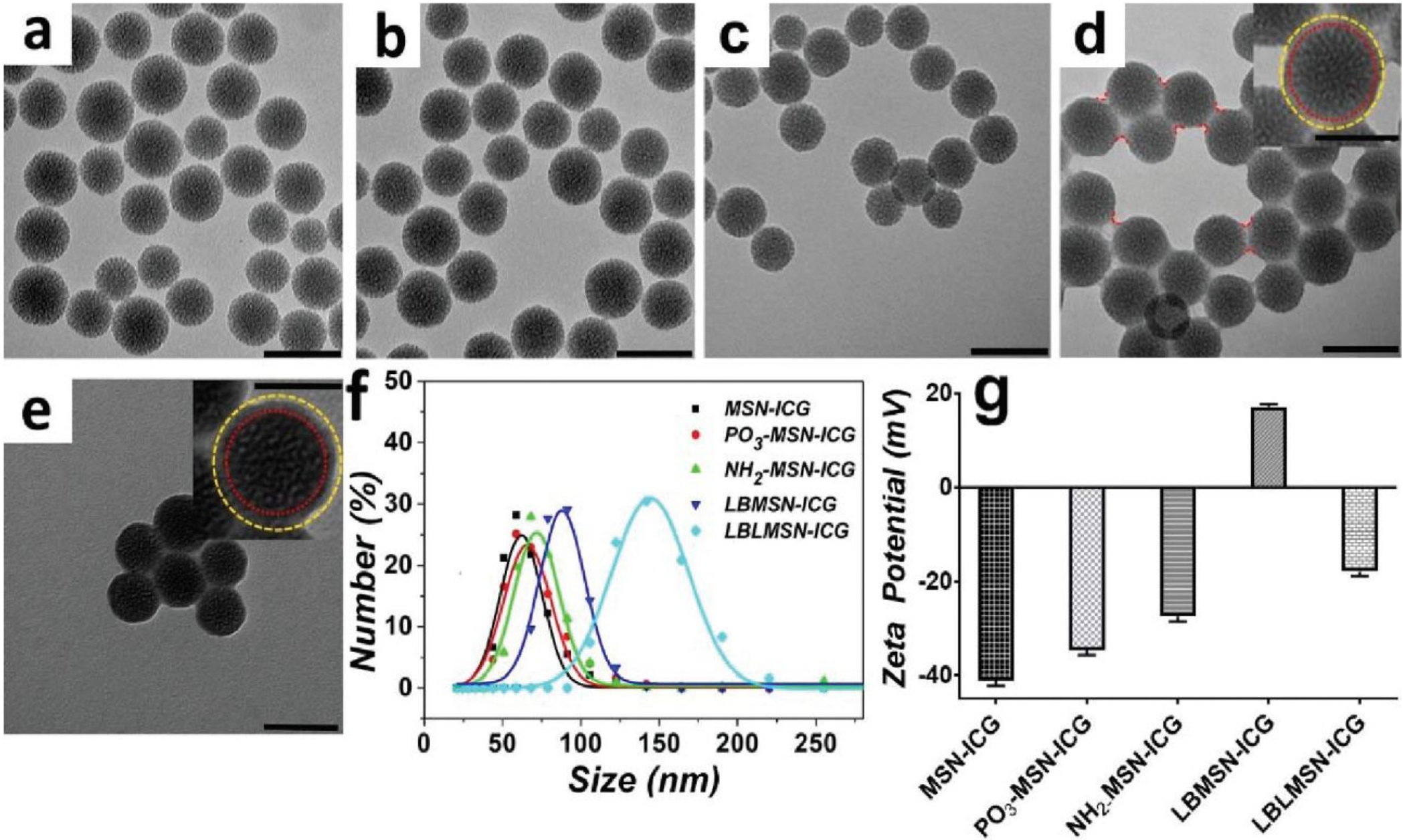
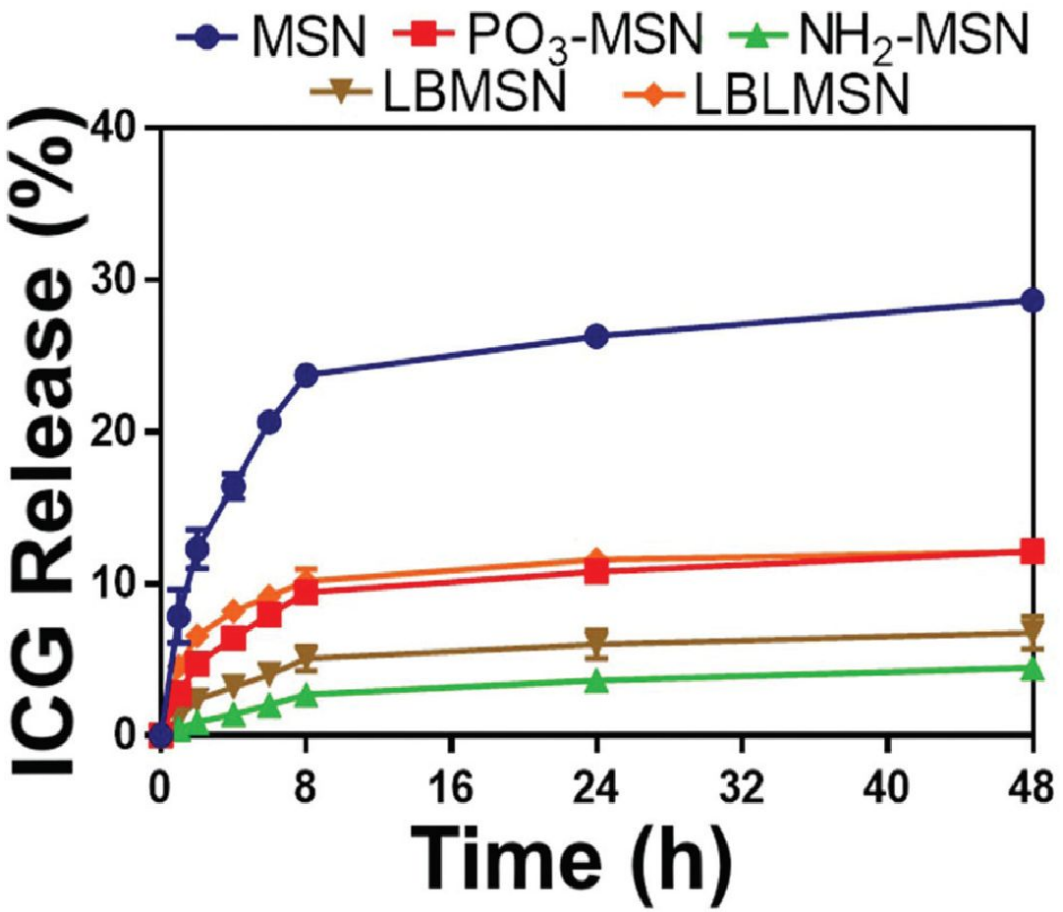
Chaudhary… Kumeria, Biomaterials Science, 2019

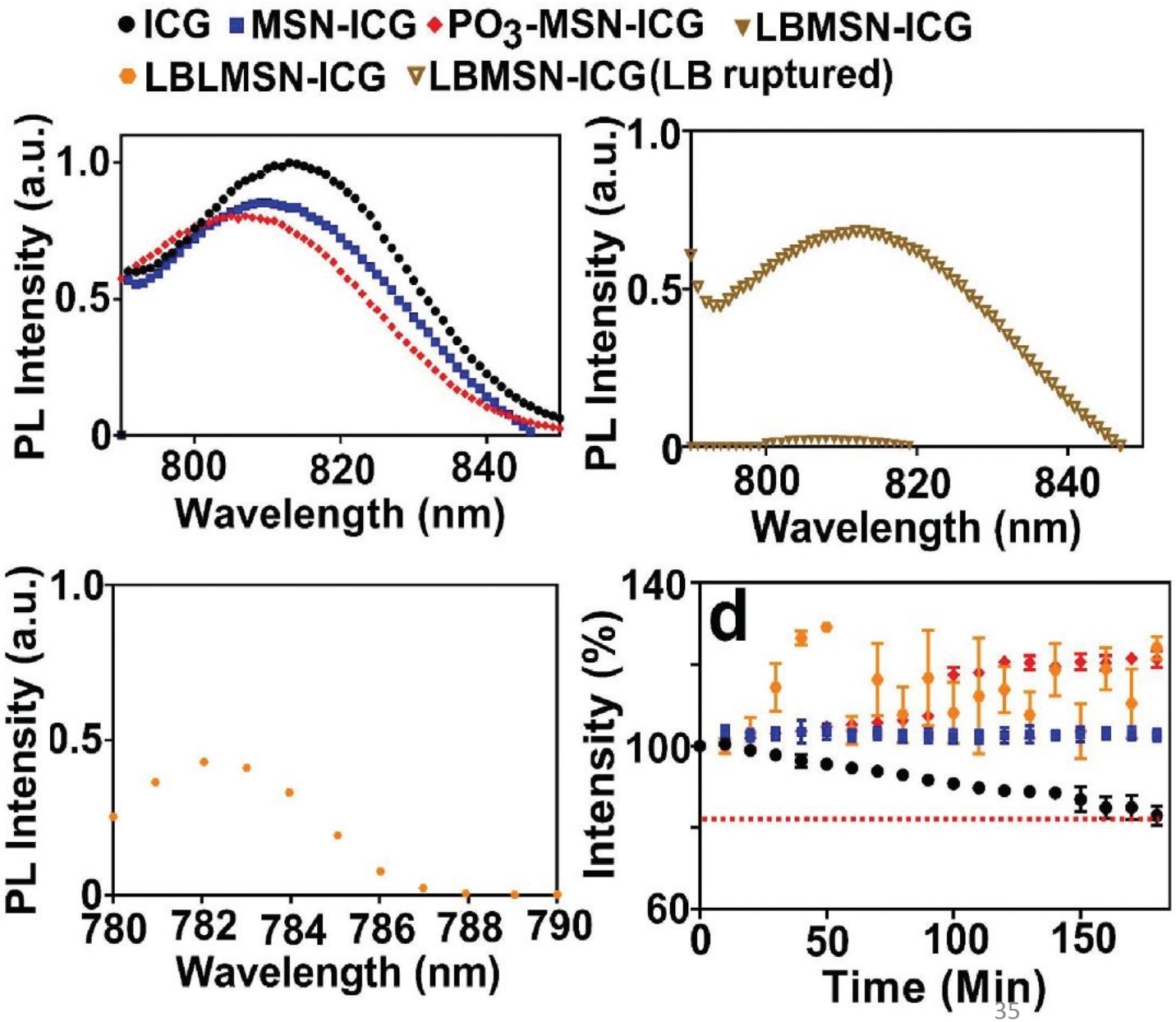
Functionalization of MSN



Chaudhary et. al, Biomaterials Science, 2019

Release and Degradation of ICG





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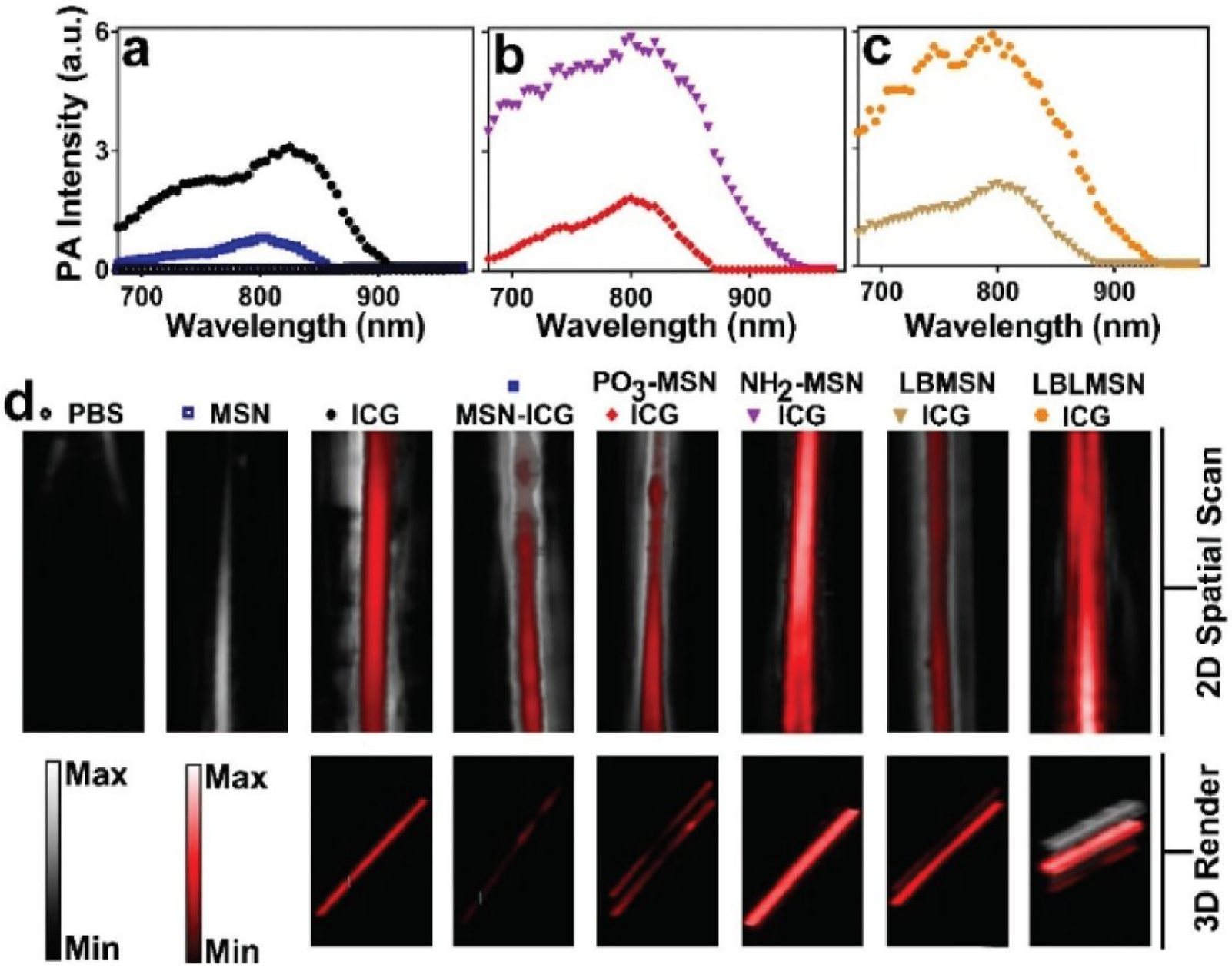
In-vitro PA imaging



The in vitro PA signal enhancement for the ICG loaded **unmodified MSNs, PO3-MSNs, and LBMSNs was close to 2.5-fold,** while almost **4-fold PA signal enhancement was observed for NH2-MSNs and LBLMSN** (at 200 µg mL−1 equivalent ICG dose), relative to pure ICG.

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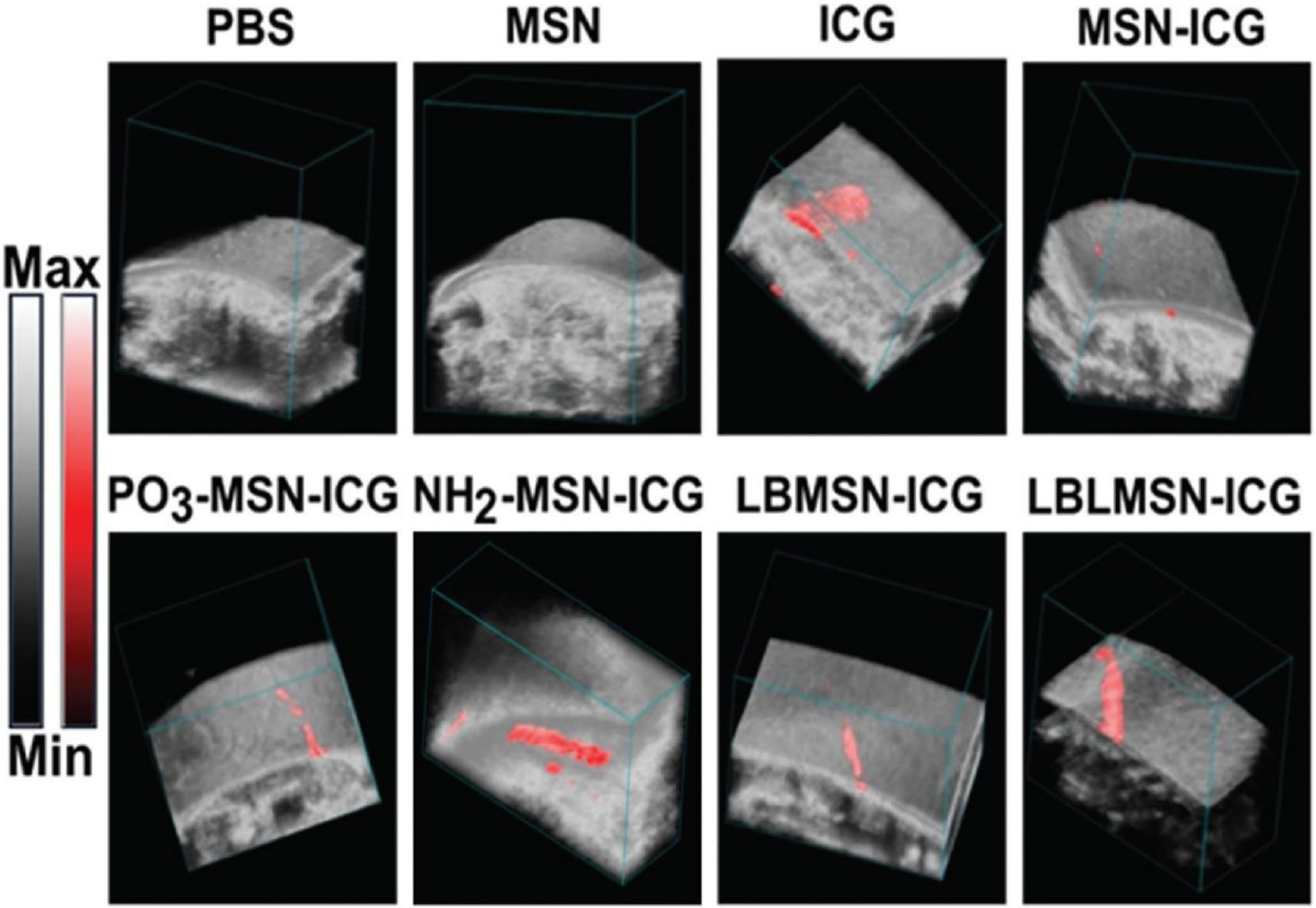
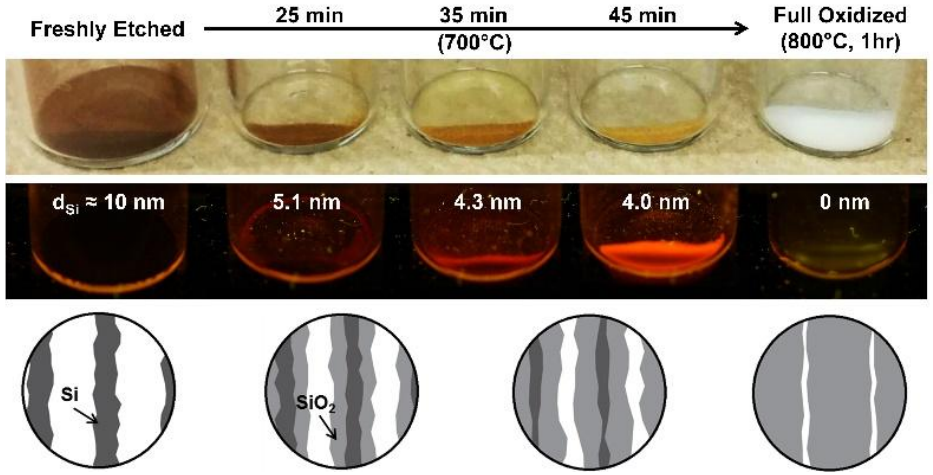
PA imaging after bolus injection

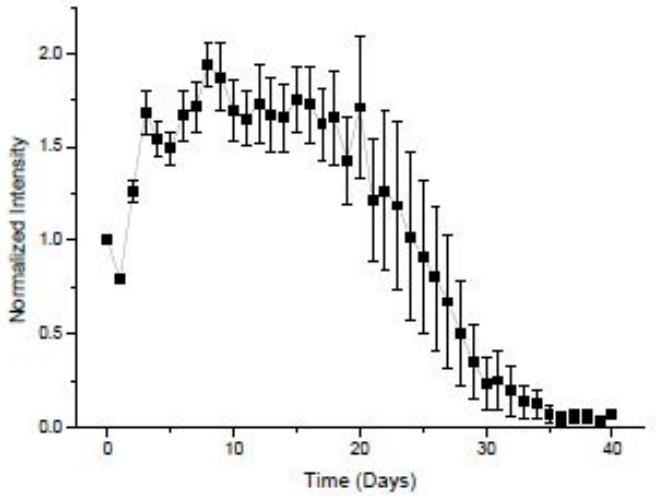


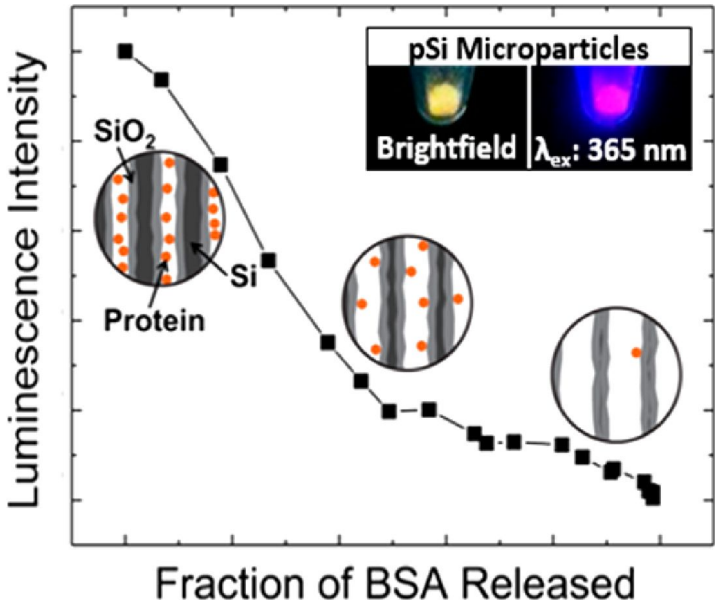
The **NH2- MSNs displayed an enhancement of 1.29-fold** compared to the same equivalent dose of pure ICG, whereas the highest PA bioimaging signal enhancement in subcutaneously injected mouse cadavers of **1.43-fold was observed for LBL modified MSNs** in comparison to pure ICG

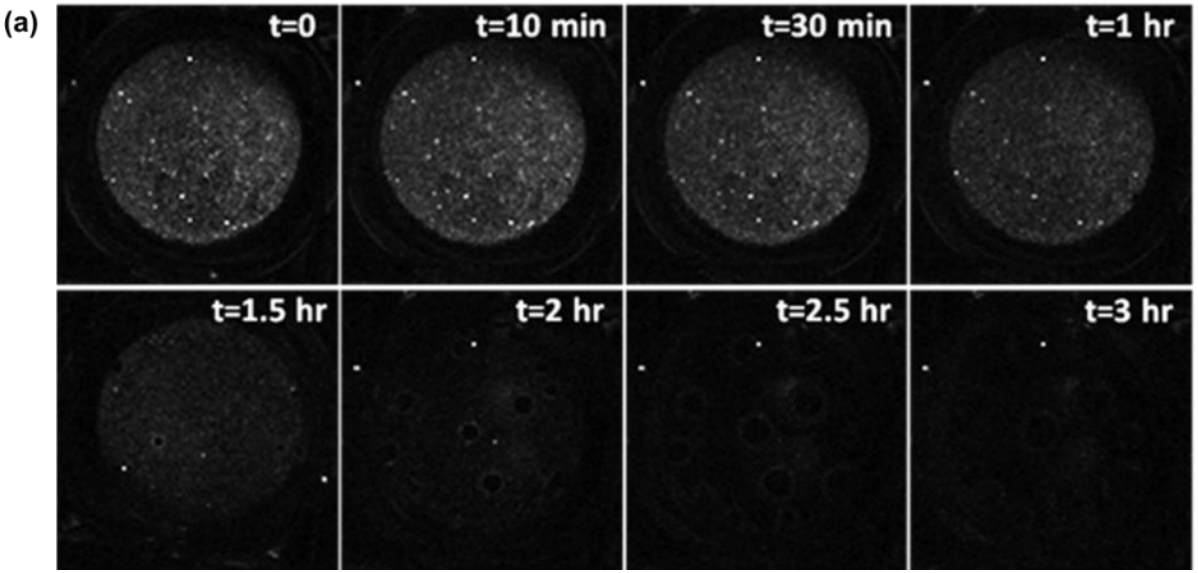
Chaudhary et. al, Biomaterials Science, 2019

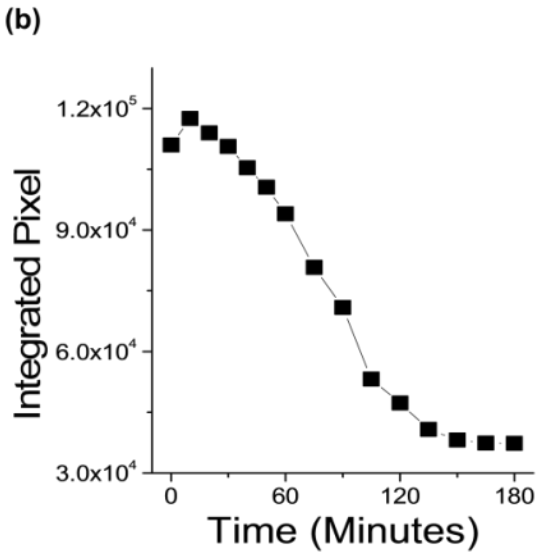
Self-reporting Ophthalmic Protein Delivery

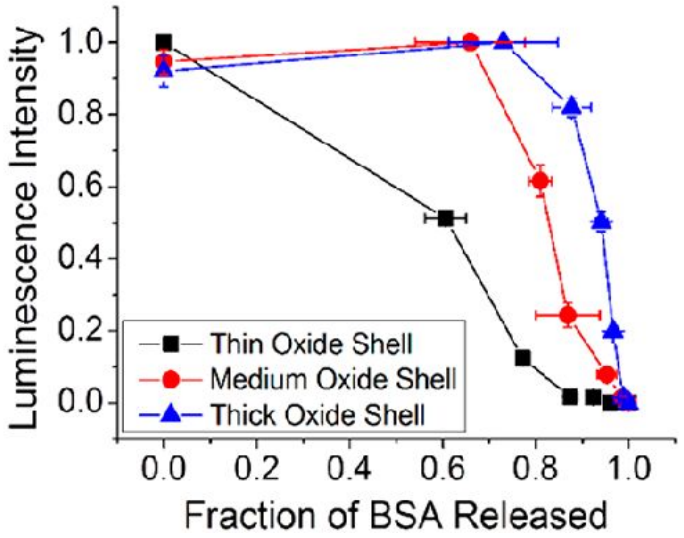












Wang, Kumeria….. ACS Applied Materials and Interfaces, 2018

Self-reporting Ophthalmic Drug Delivery

Luminescent pSi in vivo