Mesoporous Silica Nanoparticles

as Complex Bioactive Delivery Vehicles

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Characteristics of **meso**porous materials

Material (IUPAC notation)	Pore Size
microporous	<2nm
mesoporous	2-50 nm
macroporous	>50nm

- high surface area (over 1000 m^2/g)
- large pore volumes
- sharp pore size distributions
- stable compositions (chemically and thermally)
- Properties that can be designed and modified—particle size, particle shape, and surface functionalization

Published in Garcia-Bennett *Nanomedicine* **2011** 6 (5): 867-877

Abridged History of Mesoporous Silica Nanoparticles (MSNs)

"Process for producing silica in the form of hollow spheres"; Application No. US 342525 A filed on 04-Feb-1964; Publication No. US 3383172 A published on 14-May-1968

"Porous silica particles containing a crystallized phase and method" Application No. US 3493341D A filed on 23-Jan-1967; Publication No. US 3493341 A published on 03-Feb-1970

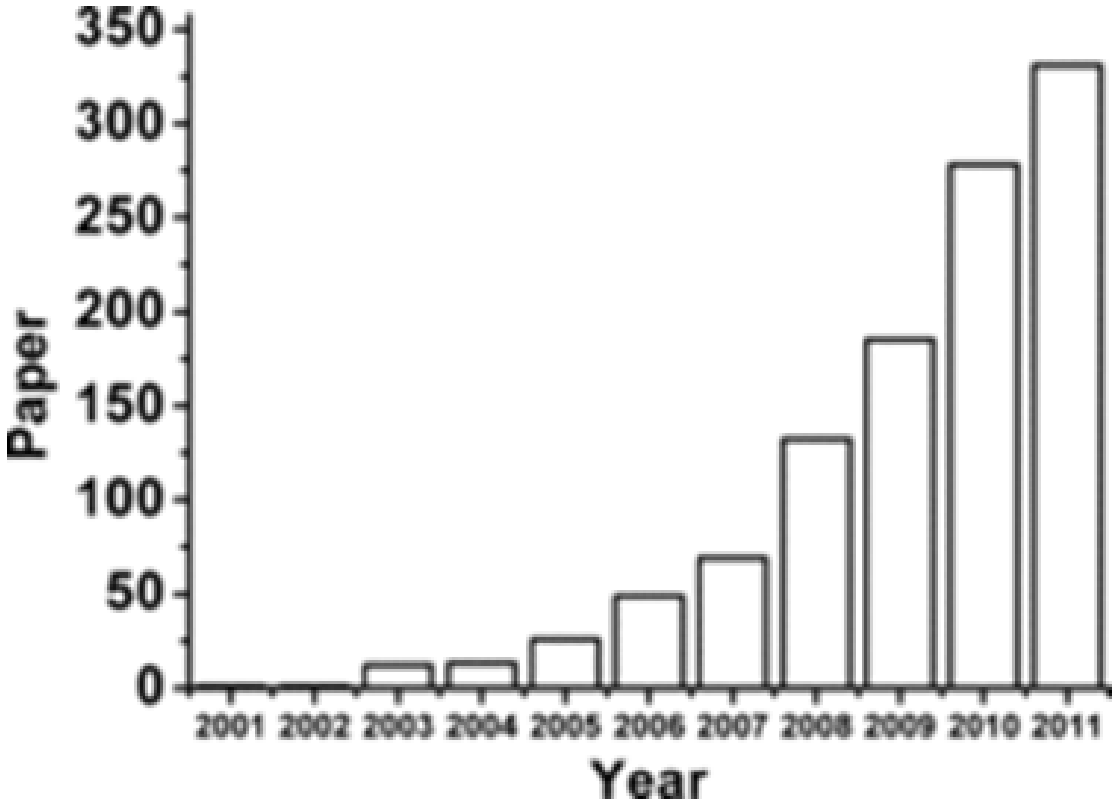
Chiola, V.; Ritsko, J. E. and Vanderpool, C. D. "Process for producing low-bulk density silica." Application No. US 3556725D A filed on 26-Feb-1969; Publication No. US 3556725 A published on 19-Jan-1971

1992 J.S. Beck et al *J Am Chem Soc*
MCM-41
(Mobil Crystalline Materials)

1998 D. Zhao et al *Science*
SBA-15
(Santa Barbara Amorphous)

MSNs—promise as drug deliverers

ISI web of science by the topic of "mesoporous silica" and "drug delivery"



Advanced Materials
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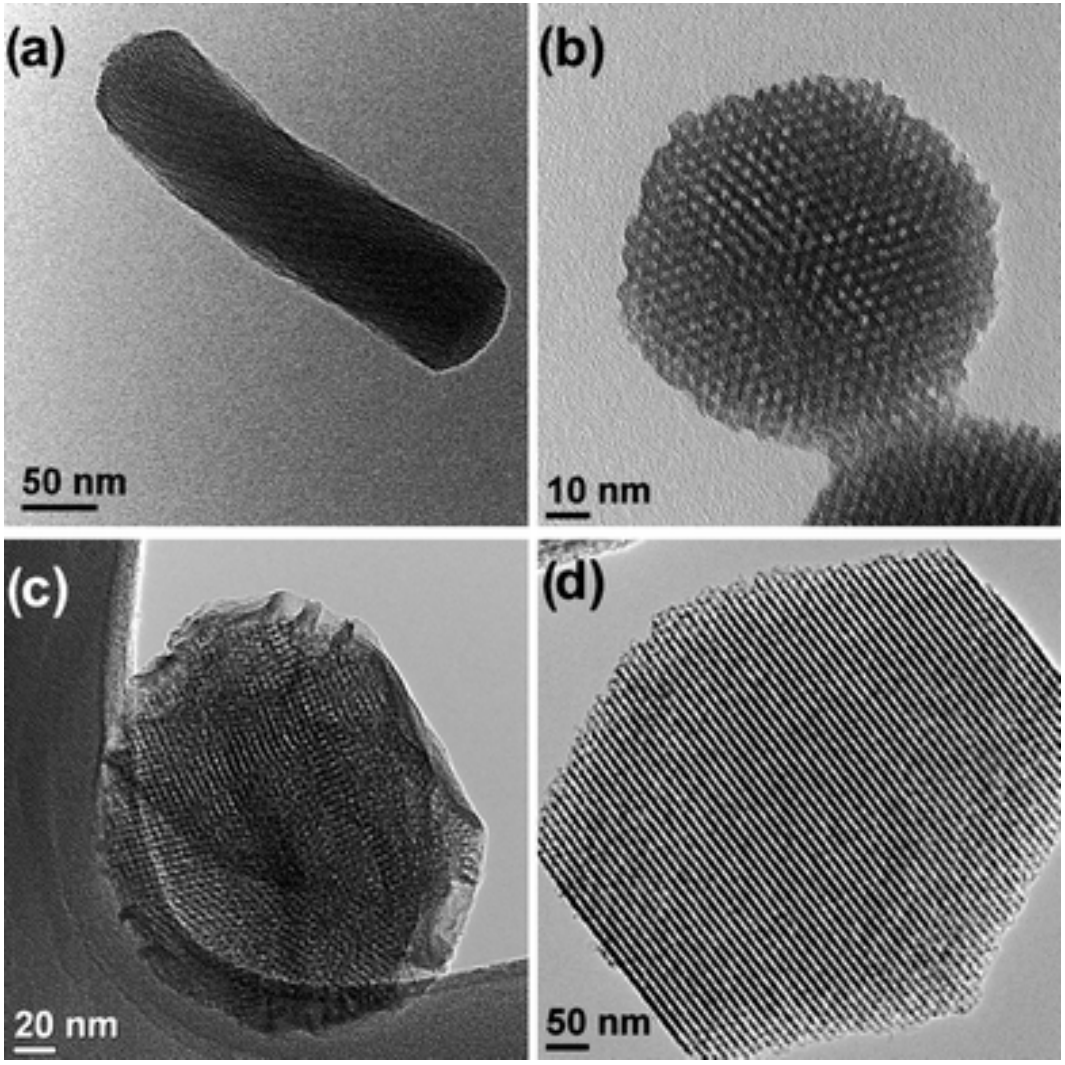
http://onlinelibrary.wiley.com/doi/10.1002/adma.201104763/full#fig1

Structural Variation of MSNs

rods with 3 nm wide helicoidal pores



spheres with 4 nm wide hexagonal pores

spheres with 3 nm wide cubic pores

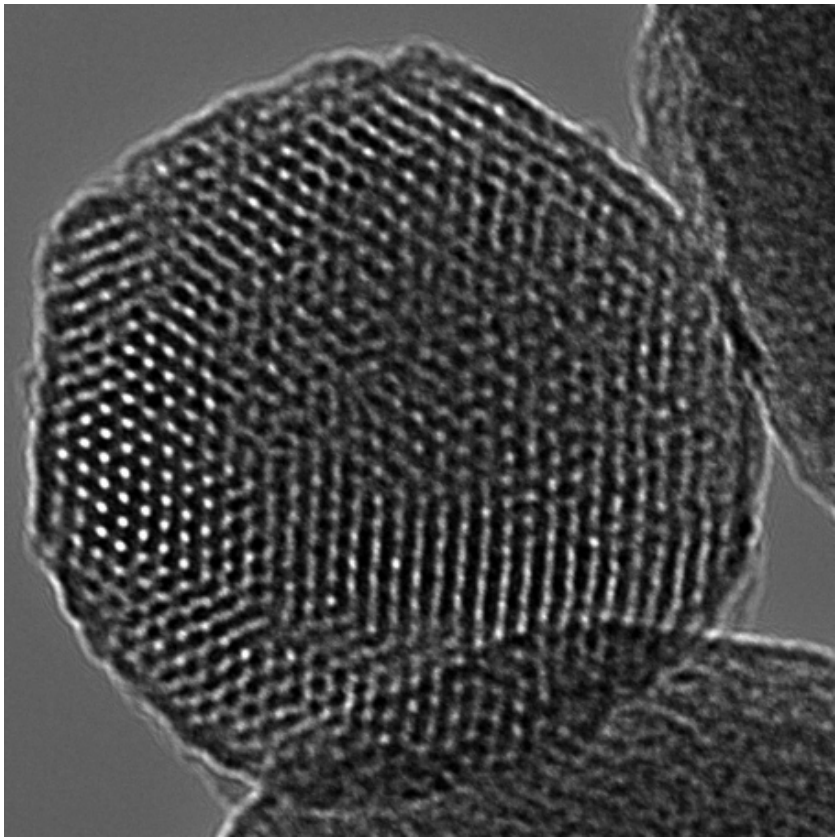
hexagonal plates with 10 nm wide hexagonal pores

Source: J. Mater. Chem., 2010, 20,7924-7937Igor I. Slowing, Juan L. Vivero-Escoto , Brian G. Trewyn , and Victor S.-Y. Lin; "Mesoporous silica nanoparticles : structural design and applications."

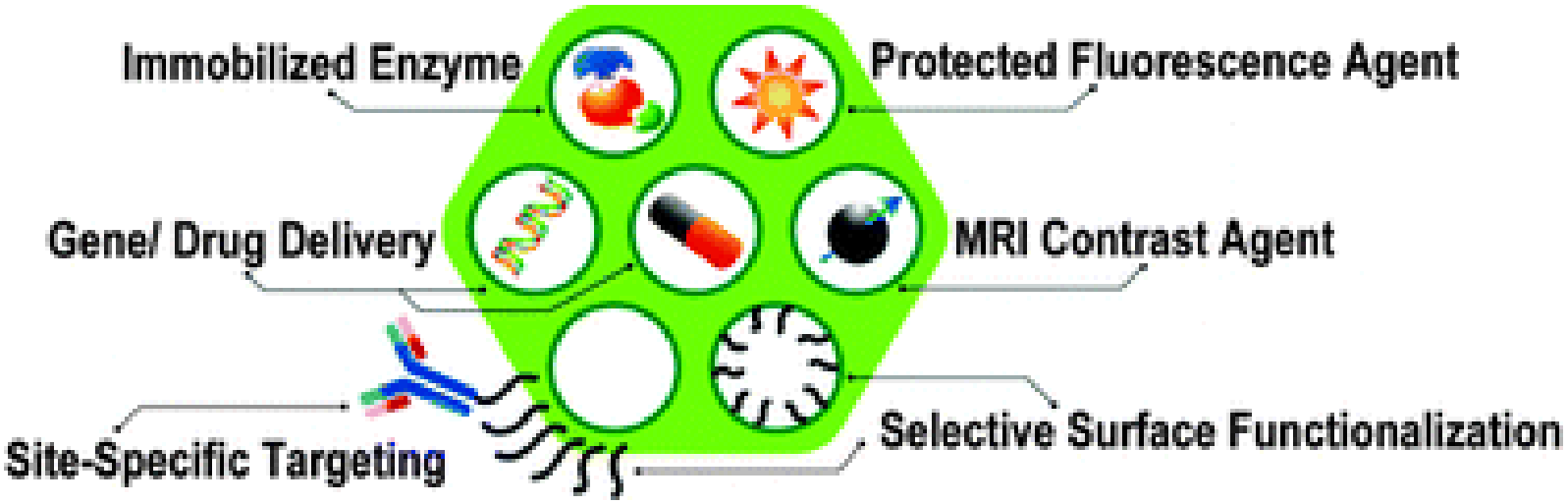
Mesoporous Silica Nanoparticles (MSNs) for Drug Delivery

Advantageous Functional Options

- Large payloads
- Multiple payloads
  - Diagnostic-Therapuetic
  - Drug A-Drug B
- Solubilization
- Targeting
- Triggering
- Mechanization

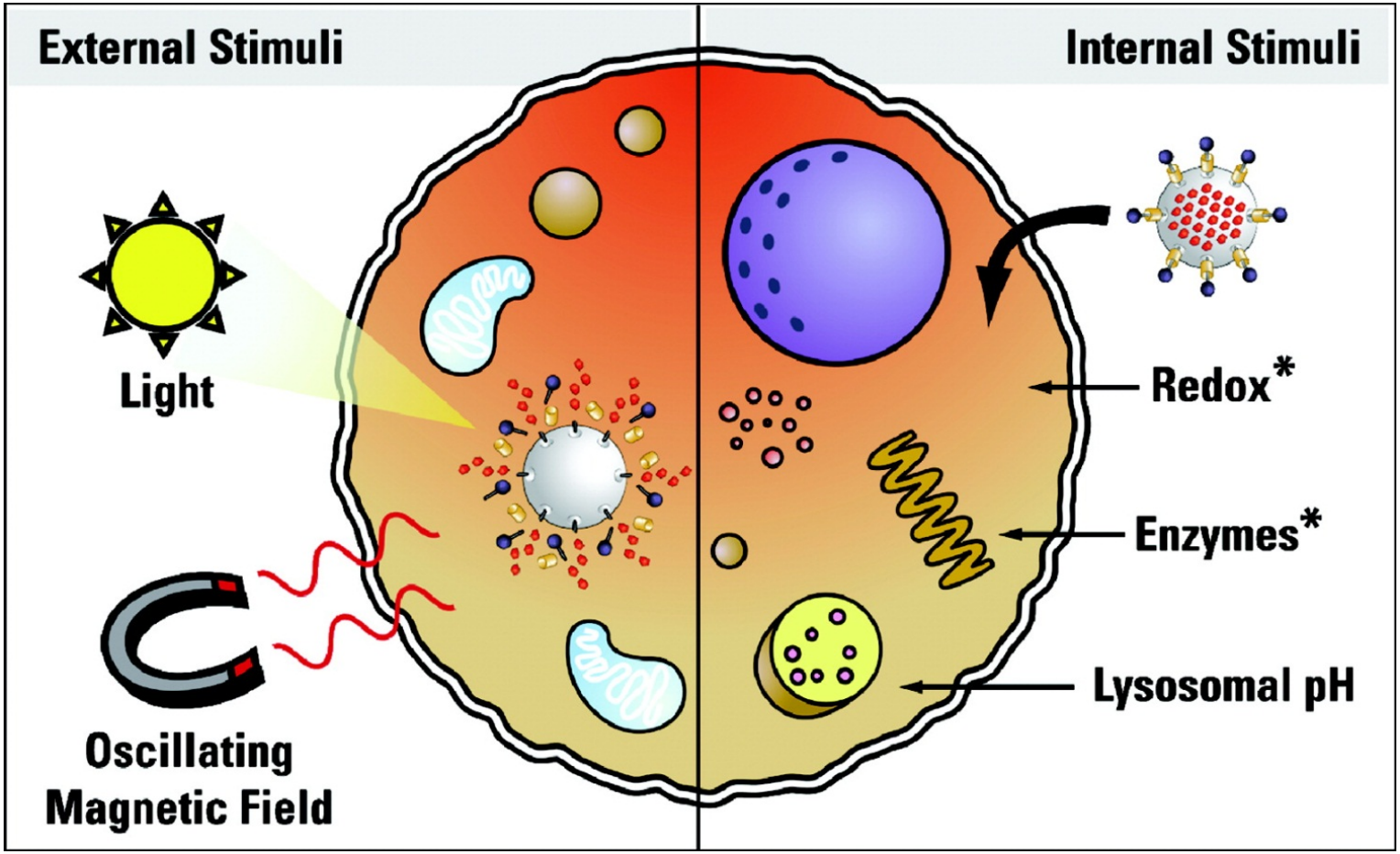


MSNs Carry Functional Cargo of Multiple Types



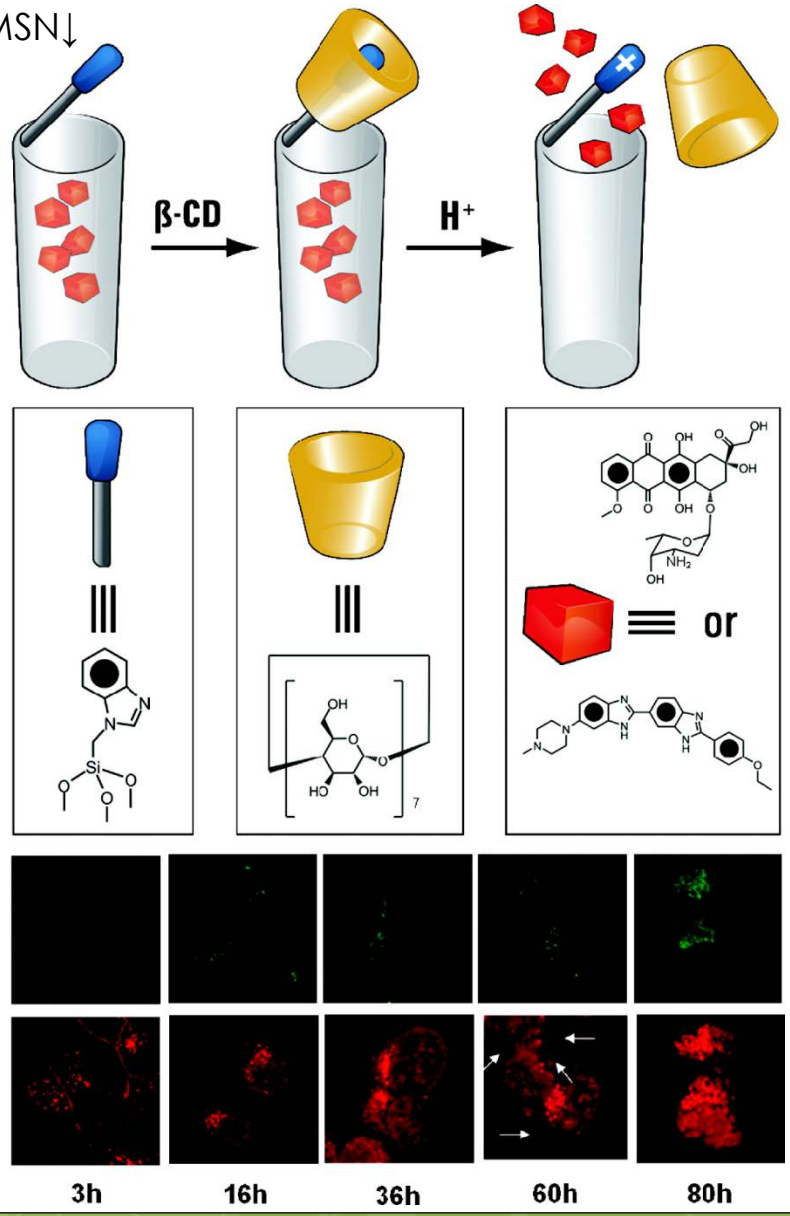
Source: Chem. Commun., 2011, 47,9972-9985
Si-Han Wu, Yann Hung, Chung-Yuan Mou; "Mesoporous silica nanoparticles as nanocarriers."

Controlled Cargo Release



Published in: Michael W. Ambrogio; Courtney R. Thomas; Yan-Li Zhao; Jeffrey I. Zink; J. Fraser Stoddart; *Acc. Chem. Res.* **2011.** 44, 903-913.

Benzimidazole on MSN↓

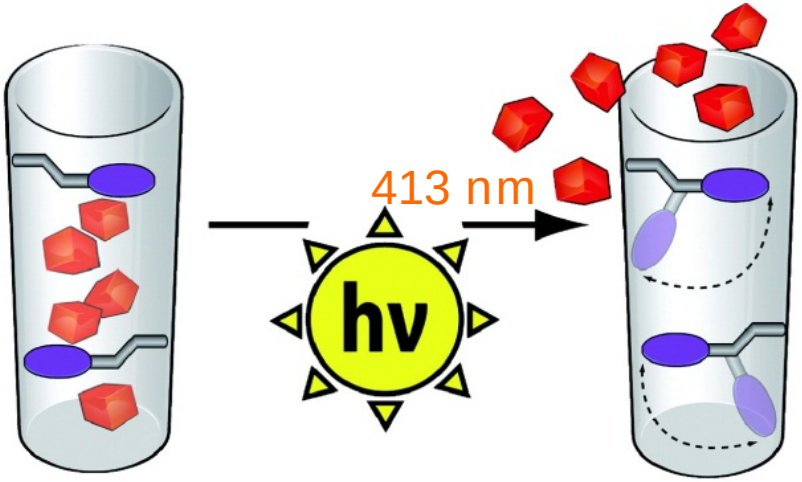


pH drops within lysosomal compartment of cells

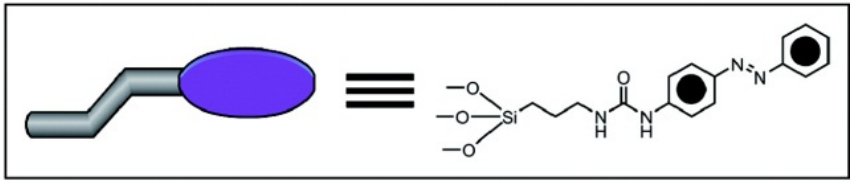
Release Controlled by pH

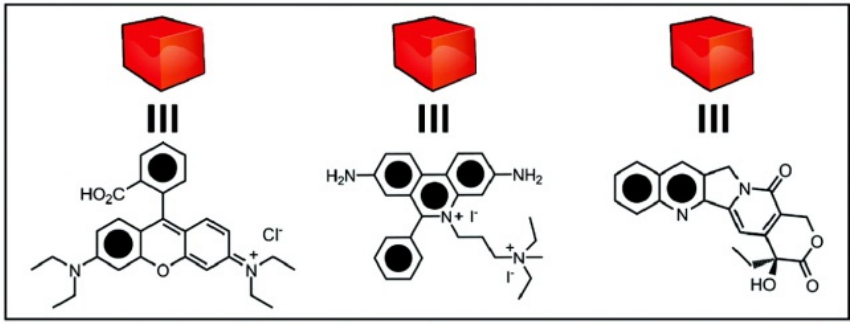
Cyclodextrin cap
Hoescht or Dox. cargo

Adapted from: Michael W. Ambrogio; Courtney R. Thomas; Yan-Li Zhao; Jeffrey I. Zink; J. Fraser Stoddart; *Acc. Chem. Res.* **2011,** 44, 903-913.Copyright © 2011 American Chemical Society



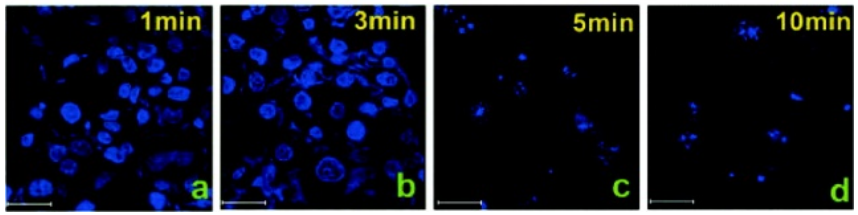
Nanoimpellers work by cis-trans isomerization of azobenzene





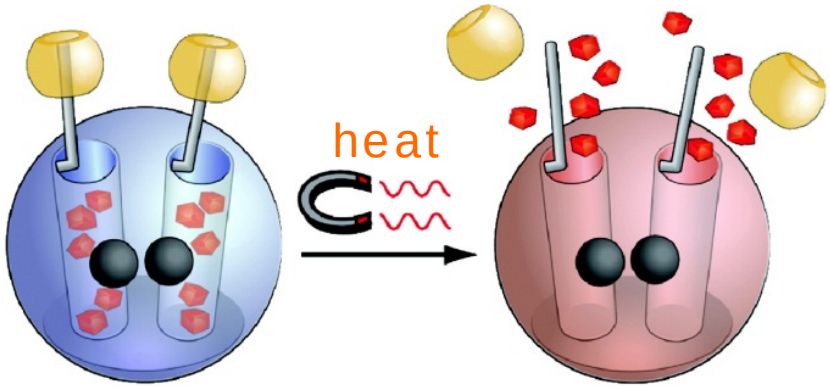
Campothecin (hydrophobic)

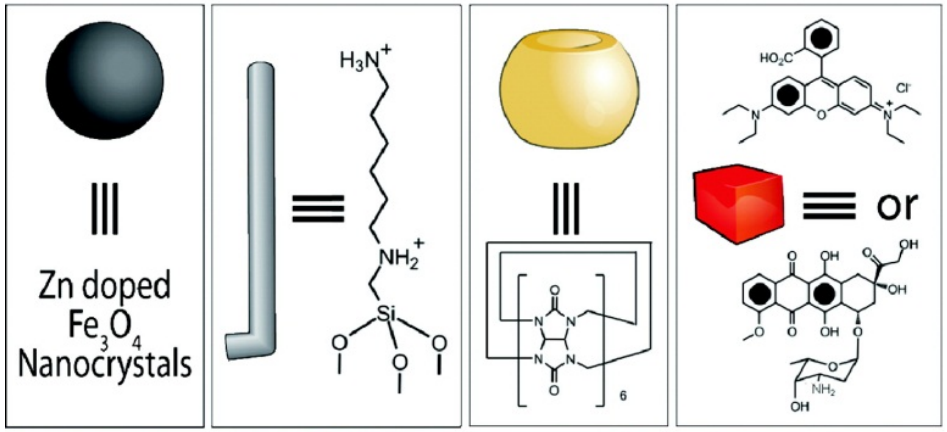
Release Controlled by Irradiation

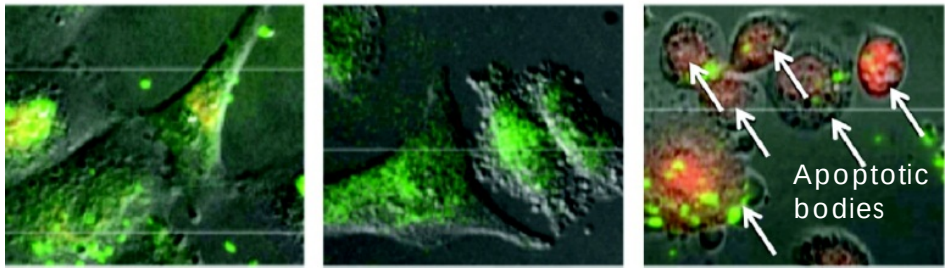


Adapted from: Michael W. Ambrogio; Courtney R. Thomas; Yan-Li Zhao; Jeffrey I. Zink; J. Fraser Stoddart; *Acc. Chem. Res.* **2011,** 44, 903-913.

Release Controlled by Oscillating Magnetic Field





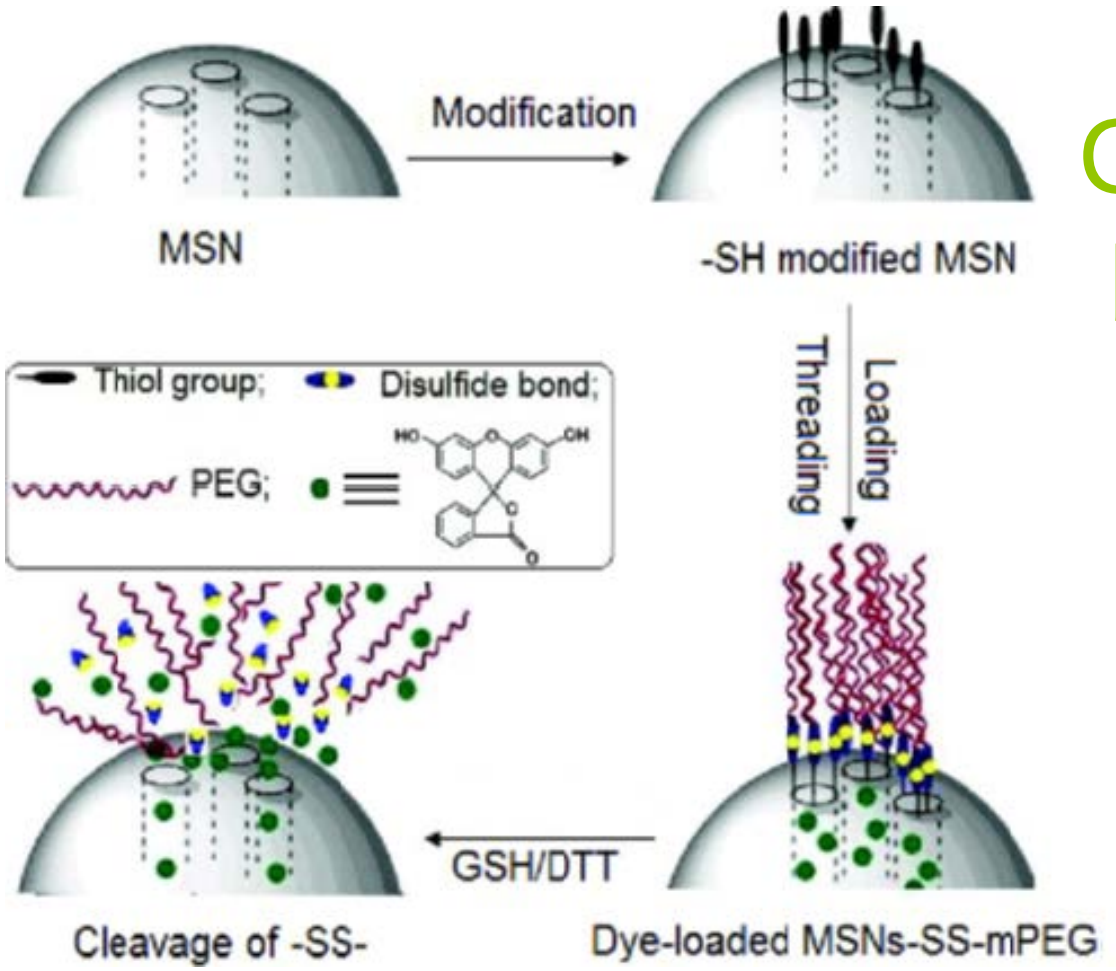


Cyclodextrin cap
Rhod. or Dox. cargo

37% cell death
w/Doxorubicin cargo

Adapted from: Michael W. Ambrogio; Courtney R. Thomas; Yan-Li Zhao; Jeffrey I. Zink; J. Fraser Stoddart; *Acc. Chem. Res.* **2011,** 44, 903-913.

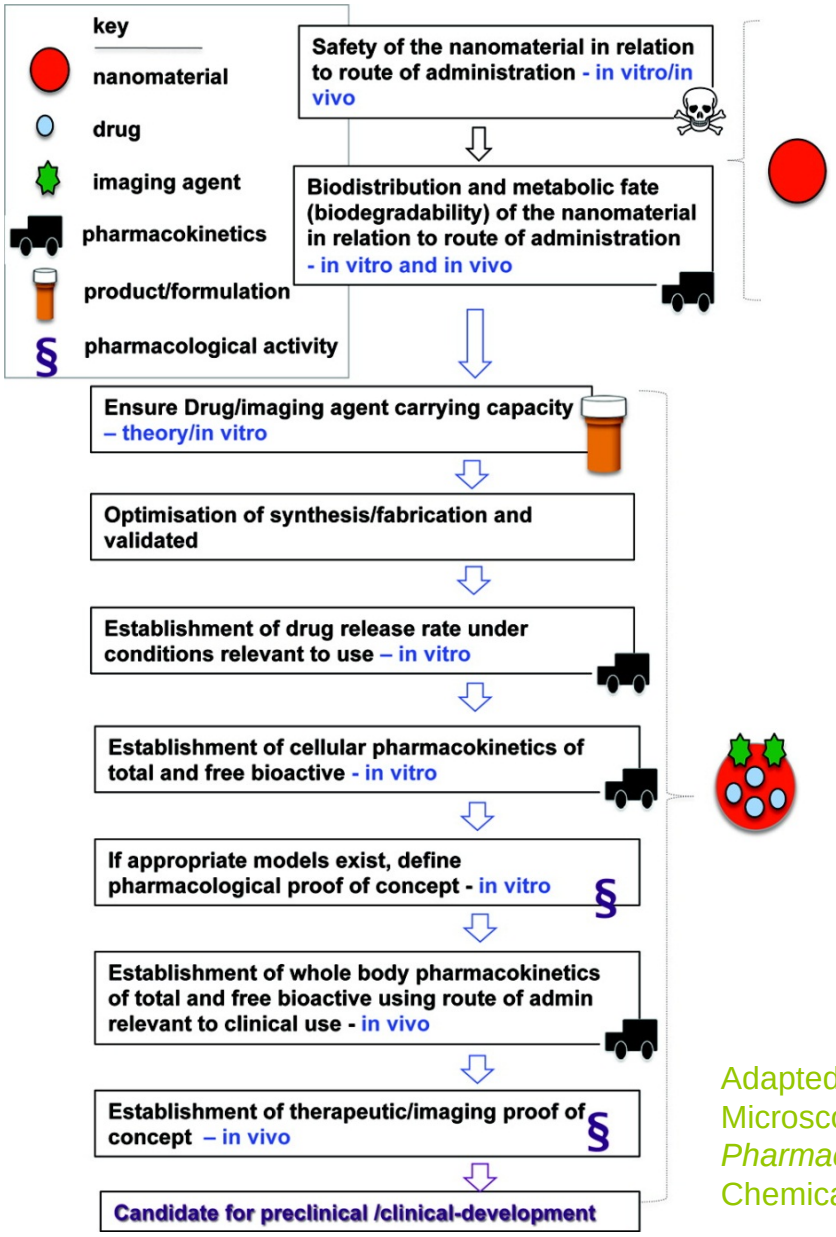
Release Controlled by Redox

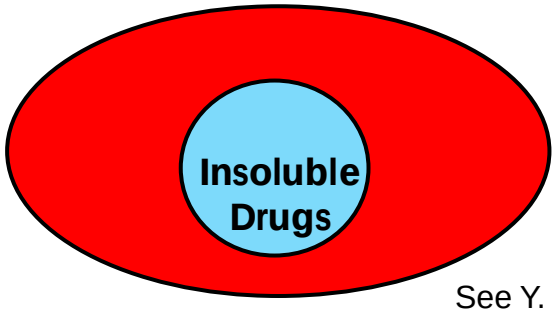


50% cell death w/Methotrexate cargo

Adapted from: Yanna Cui, Haiqing Dong, Xiaojun Cai, Deping Wang, and Yongyong Li; *ACS Appl. Mater. Interfaces*, Article ASAP online May 30 **2012,** 44, 903-913.Copyright © 2012 American Chemical Society

Stop and Go Checkpoints for Nanomedicine Design

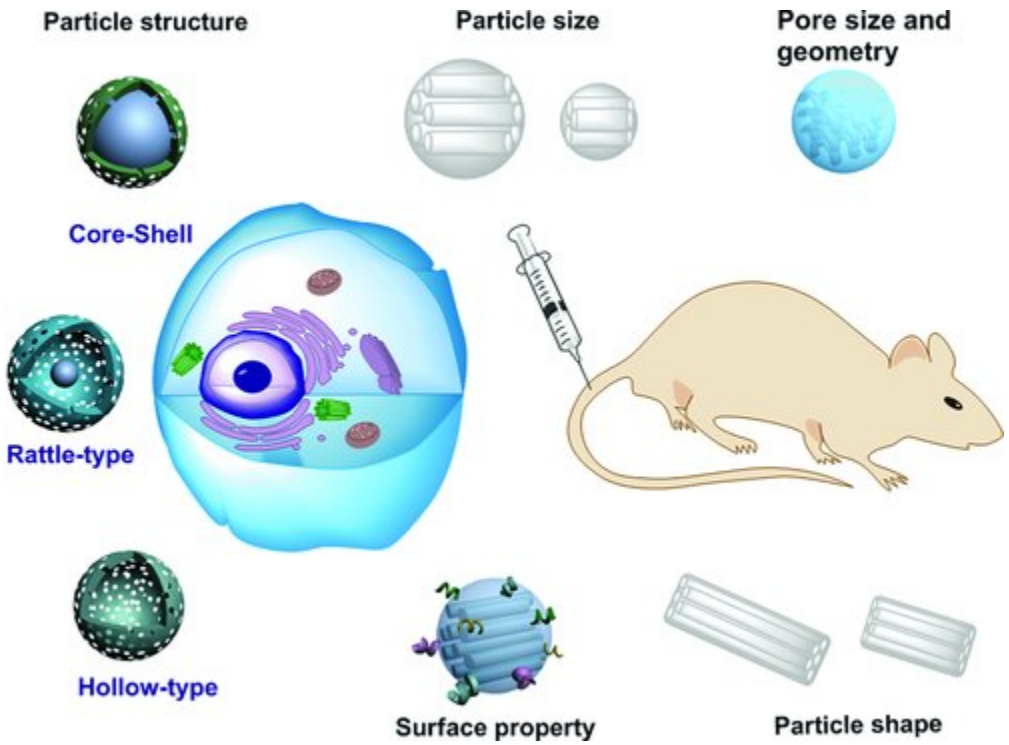




See Y. Hu et al, *Mesoporous and Microporous Materials* 147 (2012) 94-101 for example

Adapted with permission from "Nanomedicine(s) under the Microscope" by Ruth Duncan and Rogerio Gaspar; *Molecular Pharmaceutics* 2011 *8* (6), 2101-2141. Copyright ©2011 American Chemical Society.

Biocompatibility and Biotranslocation of MSNs

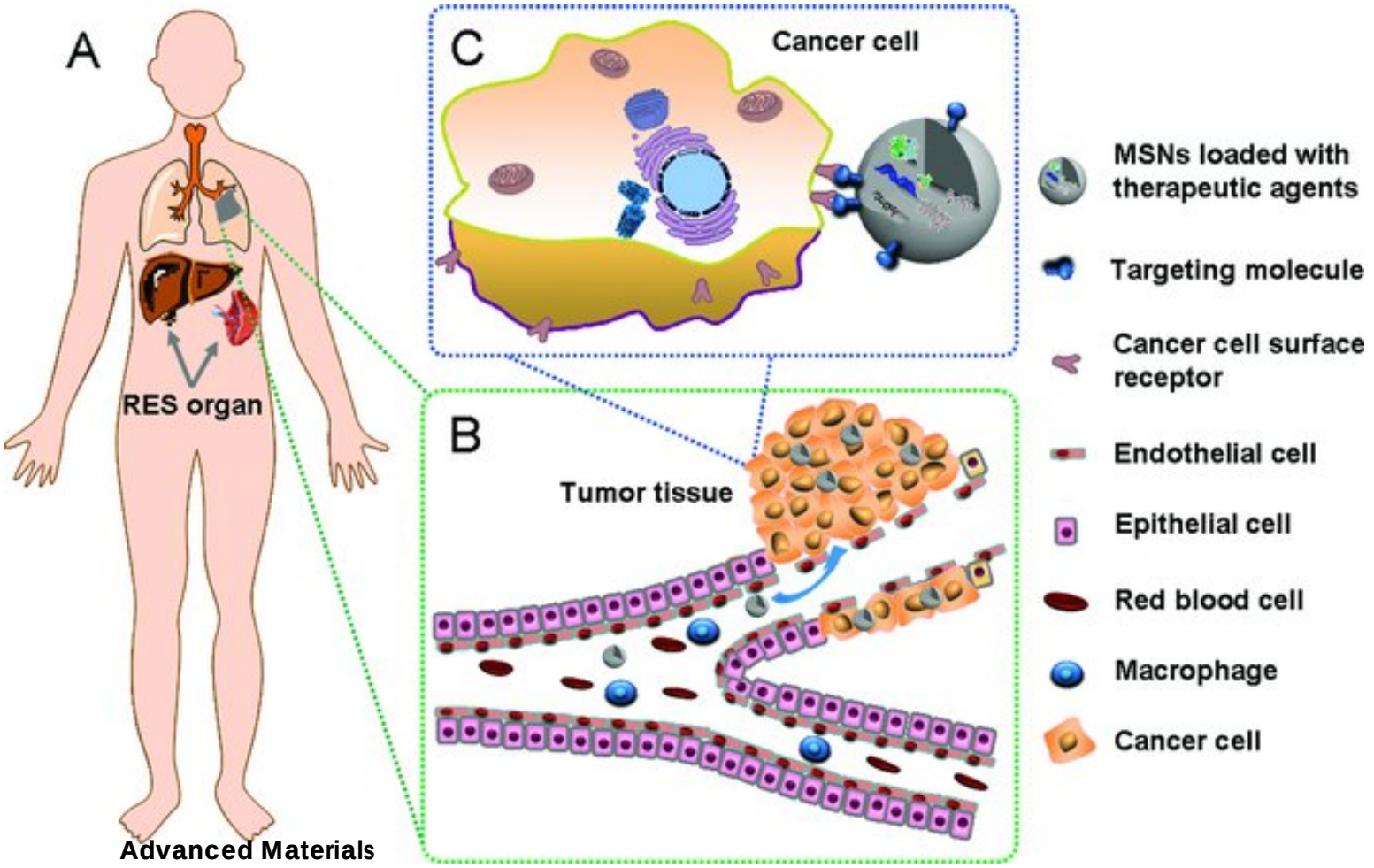


in vitro
cellular uptake, intracellular translocation and cytotoxicity

in vivo
biodistribution, biodegradation, excretion, and toxicity

Advanced Materials Volume 24, Issue 12, pages 1504-1534, 29 FEB 2012 DOI: 10.1002/adma.201104763
http://onlinelibrary.wiley.com/doi/10.1002/adma.201104763/full#fig15

Biolocalization of loaded MSNs



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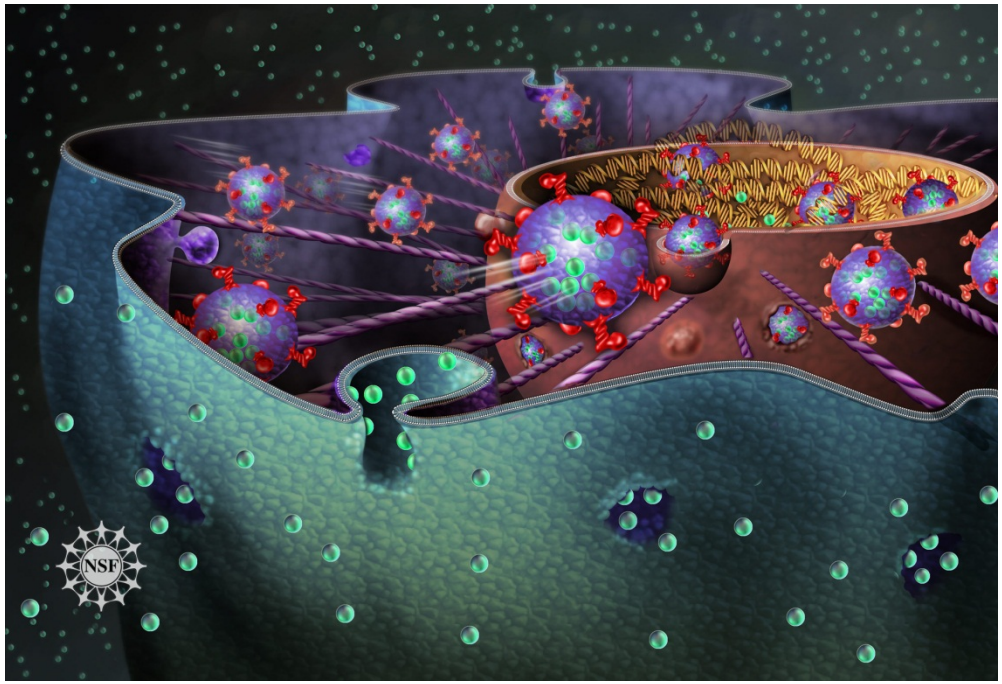
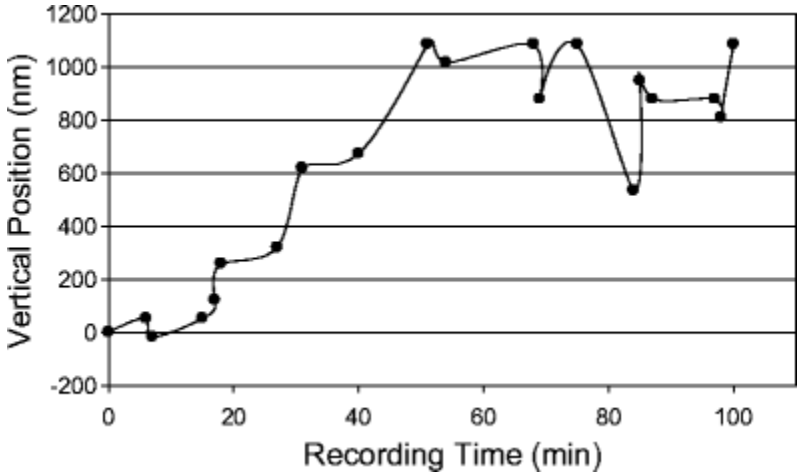
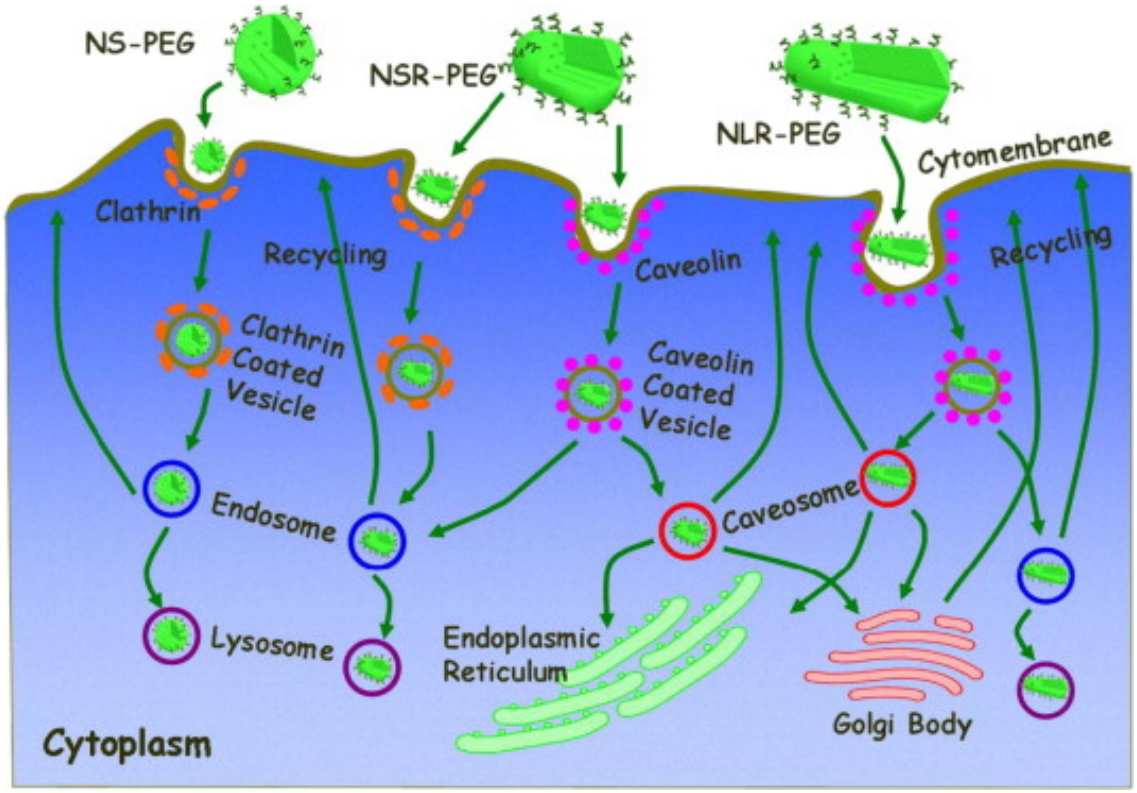


Endocytosis of MSNs

“Endocytosis of a single mesoporous silica nanoparticle into a human lung cancer cell observed by differential interference contrast microscopy” Wei Sun et al *Analytical and Bioanalytical Chemistry* (2008) 391:2119–2125

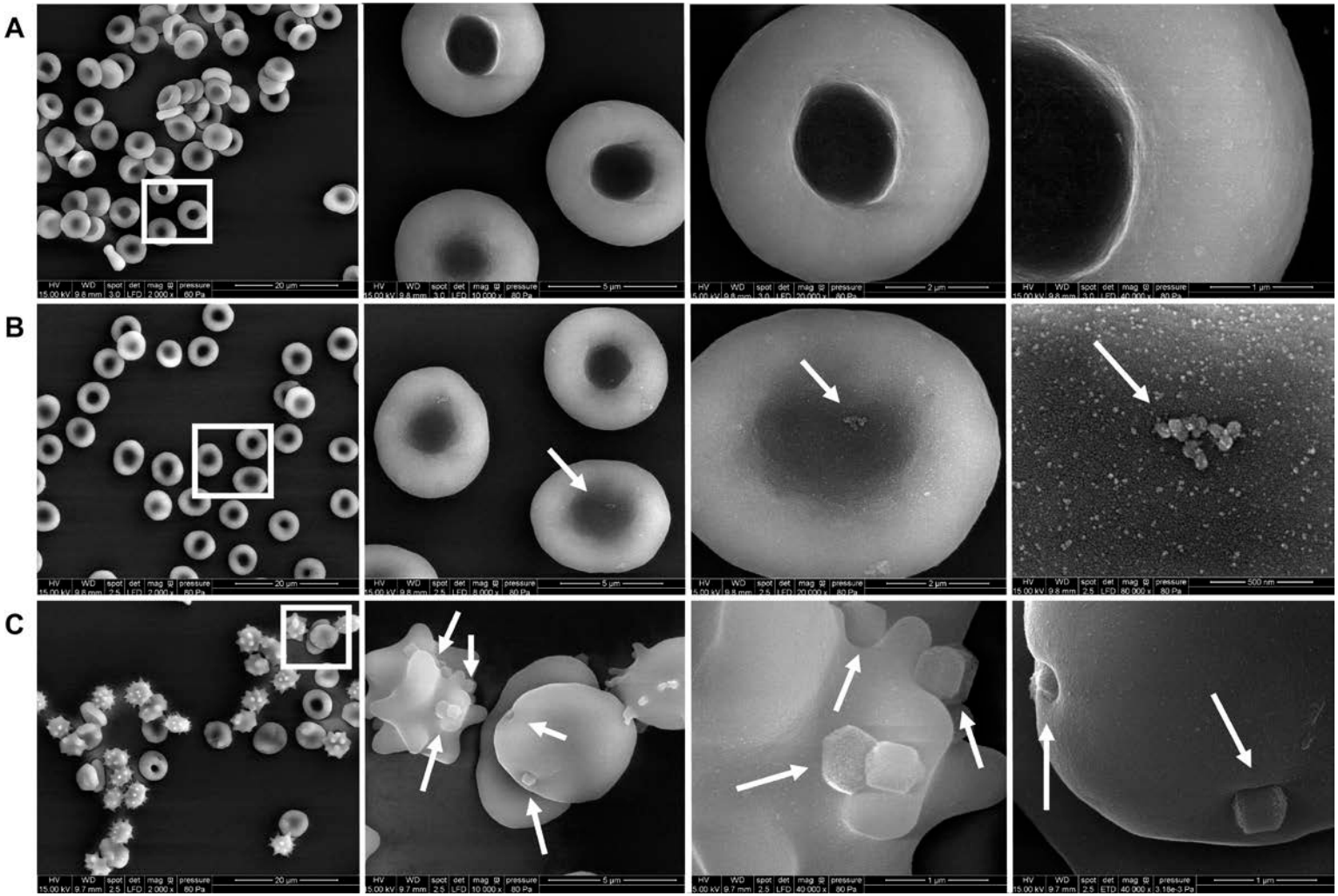


Trafficking of PEGylated MSNs varies by shape

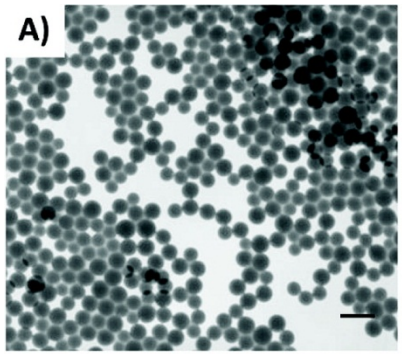


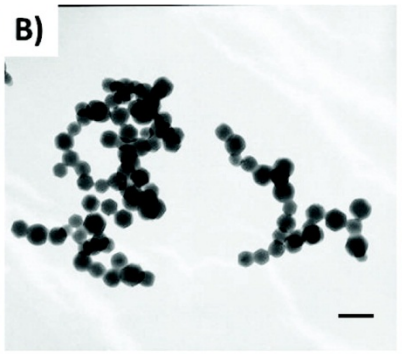
N Hao et al The shape effect of PEGylated mesoporous silica nanoparticles on cellular uptake pathway in Hela cells *Microporous and Mesoporous Materials* 162 (2012) 14–23

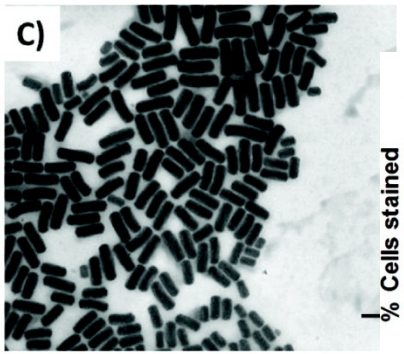
Hemolysis by MSNs Up Close

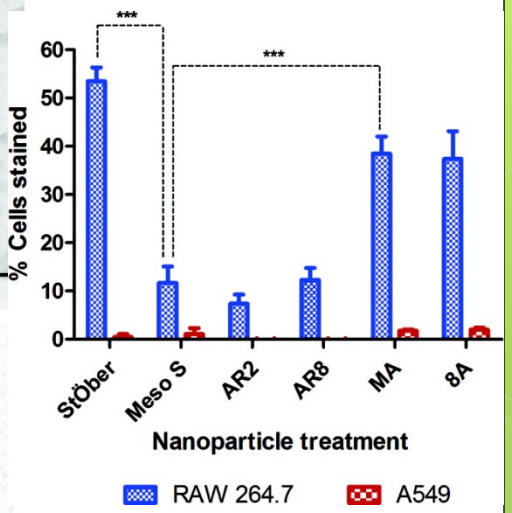


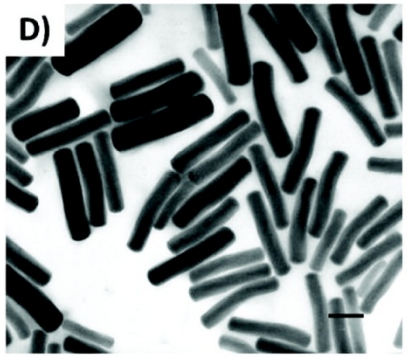
Published in: Yannan Zhao; Xiaoxing Sun; Guannan Zhang; Brian G. Trewyn; Igor I. Slowing; Victor S.-Y. Lin; *ACS Nano* **2011,** 5, 1366-1375.

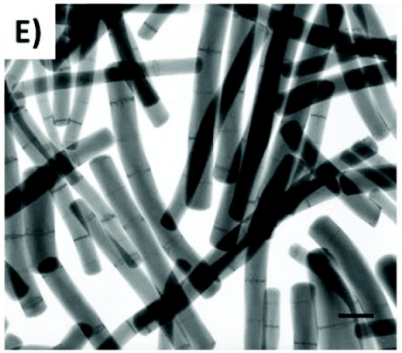


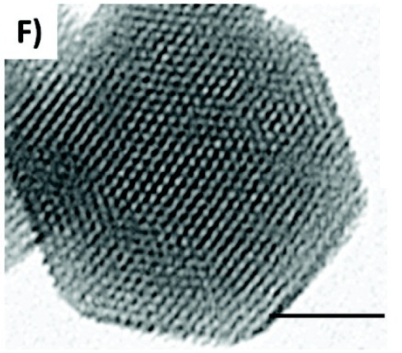




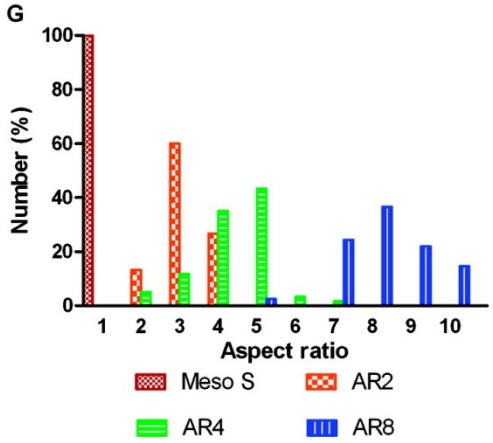


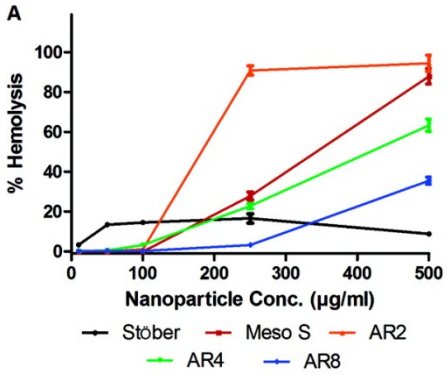


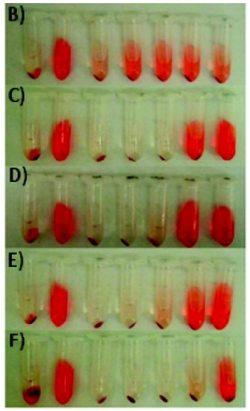




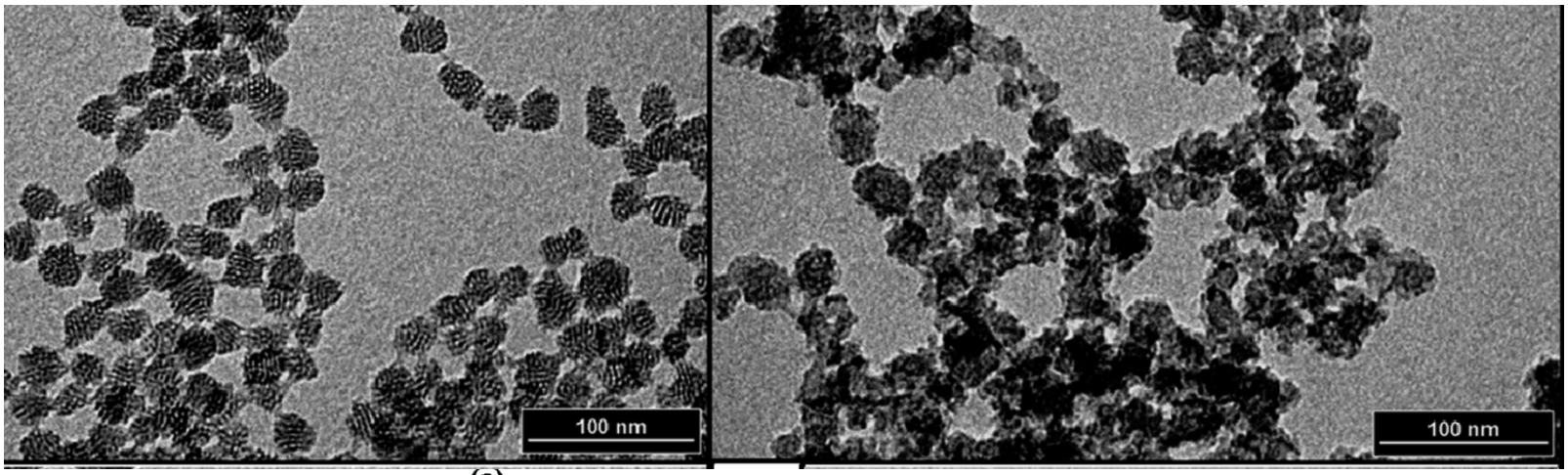
Results Differ by Geometry, Porosity, Cell Type

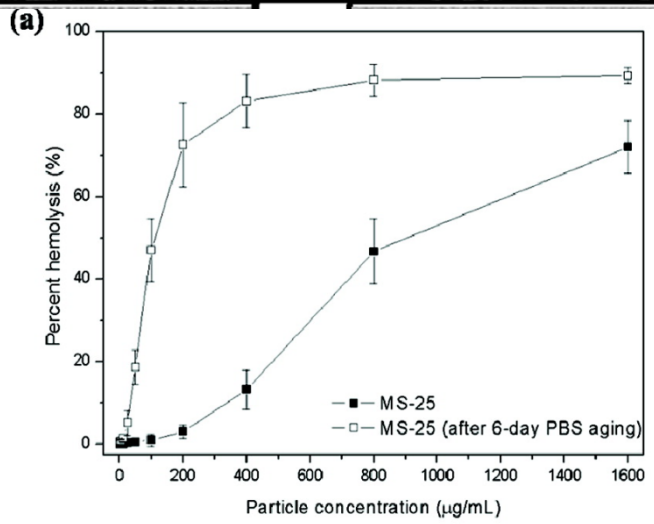






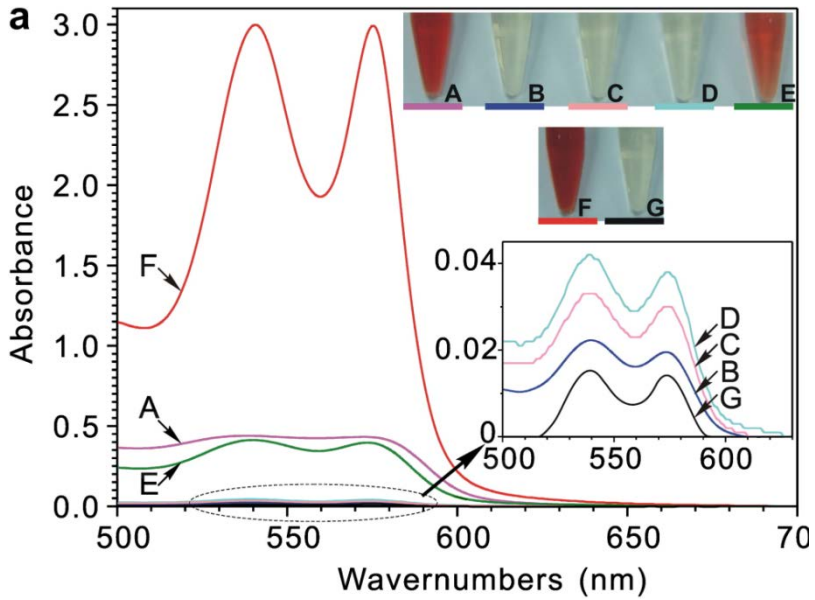
Particle Aging Effects?

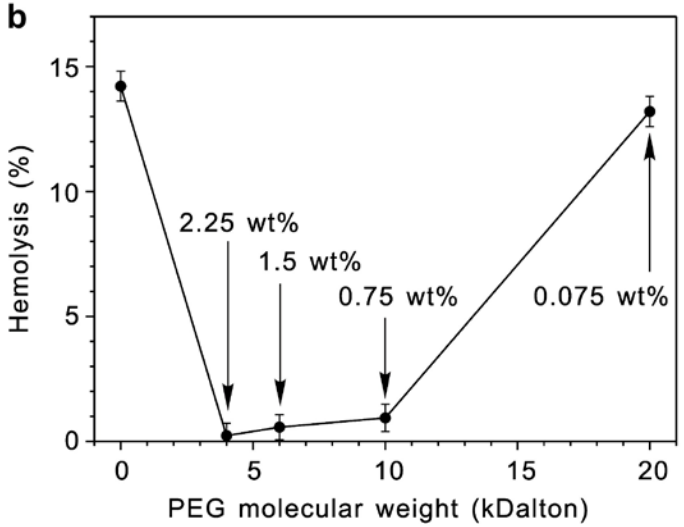




Adapted from: Yu-Shen Lin; Christy L. Haynes; *J. Am. Chem. Soc.* **2010,** 132, 4834-4842.

PEGylation and Inhibition of Hemolysis



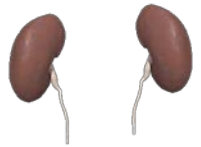


PEG drawbacks:

-Side effects from increased exposure to normal tissues

-Increased diameter alters mobility

-Not biodegradable, potential intracellular accumulation or tubular reabsorption



MSNs as complex bioactive delivery vehicles: much more to be learned.

Qianjun He,Jiamin Zhang,Jianlin Shi,Ziyan Zhu,Linxia Zhang,Wenbo Bu,Limin Guo,Yu Chen; *Biomaterials* **2009,** 31(6), 1085-1092. and "Nanomedicine(s) under the Microscope" by Ruth Duncan and Rogerio Gaspar; *Molecular Pharmaceutics* 2011 *8* (6), 2101-2141.