Theranostics: A combination of diagnostics and therapy

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Theranostics: the possible scenarios

- Therapeutic product followed by diagnostic

  eg: a drug that shows efficacy, but not for all; new diagnostics used to identify the patients for whom it will work

- Diagnostic product followed by therapeutic

  eg: diagnostic that distinguishes patients or disease type and allows selection of therapy

- Co-development

  eg: Herceptin and HerceptTest for breast cancer

Nanotechnology can permit combinations (co-development) with single particles

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Theranostics

- Personalized medicine: *pharmacogenetics*
- Take diagnosis from the biochemistry lab to the “point-of-care”: *lab-on-chip*
- Dual use particles/devices.

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Diagnosis and Therapy

Genomics Proteomics Metabolomics

Imaging → MRI
Fluorescence
Ultrasound

Therapy → Drug release
Hyperthermia
X-ray
Free radicals

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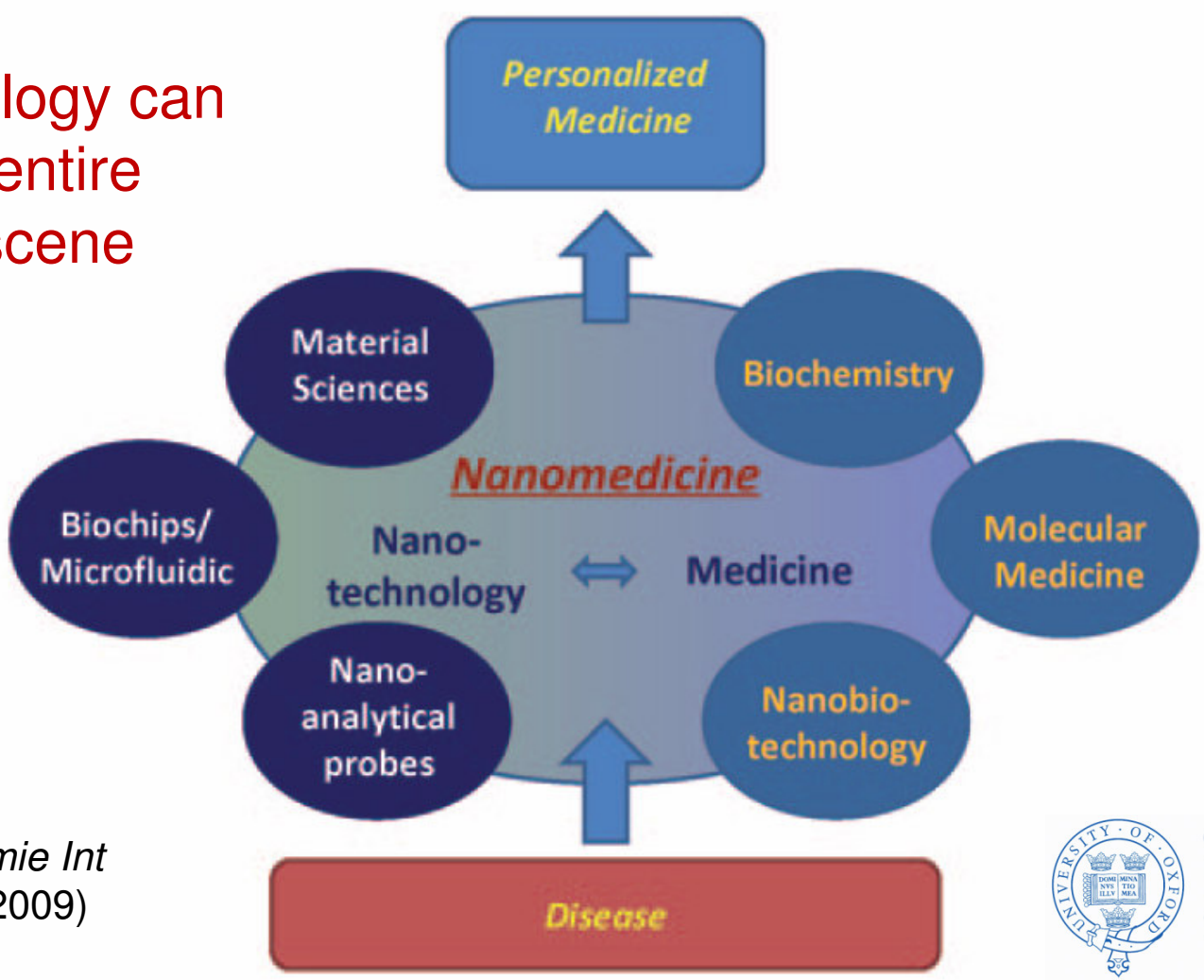
Nanomedicine

Nanotechnology can change the entire healthcare scene



Riehemann et al.
Angewandte Chemie Int Ed. **48**, 872-897 (2009)

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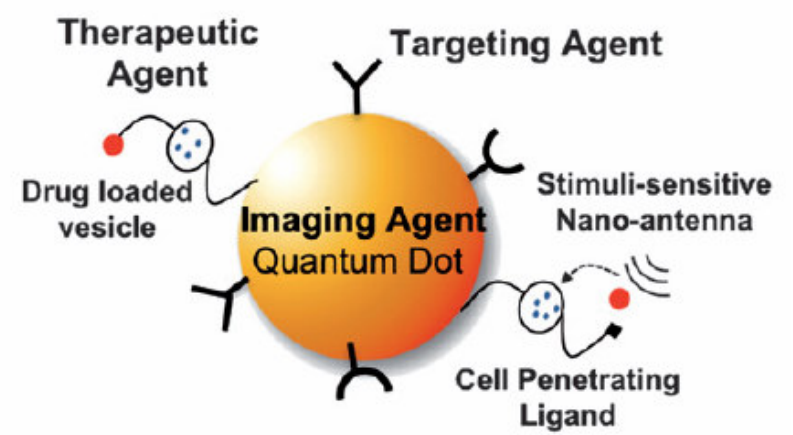
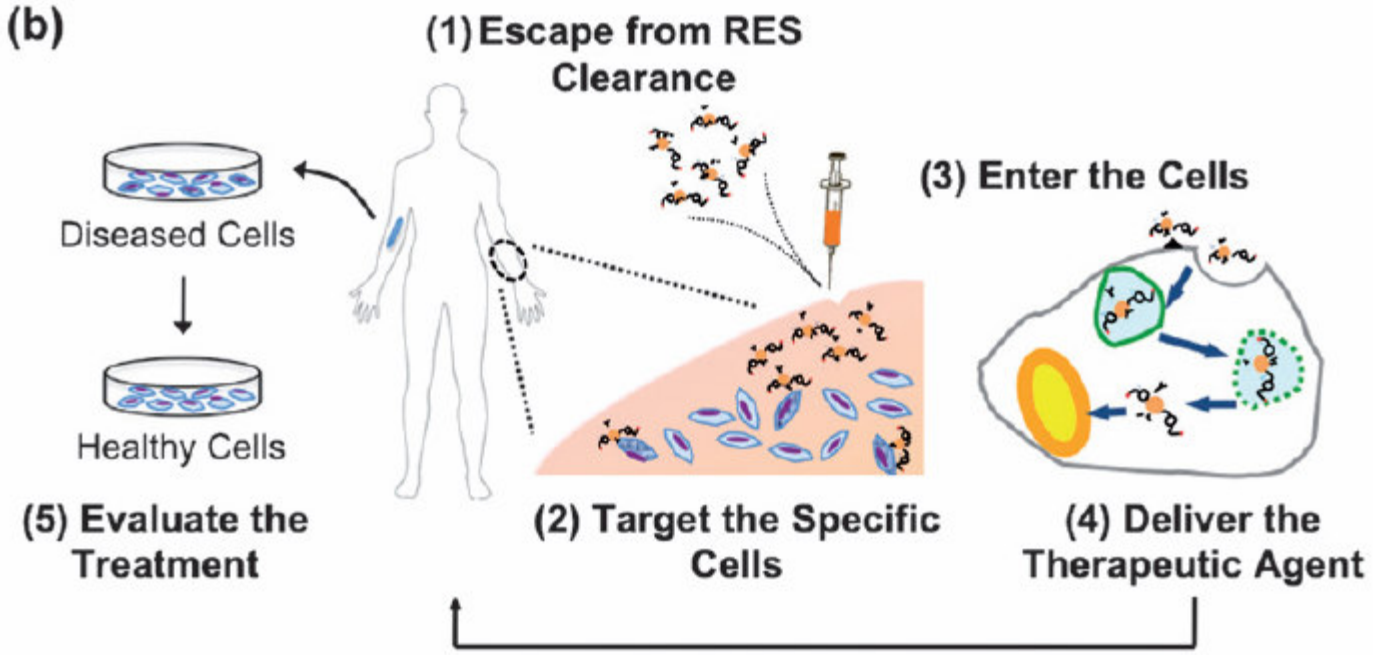
Figure 1. Technologies involved in the field of nanomedicine.

One concept for delivering therapy and then examining the effect



Ho and Leong *Nanoscale* **2**, 60-68 (2010)



Post treatment evaluation using fluorescence microscopy

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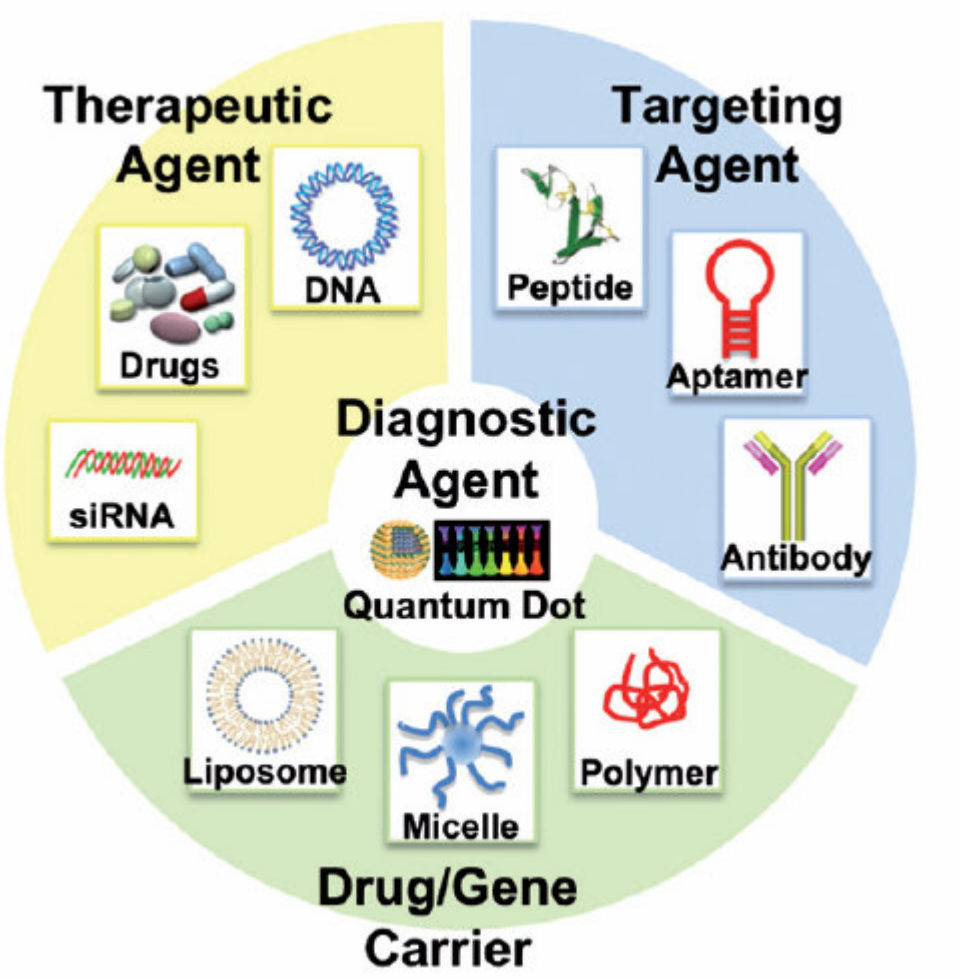
The possible combinations built around quantum dots



Note that quantum dots may have possible toxicity and stability issues

Ho and Leong *Nanoscale* **2**, 60-68 (2010)

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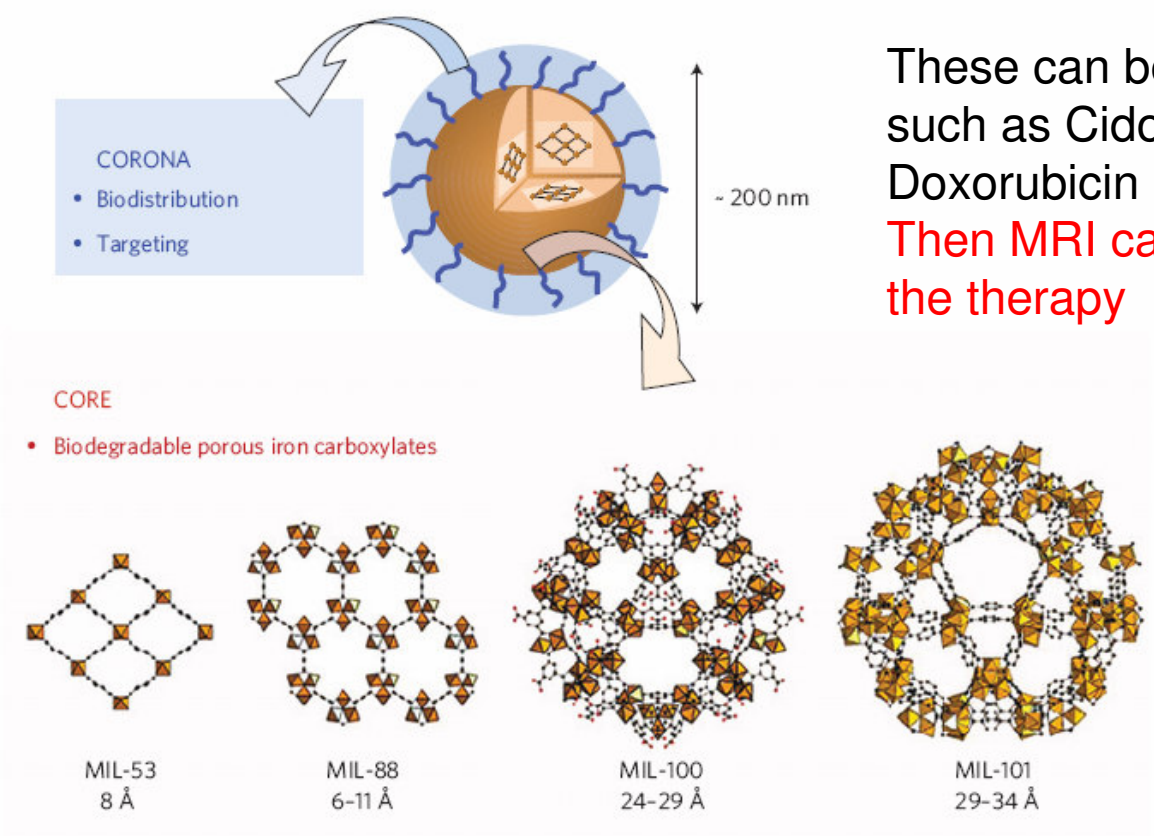
Porous Carriers 1



These can be loaded with drugs such as Cidofovir, Busulfin, Doxorubicin etc....
Then MRI can be used to follow the therapy

Horcajada et al *Nature Materials* **9**, 172-178 (2010)

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MRI results of Horcajada et al

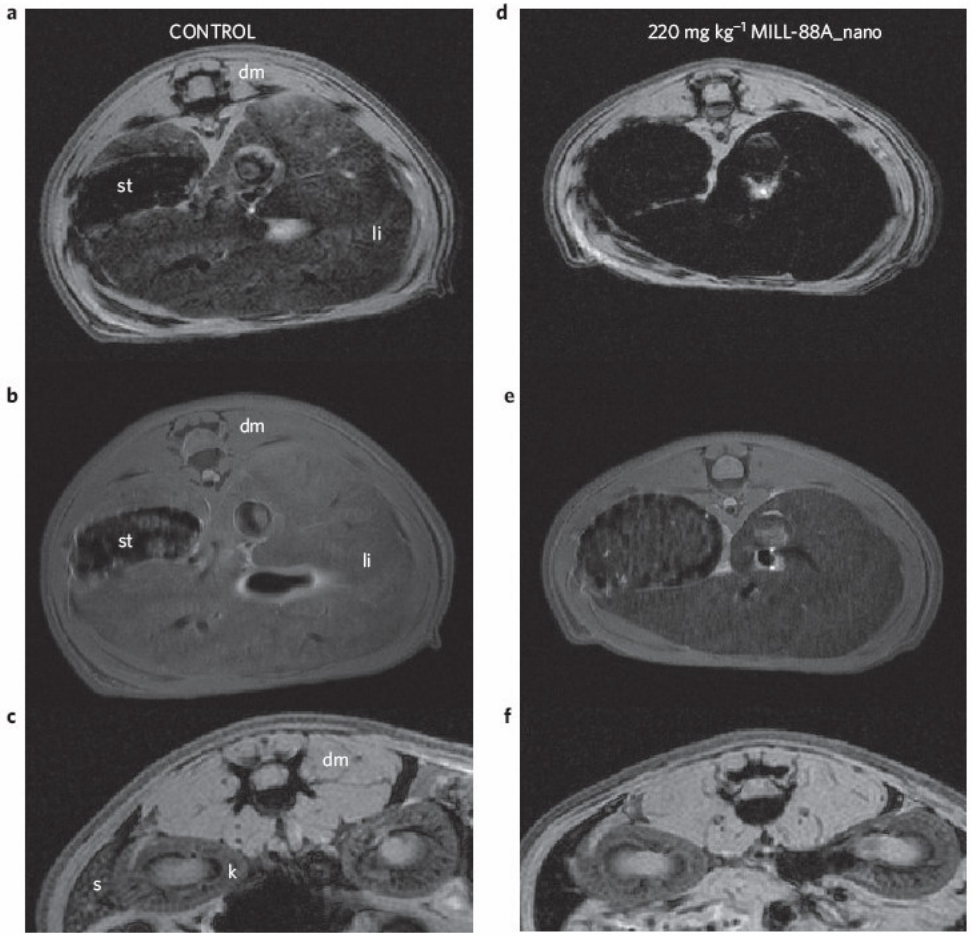

Figure 4 | Magnetic resonance images. The images were acquired with gradient echo (**a**, **c**, **d**, **f**) or spin echo (**b**, **e**) sequence of control rats (left; **a**–**c**) and rats injected with 220 mg kg^{-1} MIL-88A (right; **d**–**f**), in liver (**a**, **b**, **d**, **e**) and spleen (**c**, **f**) regions. 30 min after injection, product effect is observable on the liver and spleen. (dm, dorsal muscle; k. kidney; li, liver; s, spleen; st, stomach.)

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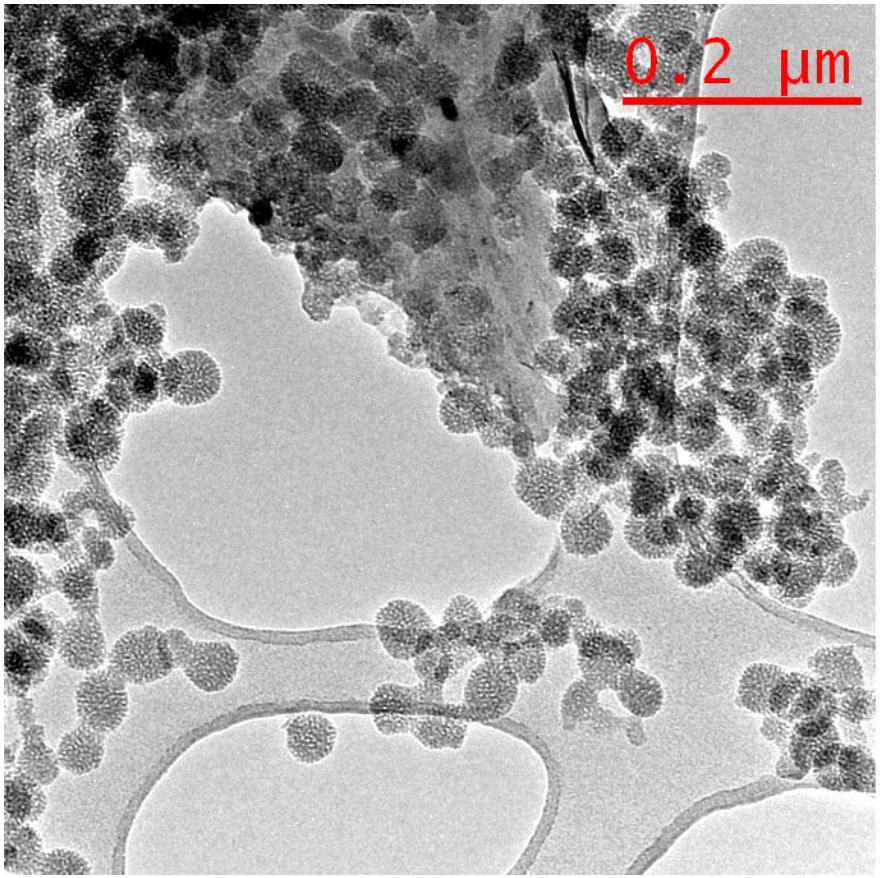
Silica building blocks for porous nanoparticles



These 50nm porous silica nanoparticles could be used as the basis for drug-loaded particles.
They can be targeted at specific sites using surface moieties .

Townley et al 2010 unpublished

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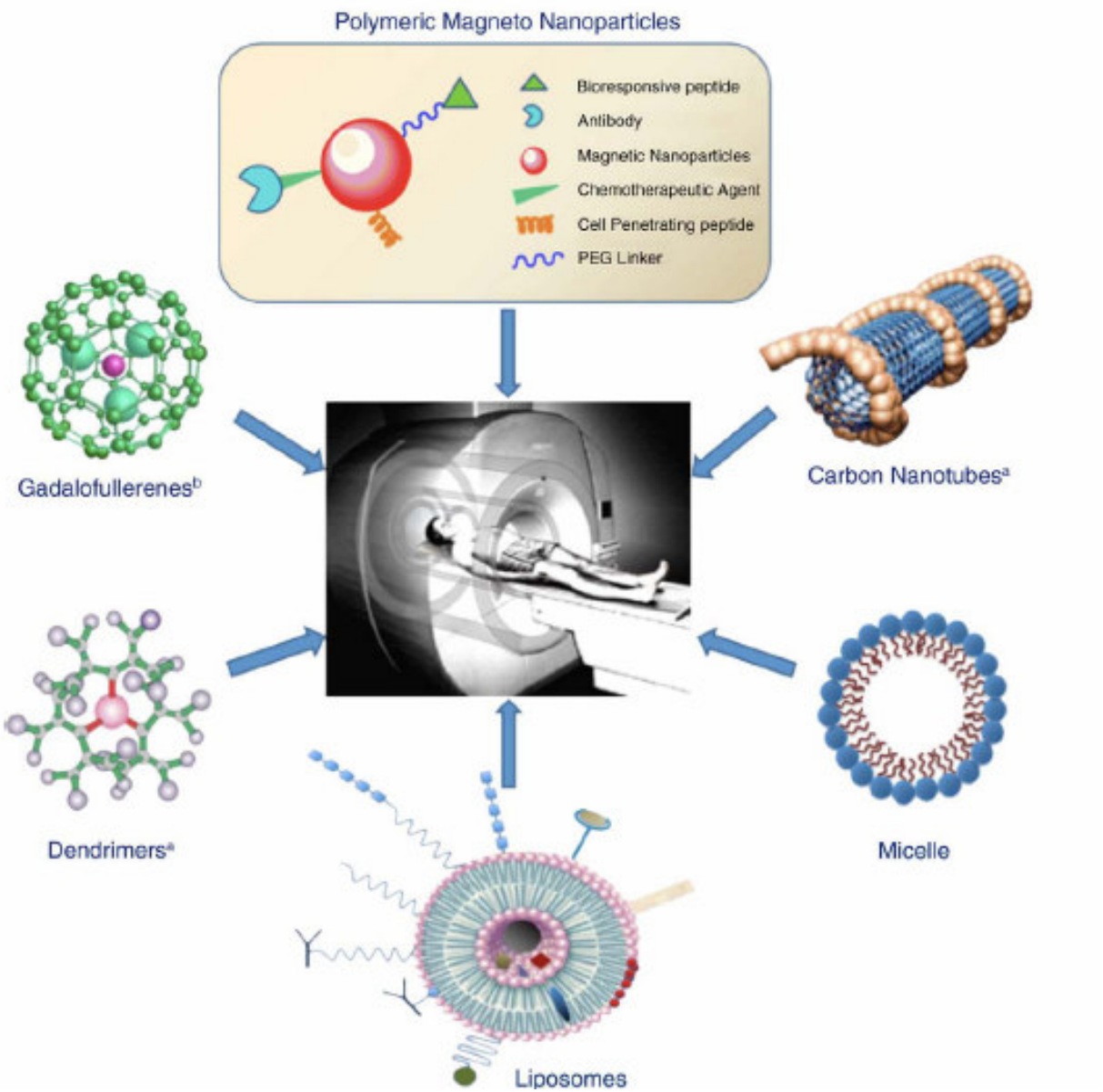
Magnetic Theranostic Particles



Mody et al *Advanced Drug Delivery Reviews* **61**, 795-807 (2009)

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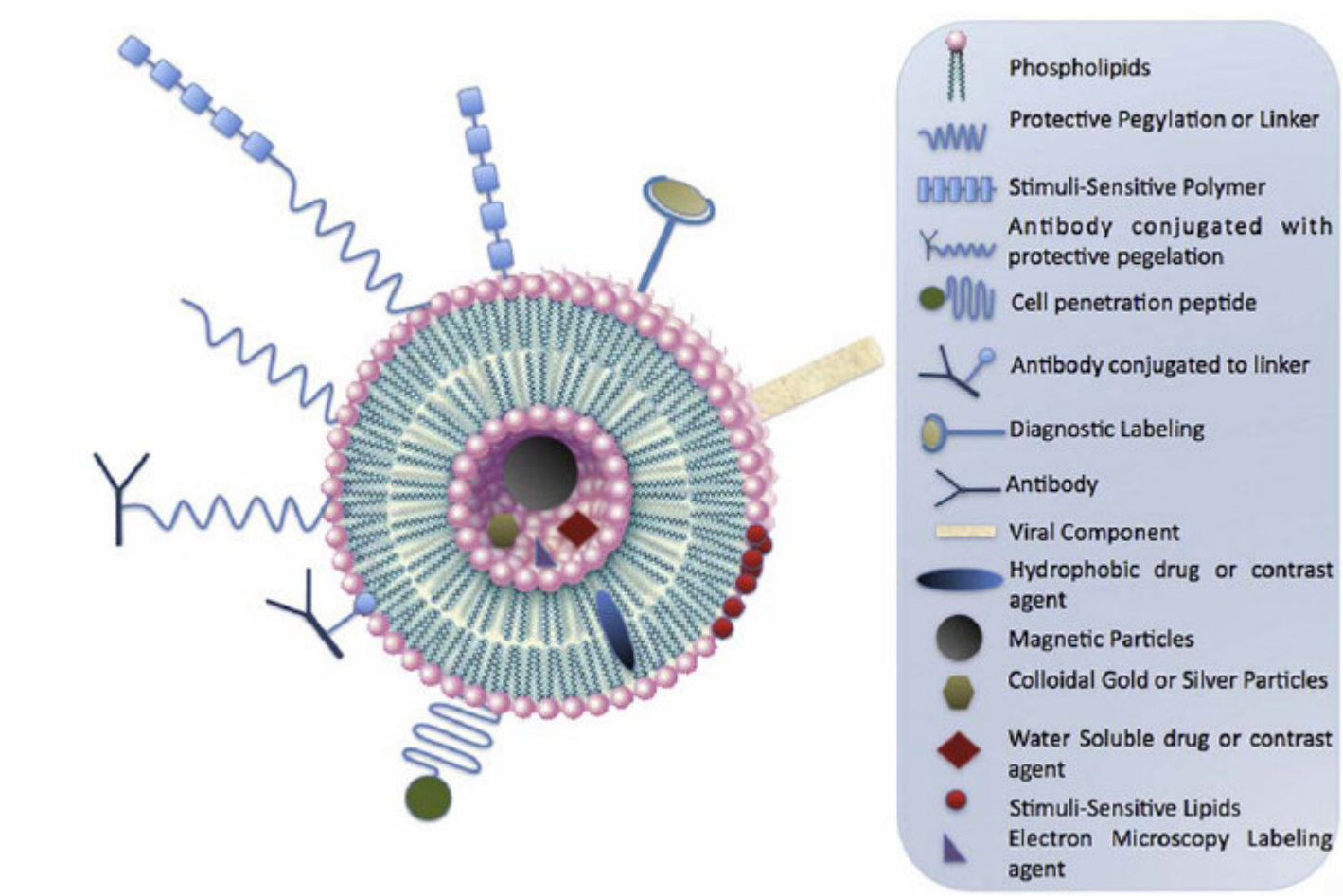
Magnetic Theranostic particles 2



Mody et al *Advanced Drug Delivery Reviews* **61**, 795-807 (2009)

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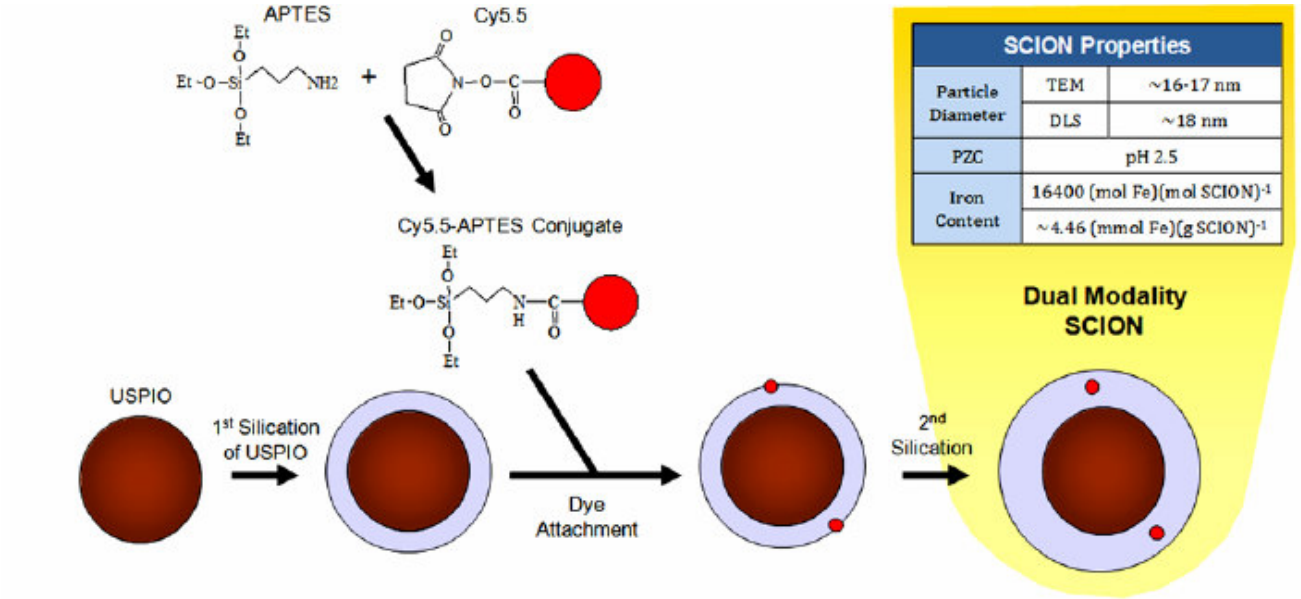
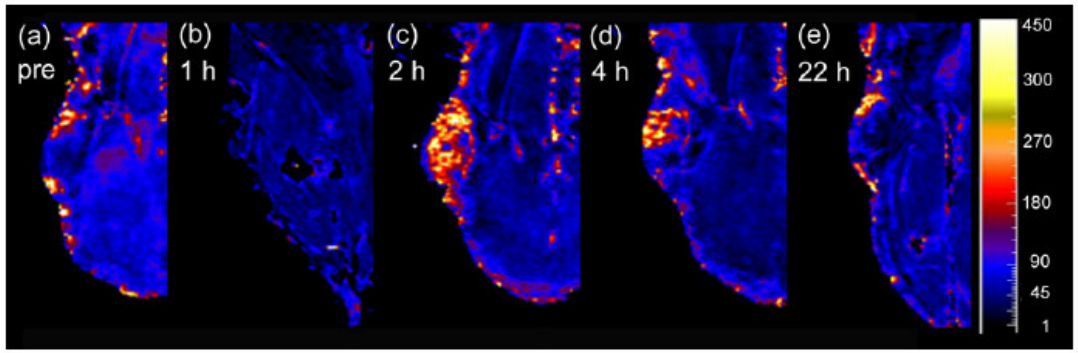
Magnetic nanoparticle building blocks



SCION Properties		
Particle Diameter	TEM	~16-17 nm
	DLS	~18 nm
PZC	pH 2.5	
Iron Content	16400 (mol Fe)(mol SCION)$^{-1}$	
	~4.46 (mmol Fe)(g SCION)$^{-1}$	



Note the SCION retention after 2 hours via the Enhanced Permeability and Retention effect for leaky tumours

Bumb et al *Nanotechnology* **21**, 175704 (2010)

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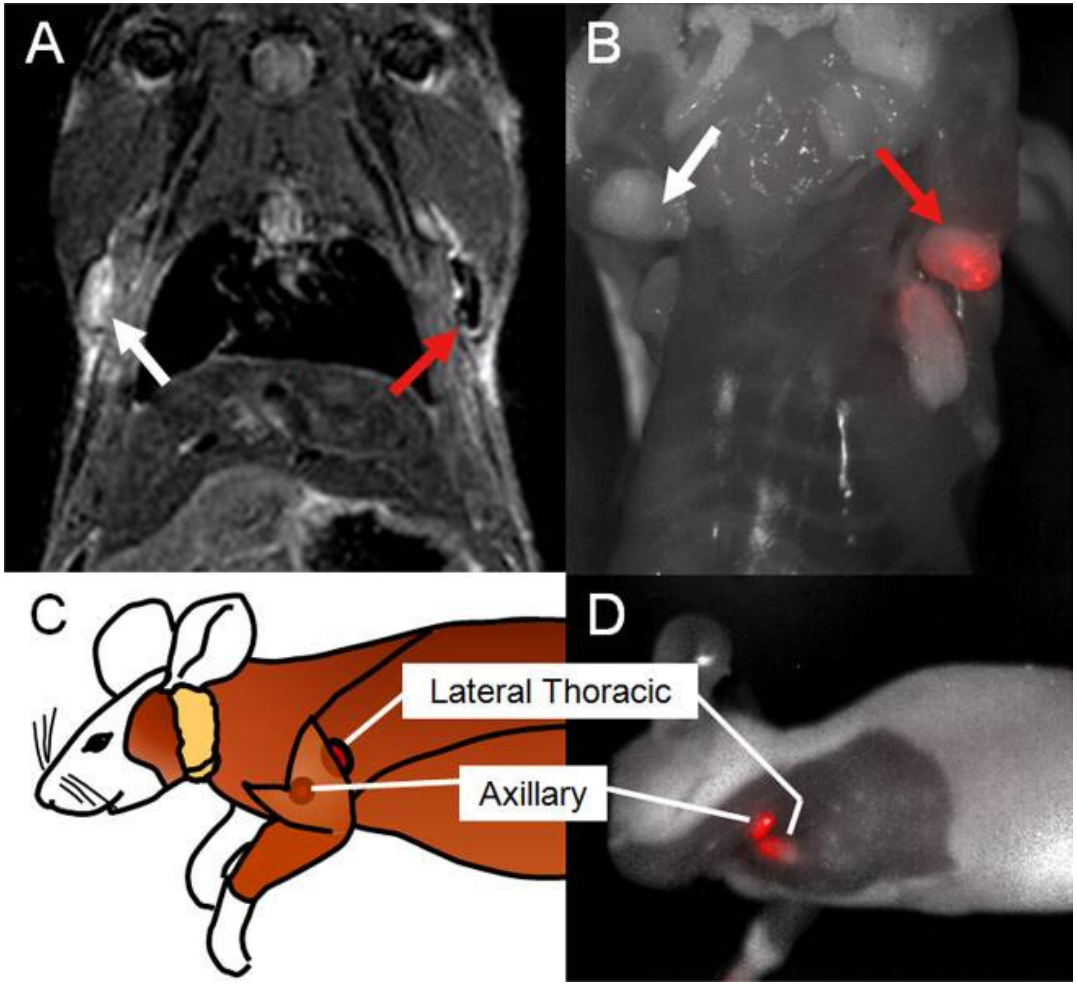
Example of the use of these SCION particles in animals



Sentinel lymph node imaging with SCION. The white arrows in (A) T2-weighted MR and (B) optical imaging point to control nodes on which side no injection of SCION was given to the foot pad. The red arrows indicate nodes that were clearly visualized after SCION footpad injection, where in MR the node darkened and in spectrally unmixed optical imaging the NIR fluorescence was captured. The illuminated nodes are the axillary and lateral thoracic lymph nodes, as pointed out in (C) and (D).

Bumb et al (2009)

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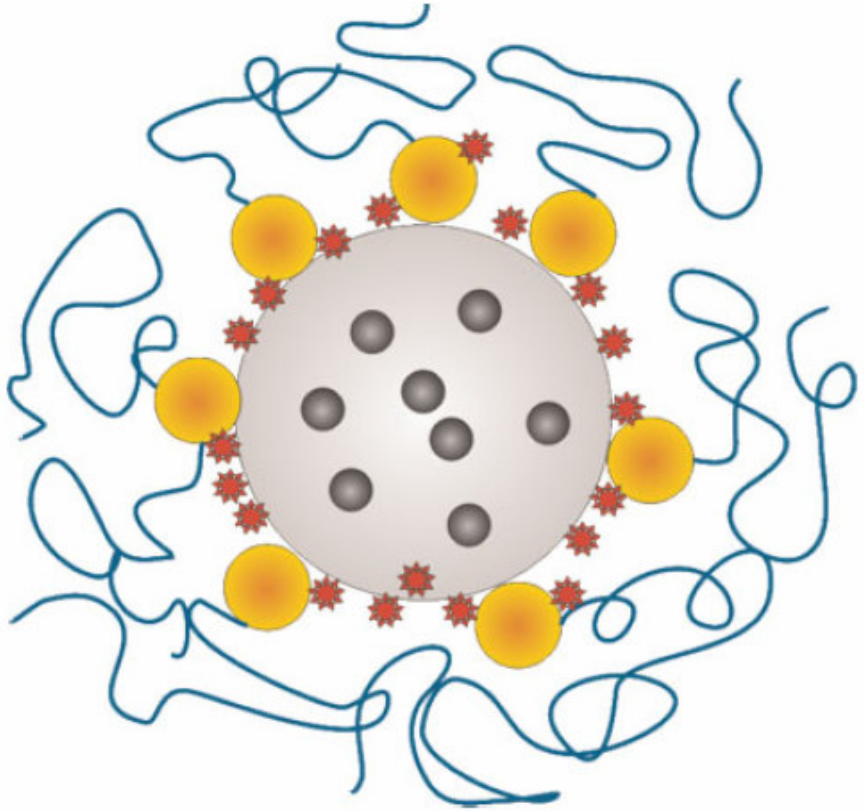
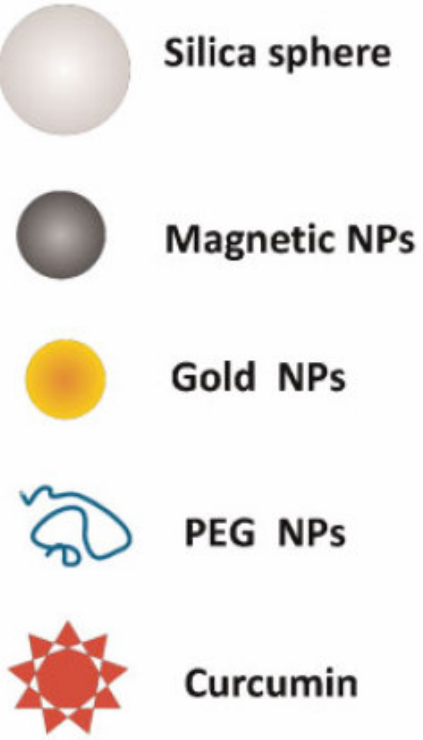
Composite drug-loaded particles





Scheme 1. Schematics of drug-loaded magnetoplasmonic assemblies (MPA) with PEG "camouflage" coating.

Gold particles increase the optical visibility via surface plasmon resonance scattering

Chen et al Macromol.Rapid Commun. 31, 228-236 (2010)

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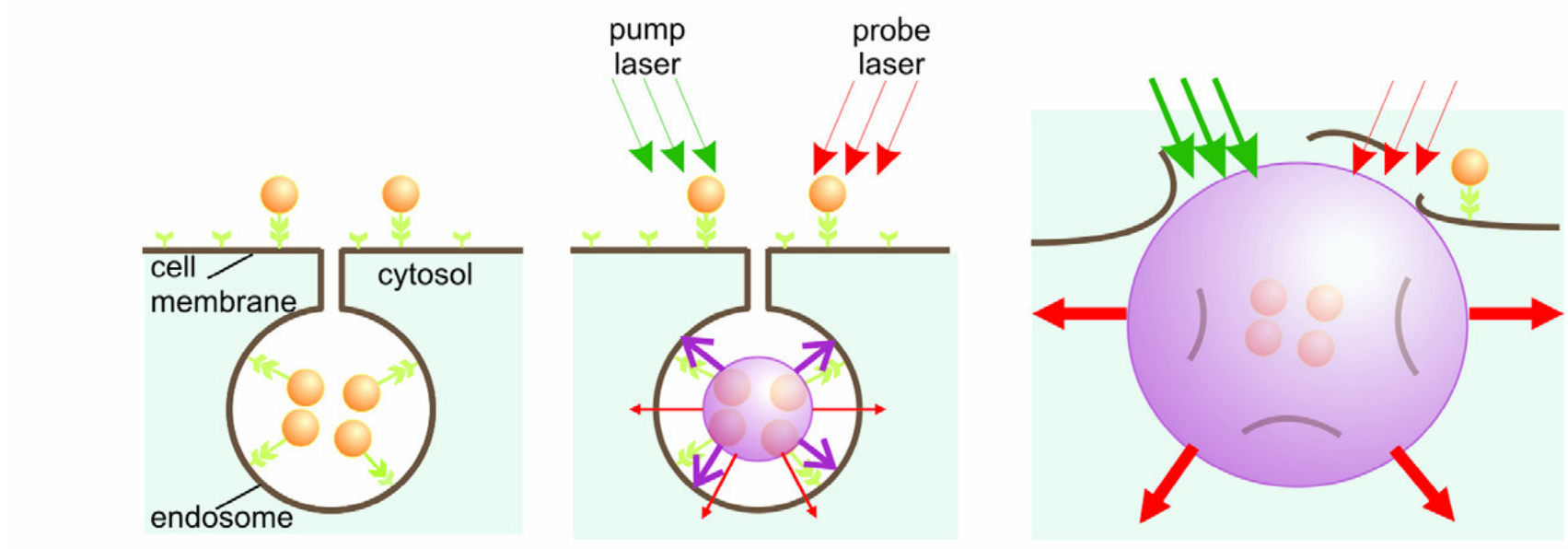
Plasmonic nano-bubble approach



Gold NP-antibody conjugates taken into cell

Probe laser tuned to *plasmon resonance* creates diagnostic image via light scattering

High power laser pulse can be used to destroy the cell

Lukianova-Hleb et al. *Nanotechnology* **21**, 1-10 (2010)

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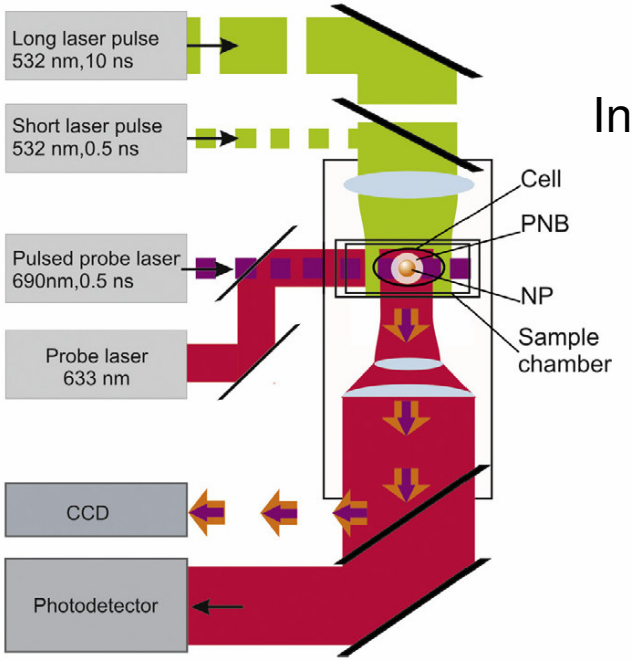
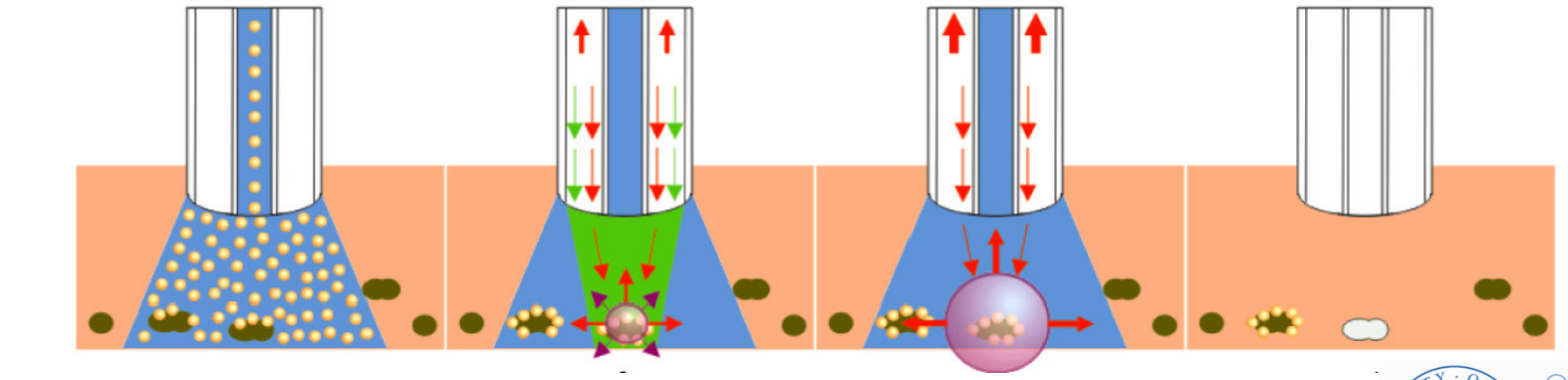
Plasmonic nano-bubble approach



In-vitro set-up

Possible future manifestation for sub-cutaneous tumours



Lukianova-Hleb et al. *Nanotechnology* **21**, 1-10 (2010)

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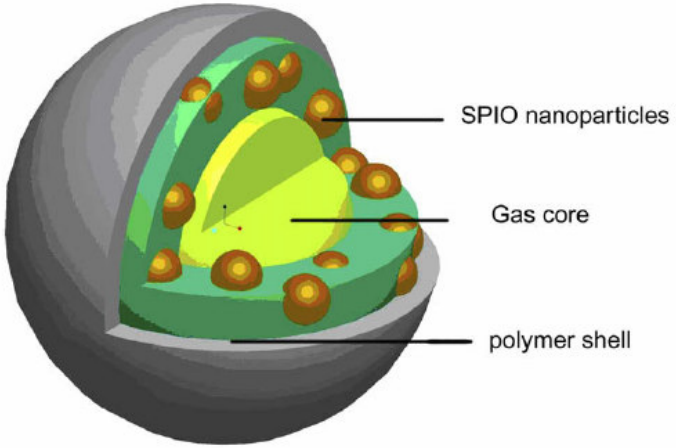
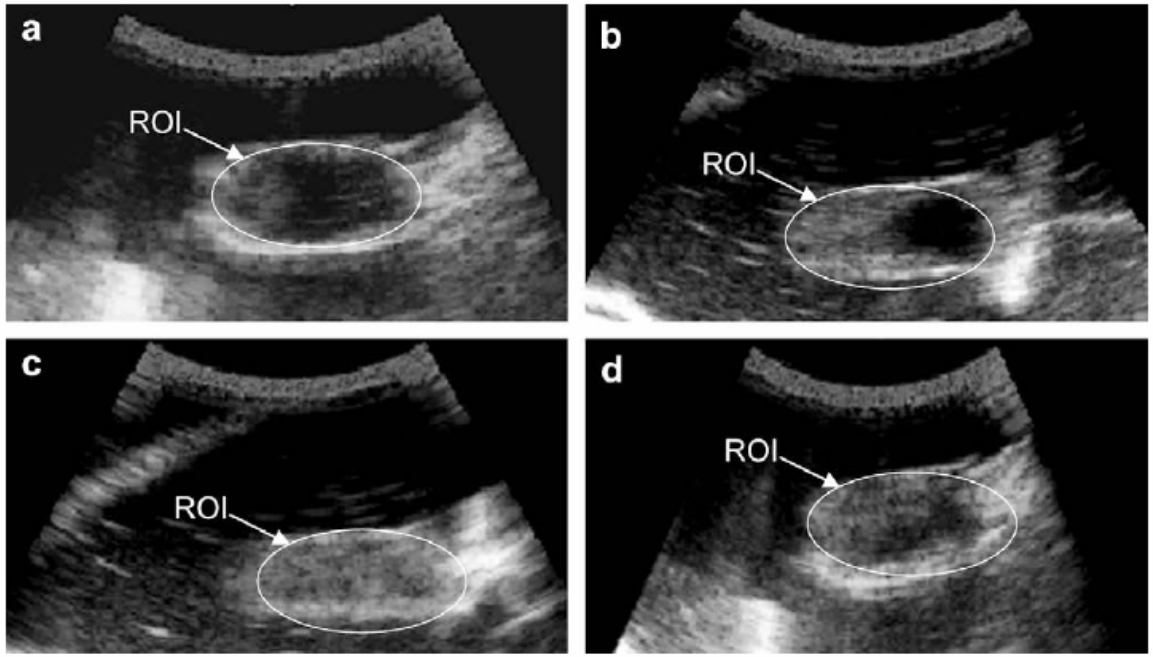
Ultrasound enhancement with microbubbles (with MR contrast)

Ultrasonic contrast changed by mechanical compliance differences between particle and surroundings



Yang et al. *Biomaterials* **30**, 3882-3890 (2009)

a) No microbubbles
b) Microbubble without SPIO
c) Microbubble with SPIO low concentration
d) Microbubble with SPIO high concentration



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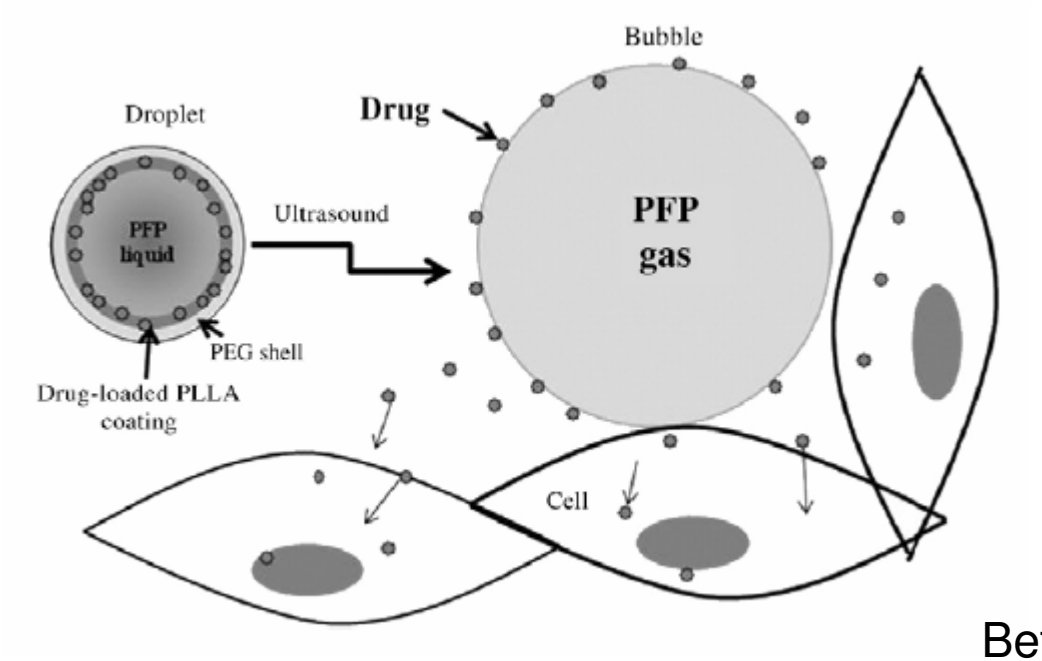
Ultrasound bubble treatment

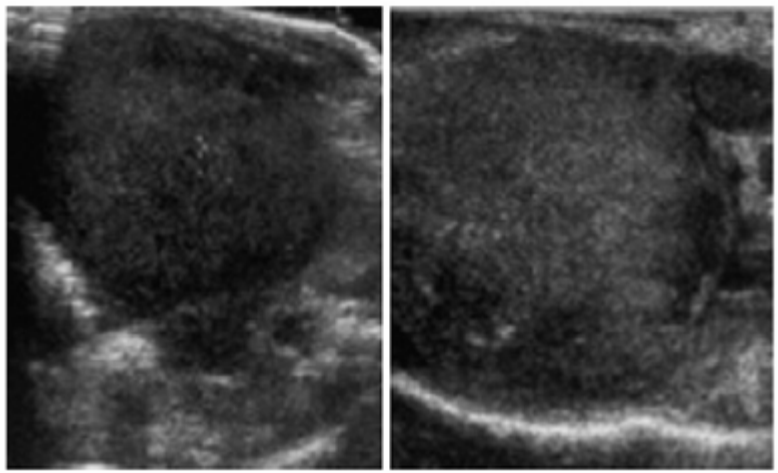


Focussed high intensity ultrasound can be used for directed therapy

Rapoport et al. *J of Controlled release* **138**, 268-276 (2009)

Before

After



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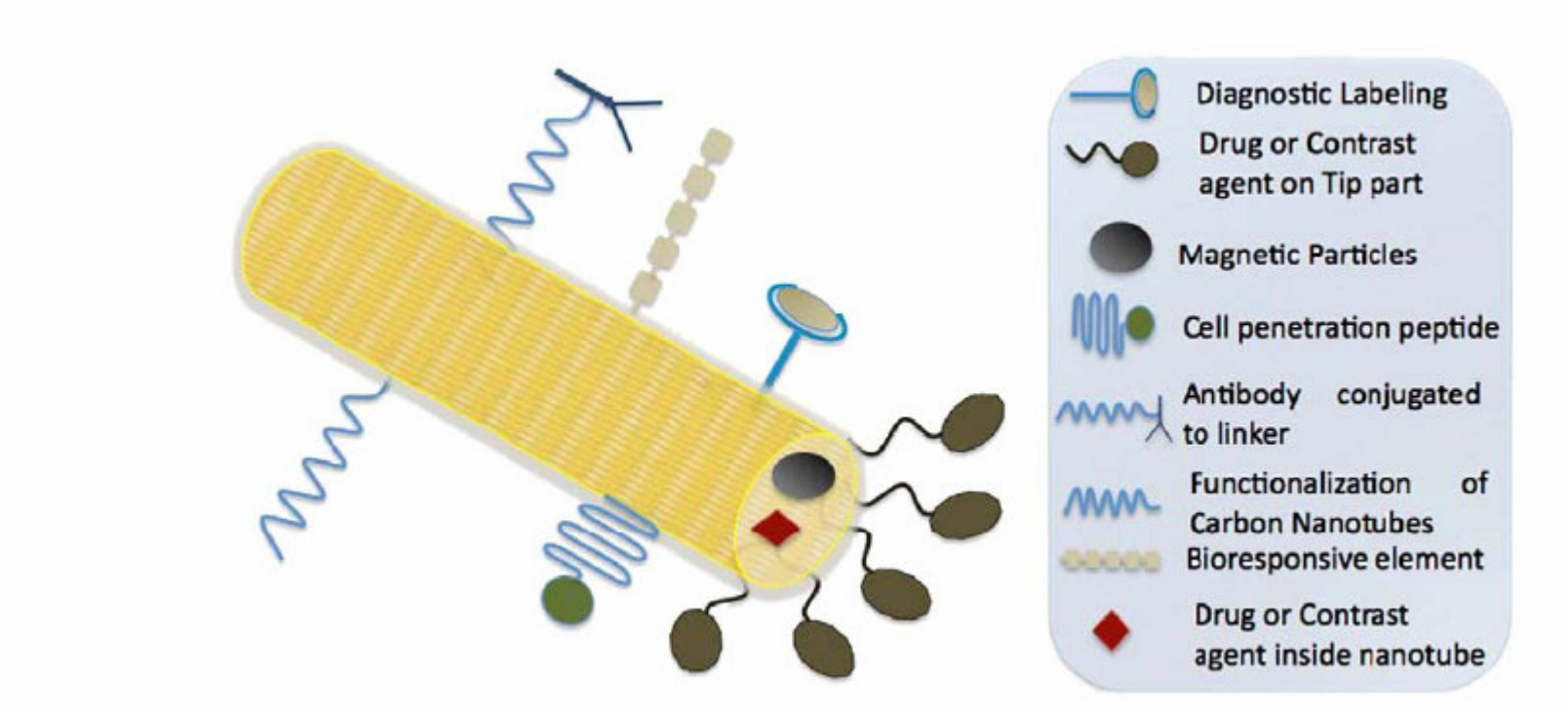
Carbon nanotubes as the basis



The improvements in manufacturing and cleaning these will increase their utilization.

Mody et al *Advanced Drug Delivery Reviews* **61**, 795-807 (2009)

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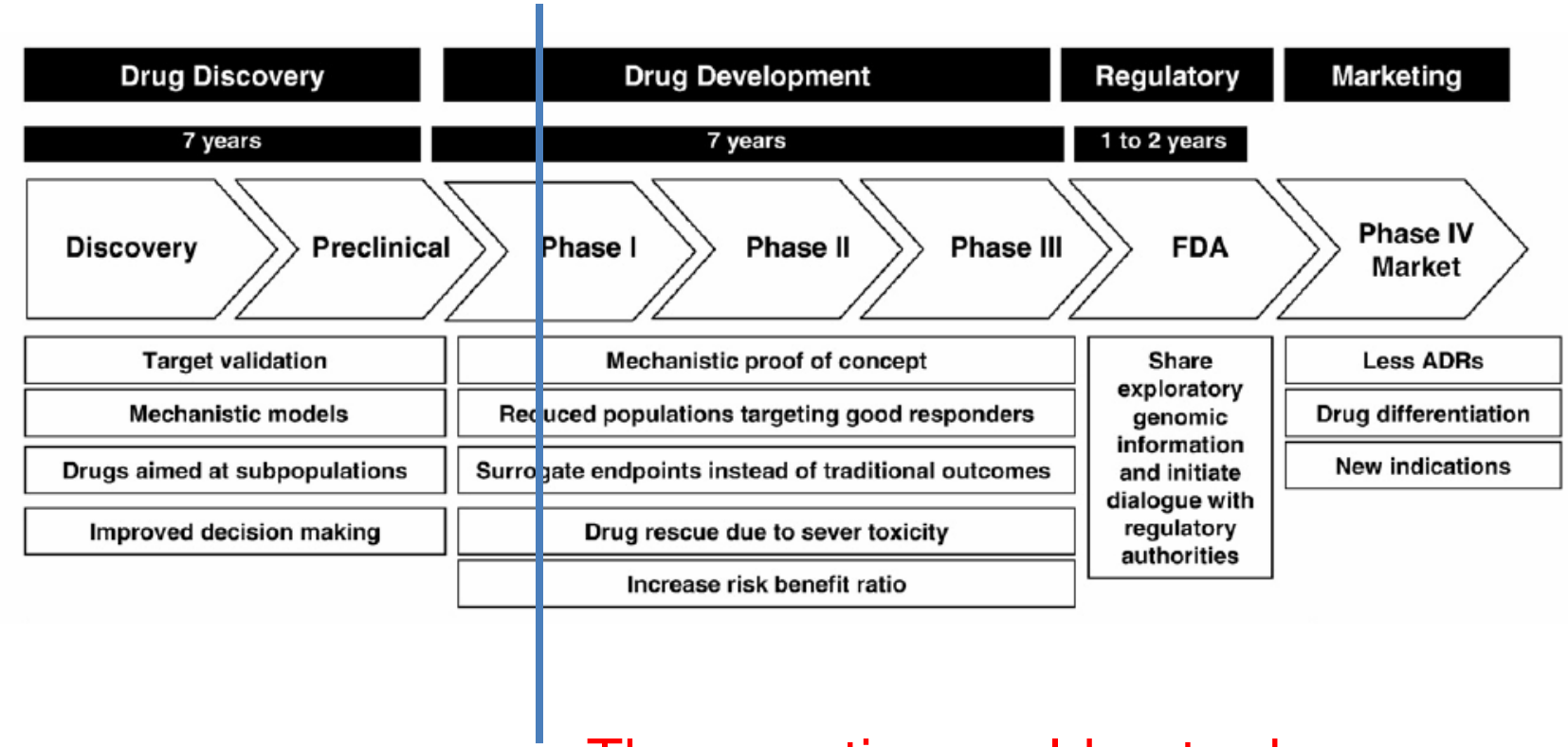
The timescales for new developments



Theranostics could enter here for established drugs and markers

Adapted from: Amir-Aslani and Mangematin *Technological Forecasting & Social Change* ***77,*** 203-217 (2010)

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Implications of Theranostic Nanostructures

- Drug or Device?
- Patient-Physician implications: choice of therapy might be removed
- Precautionary principle and issues of unknown effects of nanoparticles
- Funding and “supply chain”, especially for clinical trials

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