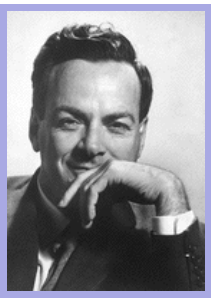
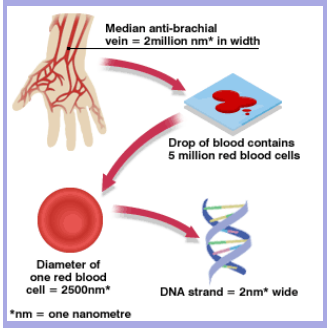


In 1959, ---------- gave a speech at Caltech called "There's Plenty of Room at the Bottom". This officially started the advance of Nanotech.

http://www.myspace.com/infinitespiral

What is the scale of 'Nano'?



"Nano" comes from the Greek "dwarf".

-a nanometer (nm) is a billionth of a meter.
-1/50,000th the width of a human hair.

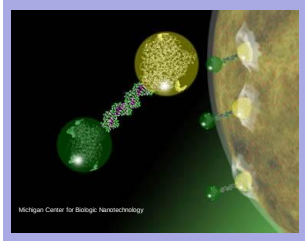
-Normal office paper is about 100,000nm thick.

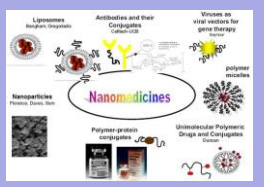
BBC Website

Nanoparticles for Cancer Therapy

Basnagge Devika Chithrani

Ryerson University, Toronto, Ontario, Canada
Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, Ontario Canada





http://nanoparticledrugdelivery.blogspot.com/2007/09/introduction-to-nanopharmaceuticals.html

Gold Nanoparticles for Improved Outcome in Cancer Therapy

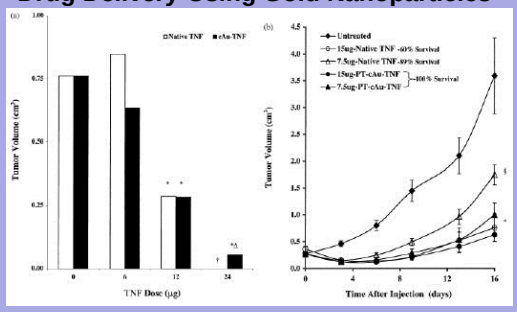
Basnagge Devika Chithrani

Ryerson University, Toronto, Ontario, Canada
Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, Ontario Canada

Why Au NPs?

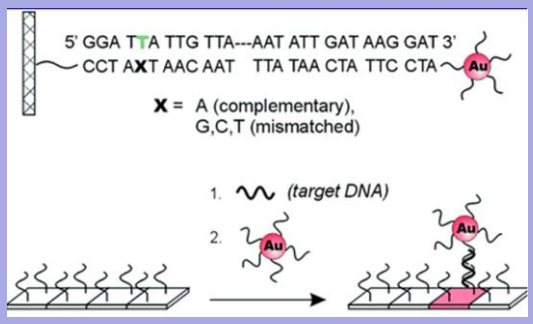
- Tunability (in size and shape)
- Easy to attach ligands
- Stability, BIOCOMPATIBILITY
- Easiness of making them
- Imaging – Hyperspectral imaging
- Therapy-radiosensitizers and anticancer drug carriers

Drug Delivery Using Gold Nanoparticles



Paciotti, G. F., L. Myer, D. Weinreich, D. Goia, N. Pavel, R. E. McLaughlin, and L. Tamarkin."Colloidal Gold:A Novel Nanoparticle Vector for Tumor Directed Drug Delivery."Drug Delivery, 2004.

DNA Detection



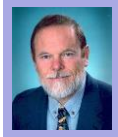
Chad Merkin and co-workers, Science, 277, 1078-81, (1997)

Heating Things up

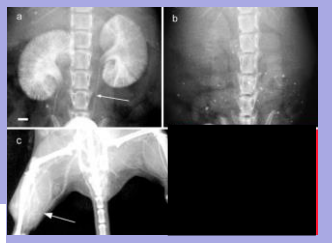
The gold coat of the nanoshell absorbs the externally applied light-energy, turning it into heat.

J. West and co-workers, Nature Reviews Cancer **3**, 887 (2003)

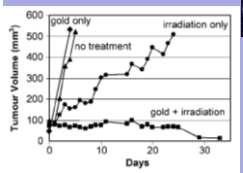
Gold is a Better X-Ray Contrast Agent



James F. Hainfeld

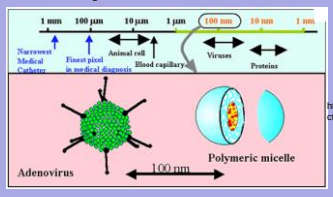


www.nanoprobes.com

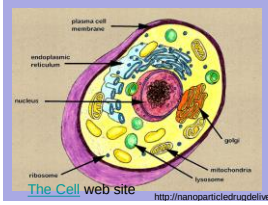


Hainfeld et al., Phys. Med. Biol. **49** (2004) N309–N315

Can We Optimize Bio-nano Interface ?



http://www.newkast.or.jp/english/projects/pro_yokoyama.html

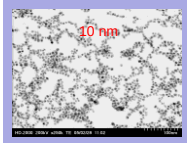


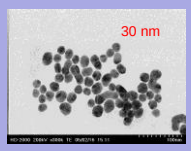
The Cell web site

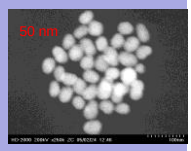
Size of the NPs matters!!!!!!!!!!!!!!!

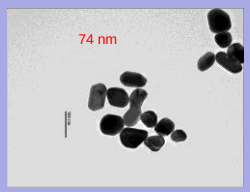
http://nanoparticledrugdelivery.blogspot.com/2007/09/introduction-to-nanopharmaceuticals.html

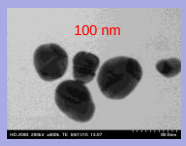
Gold Nanoparticles with Different Sizes



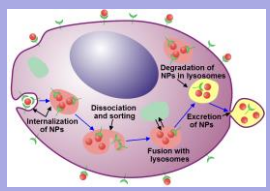


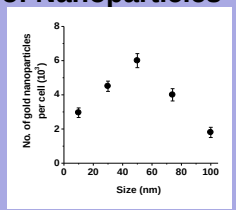




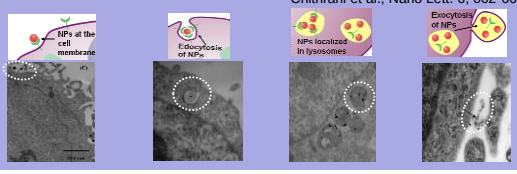


Intracellular Uptake of Nanoparticles

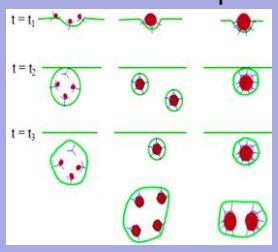


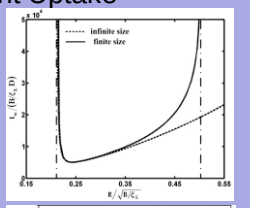


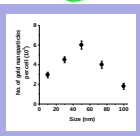
Chithrani et al., Nano Lett. 6, 662-668

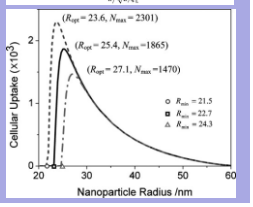


Size Dependent Uptake



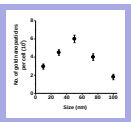




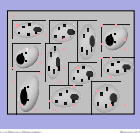


Chithrani., Mol. Mem. Biol.,27, 299 (2010)

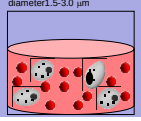
Gold NPs as Sensitizers



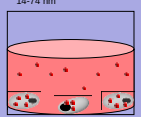
1.9 nm gold NPs

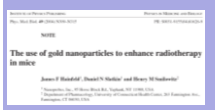


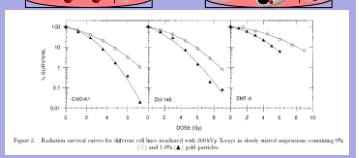
Gold microspheres with diameter1.5-3.0 μm



Gold NPs with diameters 14-74 nm

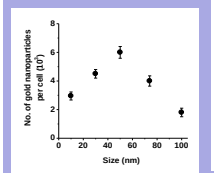


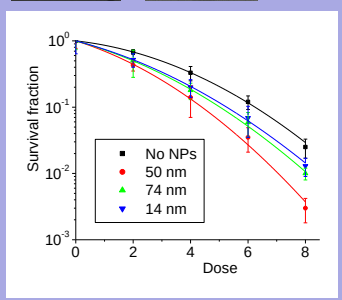




Herold et al., int. j. radiat. biol 2000, vol. 76, 1357-64

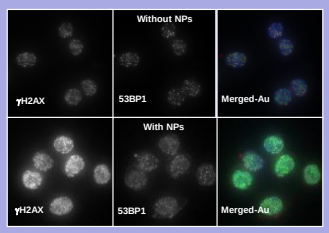
Size Dependent Radiation Response





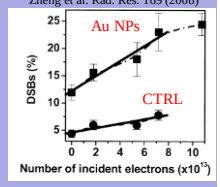
Chithrani et al.,Radiation Research 173(6):719-728 (2010

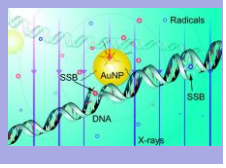
Probing of DNA Damage at X-ray Energies



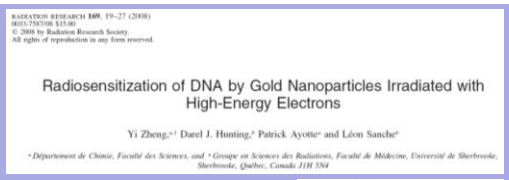
Chithrani et al., Radiation Research 173(6):719-728 (2010)

Zheng et al. Rad. Res. 169 (2008)





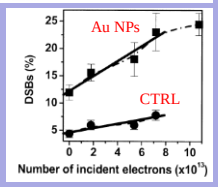
Carter et al. *J Phy Chem B* **2007**; 111, 11622-5.



Radiosensitization of DNA by Gold Nanoparticles Irradiated with High-Energy Electrons

Yi Zheng,[a,1] Darel J. Hunting,[b] Patrick Ayotte[a] and Léon Sanche[a]

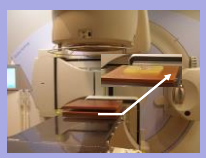
"Since short range low-energy secondary electrons are produced in large amounts by any type of ionizing radiation…targeting the DNA of cancer cells with gold nanoparticles may offer a novel approach that is generally applicable to radiotherapy treatments."

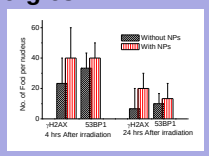


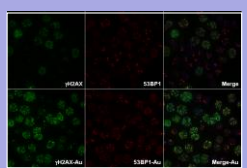
"…suggest that the radiosensitization of DNA by gold NPs is essentially caused by SE, most of which have energies below 200 eV."

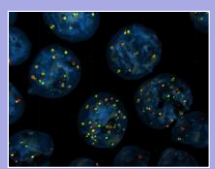
Zheng et al. Rad. Res. 169 (2008)

Radiation response at clinically relevant energies

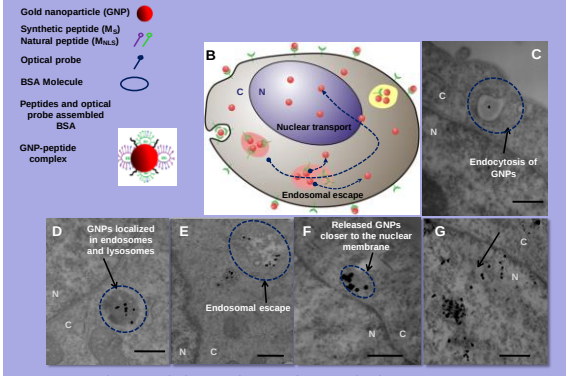




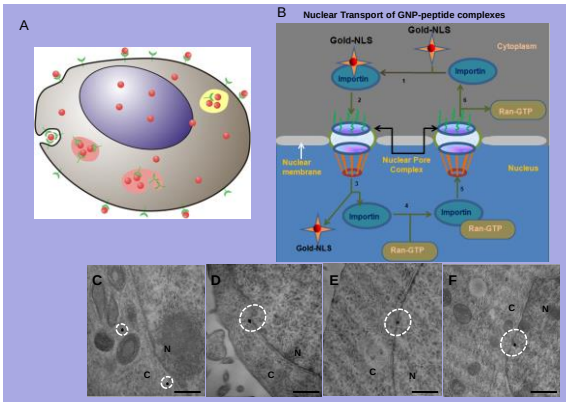




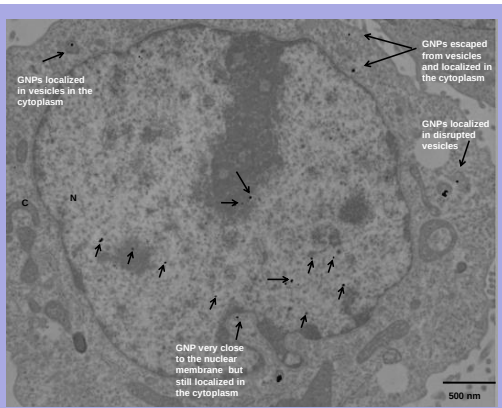
Chithrani et al., Radiation Research 173(6):719-728 (2010)



Yang et al.,, Journal of Nanoscience and Nanotechnology, 14, 4813, 2014

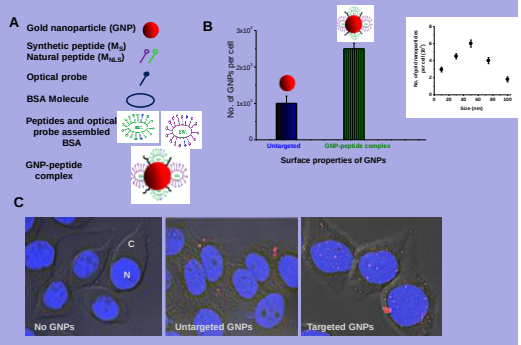


Yang et al.,, Journal of Nanoscience and Nanotechnology, 14, 4813, 2014



Yang et al.,, Journal of Nanoscience and Nanotechnology, 14, 4813, 2014

Improved uptake of smaller NPs



Yang et al.,, Journal of Nanoscience and Nanotechnology, 14, 4813, 2014

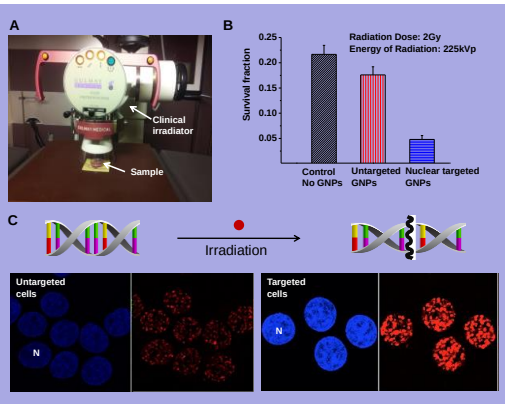
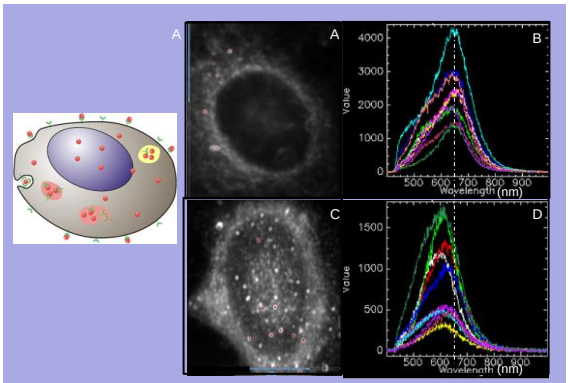


Figure 5



Yand et al., Journal of colloids and interface communications, in press, 2014

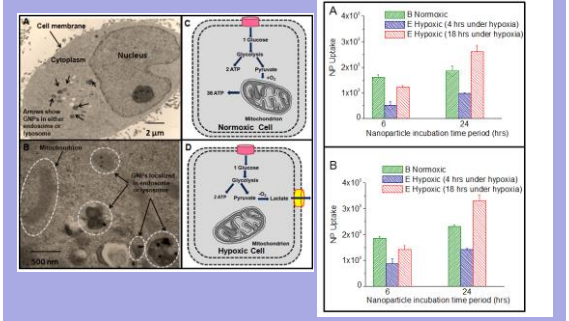
Summary

- Gold nanoparticles can be used as a model system to study their uptake, transport, organelle distribution.
- Information can be incorporated to nanoparticle-based research for improved outcome.
- Use of GNPs as radiosensitizers is promising.

Challenges

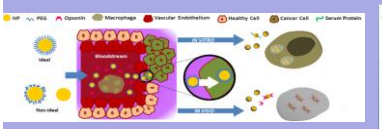
- Tumour microenvironment (Hypoxia)
- Lower uptake of PEGylated NPs

Tumour microenvironment (Hypoxia)

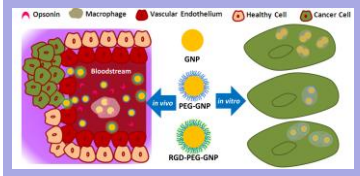


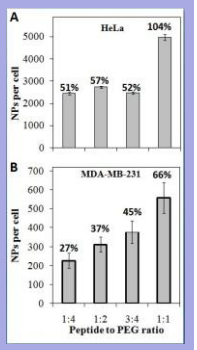
Neshatian et al., Journal of colloids and interface communications, in press, 2014

Improved uptake of PEGylated NPs

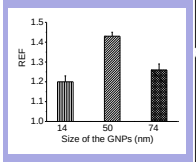


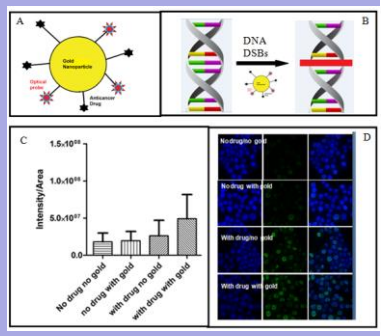
Cruje et al., RNN, 3, 20, 2014





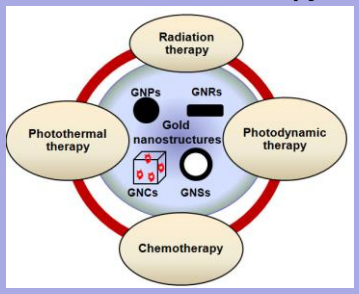
Gold NPs as anticancer drug carriers





Future Direction

Combinational Therapy

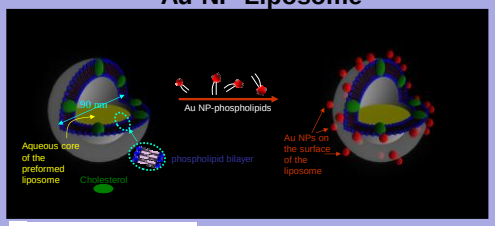


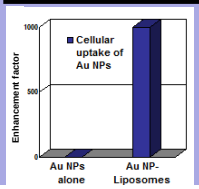
Salomeh Jelvev, B. Devika Chithrani, Cancers, 3, 1081, 2011

Challenges

- Desire to increase the therapeutic ratio (TR)
  - Sensitization of both normal and tumor tissues will not improve the TR
- Sensitization needs to be targeted to improve the TR
- Systemic application of sensitizer requires low toxicity

Au-NP Liposome





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