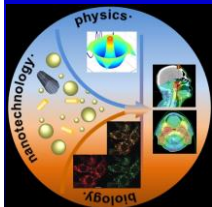


Gold nanoparticles as radiosensitizers



Sunil Krishnan, MD
John E. and Dorothy J. Harris Professor
Director, Center for Radiation Oncology Research
MD Anderson Cancer Center

DISCLOSURE

Relevant Financial Relationship(s)

Grant or research support from:
NIH, DoD, CPRIT, Alliance for Nanohealth, Shell,
Hitachi, FUSF, Dunn Foundation, MDACC

Royalties
Taylor and Francis (book sales)

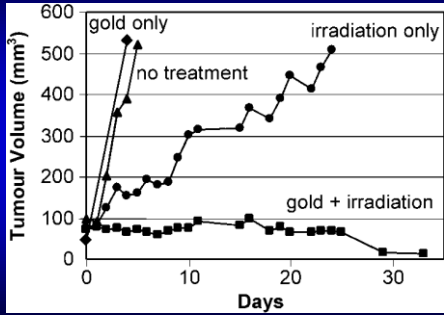
Off Label Usage

None

LEARNING OBJECTIVES

1. Identify ways in which gold nanoparticles may enhance radiosensitivity of tumors
2. Define strategies to amplify radiosensitization by gold nanoparticles
3. Cite barriers to clinical translation of this paradigm

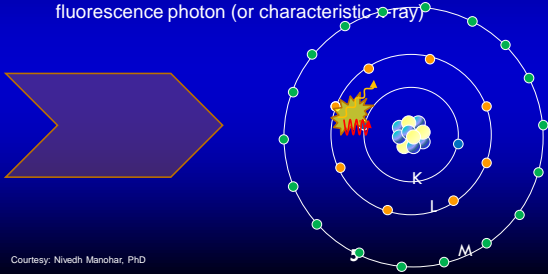
Physical dose enhancement



Hainfeld et al. Phys Med Biol 2004; 49: N309-15

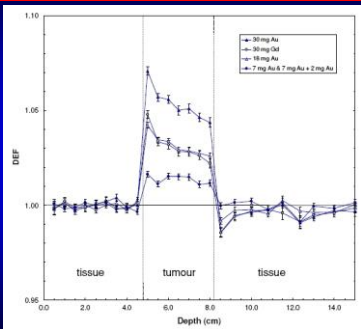
The underlying physics

- Ejection of orbital electron & emission of x-ray fluorescence photon (or characteristic x-ray)



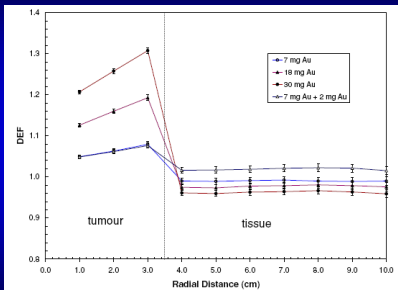
Courtesy: Nivedh Manohar, PhD

Physical dose enhancement



Cho et al. Phys Med Biol 2009

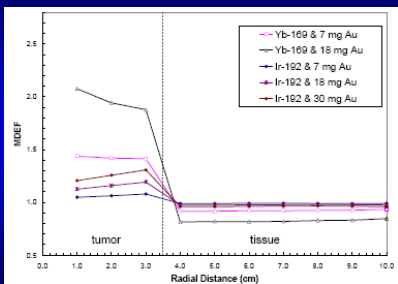
Physical dose enhancement



Cho et al. Phys Med Biol 2009



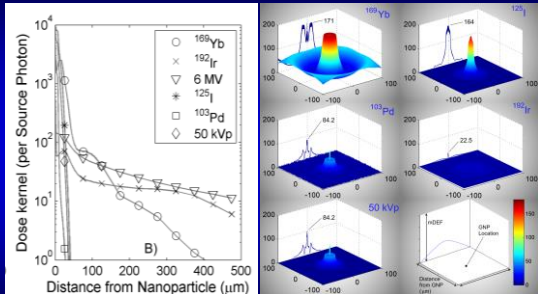
Physical dose enhancement



Cho et al. Phys Med Biol 2009, 54(16):4889-905.



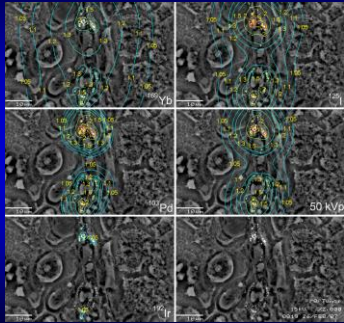
Physical dose enhancement



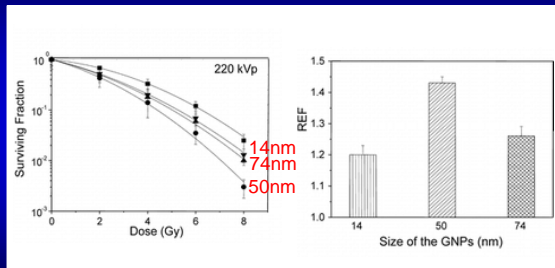
Cho, Krishnan Med Phys 2010



Physical dose enhancement

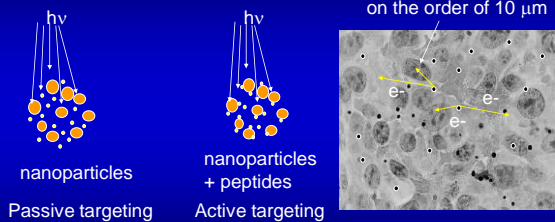


Internalization

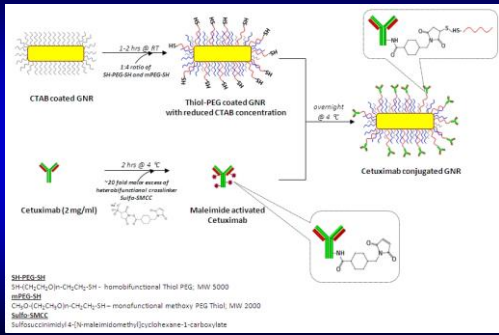


Chithrani DB, et al. Rad Res 2010 173(6):719-728.

Enhancing physical dose enhancement

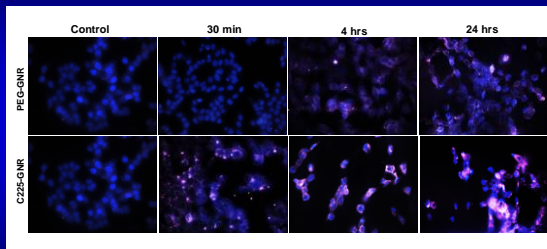


Conjugated gold nanorod

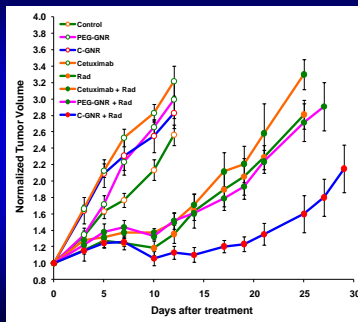


Parmesh Diagaradjane

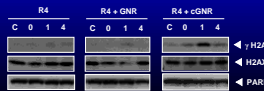
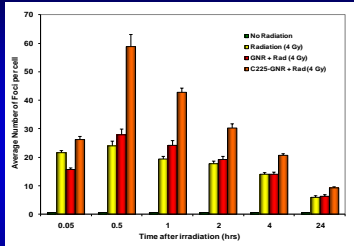
Gold nanorod



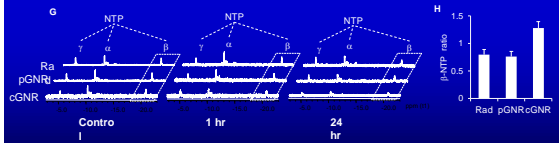
Tumor regrowth delay



DNA damage

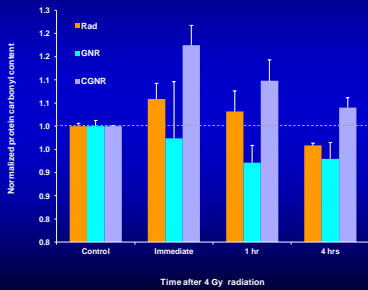


Apoptotic markers

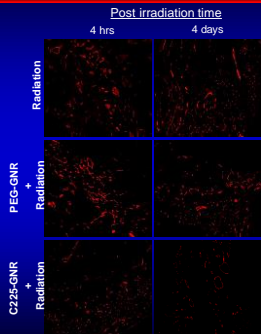


Total oxidative stress

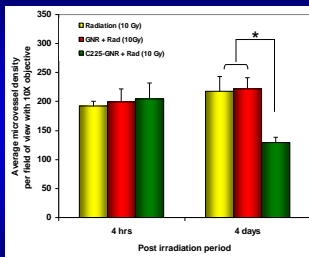
Protein carbonyl assay



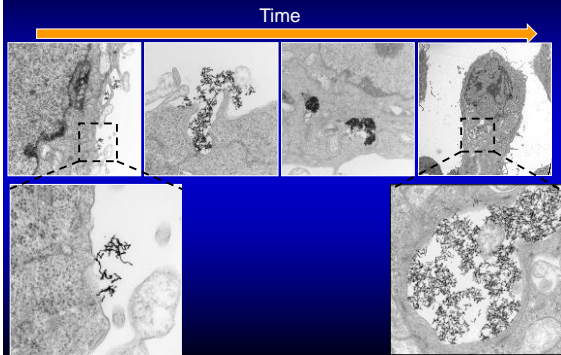
Tissue effects



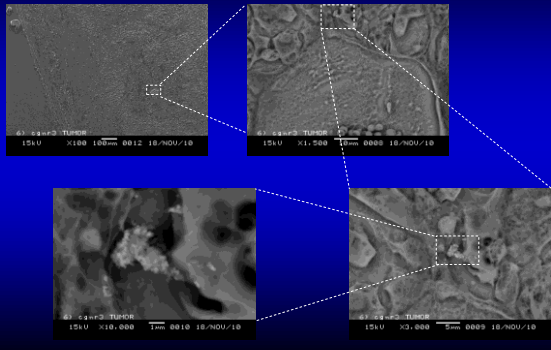
Tissue effects



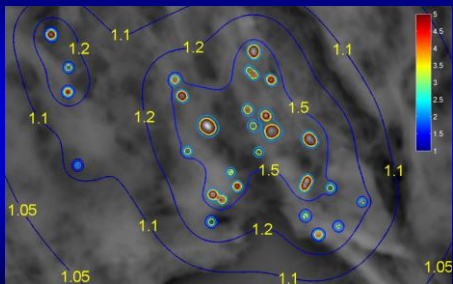
Intracellular distribution

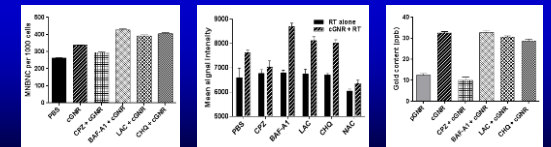
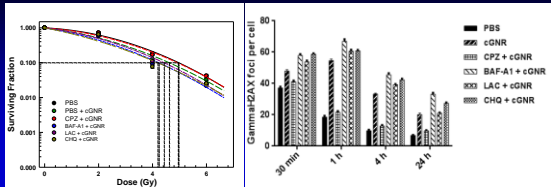


Tissue distribution

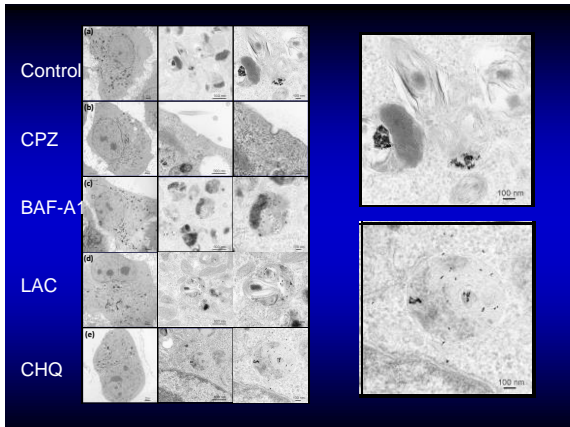


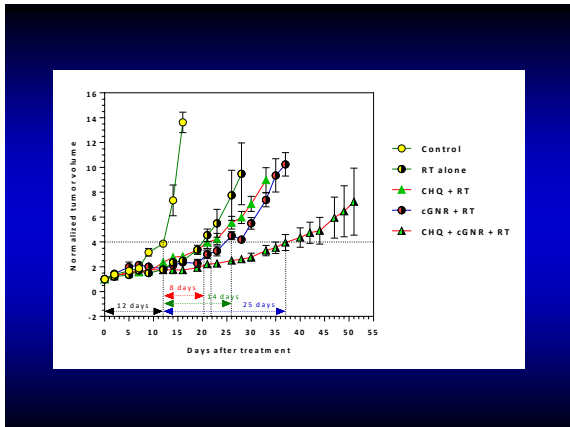
Modeling dose

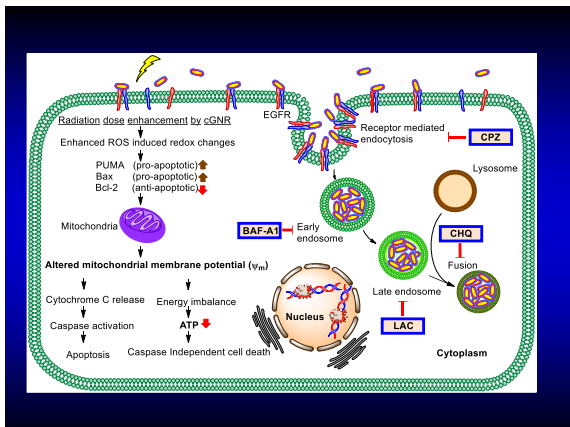




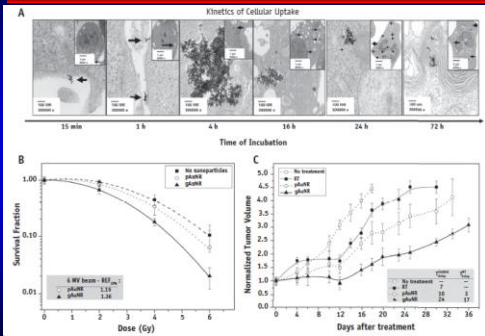
Pankaj Singh







Intracellular distribution

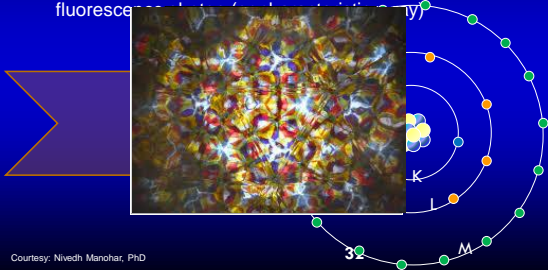


Tatiana Wolfe

Wolfe T, et al. Nanomedicine 2015;11:1277-1283

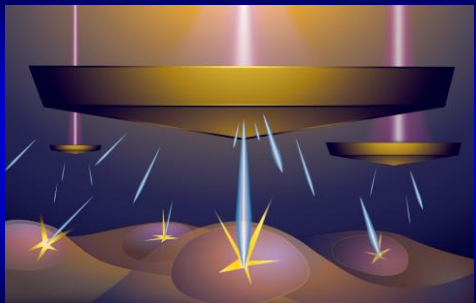
The underlying physics

- Ejection of orbital electron & emission of x-ray fluorescence



Courtesy: Nivedh Manohar, PhD

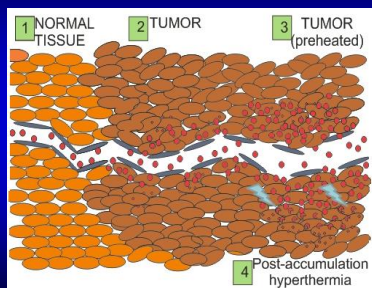
Summary



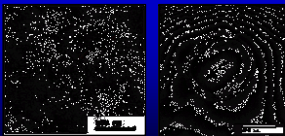
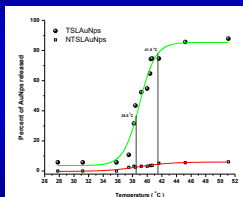
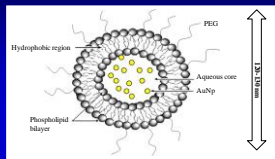
Shanta

Bhattarai SR, et al. Nanoscale. 2017 Apr 20;9(16):5085-5093.

Another approach

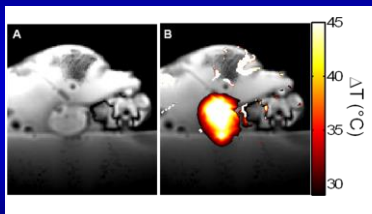


Thermosensitive liposome

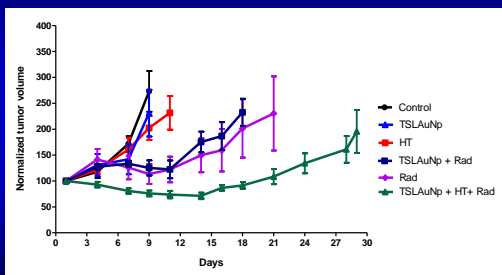


Edward Agyare

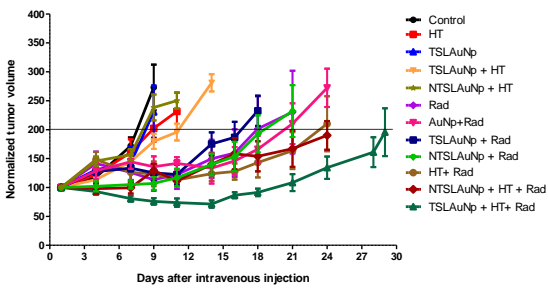
Focused ultrasound



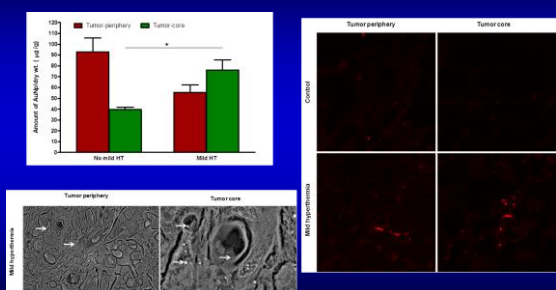
Radiosensitization



Radiosensitization

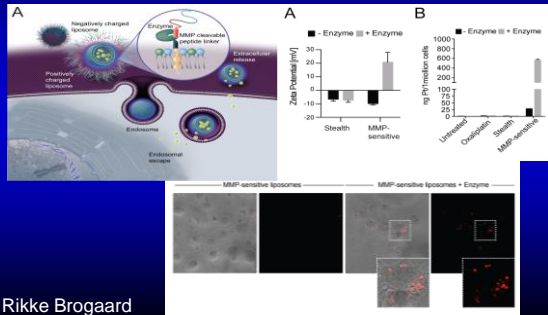


Deep penetration of tumors

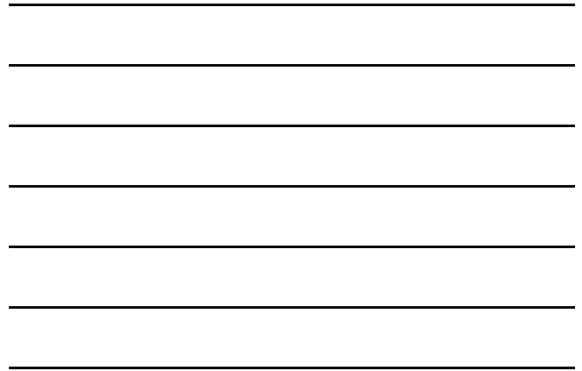


Another approach

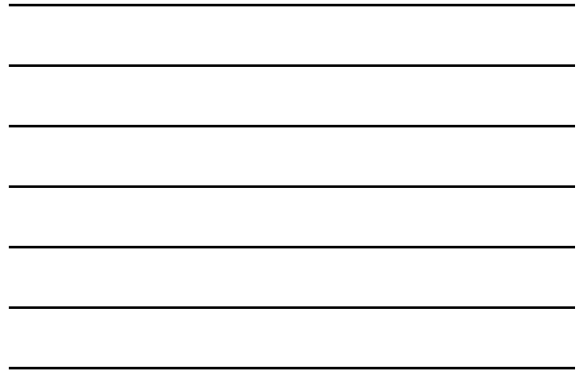
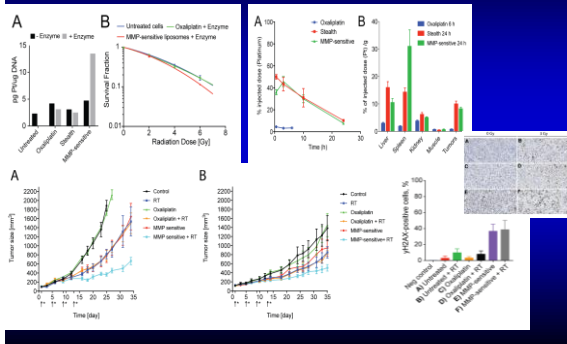
Stimulus-responsive particles



Rikke Brogaard

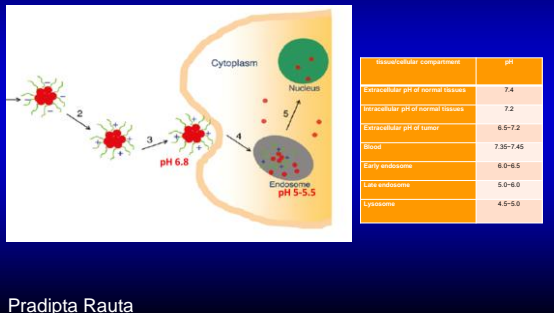


MMP-responsive

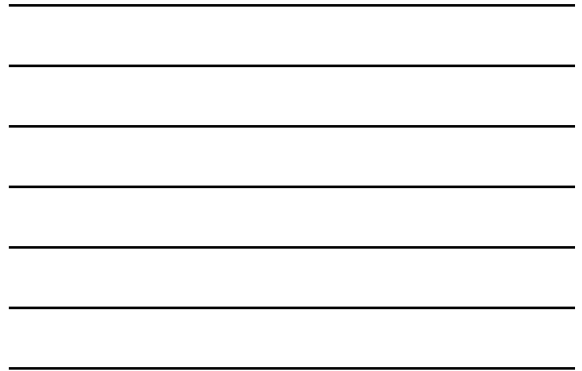


Another approach

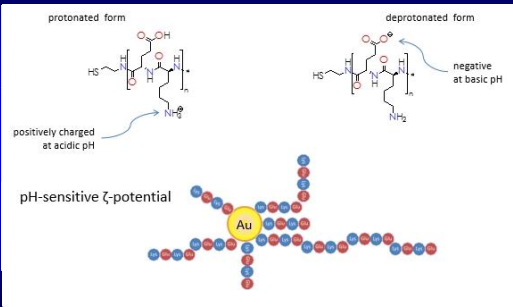
The Strange Case of Dr. Jekyll and Mr. Hyde



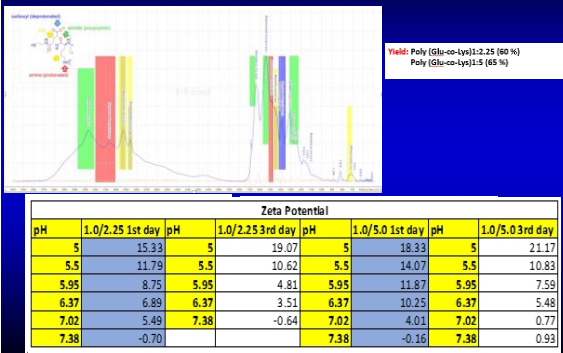
Pradipta Raut



pH-responsive

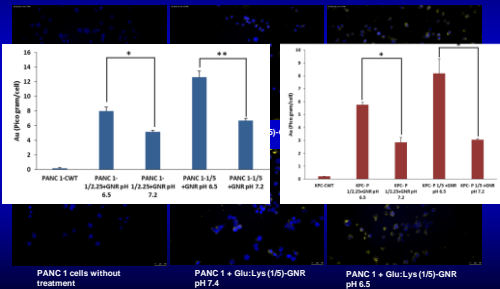


pH-responsive



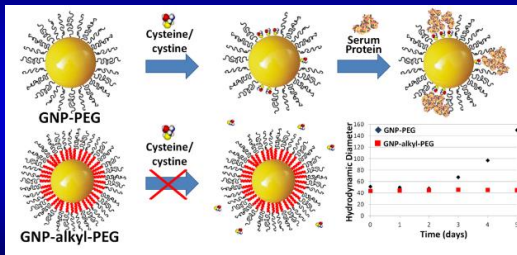
pH-responsive

In vitro study (Intracellular uptake) (24 hr treatment)



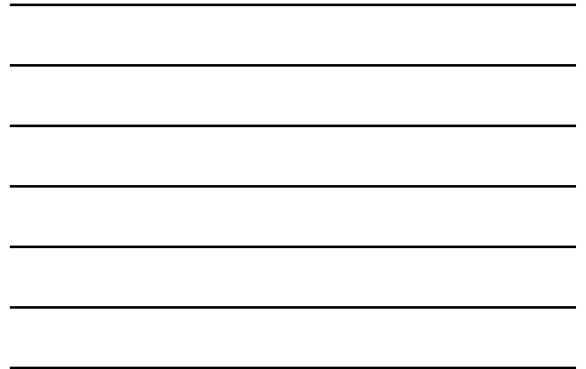
Another approach

Hydrophobic shielding - biofouling

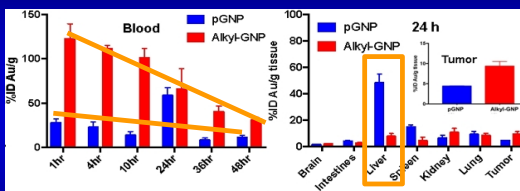


Ashok Reddy

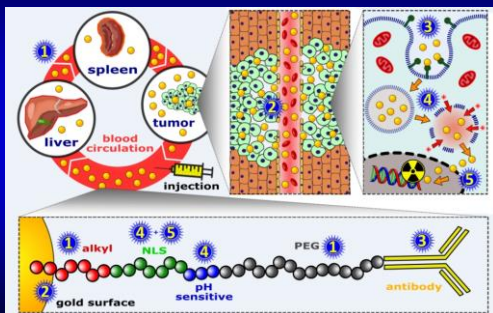
Kostia Sokolov



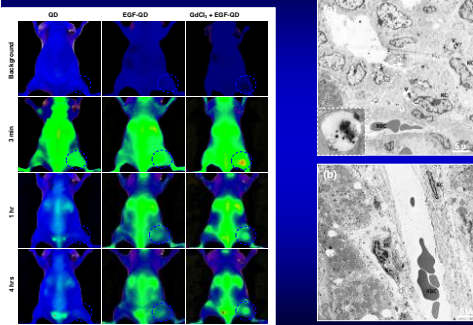
Hydrophobic shielding



Taken together

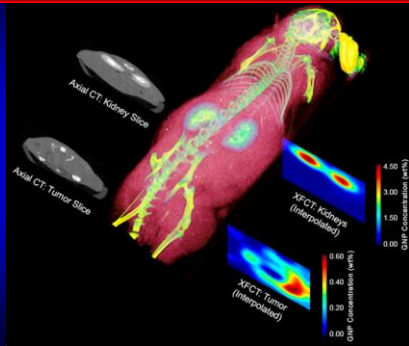


RES capture



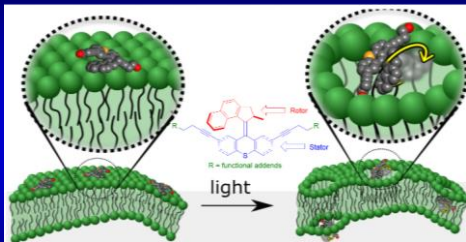
Diagaradjane et al. ACS Nano, 2010

X-ray fluorescence imaging



Manohar N, et al. Sci Rep. 2016 Feb 25;6:22079.

Molecular nanomachine

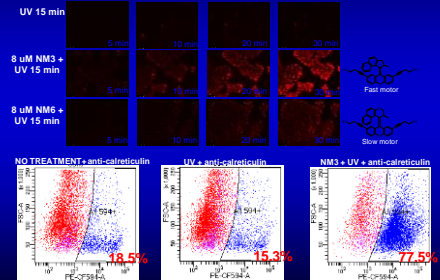


Ciceron Ayala-Orozco

Jim Tour

Molecular nanomachine

Treatment of KPC cells with 365 nm Light at 80 mW/cm²

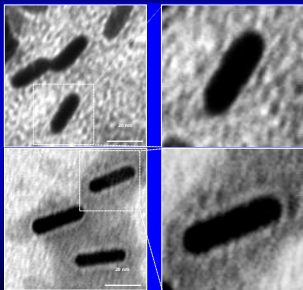


What nanoparticles work best?



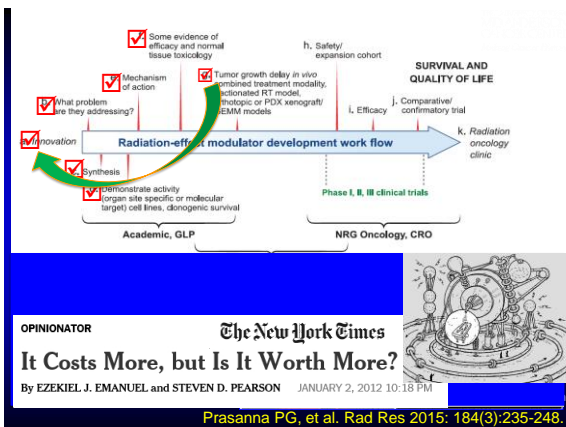
Bland?

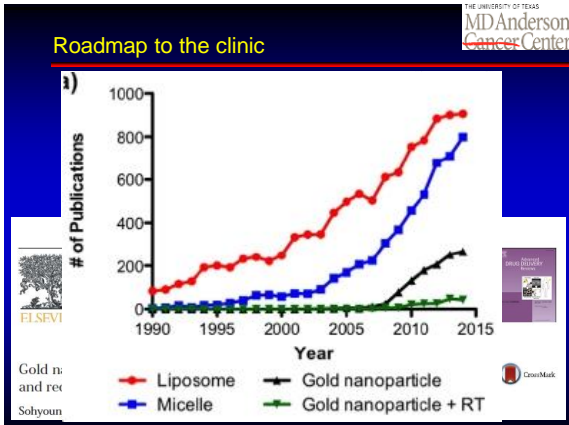
Spicy?



What nanoparticles work best?







Acknowledgements

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 Parmesh Diagaradjane
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 Shanta Bhattacharai
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Texas Southern Univ
 Huan Xie

Cancer Nanotechnology
 Principles and Applications in Radiation Oncology
 Edited by Sang Hyun Cho, PhD and Sunil Krishnan, MD
 CRC Press
 Taylor & Francis Group

