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

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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
The underlying physics

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

Courtesy: Nivedh Manohar, PhD

Physical dose enhancement


Physical dose enhancement

Physical dose enhancement


Physical dose enhancement


Physical dose enhancement

Cho, Krishnan Med Phys 2010
Physical dose enhancement

Internalization

Enhancing physical dose enhancement

Conjugated gold nanorod

Gold nanorod

Tumor regrowth delay

Normalized Tumor Volume

Days after treatment

Control
PEG-GNR
C-GNR
Cetuximab
Rad
Cetuximab + Rad
PEG-GNR + Rad
C-GNR + Rad
Biodistribution

Clonogenic survival

DNA damage
**Tissue effects**

- Post irradiation time:
  - 4 hrs
  - 4 days

- Radiation
- PEG- GNR + Radiation
- C225-GNR + Radiation

**Average microvessel density per field of view with 10X objective**

- Radiation (10 Gy)
- GNR + Rad (10 Gy)
- C225-GNR + Rad (10 Gy)

**Intracellular distribution**

- Time

- Intracellular distribution images
Control
CPZ
BAF-A
LAC
CHQ

Days after treatment

Normalized tumor volume

0 5 10 15 20 25 30 35 40

Control
RT alone
CHQ + RT
cGNR + RT
CHQ + cGNR + RT
12 days
8 days
14 days
25 days

Radiation dose enhancement by cGNR
Enhanced ROS induced mito changes
PLA2A
Cytochrome C release
Apoptosis
ATP
Cytochrome B
Caspase activation
Cytochromes
ROS
Lysosome
Caspase independent cell death

Pre-apoptotic
Pre-apoptosis
Post-apoptosis
Post-apoptotic
Mitochondria

Altered mitochondrial membrane potential (Δψm)

Fusion
Lac
cGNR
CPZ
Cytochrome
Intracellular distribution


Tatiana Wolfe

The underlying physics

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

Courtesy: Nivedh Manohar, PhD

Summary


Shanta
Another approach

Thermosensitive liposome

Focused ultrasound

Edward Agyare
Another approach

Stimulus-responsive particles

Rikke Brogaard

MMP-responsive

The Strange Case of Dr. Jekyll and Mr. Hyde

Pradipra Rauta
**pH-responsive**

**pH-sensitive ζ-potential**

Table: Poly (Glu-methacrylic acid 30:70)

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</tbody>
</table>

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

Hydrophobic shielding - biofouling

GNP-PEG

Cytoskeleton/cytoskeleton

Protein

Taken together

Hydrophobic shielding

Enzyme

Blood

GNP

Alkyl-GNP

24 h

MCgTg expression

TNBC

Spleen

Tumor

Spleen

Blood circulation

Injection

Alkyl

PEG

Antibody
Molecular nanomachine

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

UV 15 min
0 µM NM6 + UV 15 min
0 µM NM6 + UV 10 min

NO TREATMENT + anti-calreticulin
UV + anti-calreticulin
NM3 + UV + anti-calreticulin

What nanoparticles work best?

Bland?
Spicy?

What nanoparticles work best?