Selective cancer cell toxicity and radiosensitization using different high atomic number nanoparticles

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Selective cancer cell toxicity and radiosensitization using different high atomic number nanoparticles

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Radiotherapy = 50% of cancer treatments

EFFICIENT BUT:

• Toxic for surrounding tissues
• Radioresistance of several cancers
• Need to make radiotherapy selectively toxic for cancer cells

HOW?

• Nanomaterials
Radiosensitization using nanoparticles (NPs)

Previously shown for the first time with **kilovoltage** energies X-rays radiation

With Gold NPs
1.9 nm size

![Graph showing tumor volume vs days with different treatments](image)

**Average tumor volume on mice with or without treatment**
- Intravenous gold injection (1.35 g Au/kg)
- Irradiation 30 Gy, 250 kVp, 2 min post injection
- (Hainfeld et al, 2004, Physics in Medicine and Biology 49(18))

Further characterisation and optimisation needs to be done, especially using different types of energies
THE PROJECT

Irradiation (Photons, Protons and Heavy ions)

Synthesis of Nanoparticles

Understanding Cellular Damage

Preclinical Evaluation

Theoretical Modelling & Experimentation
Main aims of research:

• Design, optimise and characterise nanoparticles for cancer radiotherapy

• Optimising radiosensitization by:
  → Selective targeting of cancer cells and organelles
  → Increasing the level of oxidative stress

• Measure toxicity and potential effect on skin and breast in vitro model of two types of NPs:
  → Gold NPs (αGal/PEGamine coated)
  → Ceria NPs (cerium oxide)
First results with skin models exposed to Gold NPs (AuNPs)

AuNPs coated with αGal/PEGamine selectively accumulate in skin cancer cells, probably in lysosomes.
First results with skin models exposed to Gold NPs (AuNPs)

Skin normal cells; 3 hrs of exposure, 10 μg/ml
AuNPs coated with αGal/PEGamine are selectively toxic for skin cancer cells and give an additive effect in combination with X-ray radiotherapy.
Cerium Oxide NPs (ceria NPs), characterization

- Offer interesting properties as a large transport and storage of oxygen \([1]\)

- Characterised as radioprotector or radiosensitiser depending on the pH\([2]\) of the environment and the energy of irradiation \([3]\)

- Few investigations on its potential as a radiosensitiser, nothing in combination with heavy elements

Cerium Oxide NPs, toxicity

Explored on *in vitro* models, with a clonogenic assay

- Ceria NPs commercially available, average size of 5 nm

- Homemade (in collaboration with chemists at the Open University) in combination with bismuth or gold

  Average size of 3 nm

**viability of cells exposed to ceria NPs for 6h**

- **skin cancer**
- **skin normal**
- **breast cancer**

**concentration of ceria NPs (μg/ml)**
Summary and future work

- **AuNPs** coated with αGal/PEGamine selectively toxic for skin cancer cells; additive effect in combination with X-ray radiotherapy

- **Ceria NPs**, in combination with bismuth, gold
  → Could increase radiation induced oxidative stress in the tumour environment

Any other types of NPs: high atomic number? Oxygen storage? Any ideas are welcome!

These NPs will be tested on different cancer cells and in combination with radiotherapy. A comparison between low energy and high energy photon will be explored.
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