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

Conference or Workshop Item

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

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Advanced Radiotherapy, Generated by Exploiting Nanoprocesses and Technologies

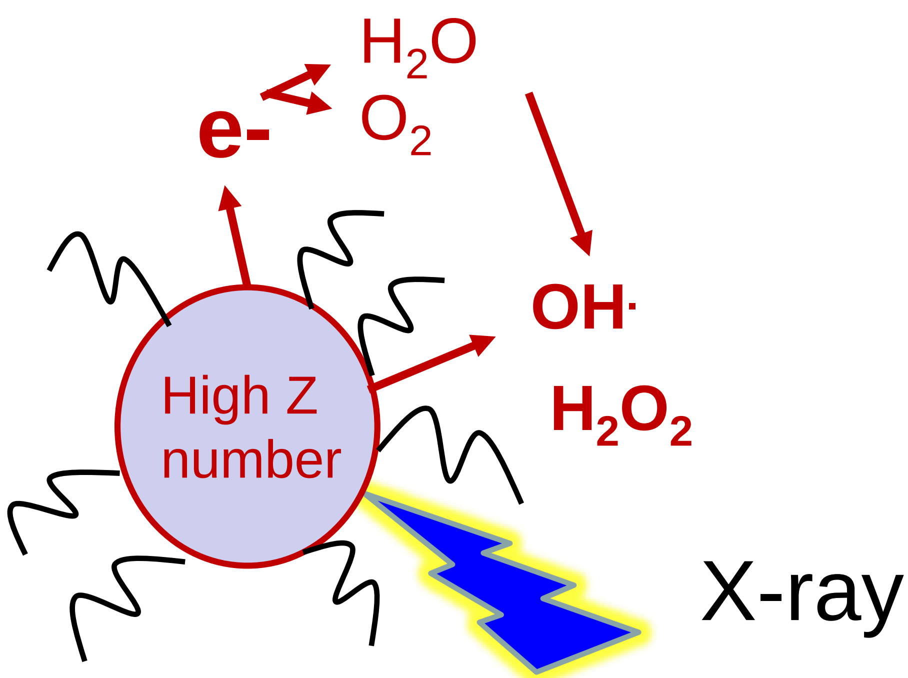
# Radiotherapy = 50% of cancer treatments

**EFFICIENT BUT:**

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

**HOW ?**

- Nanomaterials

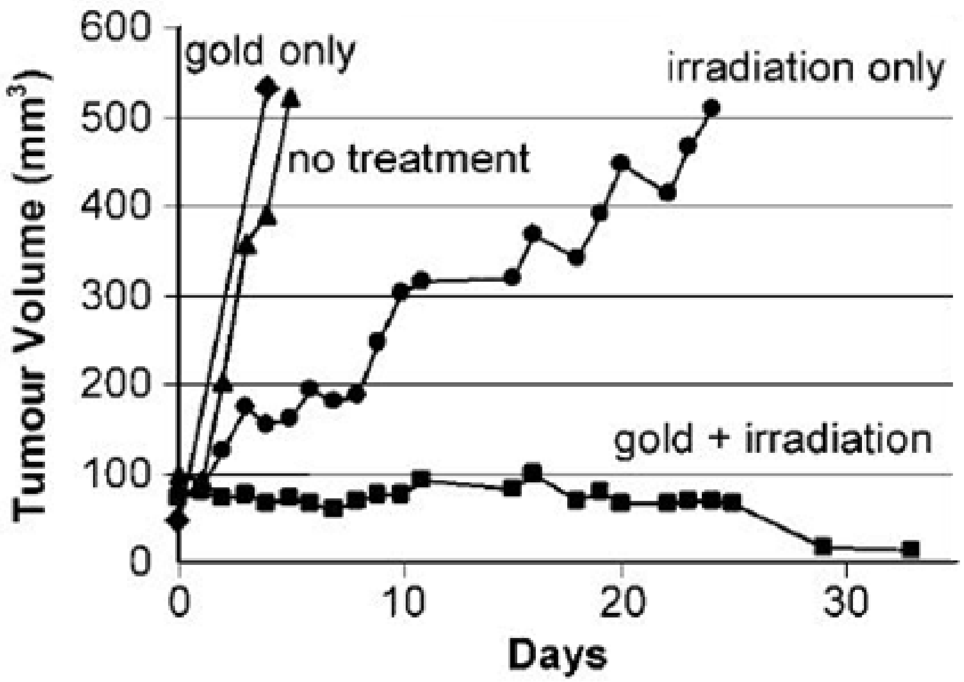


# Radiosensitization using nanoparticles (NPs)



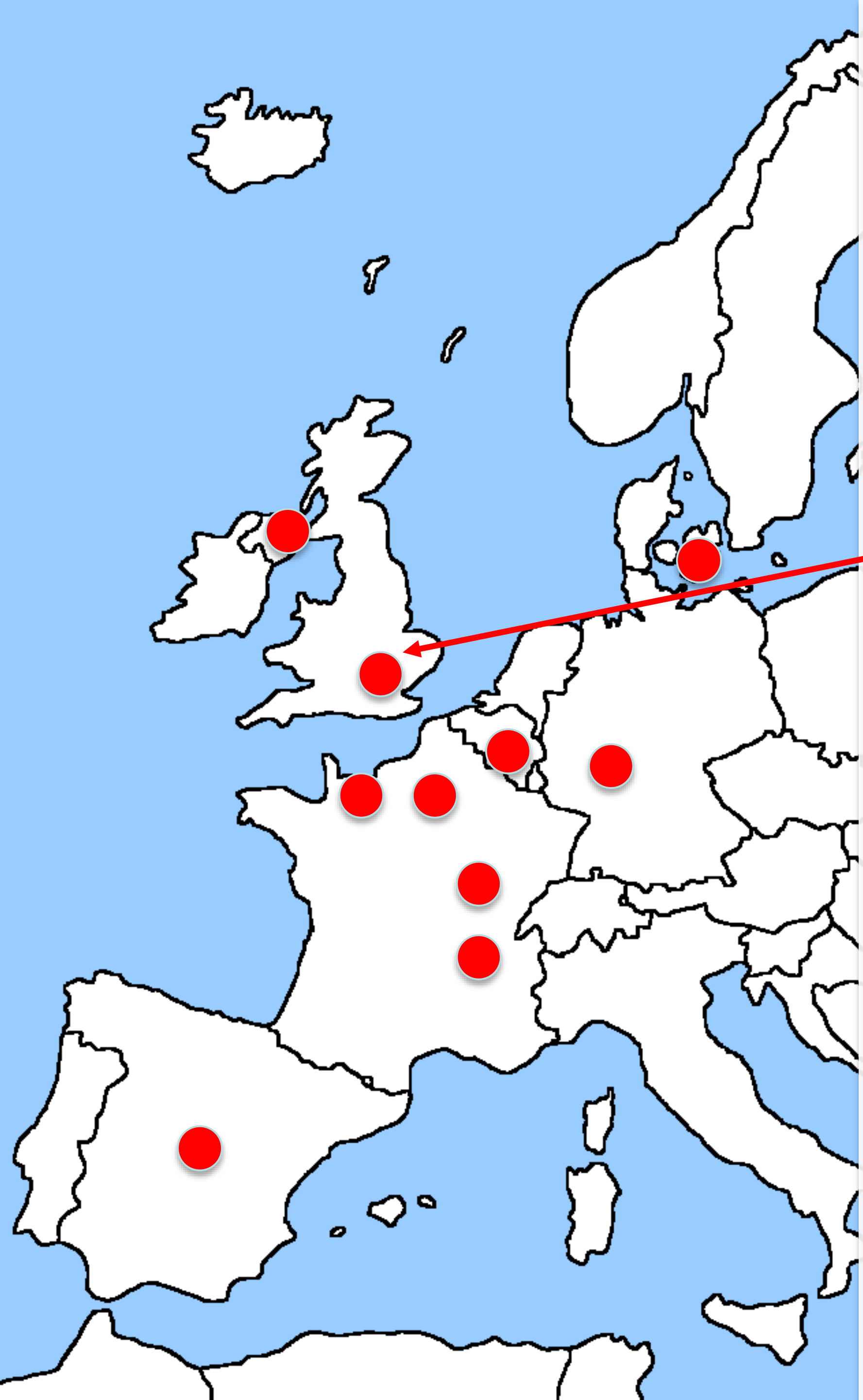
Previously shown for the first time with **kilovoltage** energies X-rays radiation

With Gold NPs
1.9 nm size




Average tumour 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 ARGENT PROJECT

Advanced Radiotherapy, Generated by Exploiting Nanoprocesses and Technologies

## Academic Partners

- GSI Helmholtzzentrum für Schwerionenforschung GmbH
- MBN Research Center
- Queen's University Belfast
- cea
- The Open University
- CSIC – Consejo Superior de Investigaciones Científicas
- cnrs – dépasser les frontières

## Industrial Partners

- nano-h – Value-Added Nanotechnology
- Quantum Wise
- CheMatech – macrocycle design technologies

## Associated Partners

- HIT – Heidelberger Ionenstrahl-Therapiezentrum
- Centre de Lutte contre le Cancer François Baclesse
- Hospital Universitario Puerta de Hierro Majadahonda – SaludMadrid – Comunidad de Madrid
- iba
- Minerva – The knowledge brokers

# THE Argent PROJECT

Advanced Radiotherapy, Generated by Exploiting Nanoprocesses and Technologies

**Irradiation**
(Photons, Protons and Heavy ions)
X-rays

**Synthesis of Nanoparticles**

NANO → **MACRO**

**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

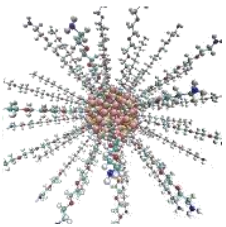
→ Increasing the level of oxidative stress

- 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)

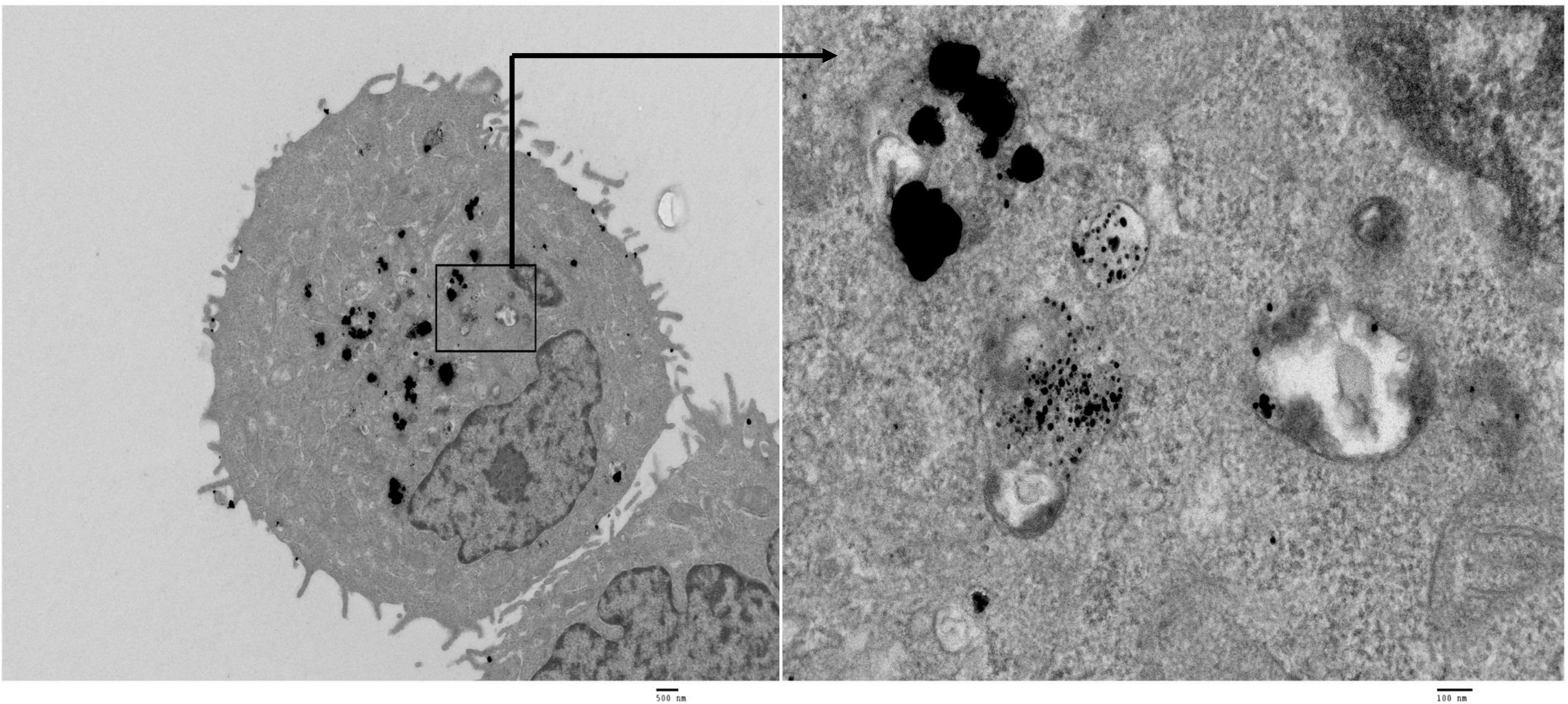
# First results with skin models exposed to Gold NPs (AuNPs)



Z = 79

Average size 4.5 nm
αGal/PEGamine

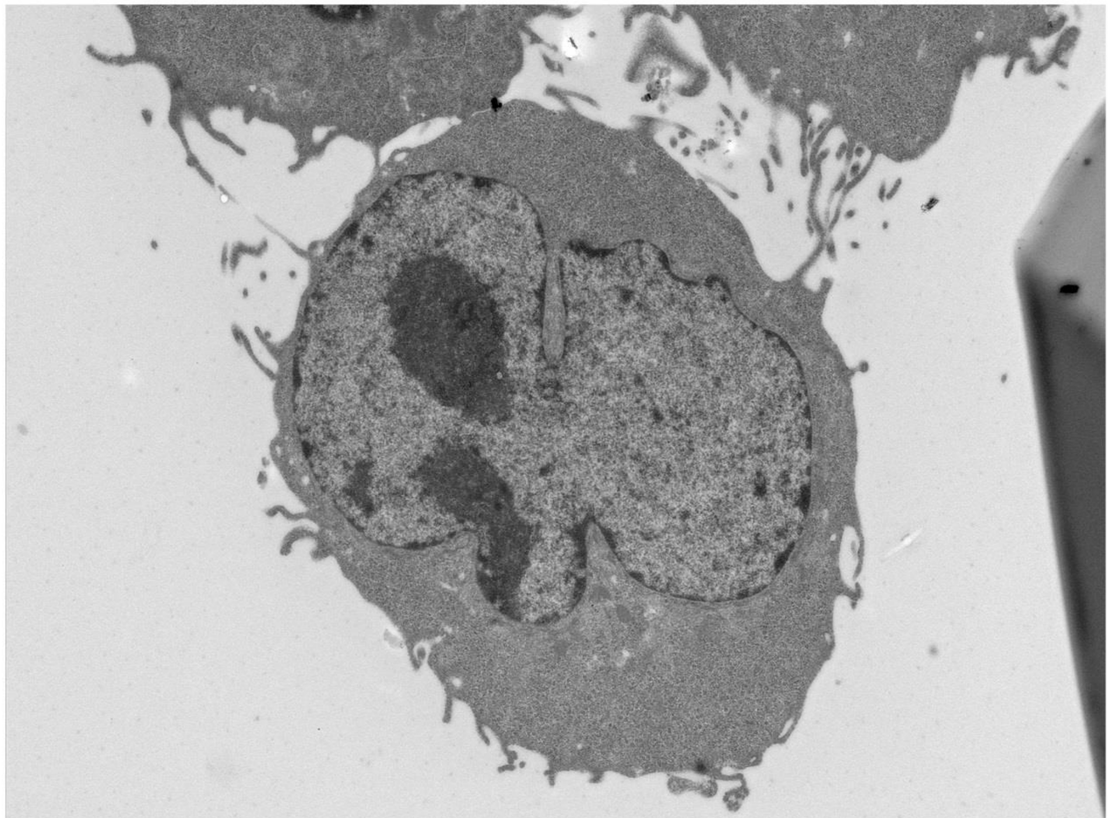
Skin cancer cells ;  3 hrs of exposure, 10 μg/ml




AuNPs coated with αGal/PEGamine selectively accumulate in skin cancer cells, probably in lysosomes

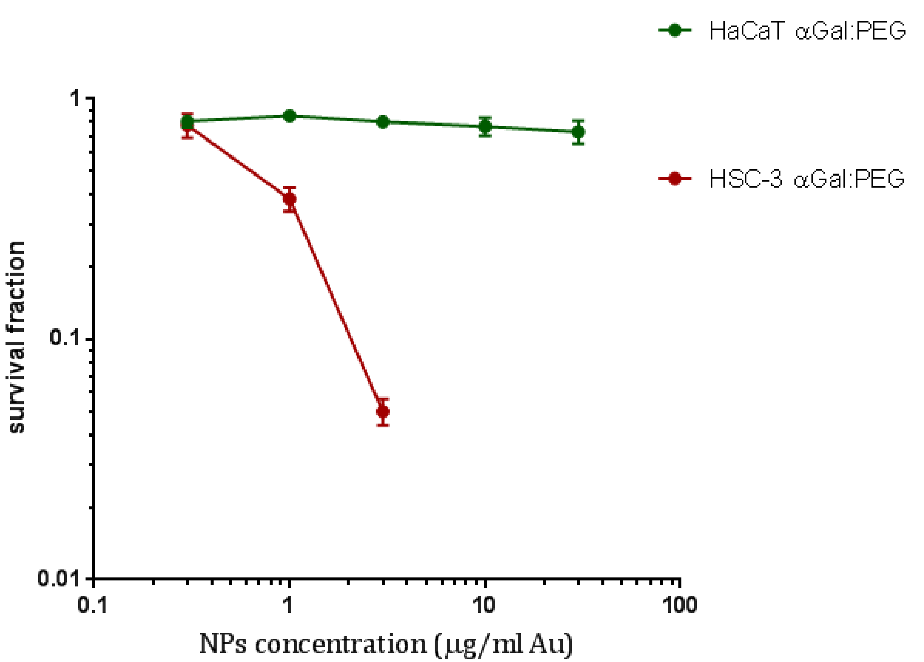
# First results with skin models exposed to Gold NPs (AuNPs)

Skin normal cells; 3 hrs of exposure, 10 µg/ml

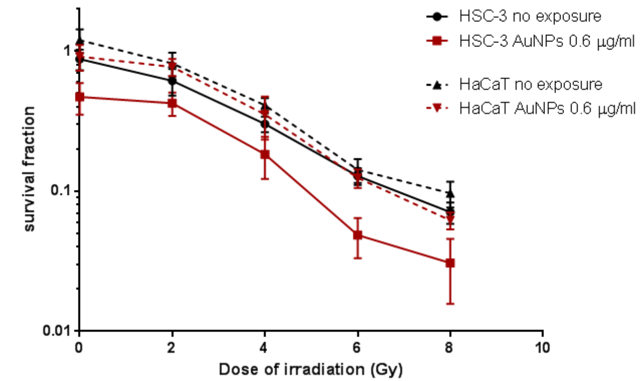


# First results with skin models exposed to Gold NPs (AuNPs)

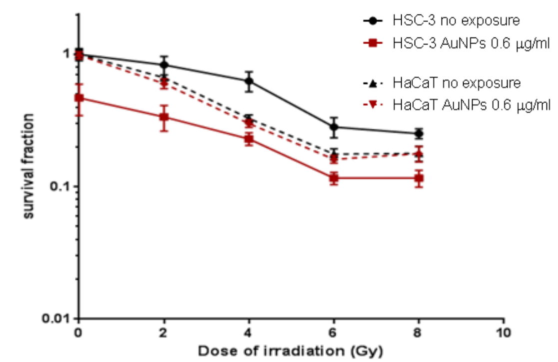
Dose vs response AuNPs 3h exposure




Cells exposed to 220 keV X-rays irradiation

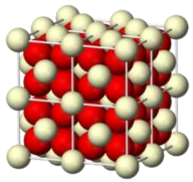



Cells exposed to 6 MeV X-rays irradiation




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



Z = 58

- 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

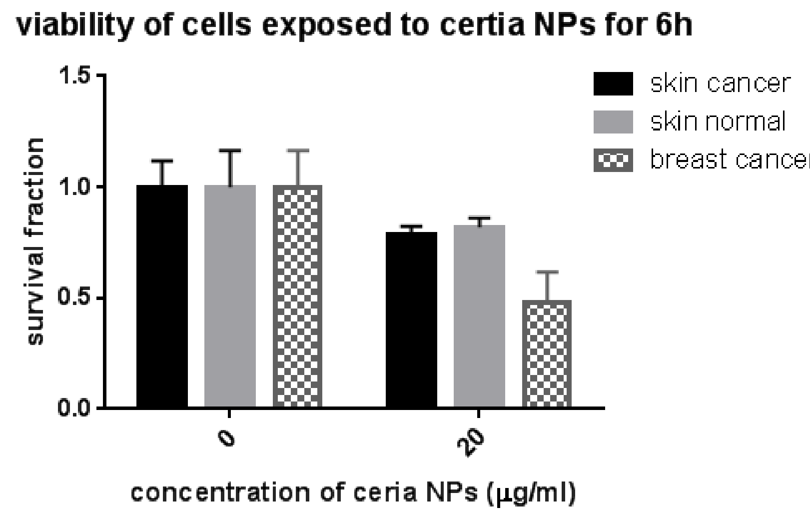
1. Goharshadi EK *et al.,(*2011). Journal of Colloid and Interface Science 356: 473-480
2. Gao Y *et al*., (2014). OncoTargets and therapy 7: 835-840
3. Briggs A *et al.,(*2013). Nanomedicine: Nanotechnology, Biology and Medicine 9: 1098-1105

# Cerium Oxide NPs, toxicity

The Open University

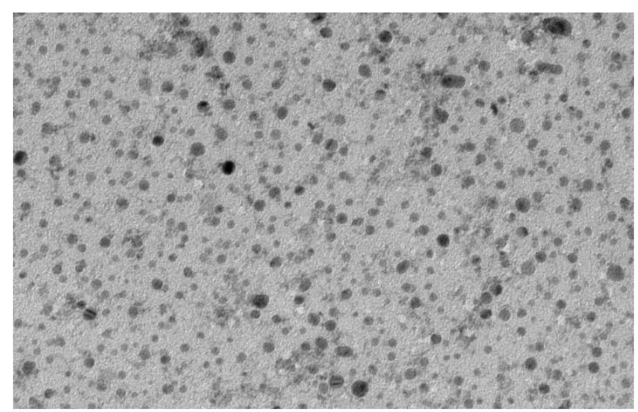
Explored on *in vitro* models, with a clonogenic assay

- 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



20 nm TEM
HV=80.0kV Direct mag: 200000×

# Summary and future work

The Open University

- **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

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

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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