Binding of nanoparticles and adenoviruses to target cancer

[1]Edward-Jones S, [6]Ada E, [5]Saini V, [1, 3]Thompson GB, [1,2] Bagaria, HG, [5]Maaike E, [1,4]Nikles DE, [1,2]Johnson DT, [5]Curiel DT

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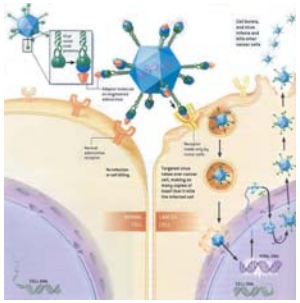
Magnetic Fluid Hyperthermia

- Hyperthermia therapy for cancer involves heating of cancerous tissue to kill cancer (typically ~45°C)
- In magnetic fluid hyperthermia (MFH) magnetic nanoparticles are heated by applying an alternating magnetic field
- How to localize magnetic nanoparticles to the cancerous tissue to prevent healthy tissue damage ? – with Adenoviruses! (that give common cold)

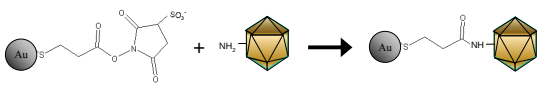
Genetically Modified Adenoviruses to Target Cancer

- Dr. Curiel's group at UAB have developed genetically modified adenoviruses that can target the cancerous tissue



Nettleback and Curiel, *Sci. Am.*, Oct. 2003

- Magnetic nanoparticles can be targeted to the cancer by binding them to these adenoviruses
- 2 nm gold particles have been conjugated to adenoviruses[1], but large nanoparticles (10-20 nm) are required for MFH
- Here we attempt to bind ~15 nm gold nanoparticles (as a model system) to adenoviruses
- Providing succinimide or sulfo-succinimide groups on nanoparticles can facilitate their conjugation to the adenoviruses (through lysine residues on adenoviruses' capsid protein as shown below)

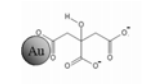


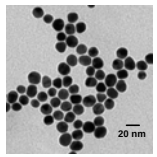
Au nanoparticle with Sulfo-succinimide functionality | Adenovirus | Au nanoparticle conjugated to Adenovirus

[1] Everts et al., *Nano Letters*, *6*, 587-591

Preparation of ~15 nm Au nanoparticles

144µl of 1.42 M of Tetrachloro aurate
+
500 ml of DI water
↓ Heated to boil
Inject 15 ml of 1% (by weight) of Sodium citrate solution in water
↓ Color changes from yellow, to blue black to violet to red
Boil for 30 minutes and cool

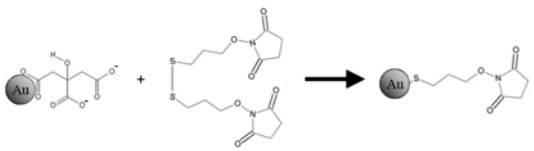




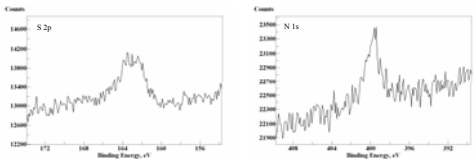
TEM image of Au nanoparticles

Frens G. *Nature* 1973

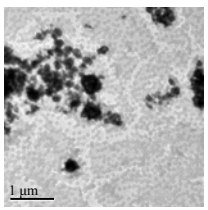
Ligand Exchange with DTSP to Introduce Succinimide Groups on Au nanoparticle's surface



Au nanoparticle with citric acid | Excess DTSP ligand | Au nanoparticle with DTSP ligand



- S2p and N1s XPS spectra confirm the presence of adsorbed DTSP on Au nanoparticles
- Ligand-exchanged particles were mixed with adenoviruses following the procedure described in Everts *et al.*[1]
- Particles appeared to have precipitated probably due to decreased negative charge from displacement of citric acid by uncharged DTSP

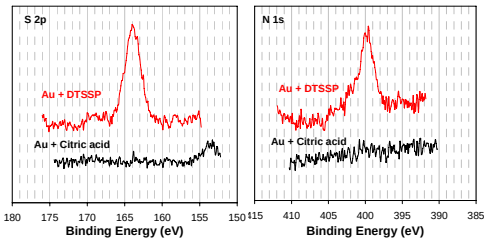


- TEM image of DTSP ligand-exchanged Au nanoparticles with adenoviruses
- Dark spots are aggregated Au particles and the light regular features (~70 nm) are adenoviruses
- Au particles did not bind to adenoviruses

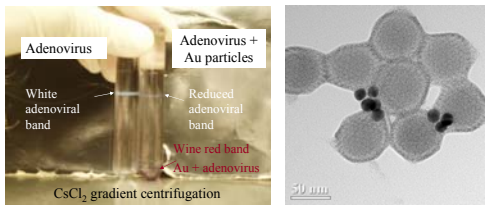
Ligand Exchange with DTSSP to Introduce Succinimide Groups on Au nanoparticle's surface

- Charged DTSSP may stabilize particles better than uncharged DTSP

Au nanoparticle with citric acid | Excess DTSSP ligand | Au nanoparticle with DTSSP ligand



- S2p and N1s XPS spectra indicate that DTSSP is present on Au nanoparticles after ligand exchange
- Particles appeared visibly stable when mixed with adenoviruses



- $CsCl_2$ gradient centrifguation suggests that Au nanoparticles with DTSSP ligands bind to adenoviruses
- TEM image of the wine red centriguation bottoms confirms that Au nanoparticles are bound to adenoviruses
- Au particles appear to cross-link between adenoviruses

Conclusions and Future work

- Au nanoparticles aggregated after ligand exchange with DTSP and hence could not bind to adenoviruses
- However, DTSSP ligand-exchanged Au particles were found to be stable and were successful in binding particles with adenoviruses
- Infectivity studies need to be performed to ensure that adenoviruses are functional after conjugation with Au particles