

“Pharmacokinetic Aspects of Nanoparticles”

It is not what does the nanoparticle to the body,
But what does the body to the nanoparticle



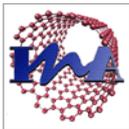
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How silver turns people blue

[editor](#), 7 November 2012 (created 7 November 2012)

Ingesting silver — in antimicrobial health tonics or for grayish-blue. Brown researchers have discovered how the silver.

Researchers from Brown University have shown for the first time how silver turns a striking shade of grayish blue.

"It's the first conceptual model giving the whole picture of the research team. "What's interesting here is that the silver particles are actually lodged deep in the stomach, absorbed into the bloodstream as a salt and then they create the telltale bluish hue. That final stage, oddly, is caused by a complex series of chemical reactions in the acidic environment of the gastrointestinal tract; on the membranes of the skin.

Scientists have known for years argyria had something to do with silver. In 1999, researchers from Brown University showed that patients with argyria actually had silver particles lodged deep in their stomachs.

As it turns out, argyria is caused by a complex series of chemical reactions in the acidic environment of the gastrointestinal tract; on the membranes of the skin.

From silver to salt and back again

Hurt and his team have been studying the environment of silver in acidic environments, giving off charged ions. The silver ions are postdoctoral fellow at the National Institute of Standards and Technology, and could play a role in argyria.

To find out, the researchers mixed a series of chemical reactions in the acidic environment of the gastrointestinal tract; on the membranes of the skin.

They found that nanosilver corrodes in stomach acid, forming positively charged silver salt ions. Those ions

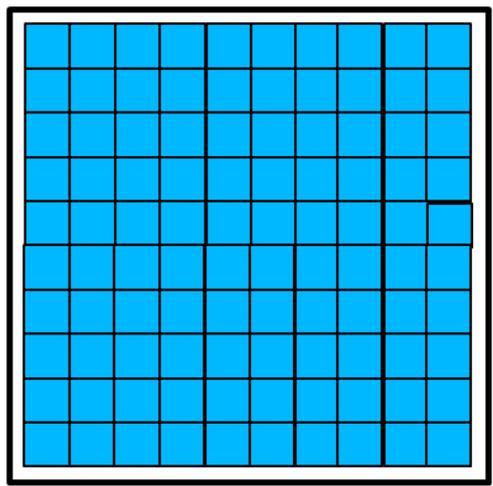


Paul Karason and his girlfriend, Jackie Northrup.

From: nano Ag^0 to AgCl to AgCl_2^- then UV to Ag^0 and to Ag_2S

THE CASE OF CISPLATIN

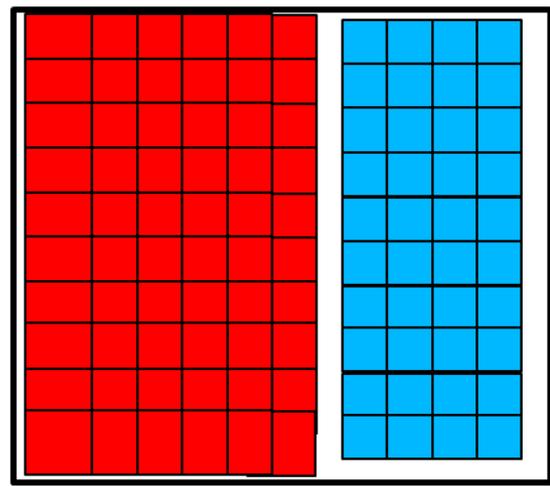
BODY → TUMOR



I

Injected Dose

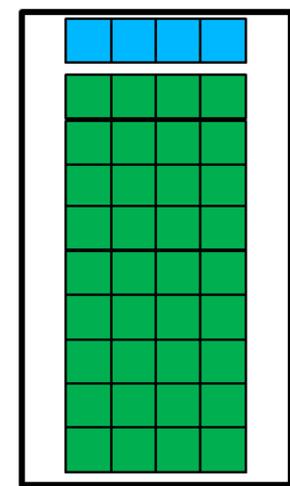
100%



II

Renal excretion
and nephrotoxicity

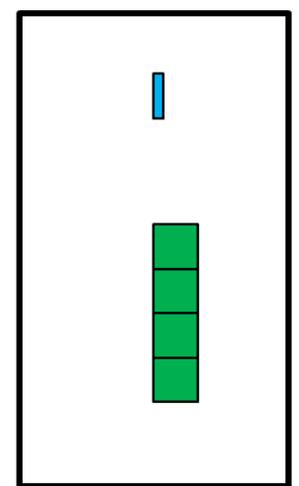
60%



III

Albumin Binding

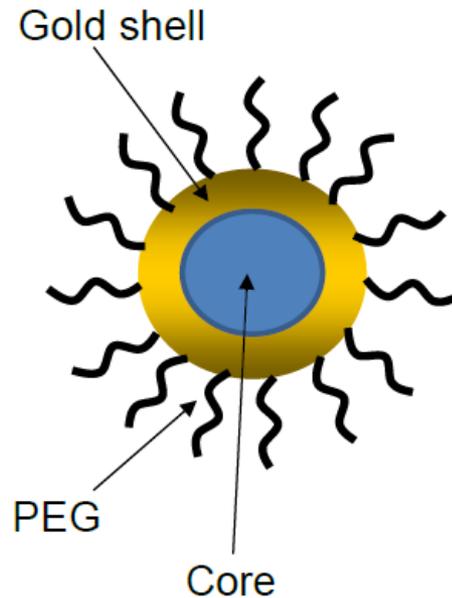
90%



IV

Free CisPt 0.12%

Bound CisPt 3%

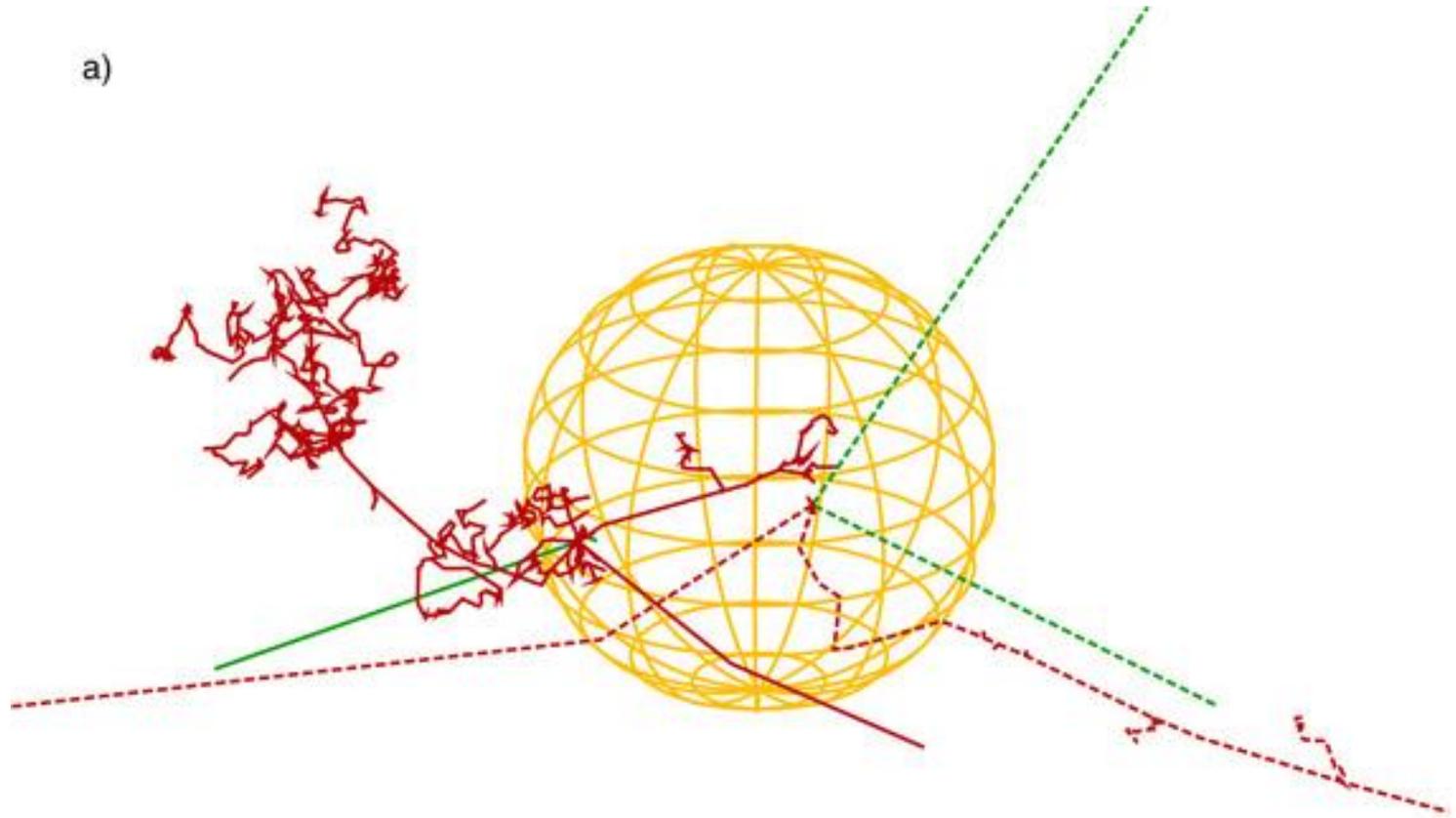


Batch 1

Batch 2

- Two batches of core shell nanomaterials appeared identical to physicochemical characterization. The 1st batch was 6 months older than the 2nd batch.
- In tox studies, 1st batch caused extensive lung lesions, 2nd batch was largely benign.
- What's causing the dramatically different safety profiles of seemingly identical batches?

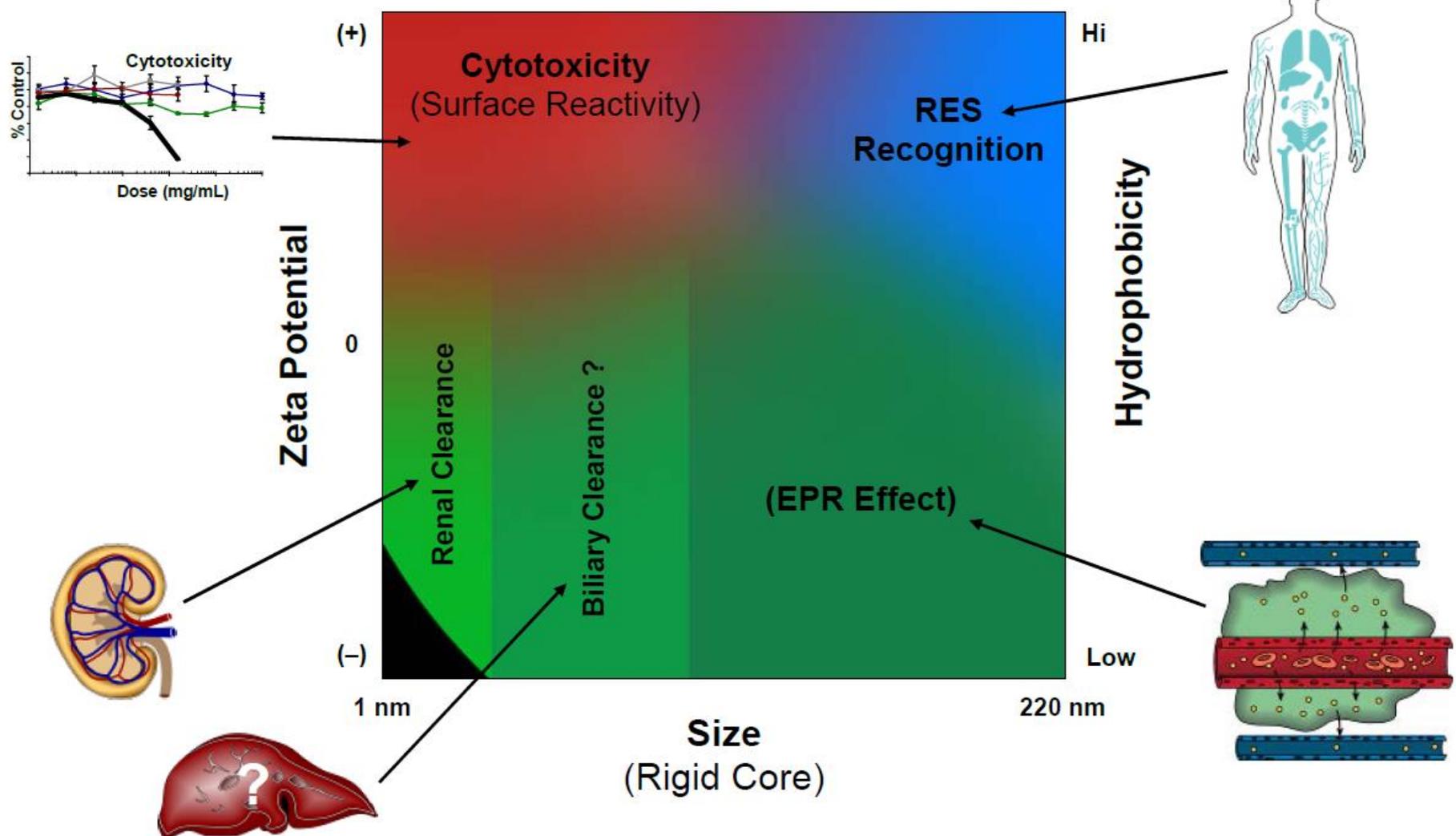
IMAGING AGENTS – RADIO ENHANCERS



Biological consequences of nanoscale energy deposition near irradiated heavy atom nanoparticles

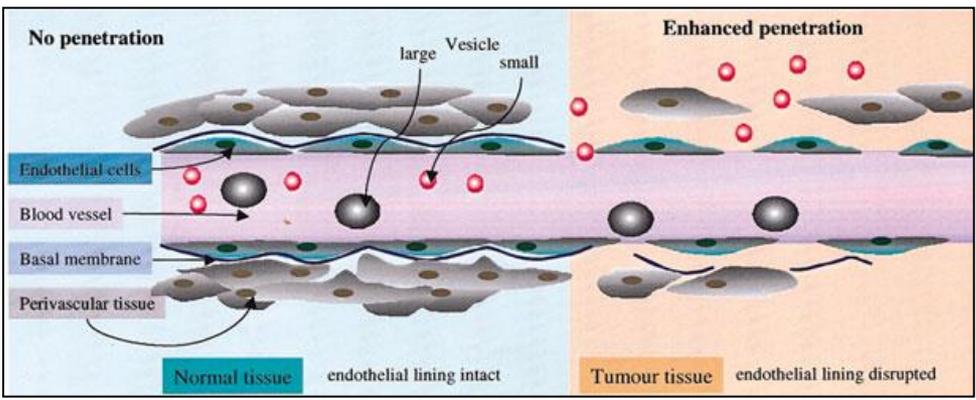
. Currell et al, Scientific Reports 1, 18 (2011)

Nanoparticle Biocompatibility

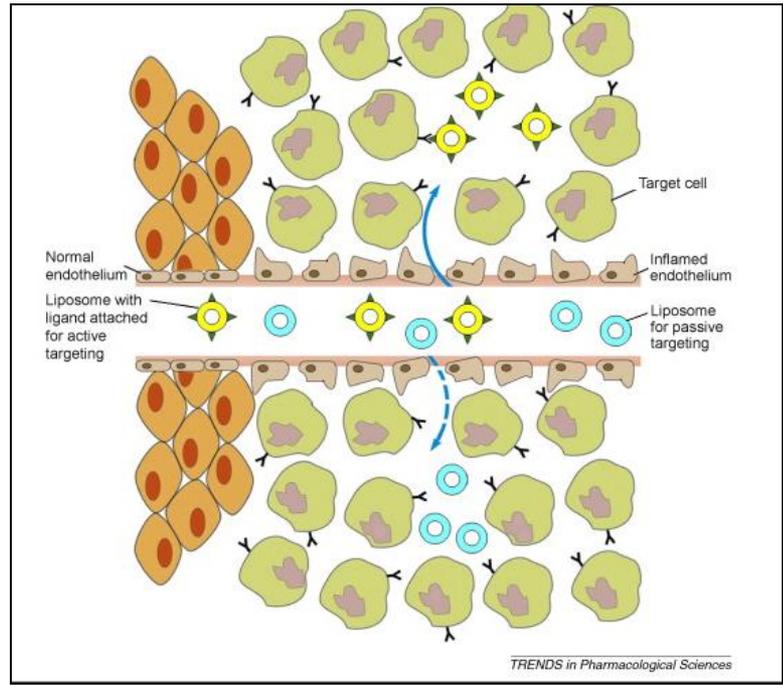


McNeil, WIRE: Nanomedicine and Nanobiotechnology 2009, 1:264-271.

PASSIVE TARGETING/ALTERED BIODISTRIBUTION



ENHANCED PENETRATION AND RETENTION EFFECT IN TUMORS



TRENDS in Pharmaceutical Sciences

ALTERED PERMEABILITY DURING INFLAMMATION

1. i.d. injection
2. Examine draining lymph nodes

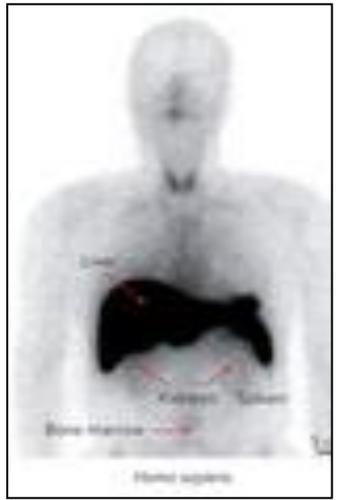
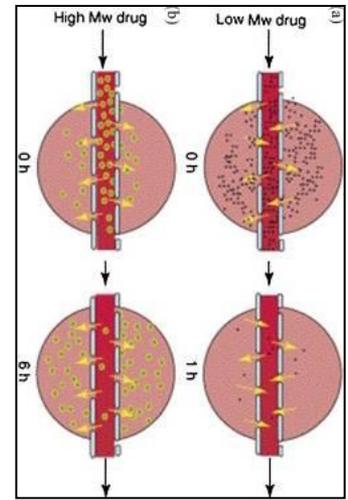
Injection Site
Tail
100nm
25nm

Draining lymph nodes
100-NPs
25-NPs

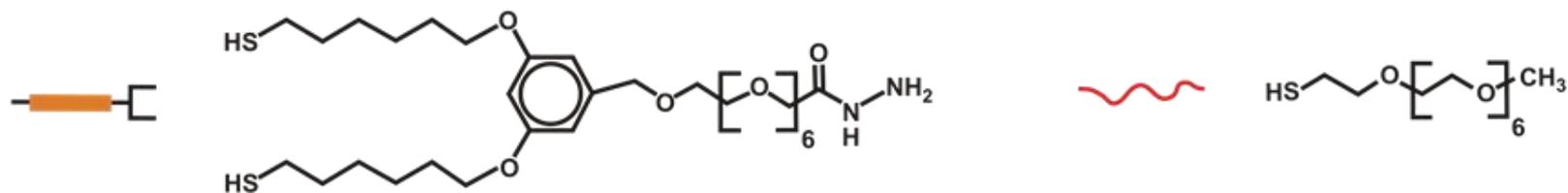
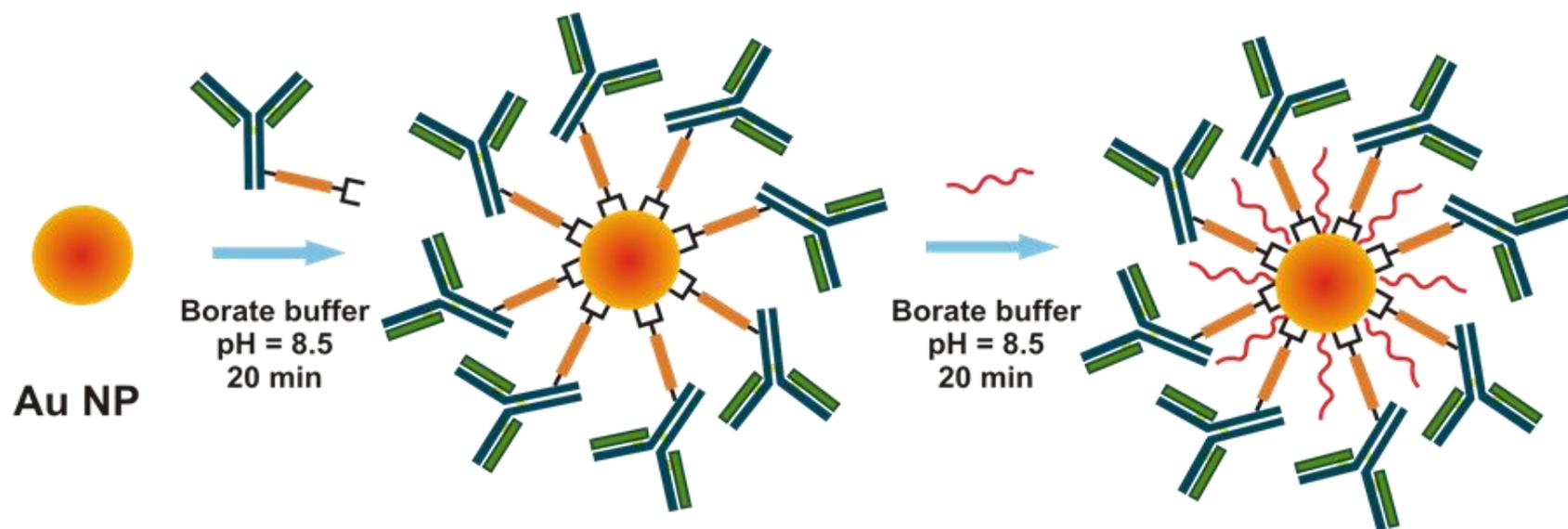
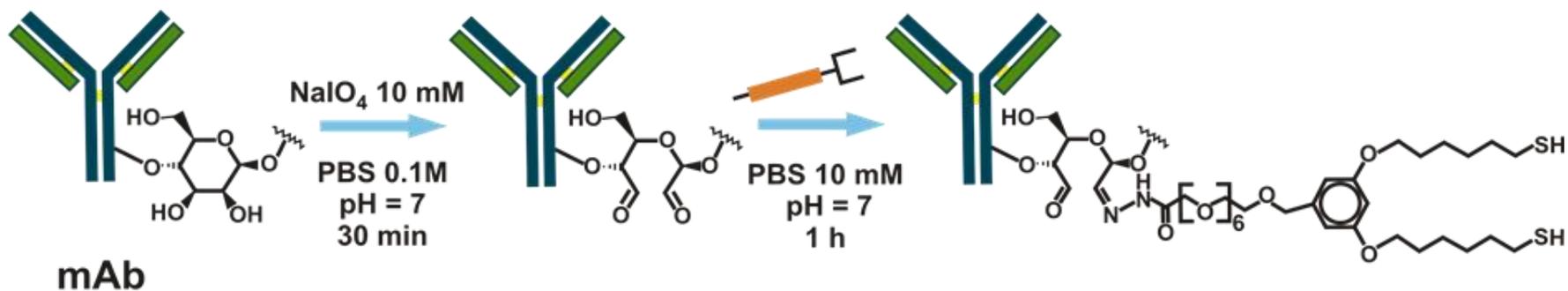
Smaller particles travel through lymphatics. Larger particles do not.

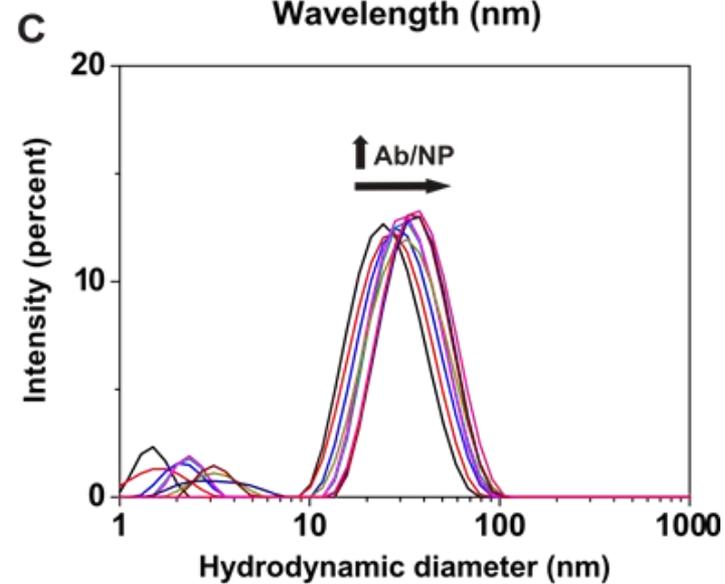
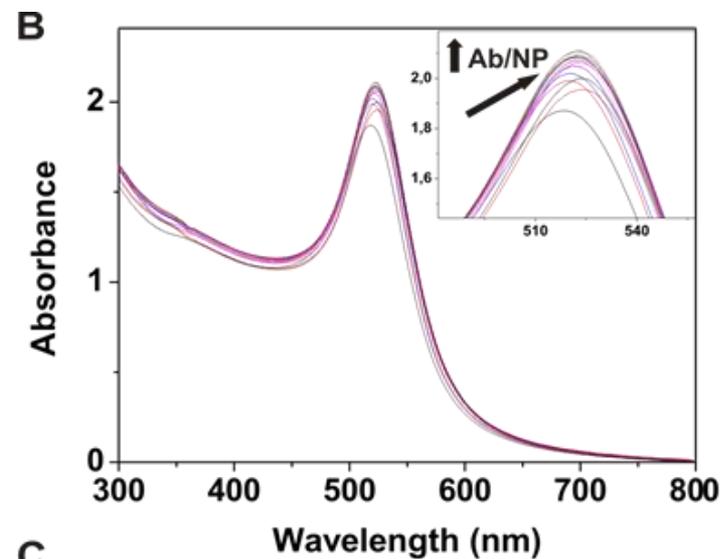
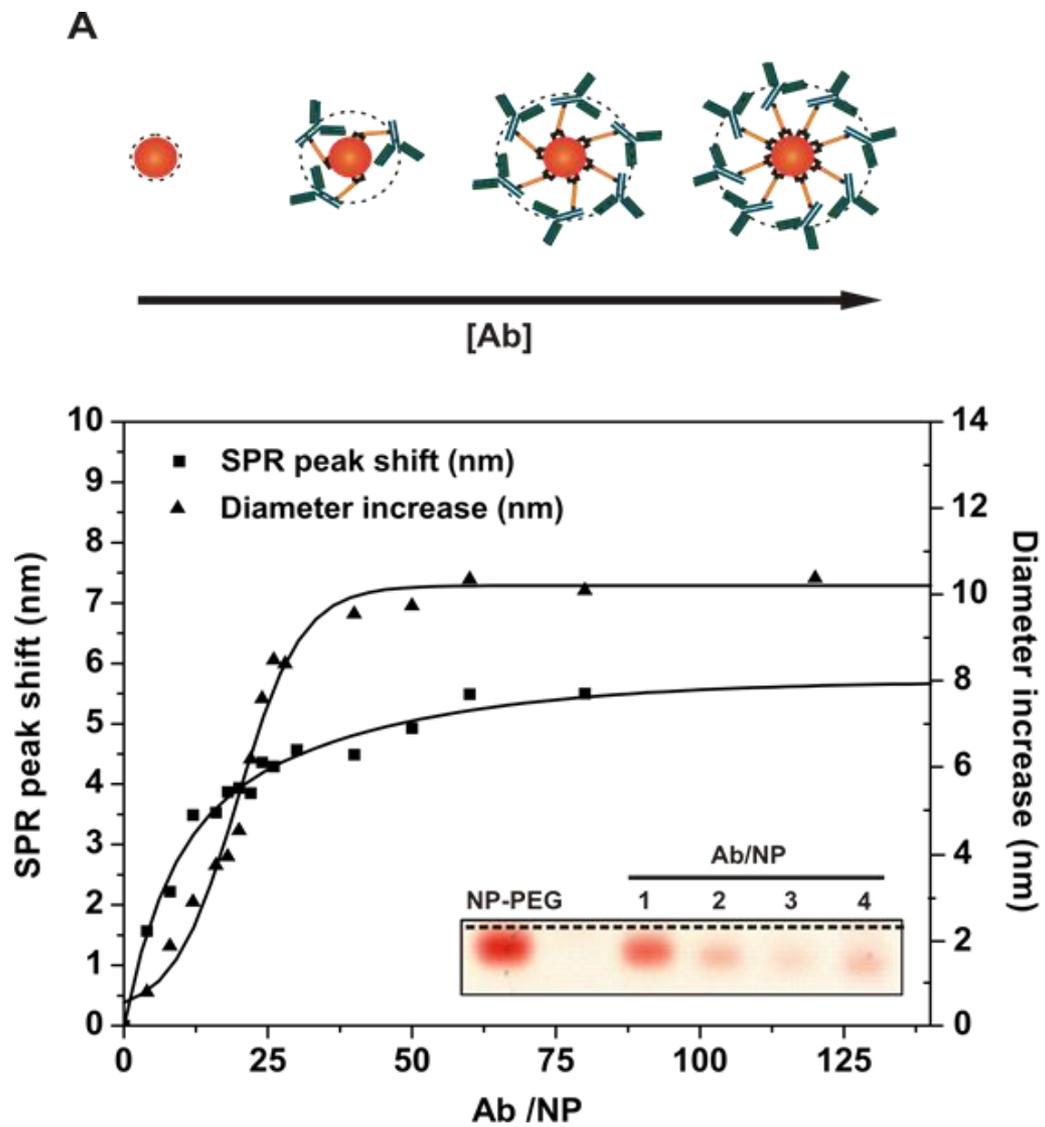
Particle distribution to lymph nodes after i.d. injection depends on their size

Reddy ST et al, *Nature Biotech.* 2007, 25 (10):1159-1164.

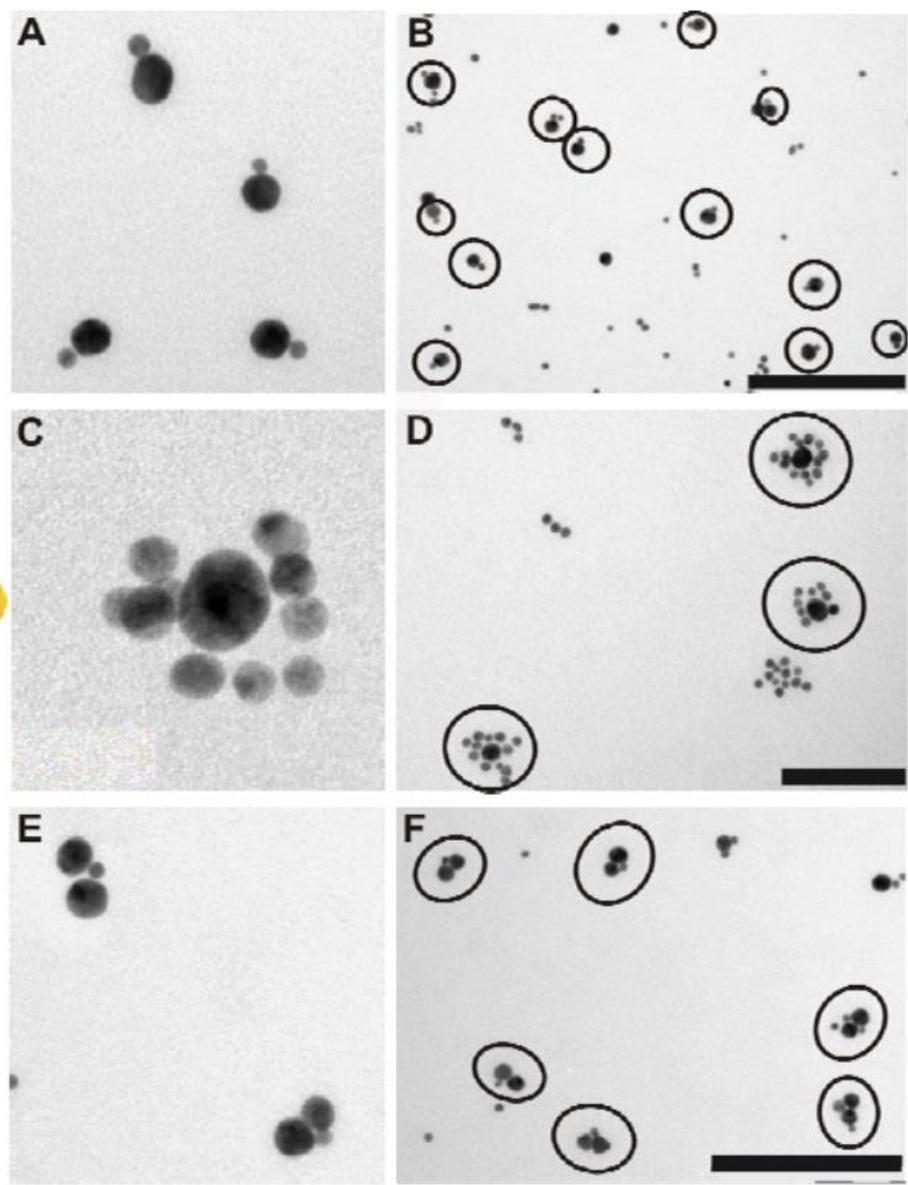
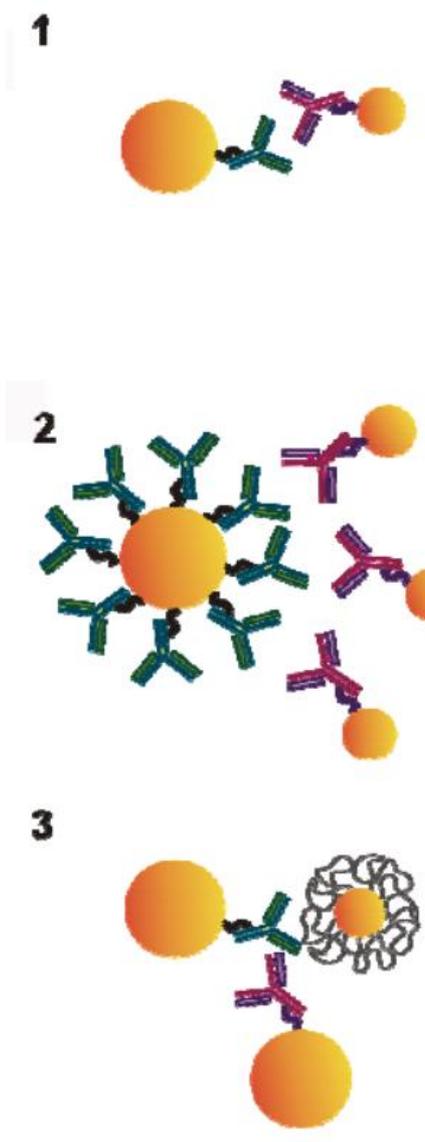


RENAL CLEARANCE AND HEPATIC ACCUMULATION OF nps

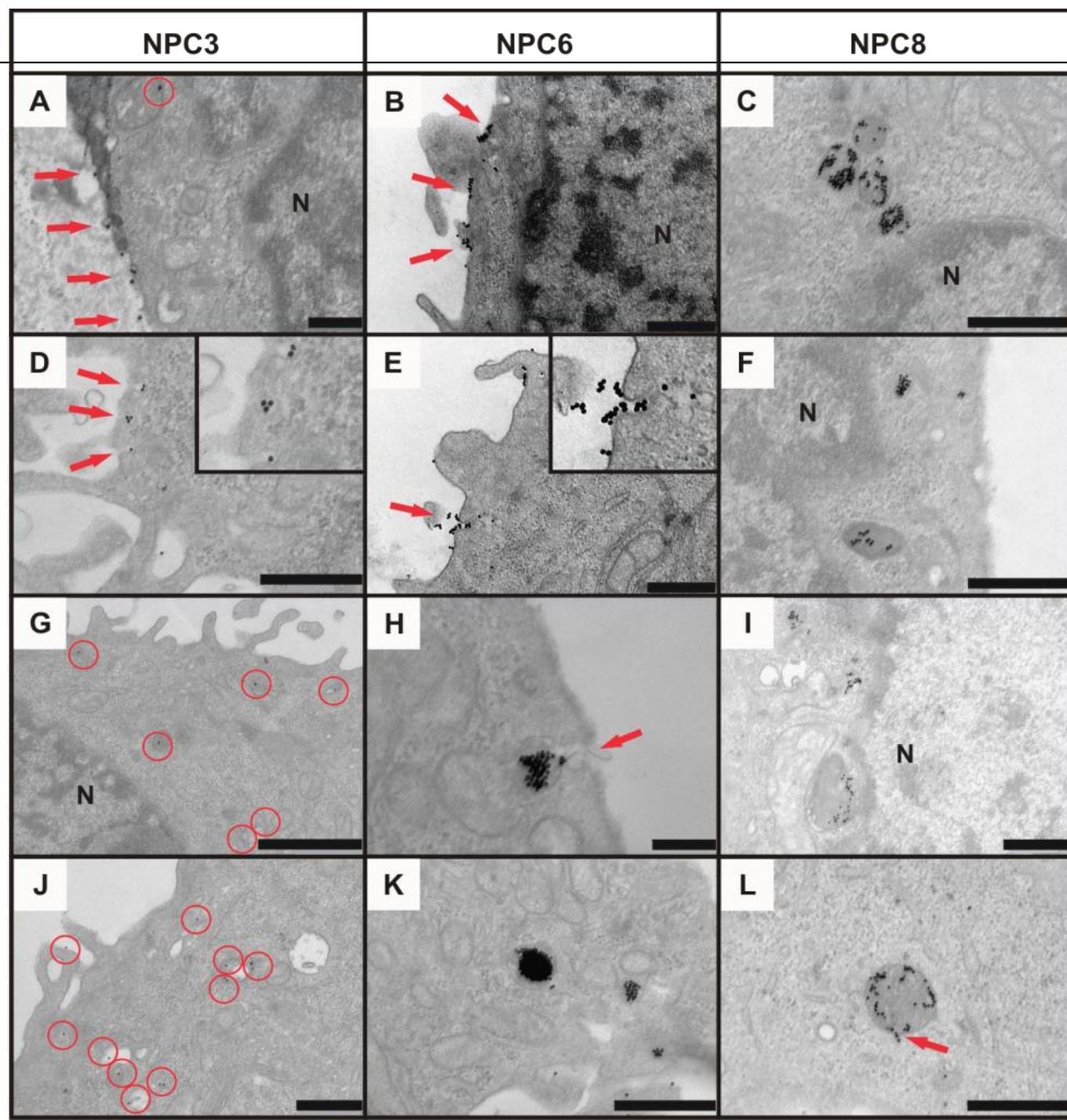




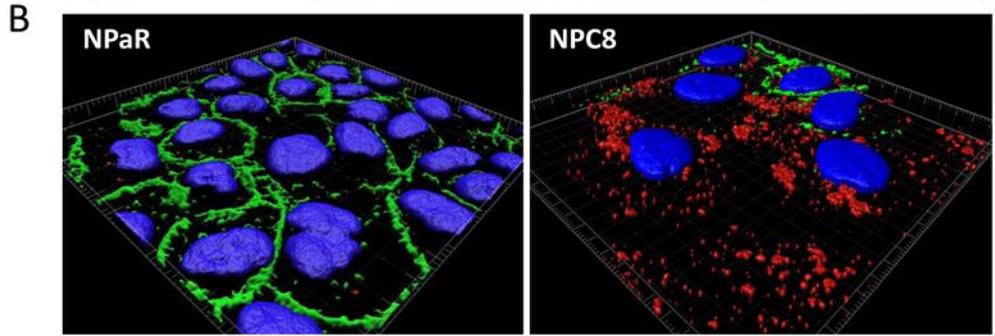
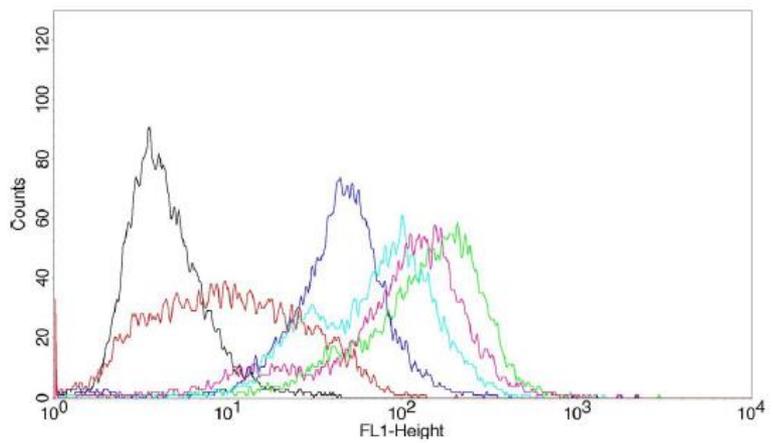
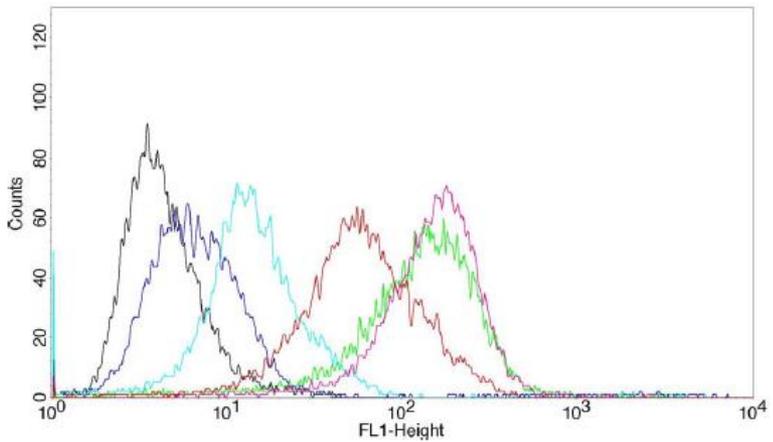
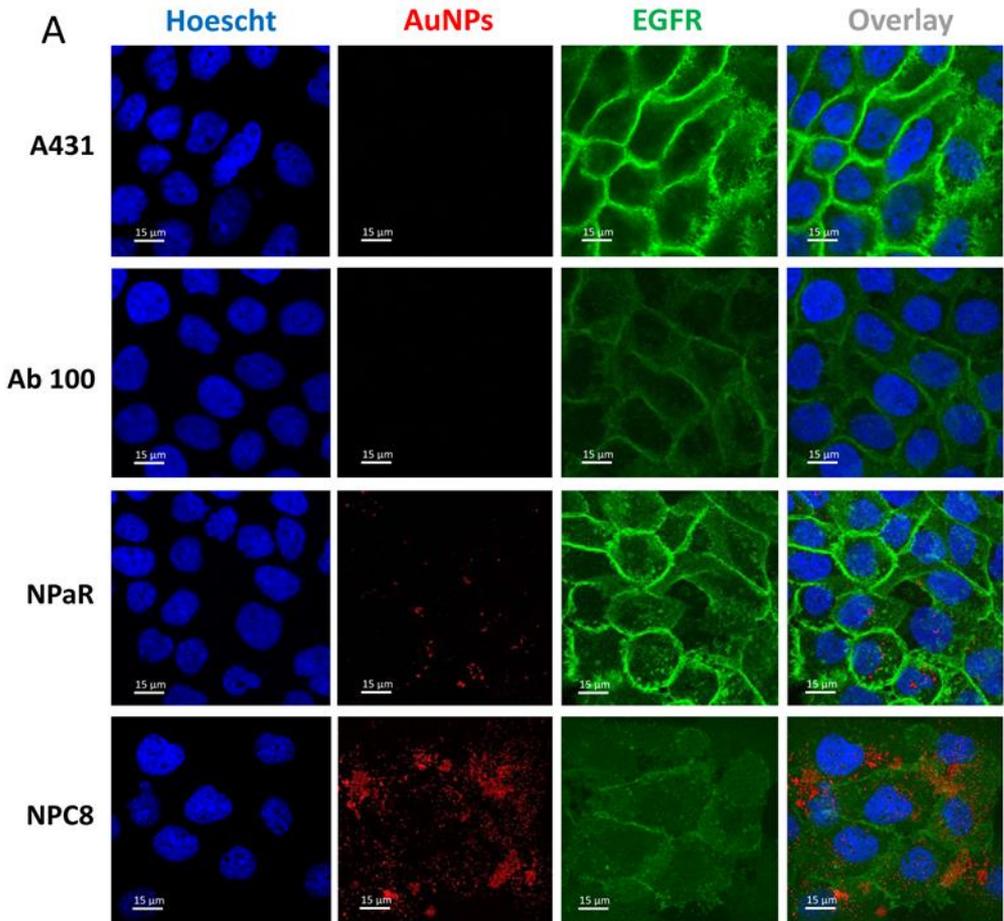
ORGANIC-INORGANIC CONSTRUCTS. Au-antibody supra structures

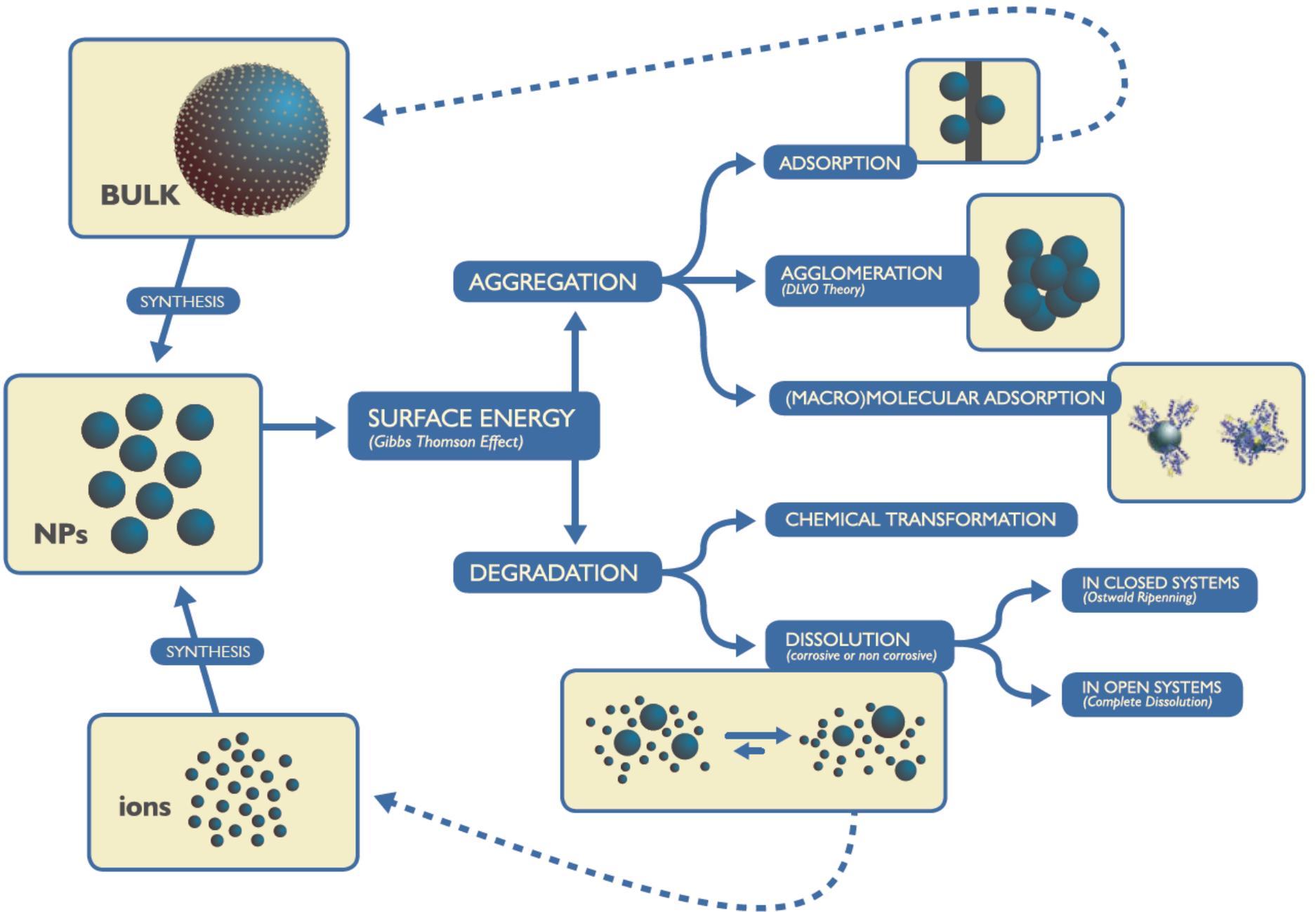


AuNPs - Cetuximab



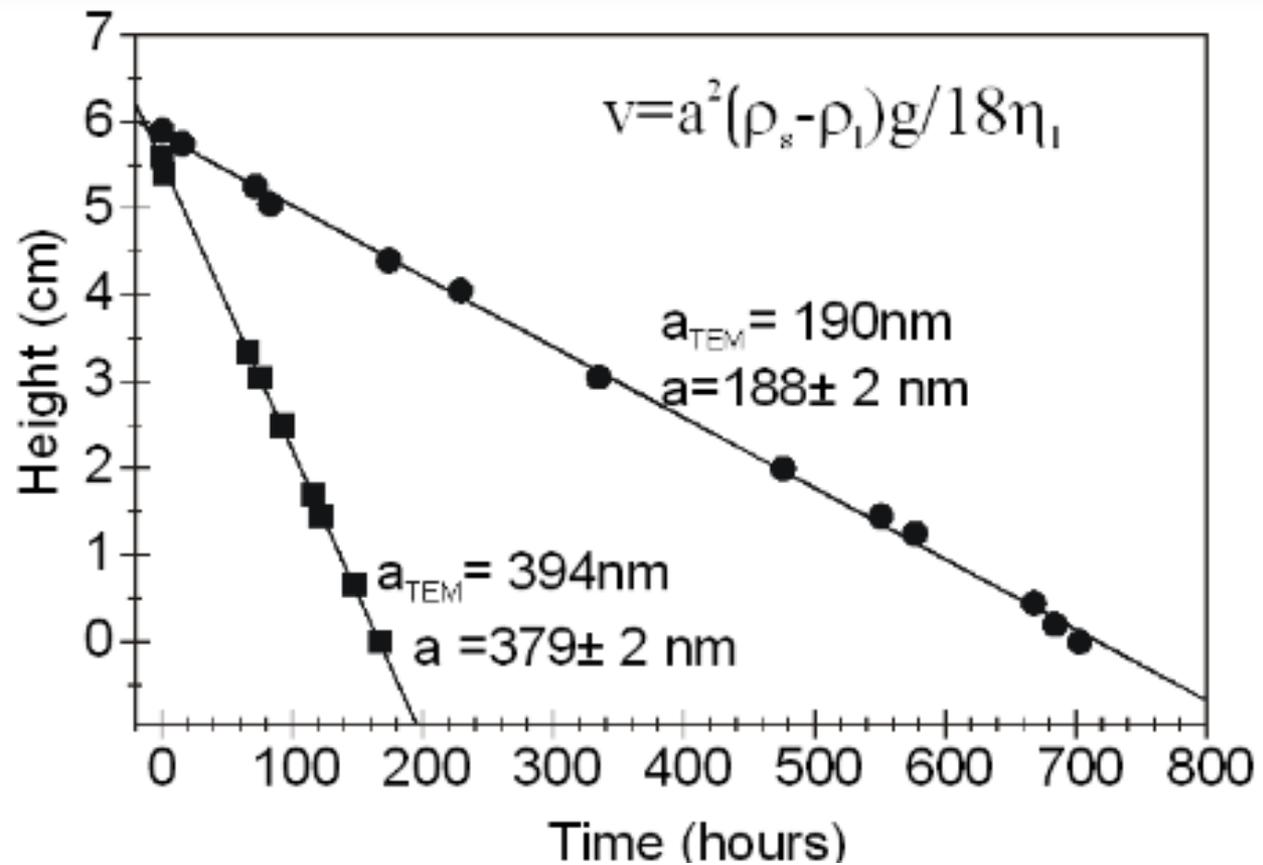
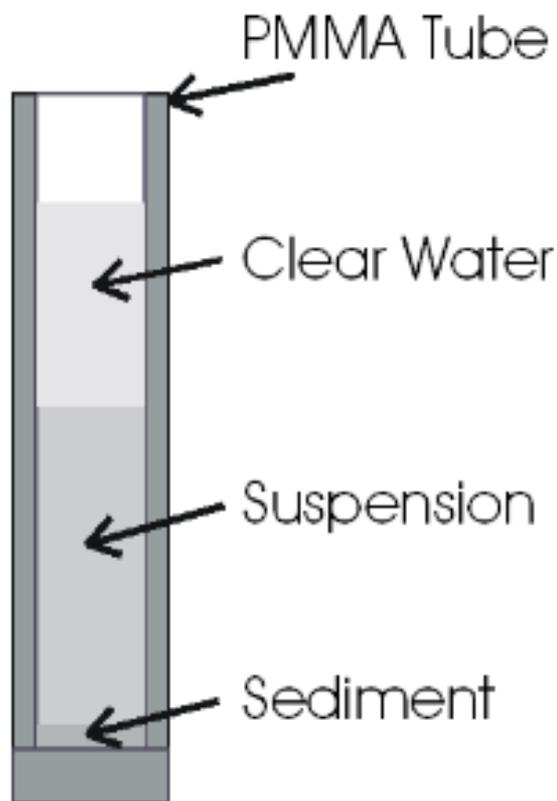
EFFECT OF ANTIBODY DENSITY ON EGFR DOWN-REGULATION

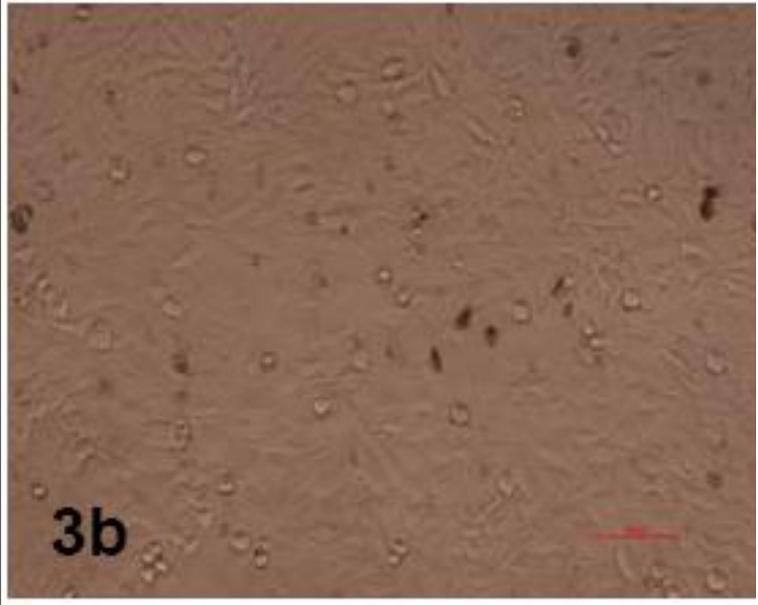
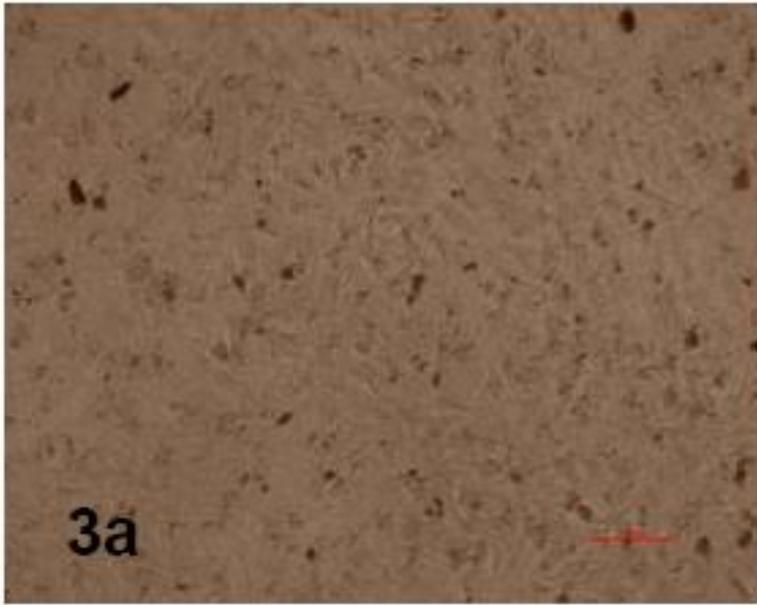
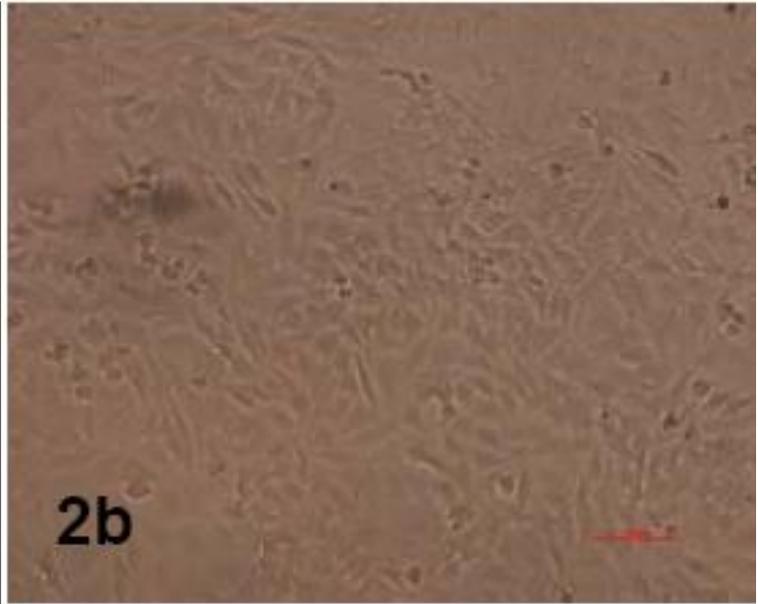
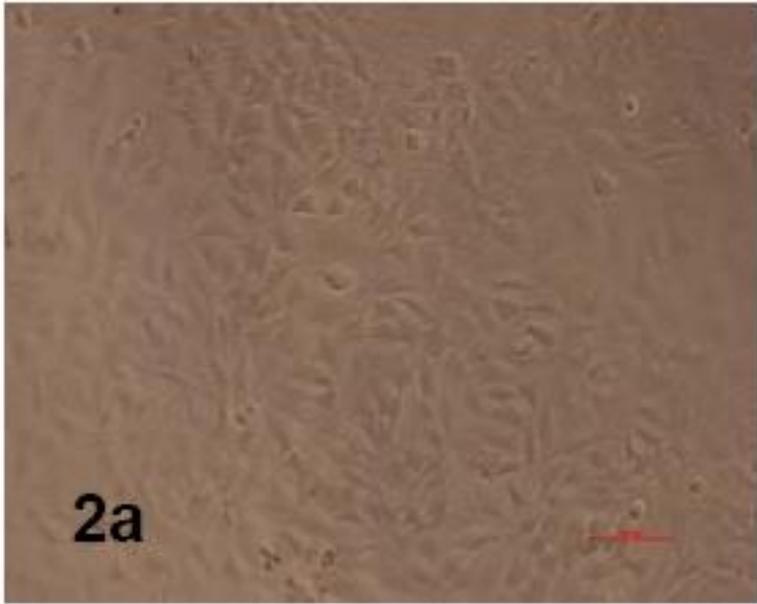


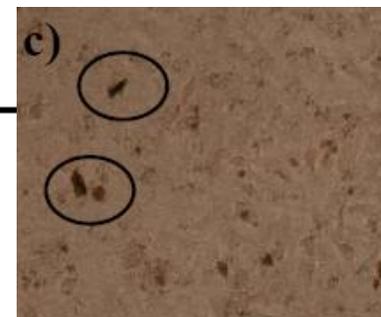
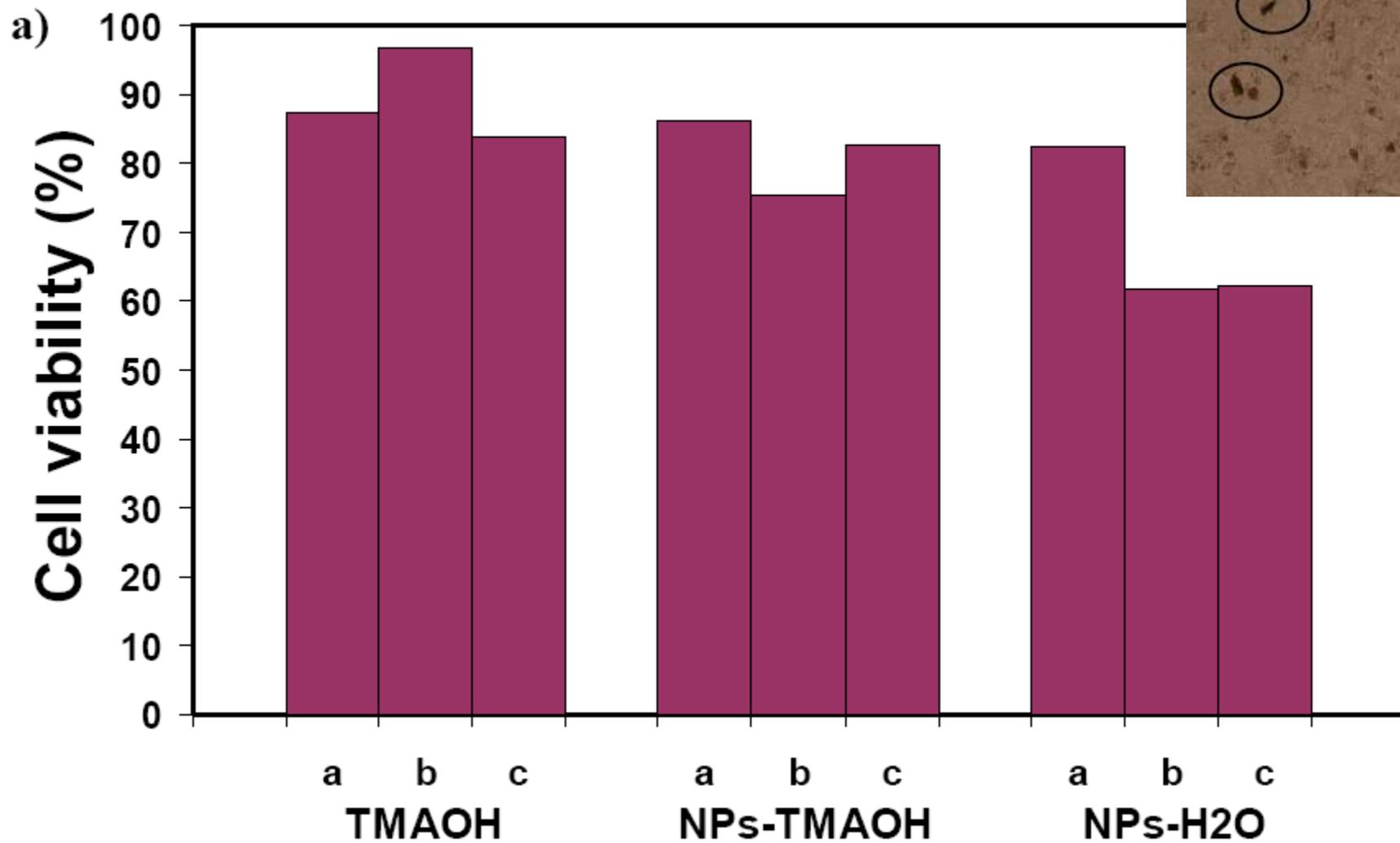


Natural sedimentation of colloids

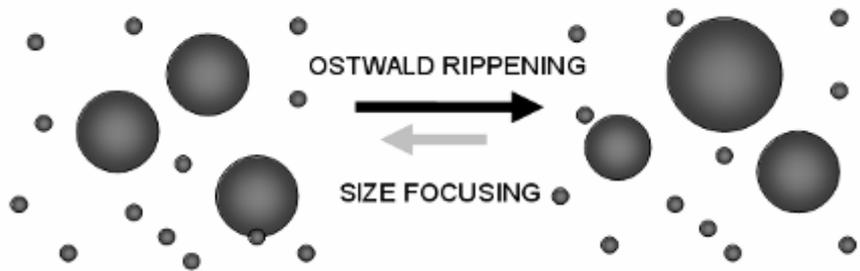
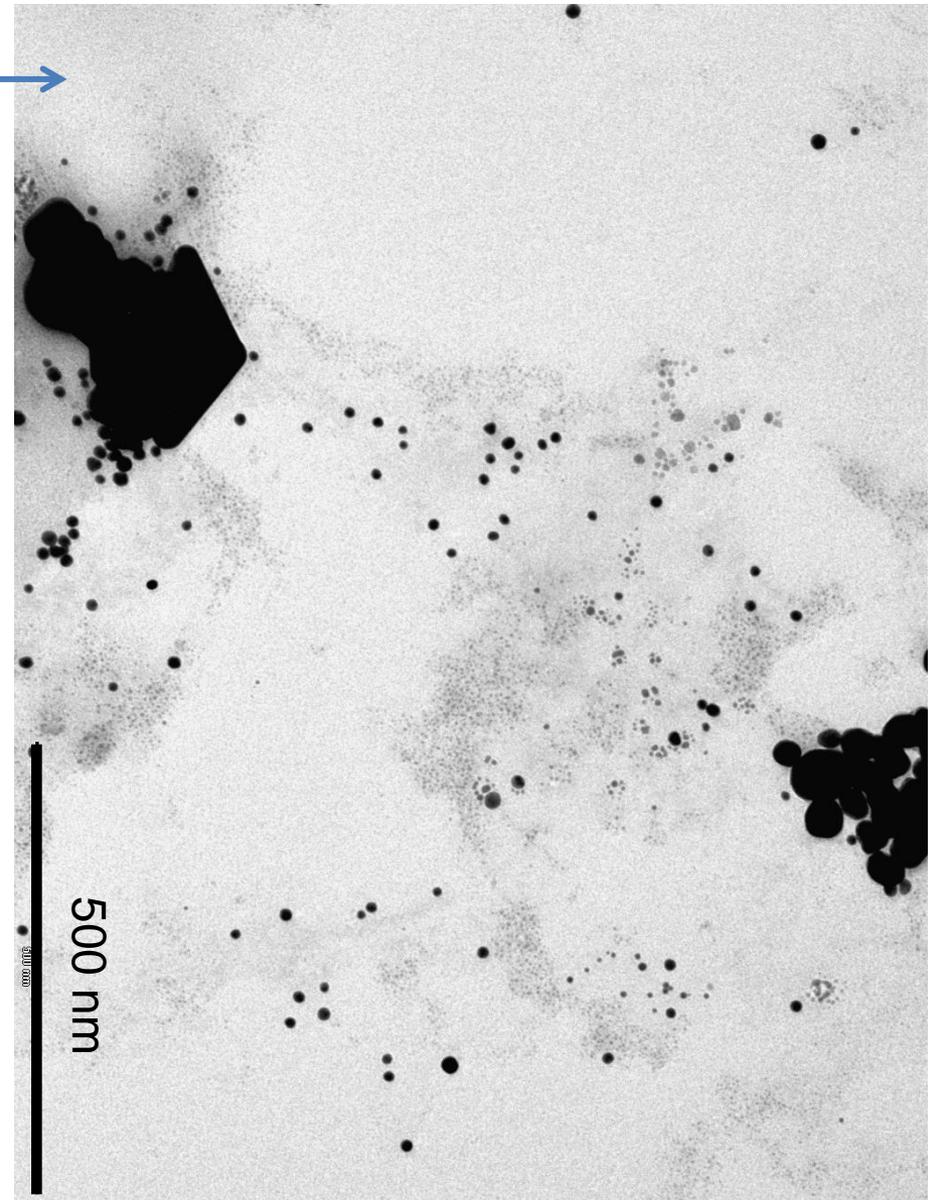
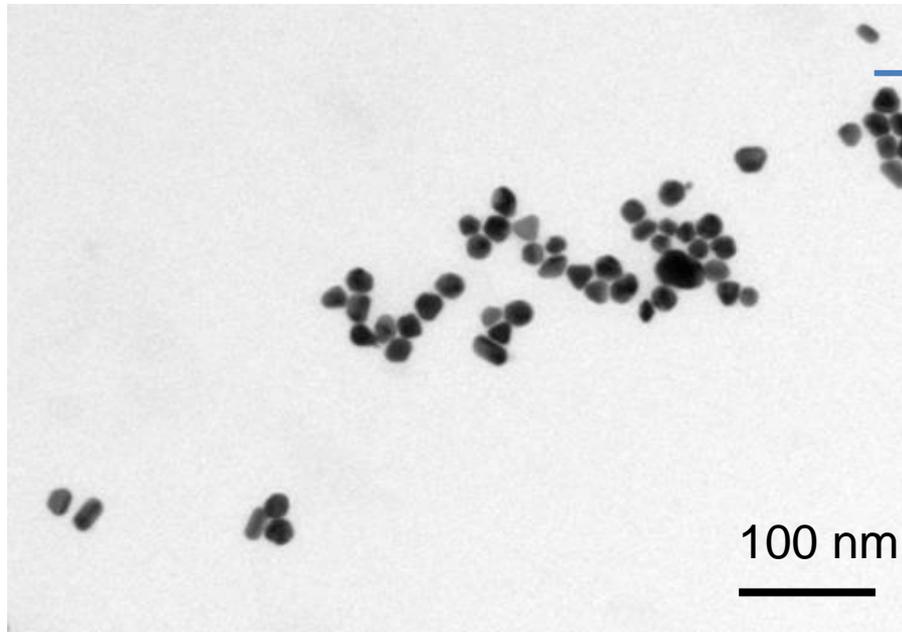
Sedimentation of the colloids

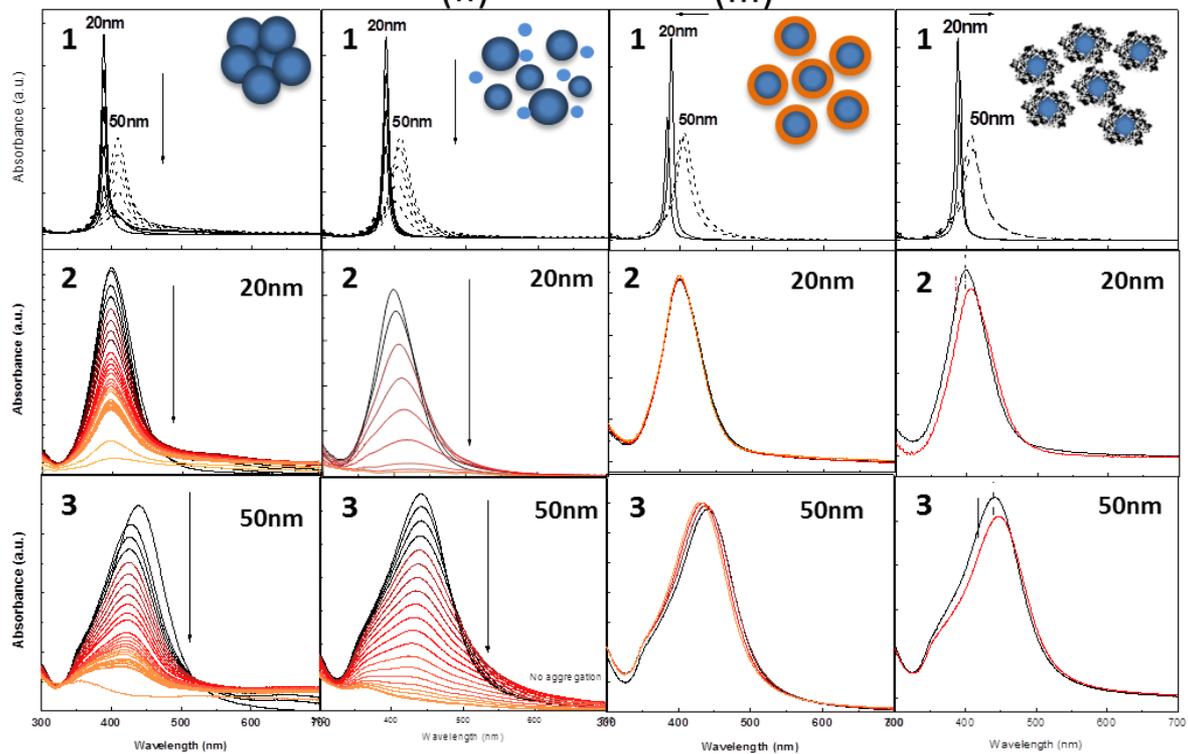
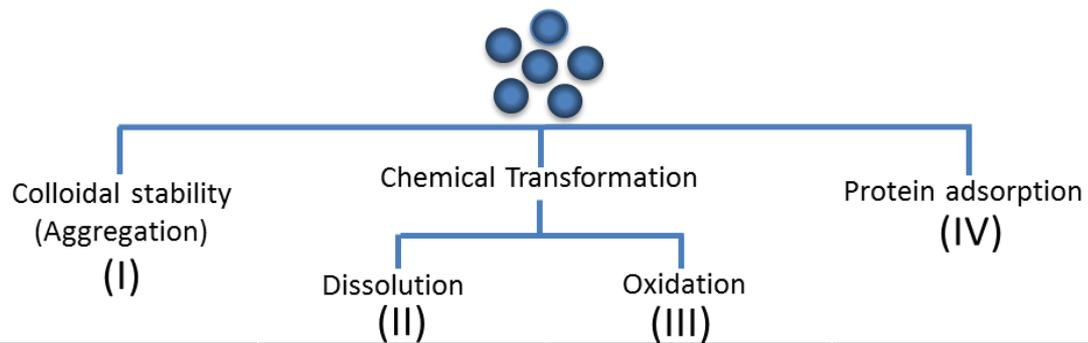


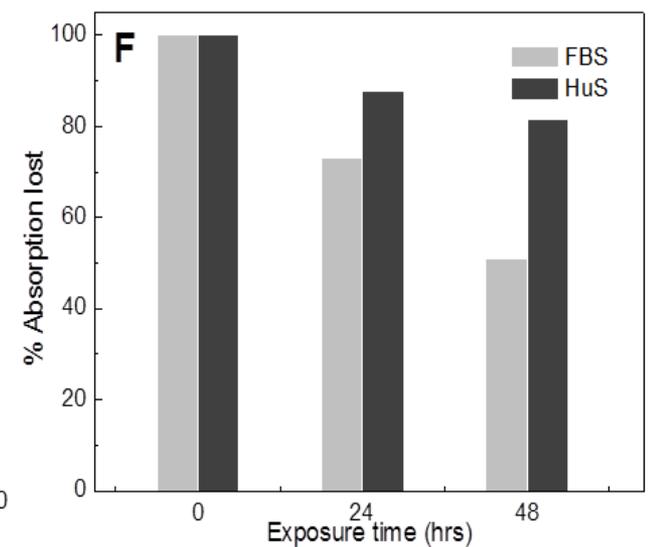
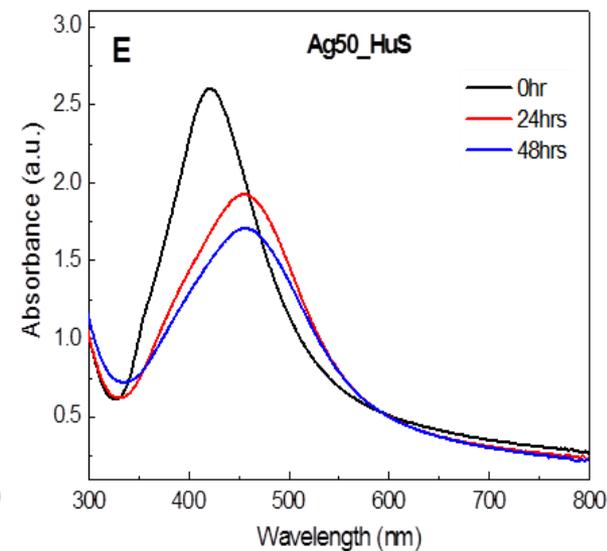
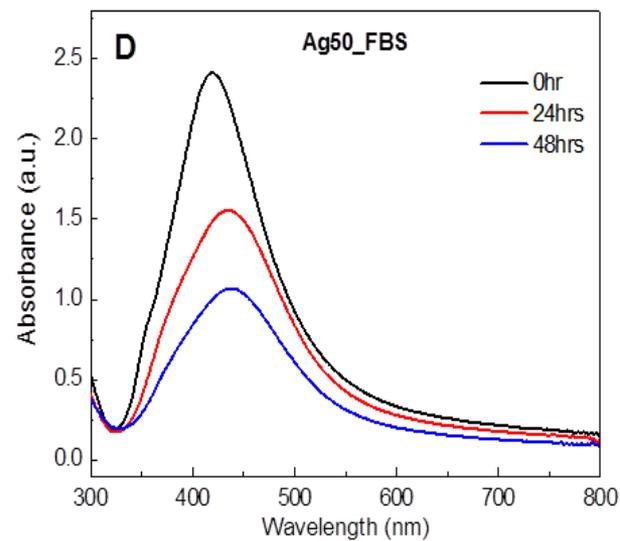
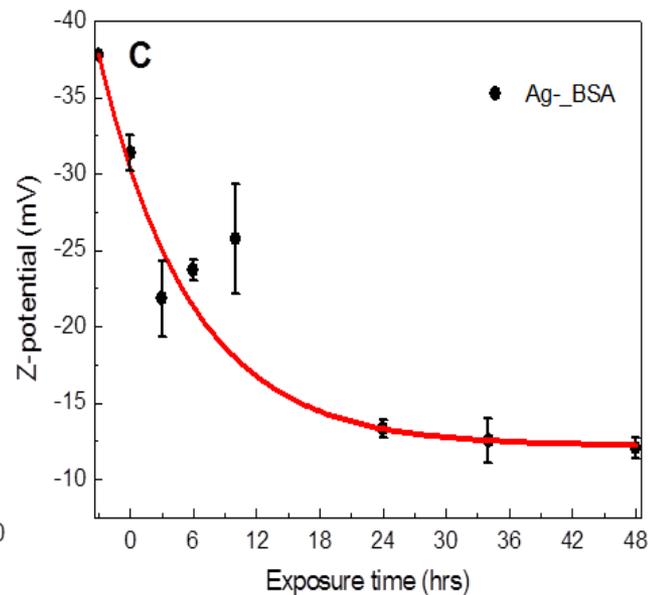
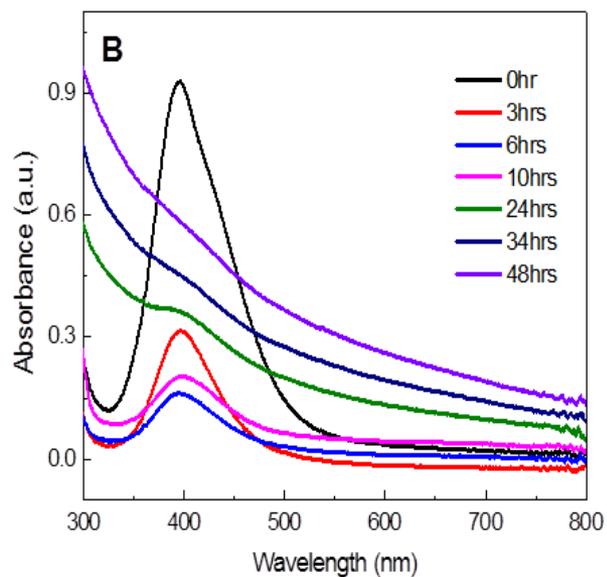
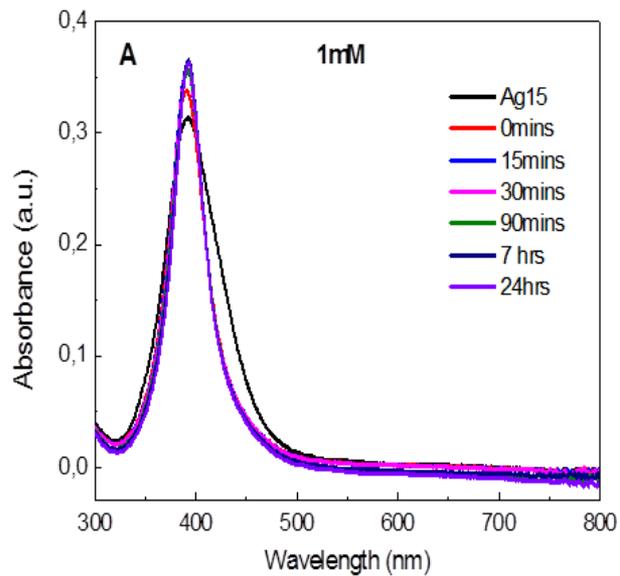




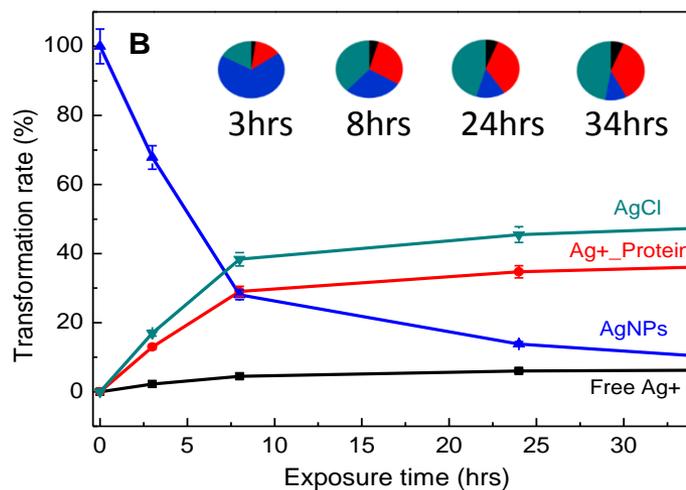
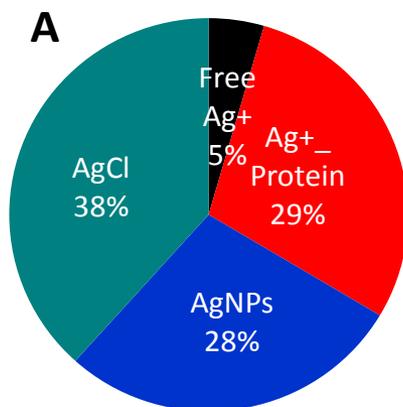
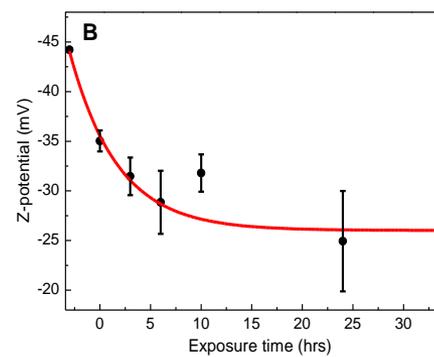
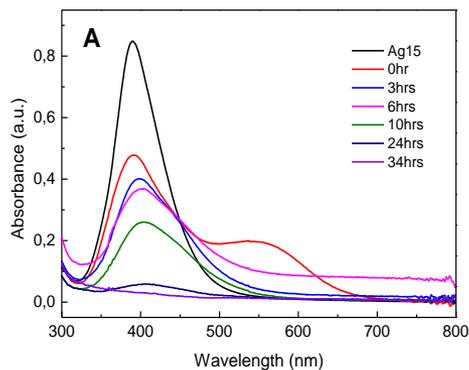
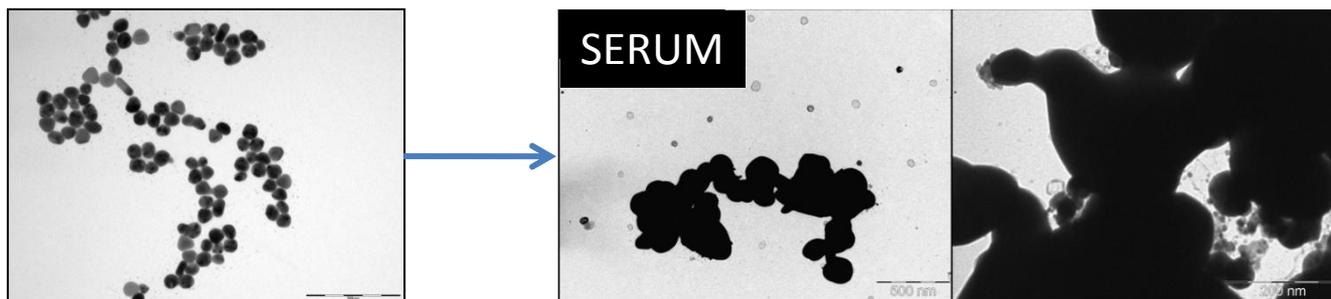
Ag NANOPARTICLE TRANSFORMATION





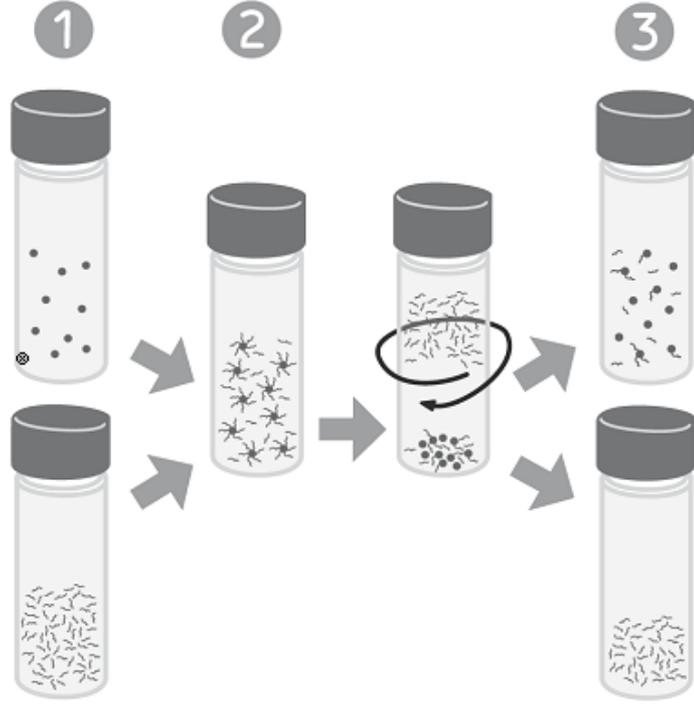
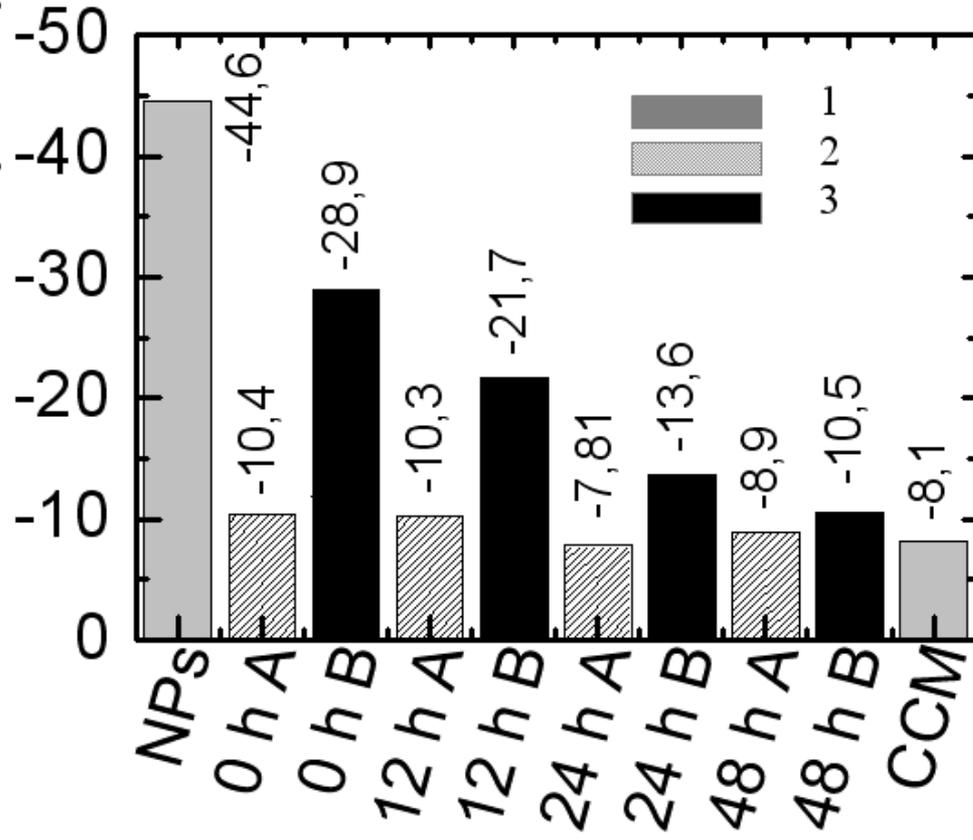


Ag NANOPARTICLE SPECIATION IN CELL CULTURE MEDIA

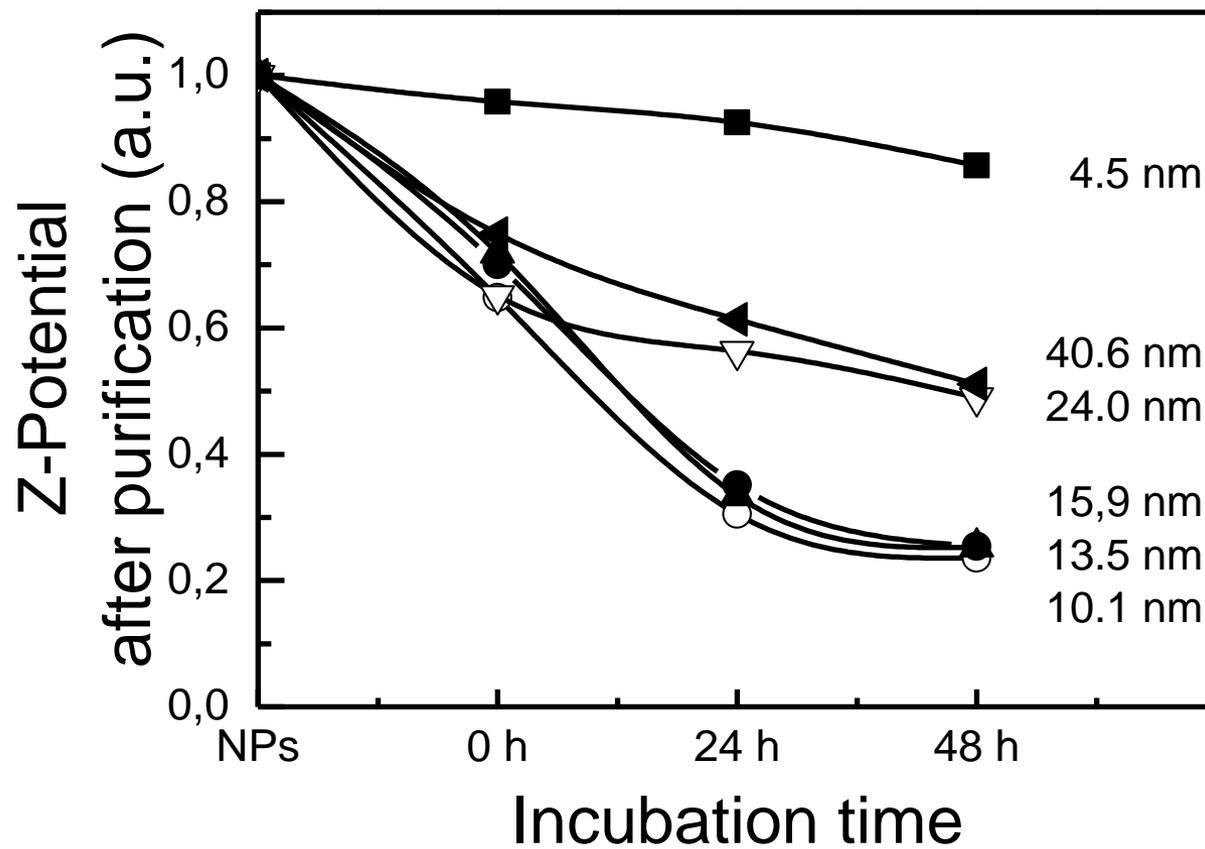


In preparation

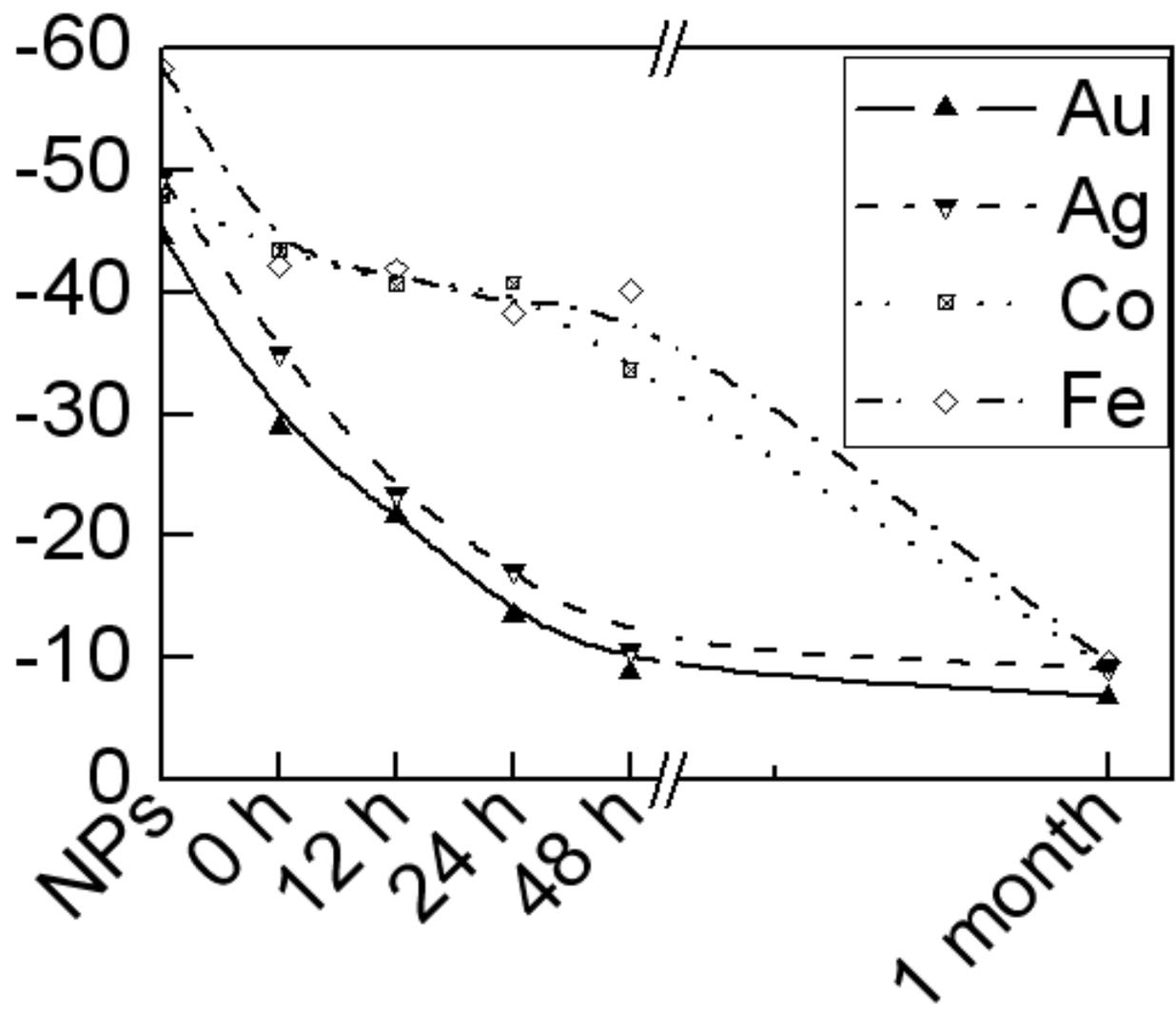
Zeta Potential (mV)



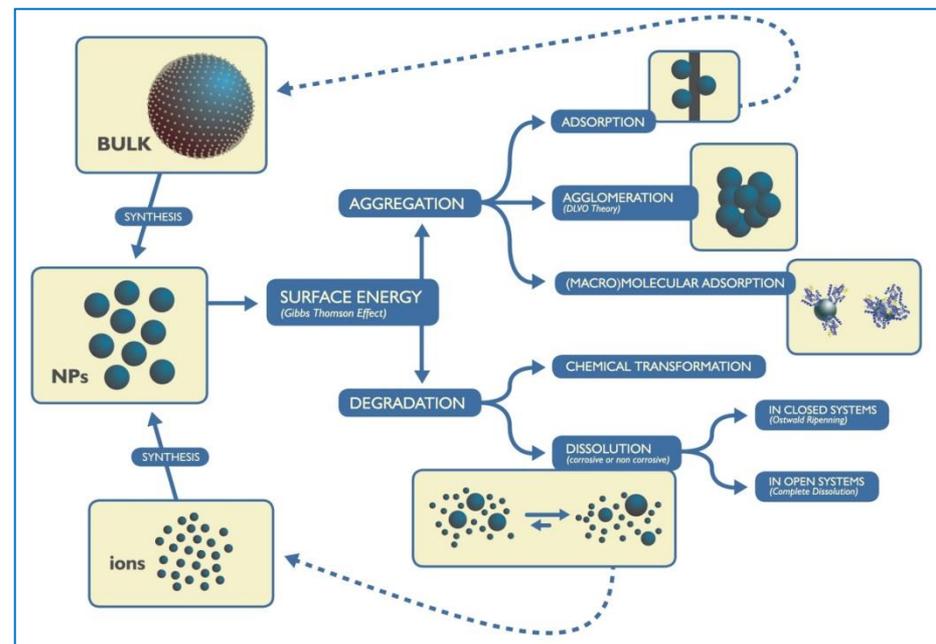
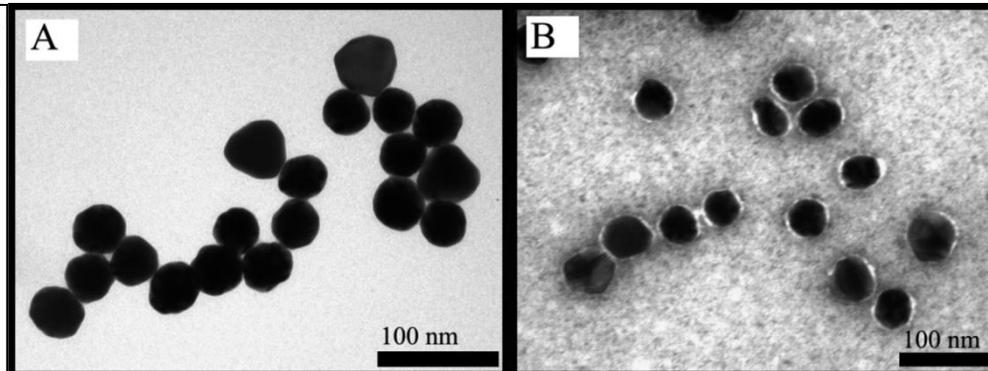
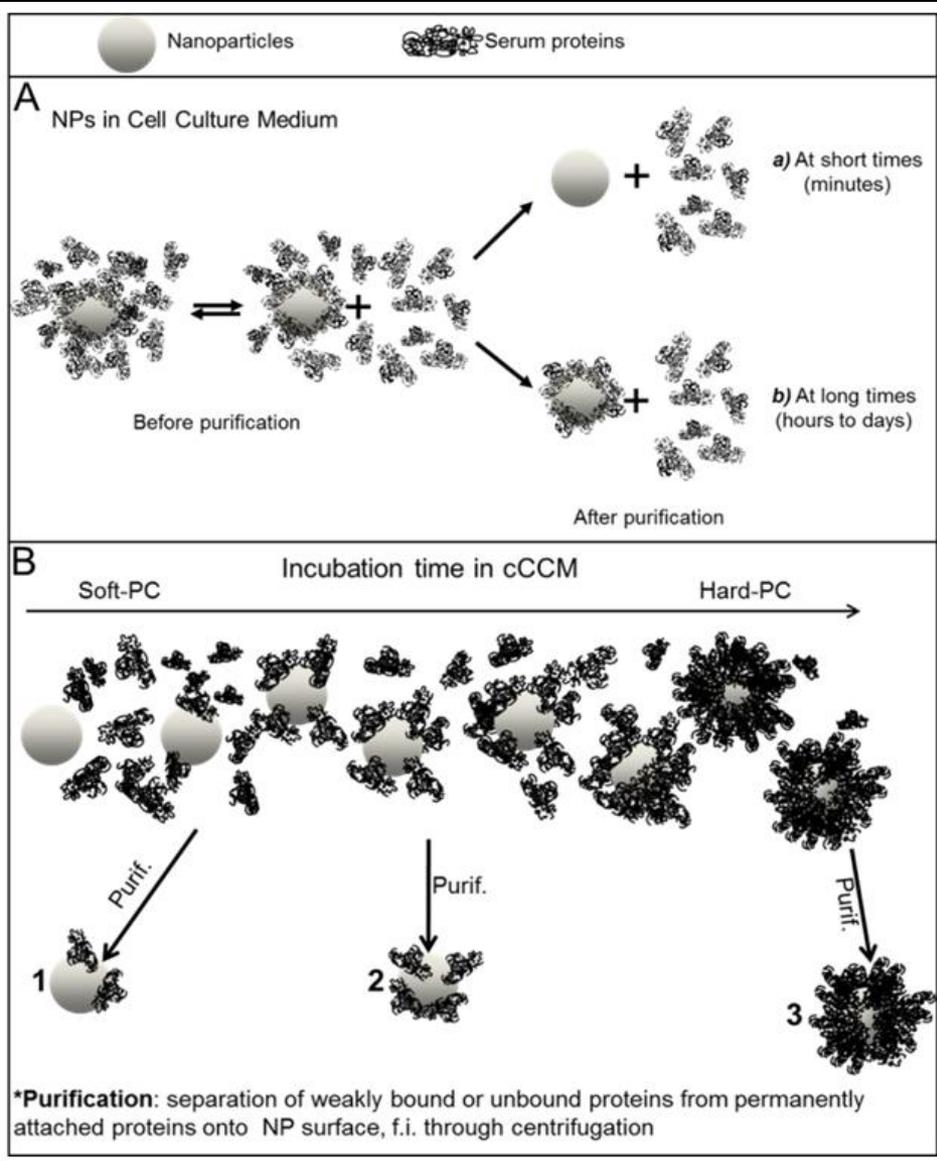
Different sizes of Au NPs



Zeta Potential

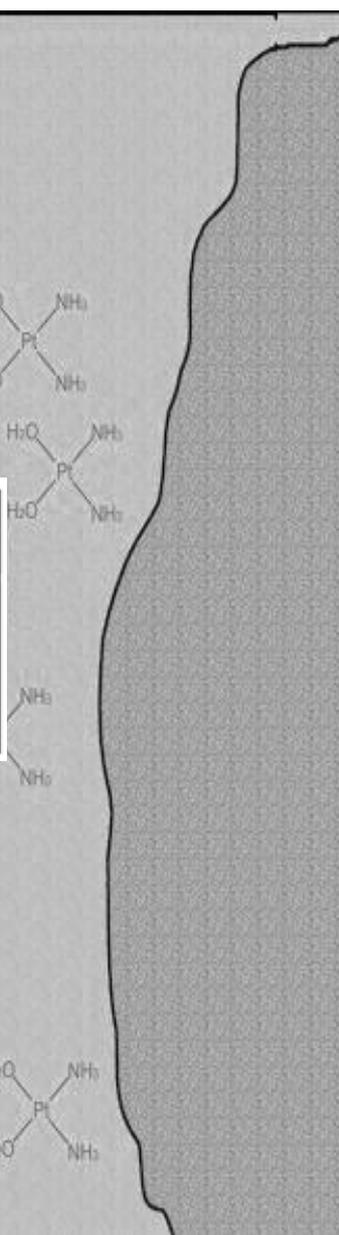
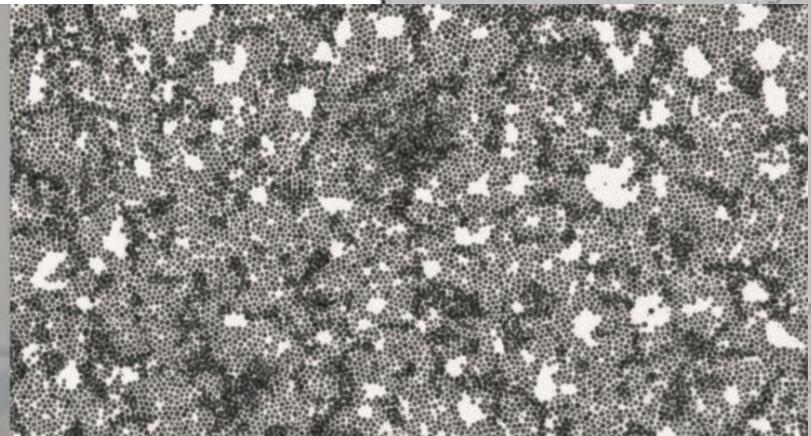
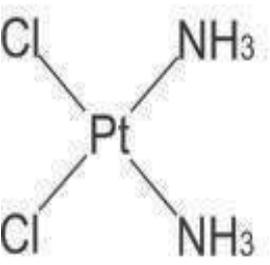
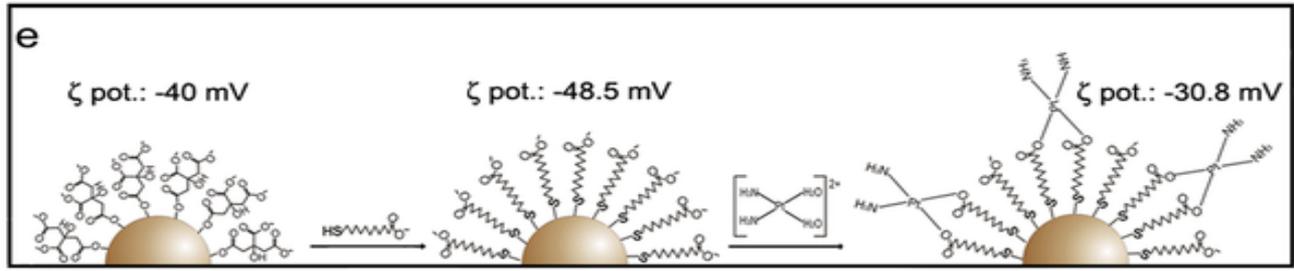
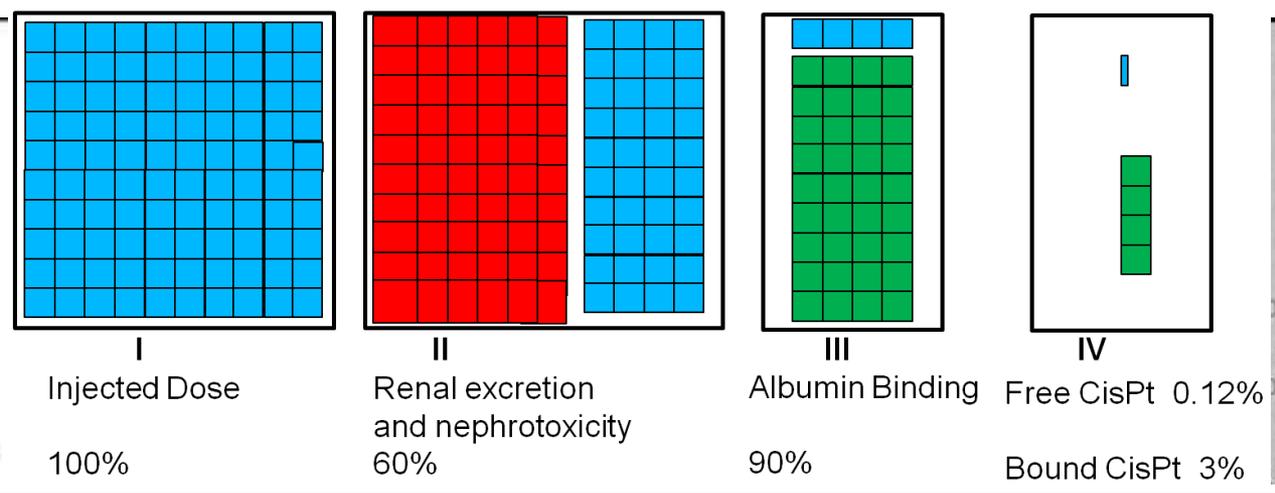
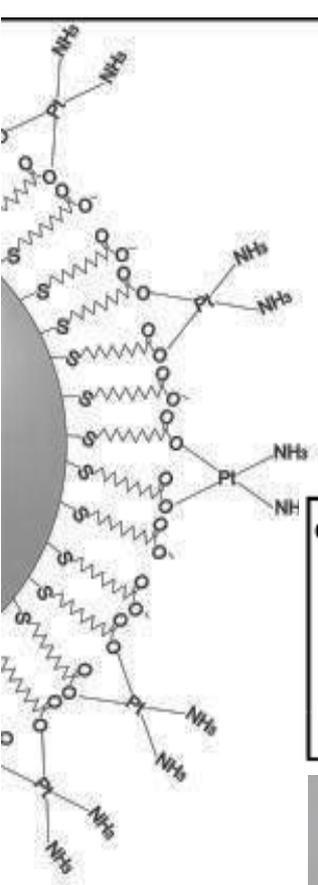


DISTRIBUTION OF NPs IN PHYSIOLOGICAL MEDIA. THE PROTEIN CORONA

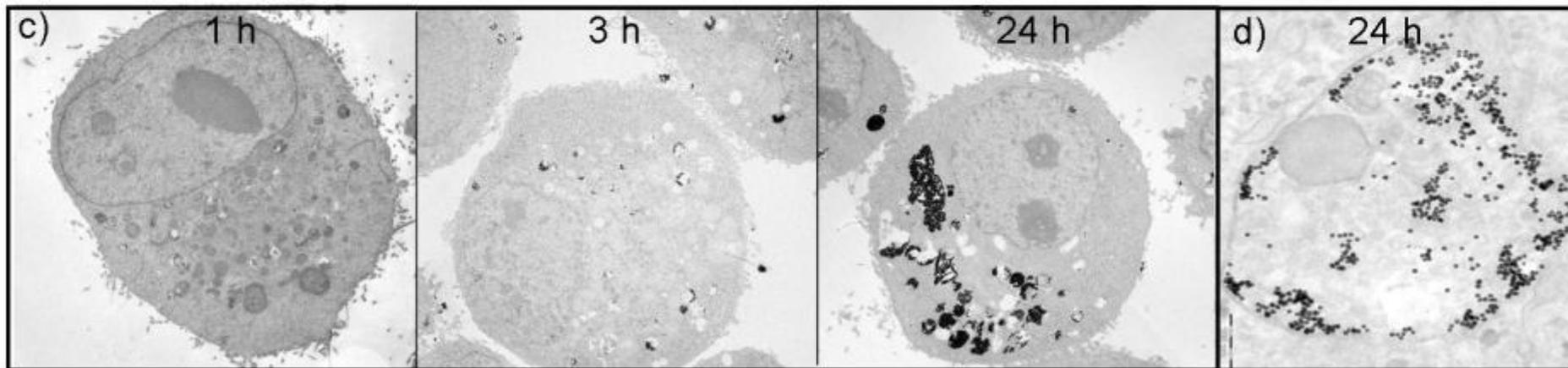
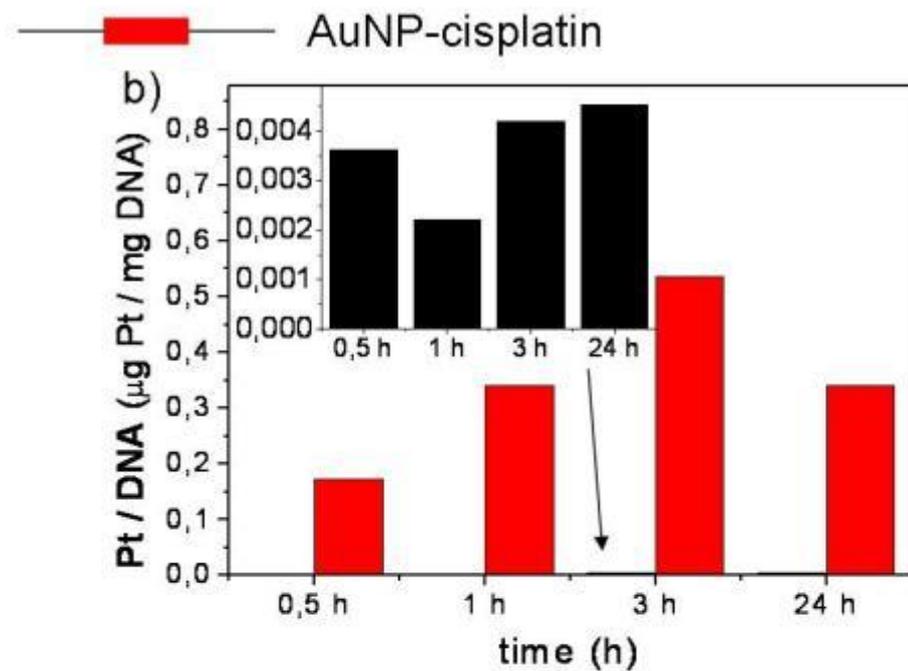
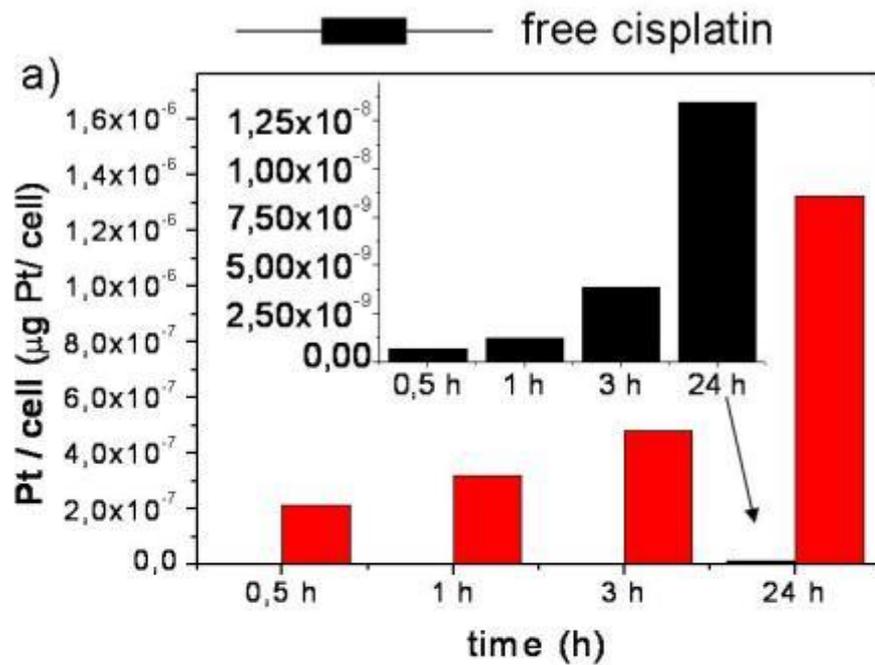


THE CASE OF CISPLATIN

BODY → TUMOR

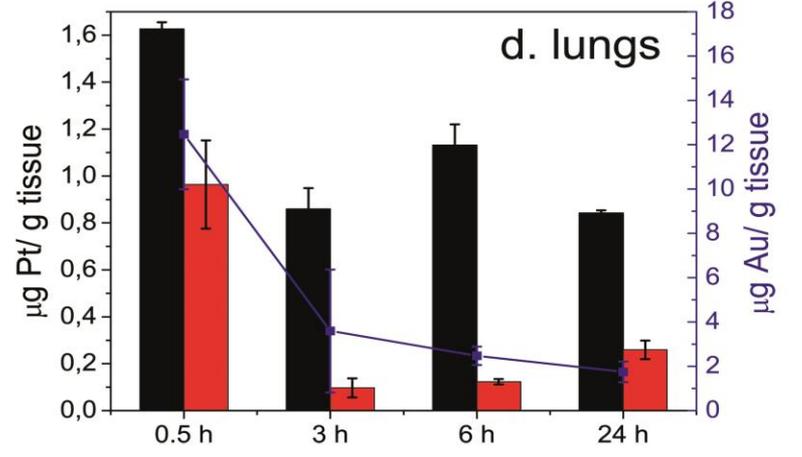
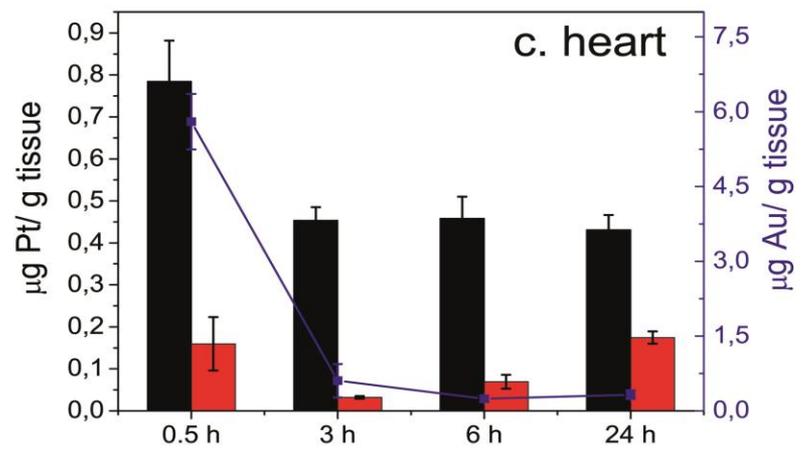
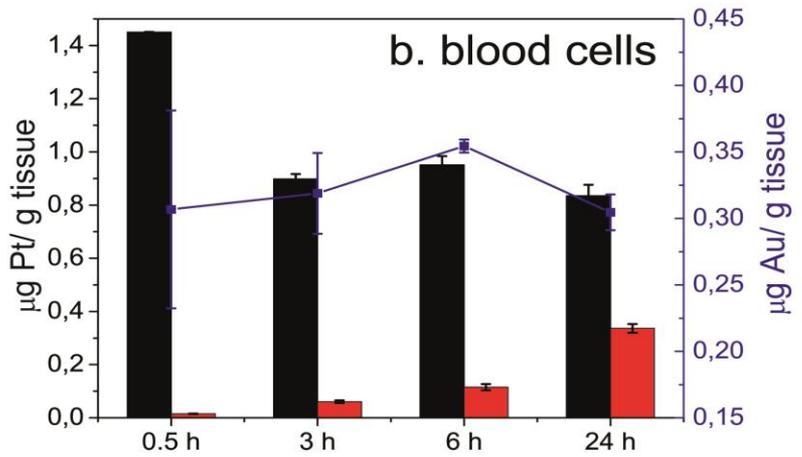
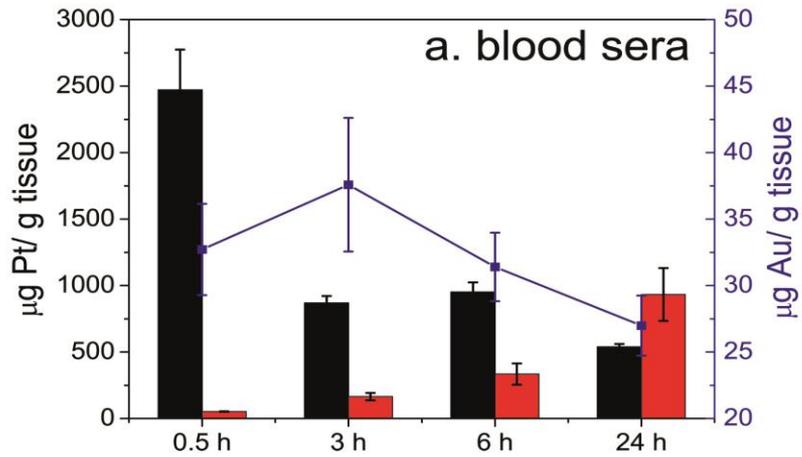


Pt CELL AND DNA ACCUMULATION.

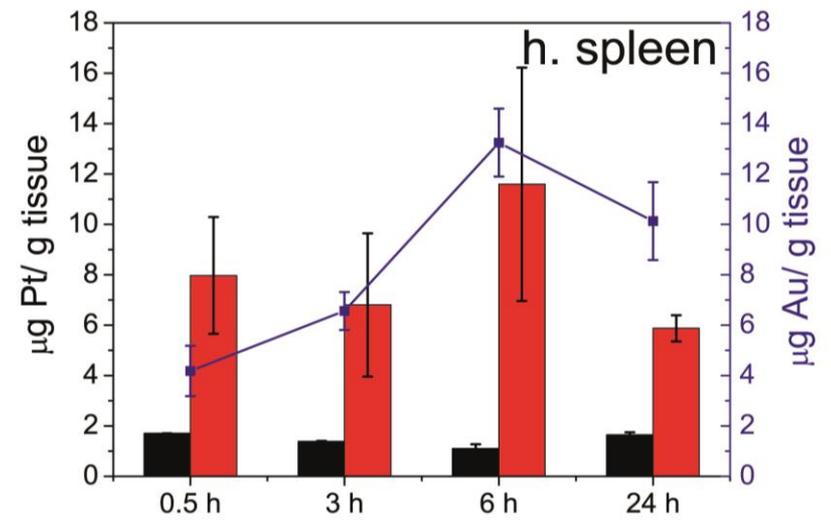
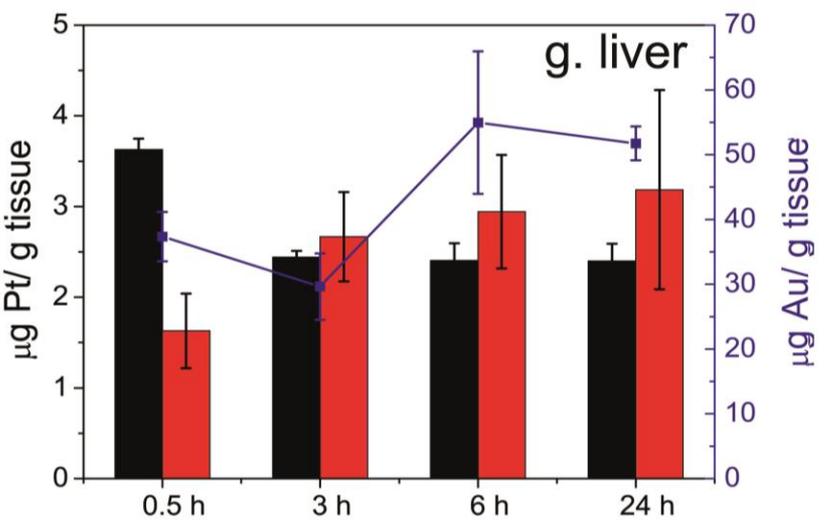
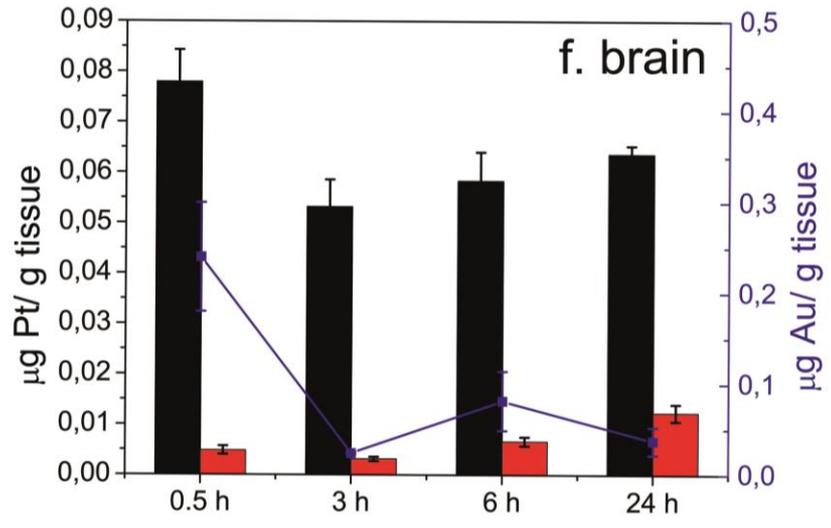
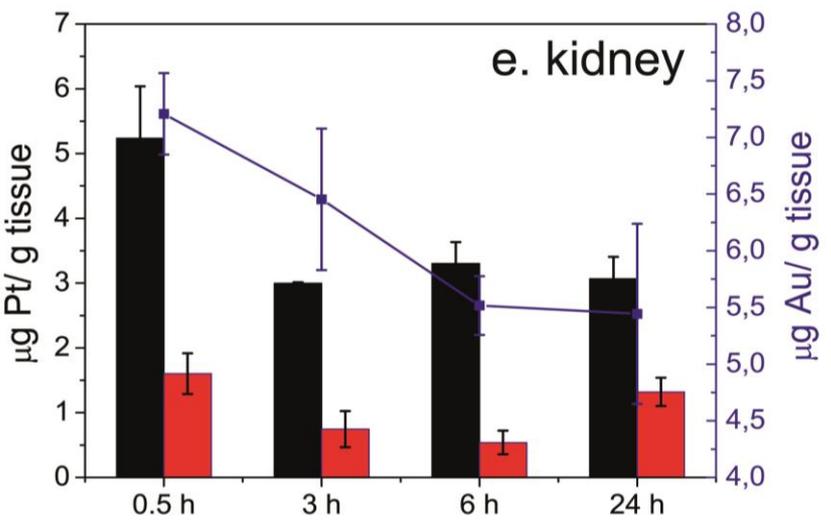


BIODISTRIBUTION IN MICE

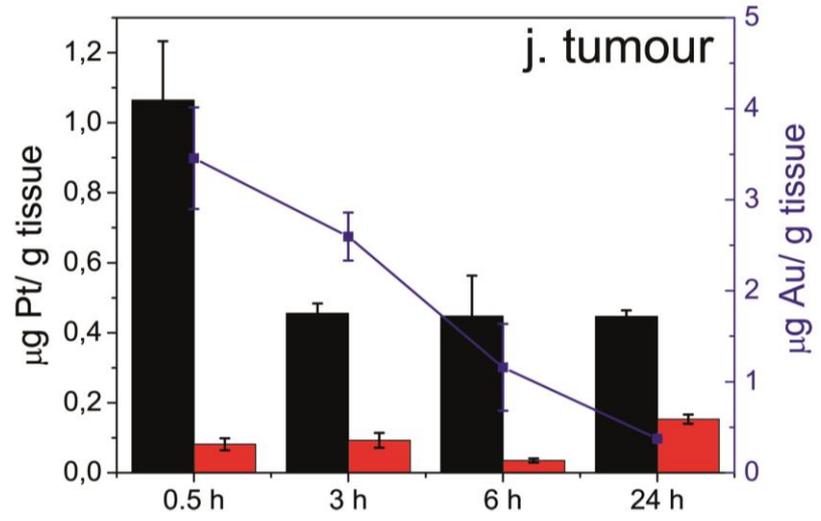
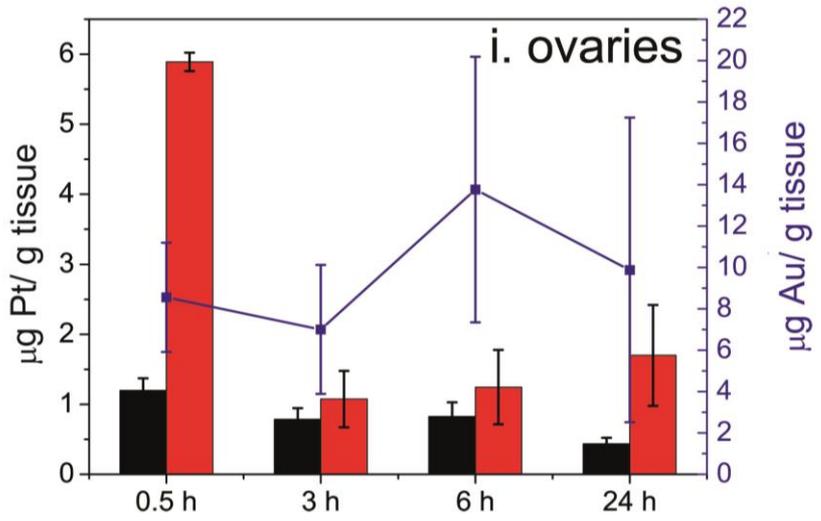
■ ^{195}Pt (free cisplatin case) ■ ^{195}Pt (AuNPs-cisplatin case) ■ ^{197}Au



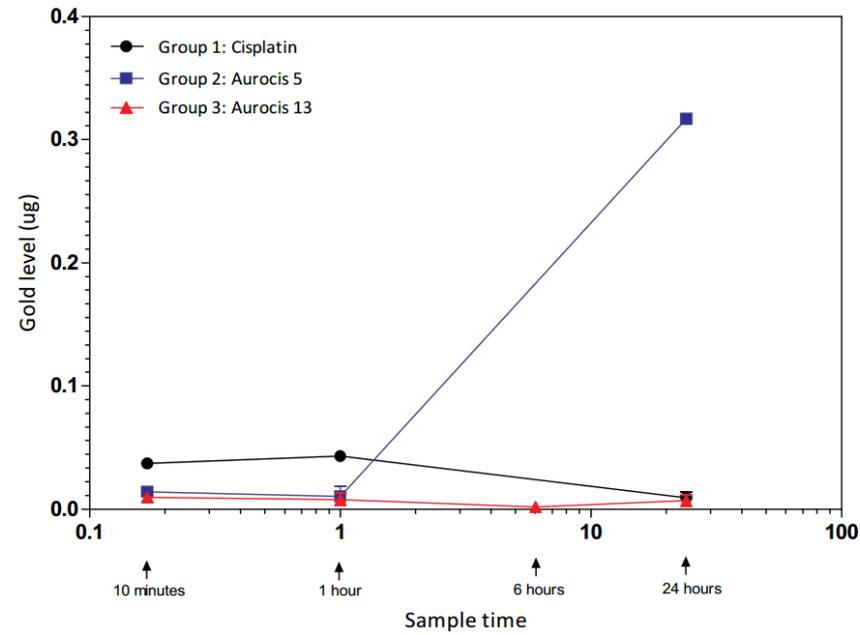
BIODISTRIBUTION IN MICE



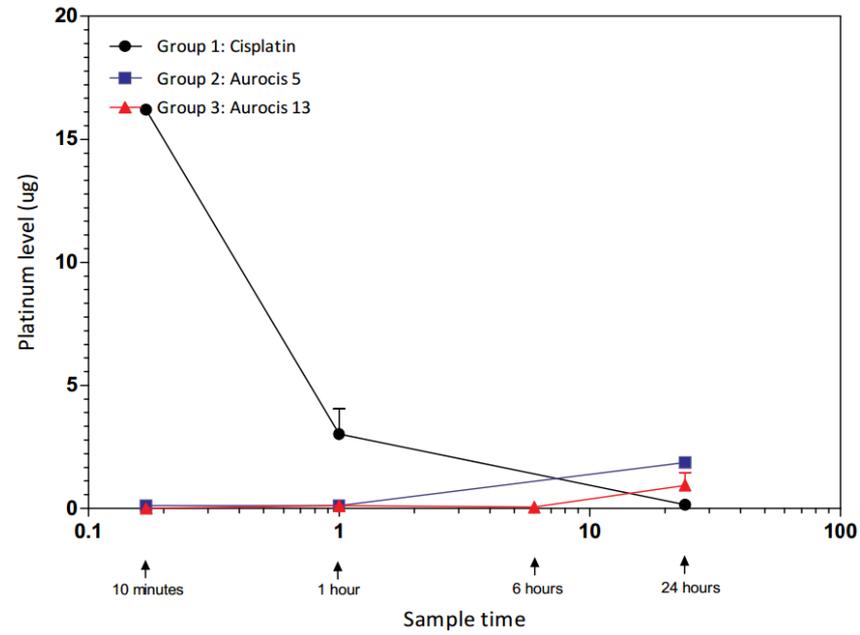
BIODISTRIBUTION IN MICE



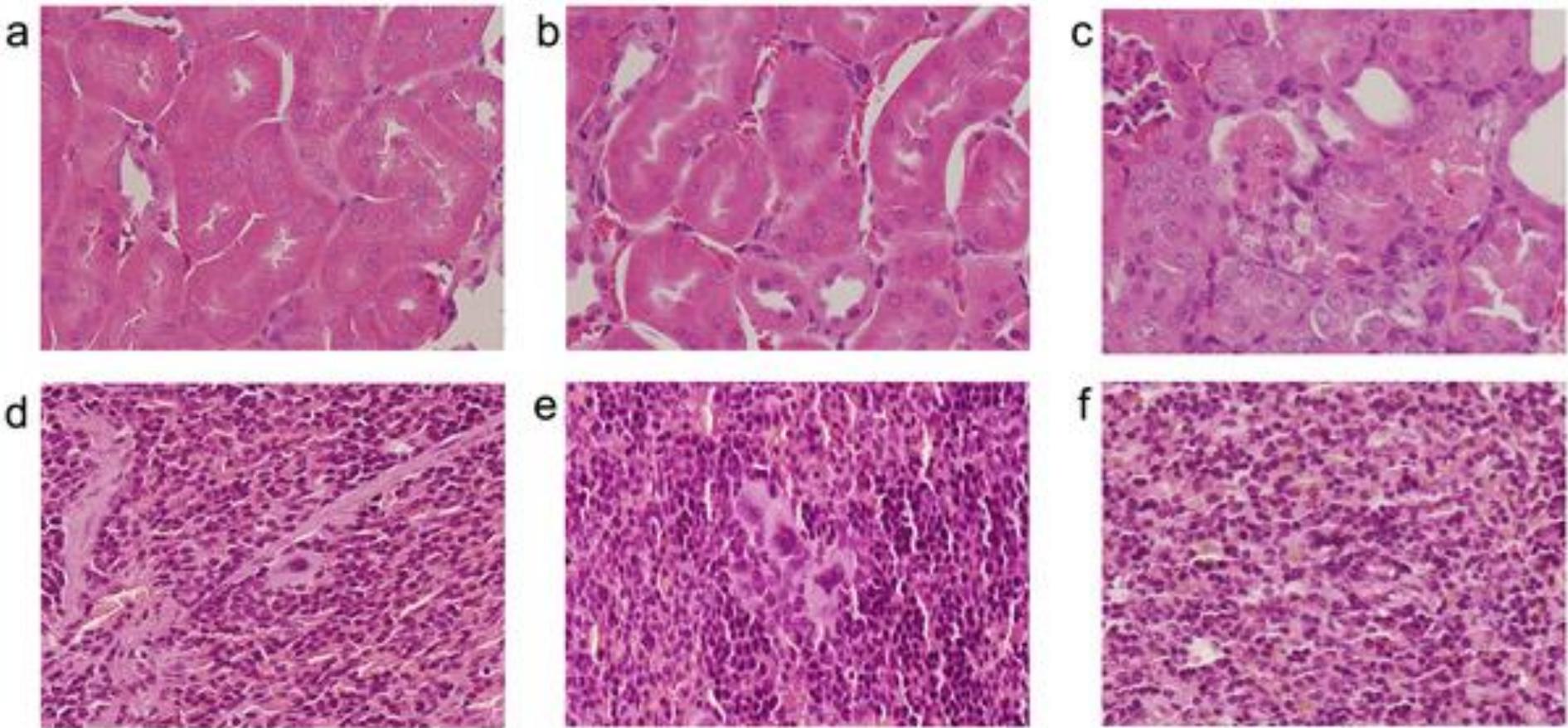
CSU 2966 Urine Gold Level total amount



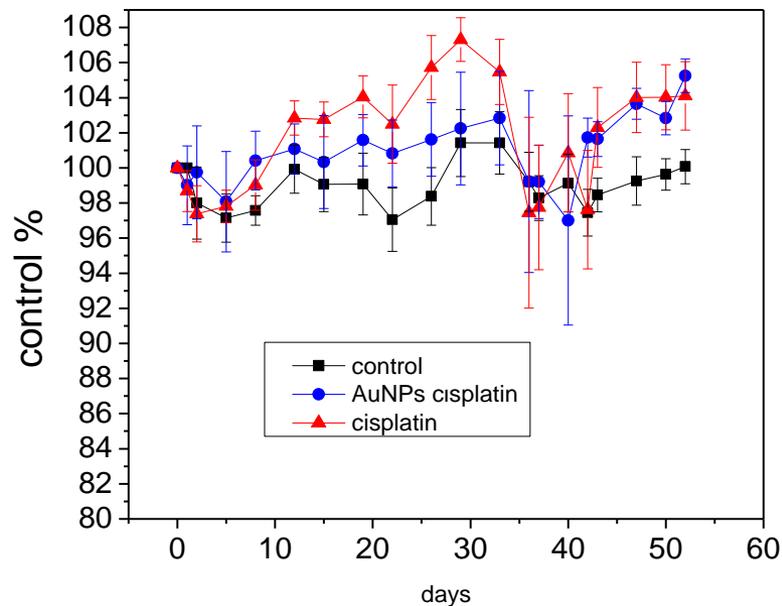
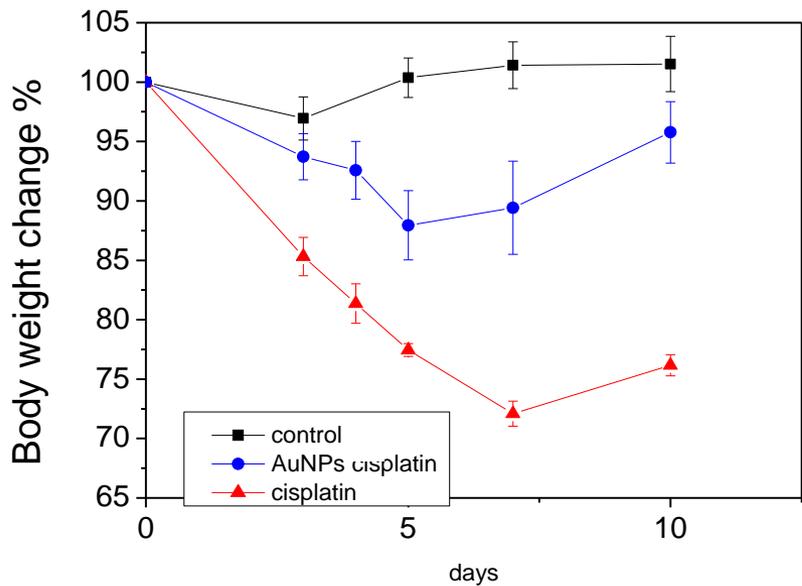
CSU 2966 Urine Platinum Level total amount



KIDNEY OBSERVATION AND BODY WEIGHT LOSS



BODY WEIGHT LOSS AS INDICATOR OF TOXICITY



. Body Weight Loss of the 2 tumour treatments presented in the main text.

AuNP- cisPt TUMORAL EFFECTS

