QEEN II: 2ND QUANTIFYING EXPOSURE TO ENGINEERED NANOMATERIALS FROM MANUFACTURED PRODUCTS WORKSHOP

SESSION B. CONSUMER EXPOSURE: FOOD, FOOD CONTACT, AND PERSONAL CARE PRODUCTS

Cytotoxicity, hemotoxicity, and in-vivo toxicity of surface modified PLGA nanoparticles

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OSHA

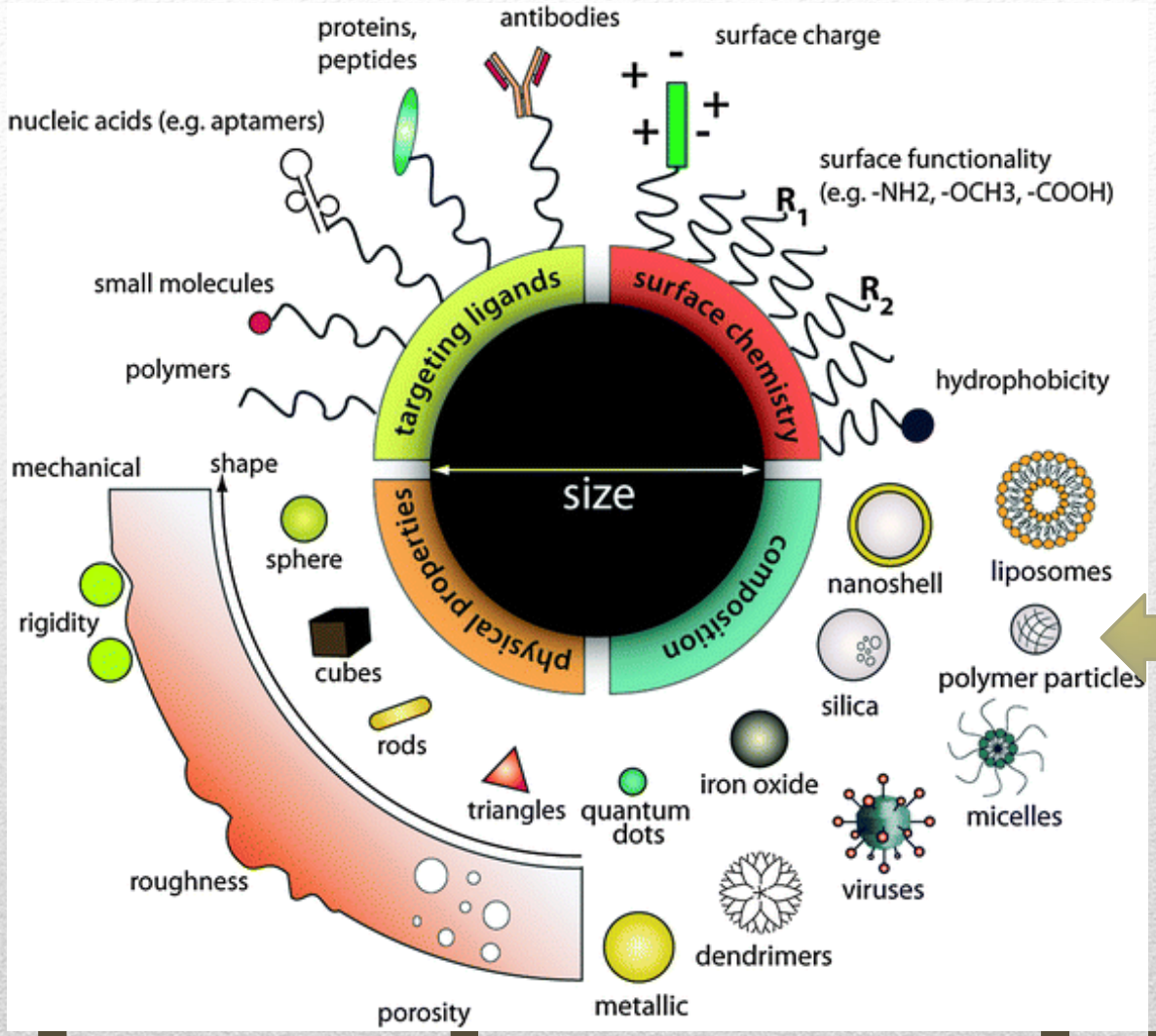
CONSUMER PRODUCT SAFETY COMMISSION · UNITED STATES OF AMERICA

Nano.gov U.S. National Nanotechnology Initiative

LSU AgCenter Research & Extension

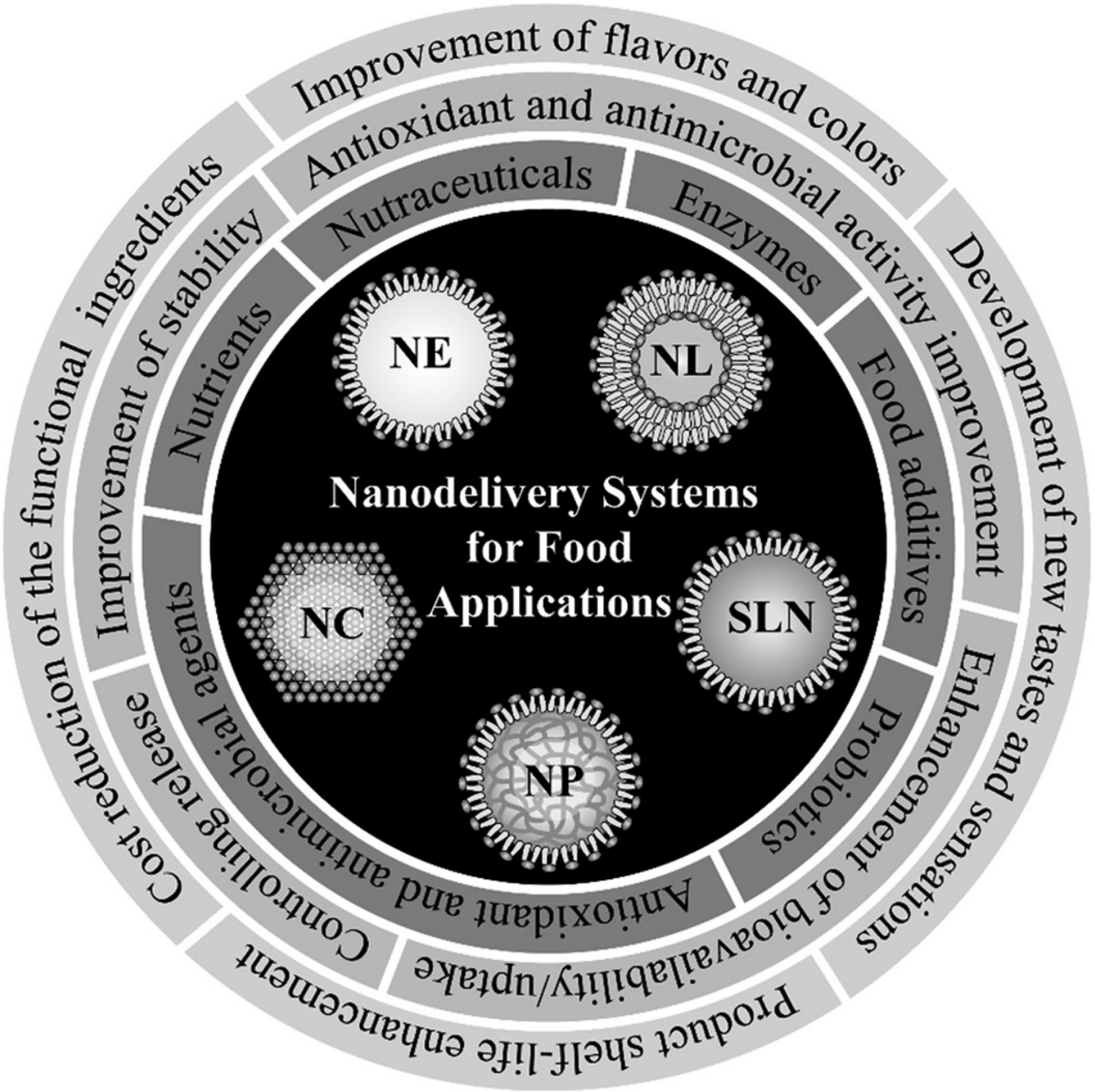
Washington DC, October 8-10

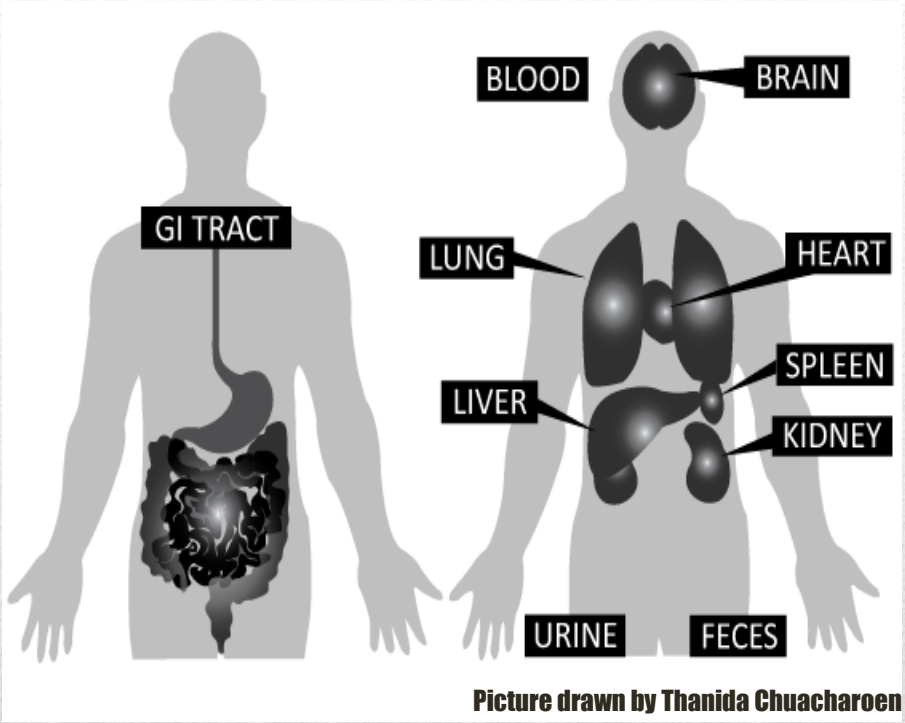
LSU



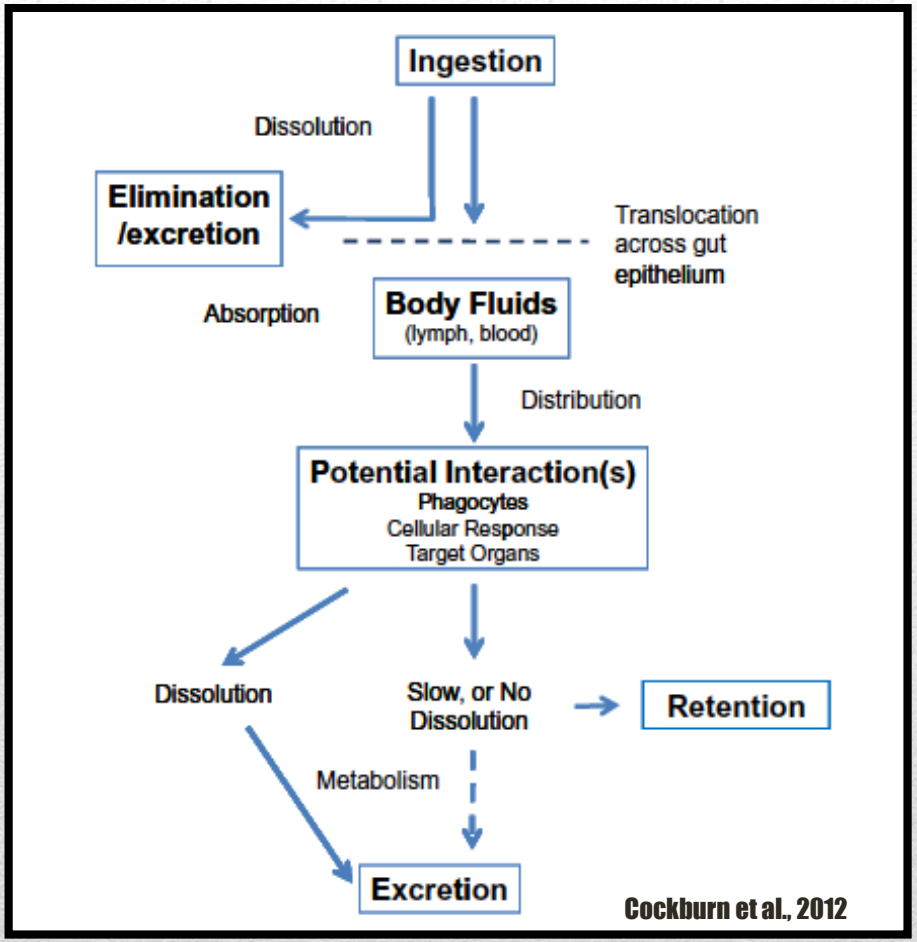
Engineered nanoparticles

Chou, L. Y. T, K. Ming and W. C. W. Chan. 2011. *Chem. Soc. Rev.* 40, 233-245.


Improvement of flavors and colors
Antioxidant and antimicrobial activity improvement
Development of new tastes and sensations
Enhancement of bioavailability/uptake
Product shelf-life enhancement
Controlling release
Cost reduction of the functional ingredients
Improvement of stability
Nutraceuticals
Enzymes
Food additives
Probiotics
Antioxidant and antimicrobial agents
Nutrients
NE
NL
Nanodelivery Systems for Food Applications
NC
SLN
NP

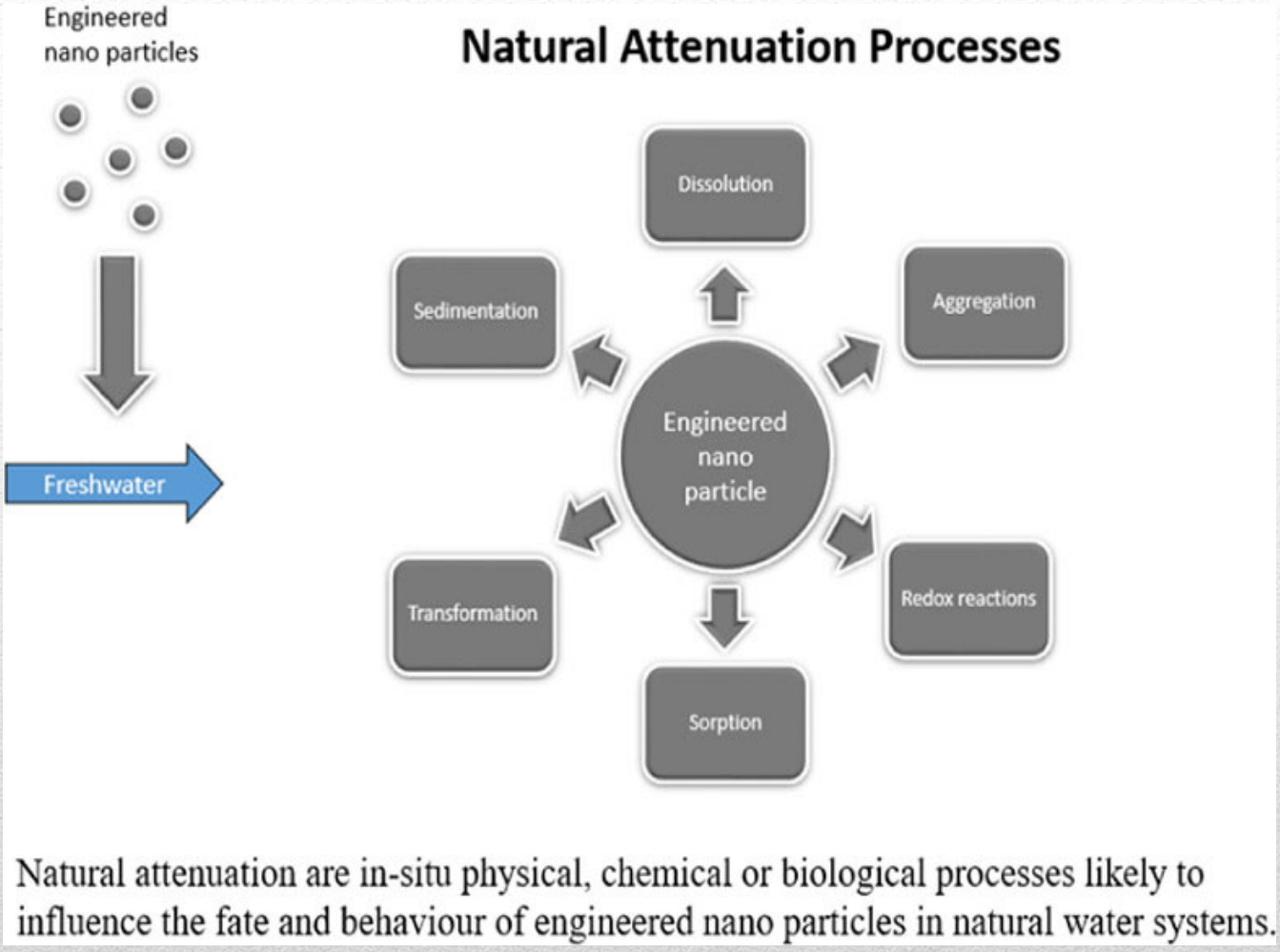


Picture drawn by Thanida Chuacharoen



Cockburn et al., 2012

Particle ADME profile

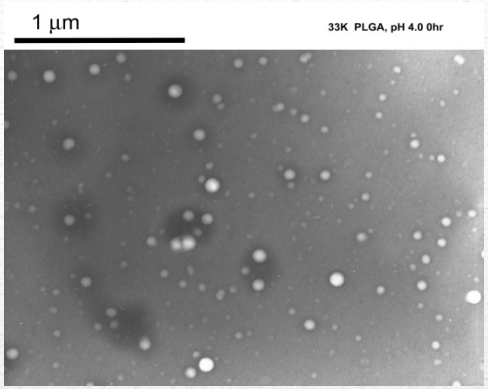


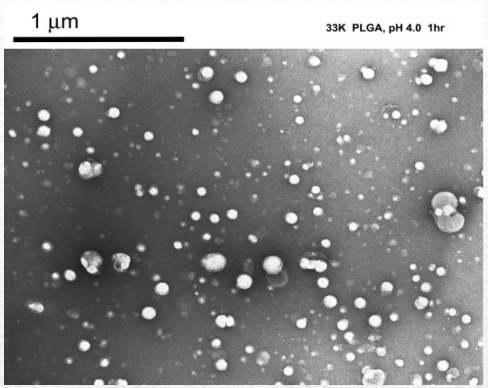
Natural attenuation are in-situ physical, chemical or biological processes likely to influence the fate and behaviour of engineered nano particles in natural water systems.

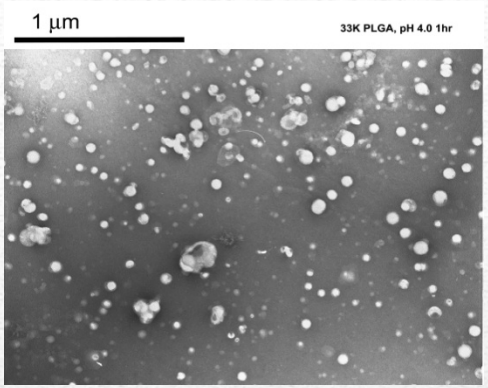
Particle Biotransformation

D.Shevlin, N.O'Brien, E.Cummins. 2018. Science of the Total environment. April, 2018.

PLGA
33K
pH 6.5

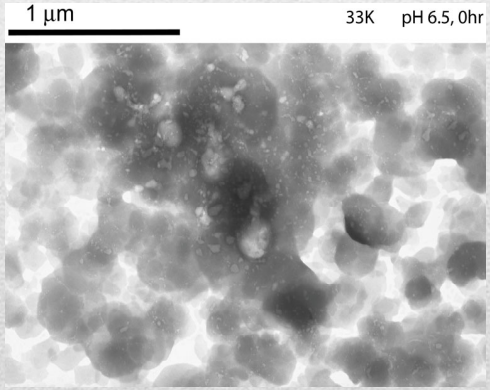


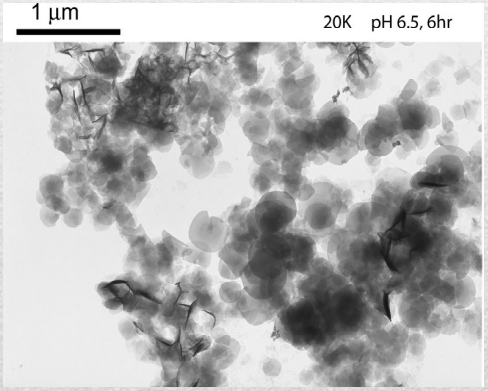


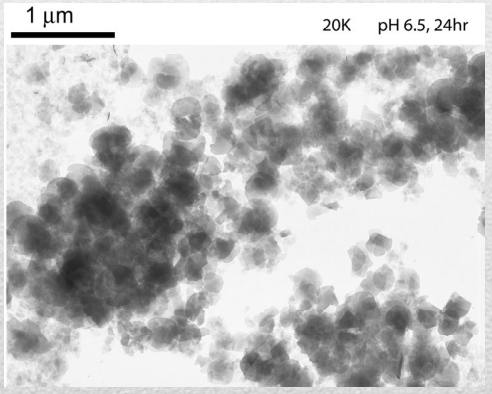


0 hrs → 6 hrs → 24 hrs

PLGA-Chi
20 K & 33K
pH 6.5



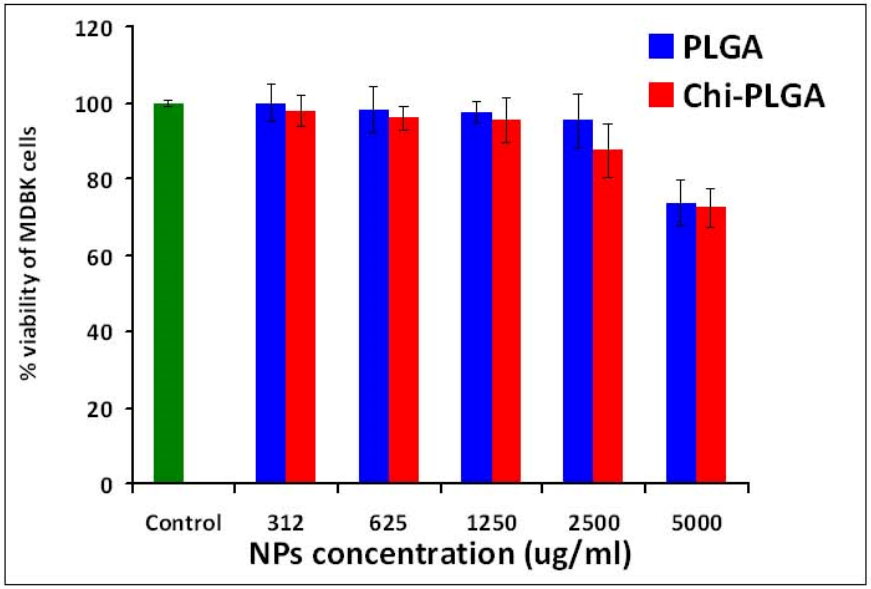




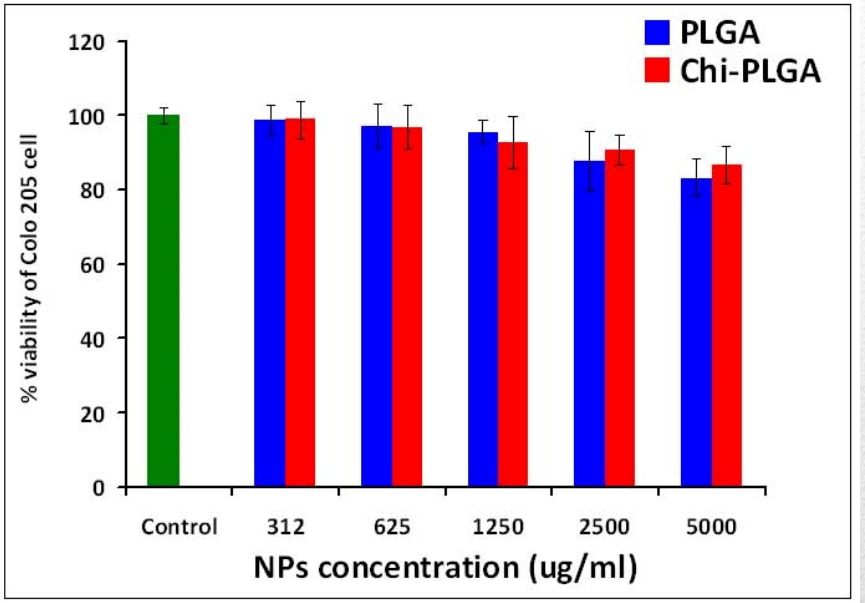
pH stability (pH=6.5)

Murugeshu, A., C. E. Astete, C. Leonardi, and C. M. Sabliov. 2011. *Nanomedicine* Vol. 6, No. 9, Pages 1513-1528.

A.



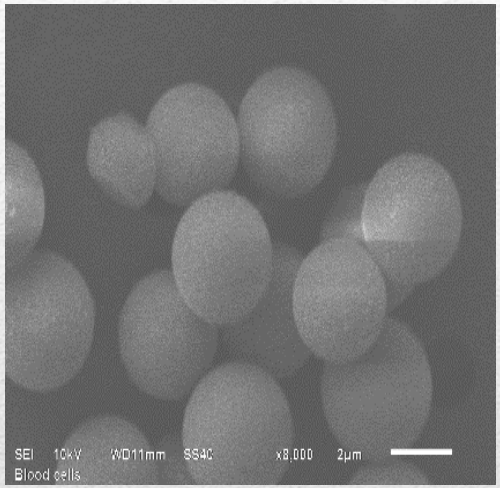
B.



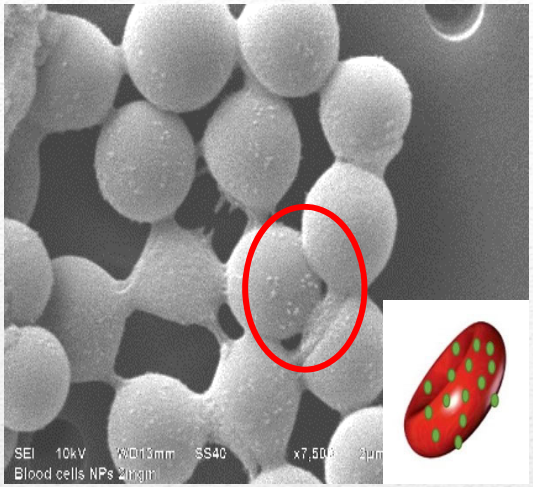
Cytotoxicity

Trif, M, P. E. Florian, A. Roseanu, M. Moisei, O. Craciunescu, C. E. Astete and C. M. Sabliov. 2015. *Journal of Biomedical Materials Research Part A.* 103(1):3599-3611

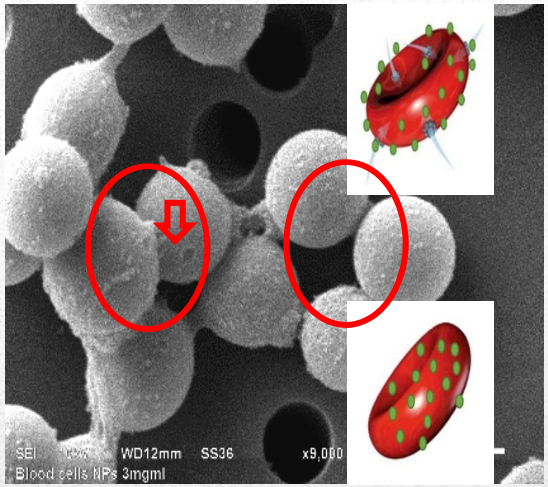
Alqahtani, S., L. Simon, C. E. Astete, A. Alayoubi, P. W. Sylvester, S. Nazzal, Y. Shen, Z. Xu, A. Kaddoumi, C. M. Sabliov. 2015. *Journal of Colloid and Interface Science.* 445: 243-251.



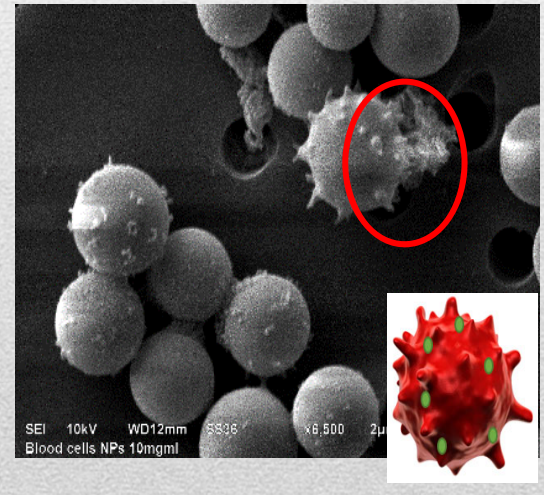
Untreated red blood cells



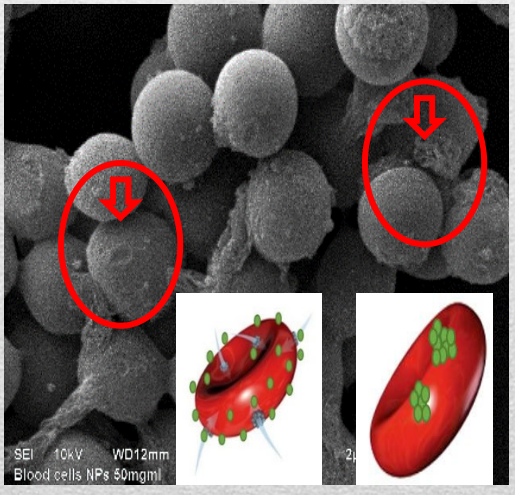
Red blood cells with 2mg/ml NPs



Red blood cells with 3mg/ml NPs

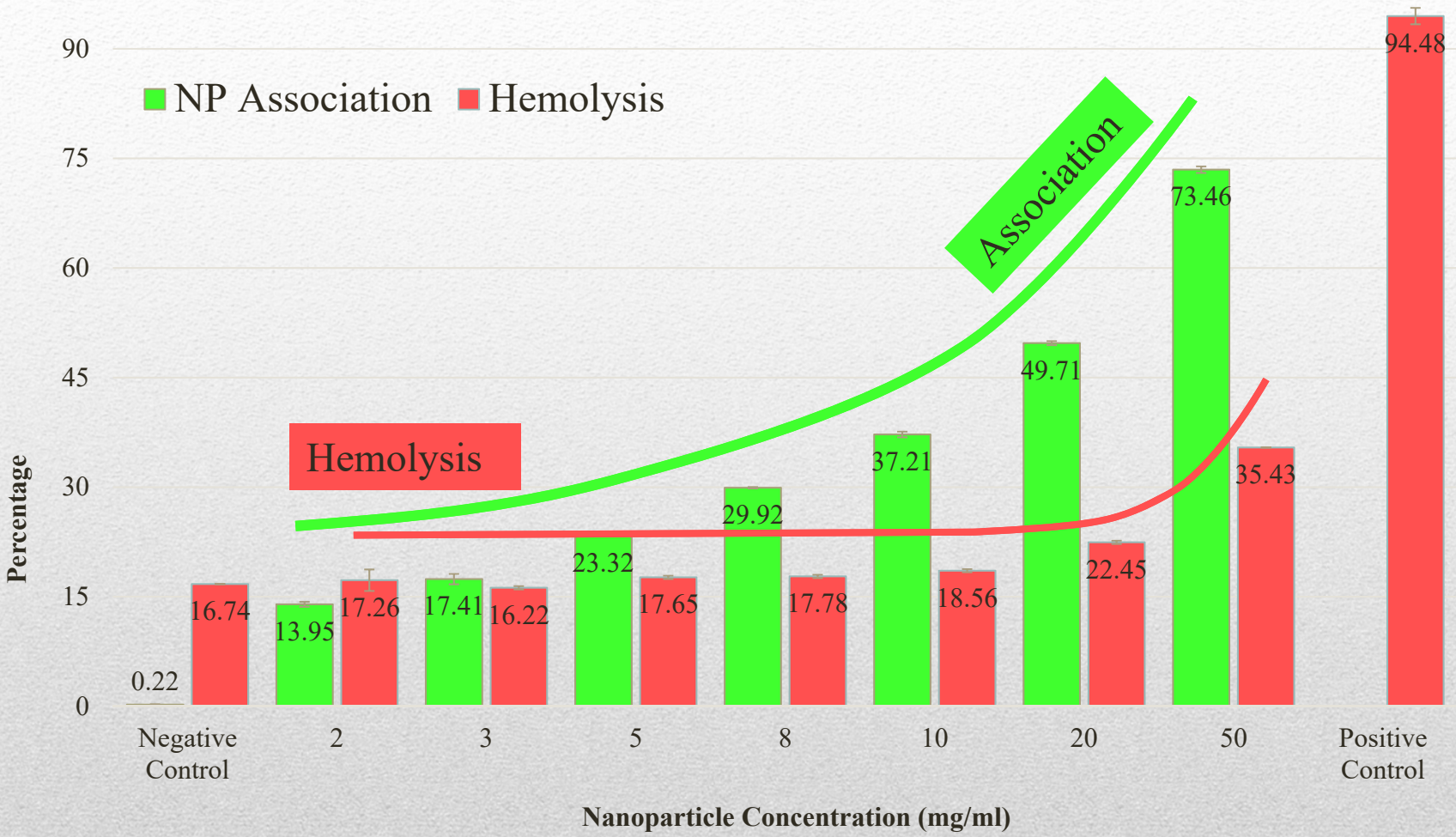


Red blood cells with 10mg/ml NPs

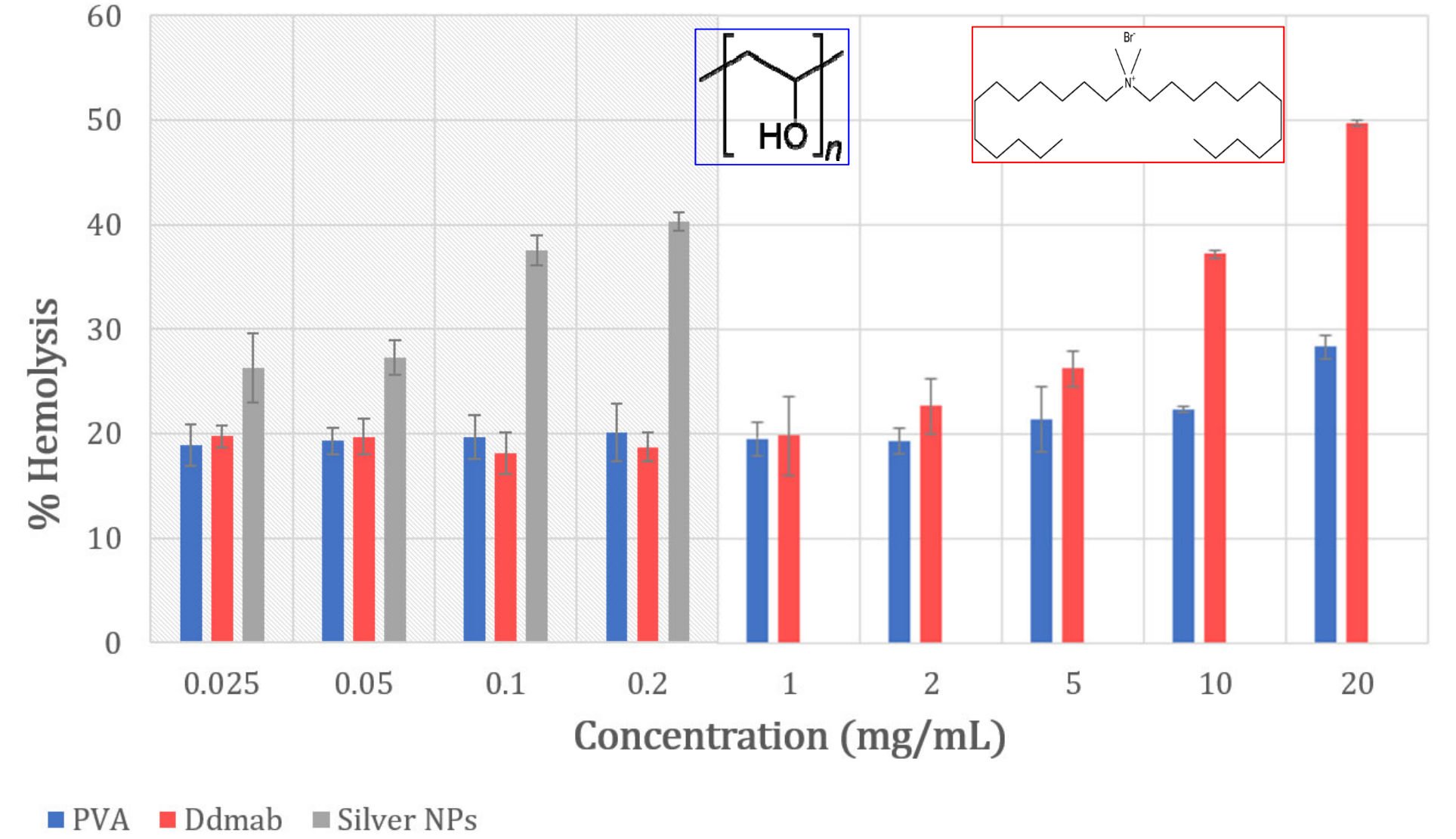


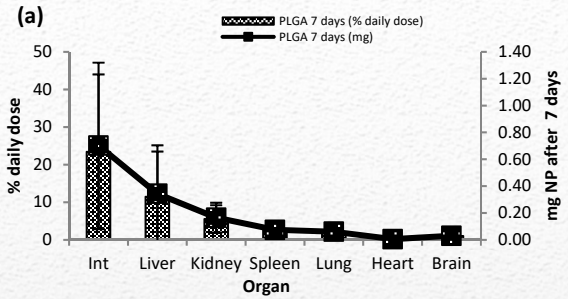
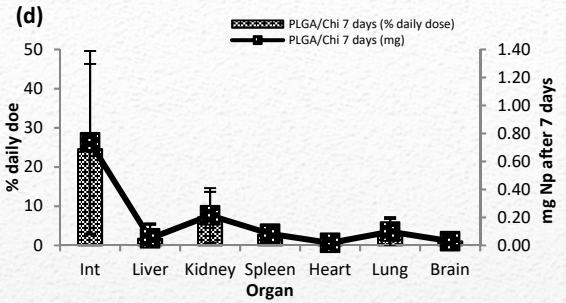
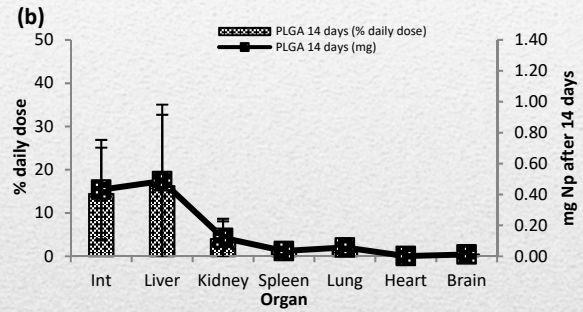
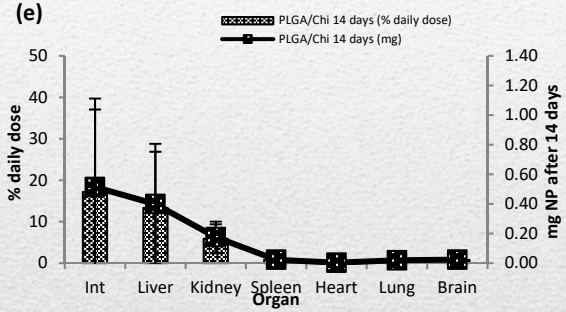
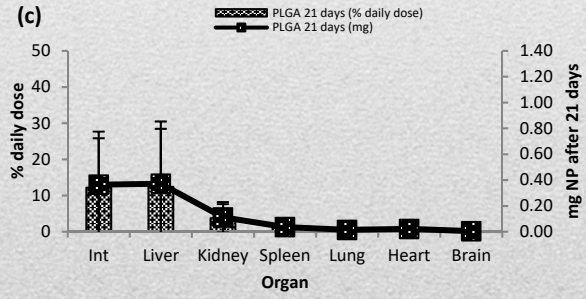
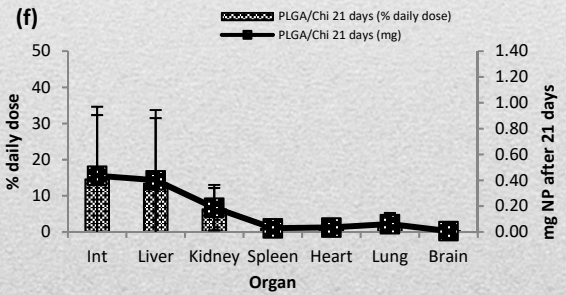
Red blood cells with 50mg/ml NPs

Nanoparticles RBC Association (SEM Image)



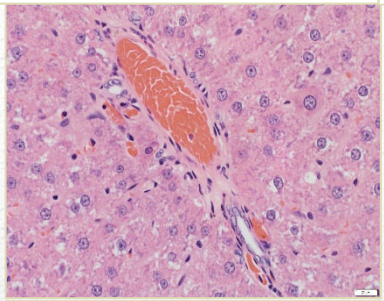
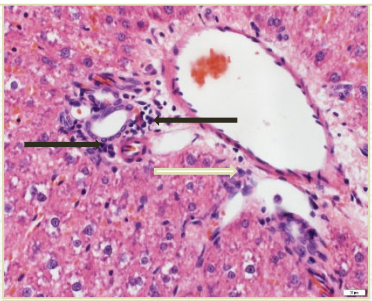
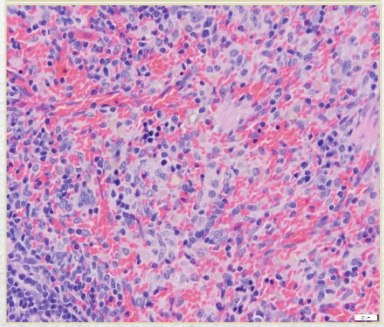
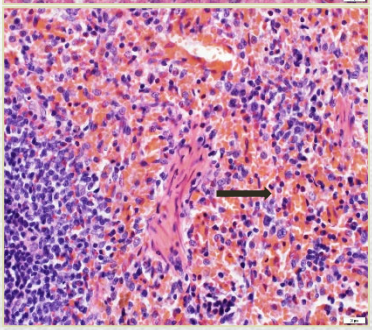
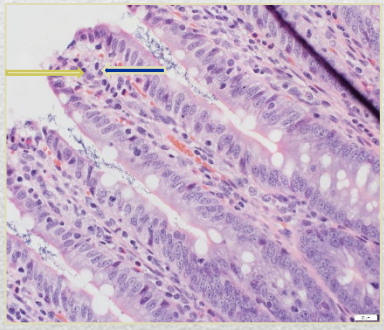
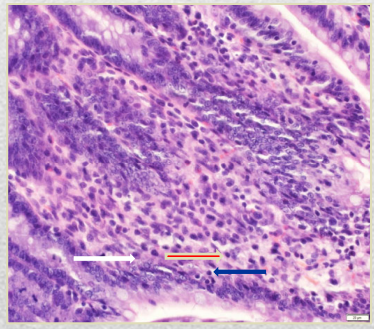
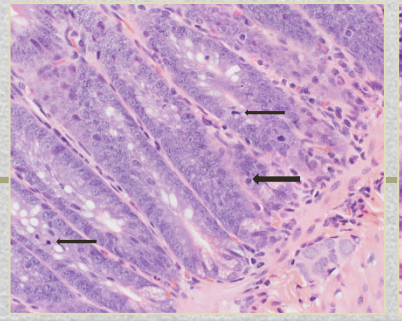
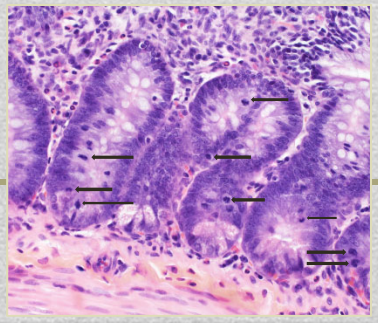
Hemotoxicity


60
50
40
30
20
10
0
% Hemolysis
HO
n
Br
N+
0.025
0.05
0.1
0.2
1
2
5
10
20
Concentration (mg/mL)
PVA
Ddmab
Silver NPs

	PLGA	PLGA-Chi
7 days		
14 days		
21 days		

In-vivo biodistribution

Navarro, S. T. Morgan, C. E. Astete, R. Stout, D. Coulon, P. Mottram and C. M. Sabliov. 2016.. *Nanomedicine*.11(13):1653-1669. (doi: 10.2217/nnm-2016-0022)

	Control	PLGA NPs	
Liver			Liver 14 days PLGA treatment shows increased numbers of lymphocytes, plasma cells (black arrow) and occasional mast cells (white arrow).
Spleen			No significant lesions have been observed in spleen.
Intestinal villi			Intestine villi show the presence of scattered lymphocytes (blue arrow), plasma cells (red arrow) and histiocytic cells (white arrow) in the lamina propria.
Intestinal crypts			Arrows indicate scattered mitotic figures (black arrows). Increased hyperplasia of intestinal crypt cells indicated increased intestinal mucosal epithelial cell turnover.

Conclusions

- **PLGA NPs were not cytotoxic,** except at high concentration (>5 mg/ml)
- Interaction between PLGA nanoparticles and RBCs was **concentration dependent**
- PLGA nanoparticles associated with RBC membrane and had **no hemotoxic effect at concentrations lower than 5 mg/ml (>5% increased over negative control),** and was dependent on the surfactant
- **Minimal inflammatory changes were observed in the hepatic portal regions of the liver and the lamina propria of the small intestine** in PLGA and PLGA-Chi dosed rats versus controls
- **The intestine had mild crypt hyperplasia, indicative of an increased intestinal mucosal epithelial turnover rate**
- **No significant histologic lesions were seen in the lung, kidney, spleen, or brain** in PLGA or PLGA-Chi dosed rats versus controls

USDA

- **Properties of nanomaterial still important** and should be documented
- **Nanomaterial biotransformation is key** to in-vivo behavior
- **Toxicity work is mainly focused on inorganic**, metal and metal oxides nanoparticles
- Interest is growing in **biodegradable particles**
- **Methods of detection of biodegradable particles** in complex media need to be developed
- **Toxicity testing needed for long term**, small concentration exposure is needed

THANK YOU!