



standardization
and innovation

2006 ANSI ANNUAL CONFERENCE

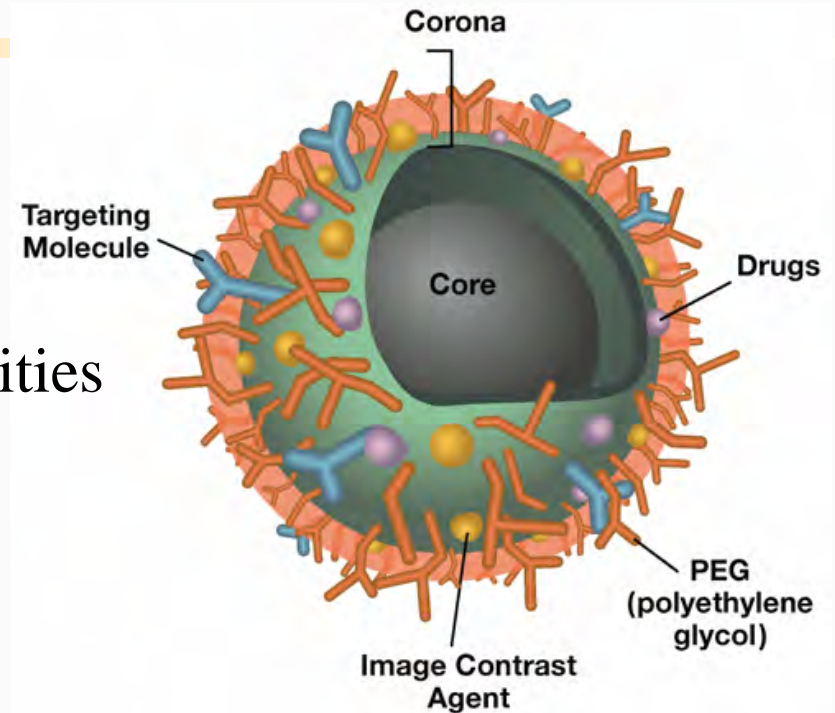


Preclinical Characterization of Nanoparticles

Presented by
Scott McNeil, Ph.D.
Director, NCL
NCI-Frederick

Cancer Nanotechnology

- Therapeutic Benefits
- Solubility
 - Carrier for hydrophobic entities
- Multifunctional capability
- Active and passive targeting
 - Ligands; size exclusion
- Reduced toxicity



McNeil, (2005), J. Leuk. Biol., 78:585-594

Active Targeting



Free Drug
30 mg/kg total

Nanodevice-bound drug
3 mg/kg total



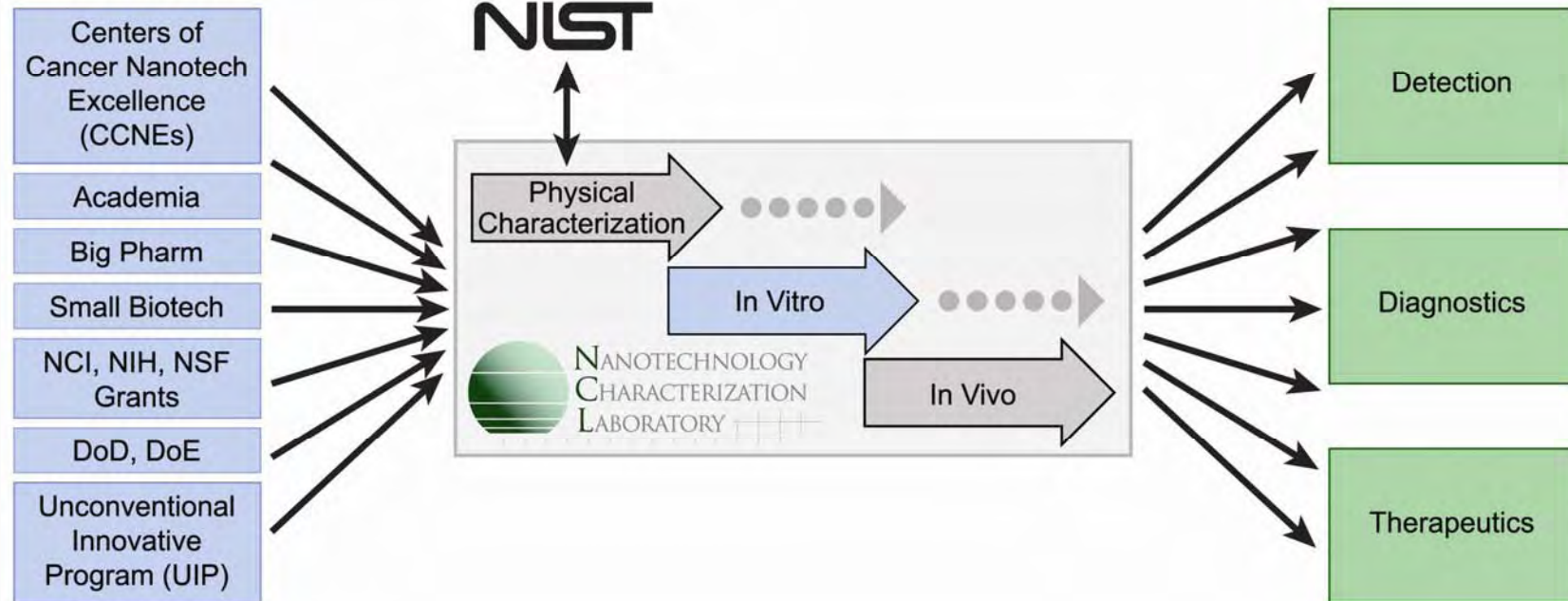
Dr. James Baker, University of Michigan



- Run by Office of Technology and Industrial Relations (OTIR)
 - Extramural Budget: \$144M over 5 years
 - Launched on Sept 13th, 2004
 - Website: <http://nano.cancer.gov/>
- Consensus among cancer researchers that significant obstacles must be overcome in order to transition 'nano' to clinical realm
 - Critical lack of available standards
 - 1st principles characterization
 - Regulatory uncertainty

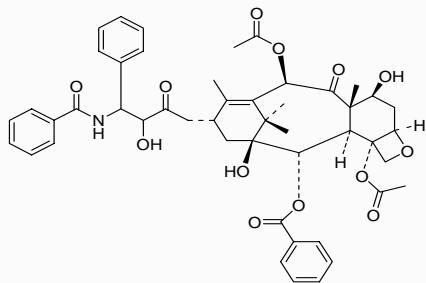
NCL Concept of Operations

Sources of Nanomaterials



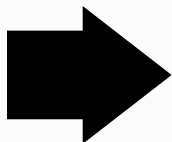
NCL is a formal collaboration between NCI, FDA and NIST

Physical Characterization



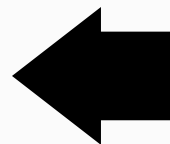
Small molecules

- Elemental analysis
- Mass
- NMR
- UV-Vis
- IR
- HPLC
- GC
- Polarimetry



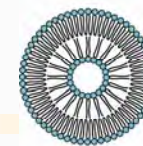
Physicochemical Parameters

- Composition
- Physical properties
- Chemical properties
- Identification
- Quality
- Purity
- Stability

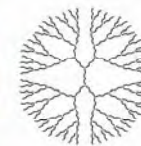


Nanomaterial

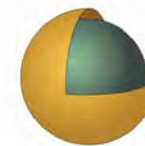
- Microscopy (AFM, TEM, SEM)
- Light scattering (Static, Dynamic)
- SEC, FFF
- Electrophoresis (CE, PAGE)
- Zeta sizer
- Fluorimetry



Liposome



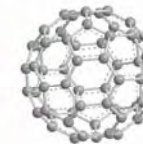
Dendrimer



Gold Nanoshell



Quantum Dot

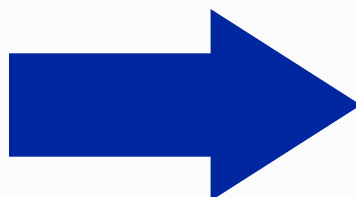



Fullerene

Same parameters – different/additional characterization methods

In Vitro Cascade

- In Vitro
- Sterility
 - Bacterial/Viral/Mycoplasma
 - Endotoxin
- Targeting
 - Cell Binding/Internalization
- Blood Contact Properties
 - Plasma Protein Binding
 - Hemolysis
 - Platelet Aggregation
 - Coagulation
 - Complement Activation
 - CFU-GM
 - Leukocyte Proliferation
 - Macrophage/Neutrophil Function
 - Cytotoxic Activity of NK Cells
- Toxicity
 - Phase I/II Enzyme Induction/Suppression
 - Oxidative Stress
 - Cytotoxicity (necrosis)
 - Cytotoxicity (apoptosis)
- Metabolic Stability





NCL Method ITA-1

Analysis of Hemolytic Properties of Nanoparticles

Nanotechnology Characterization laboratory
National Cancer Institute at Frederick
SAIC-Frederick
Frederick, MD 21702
(301)-846-6939

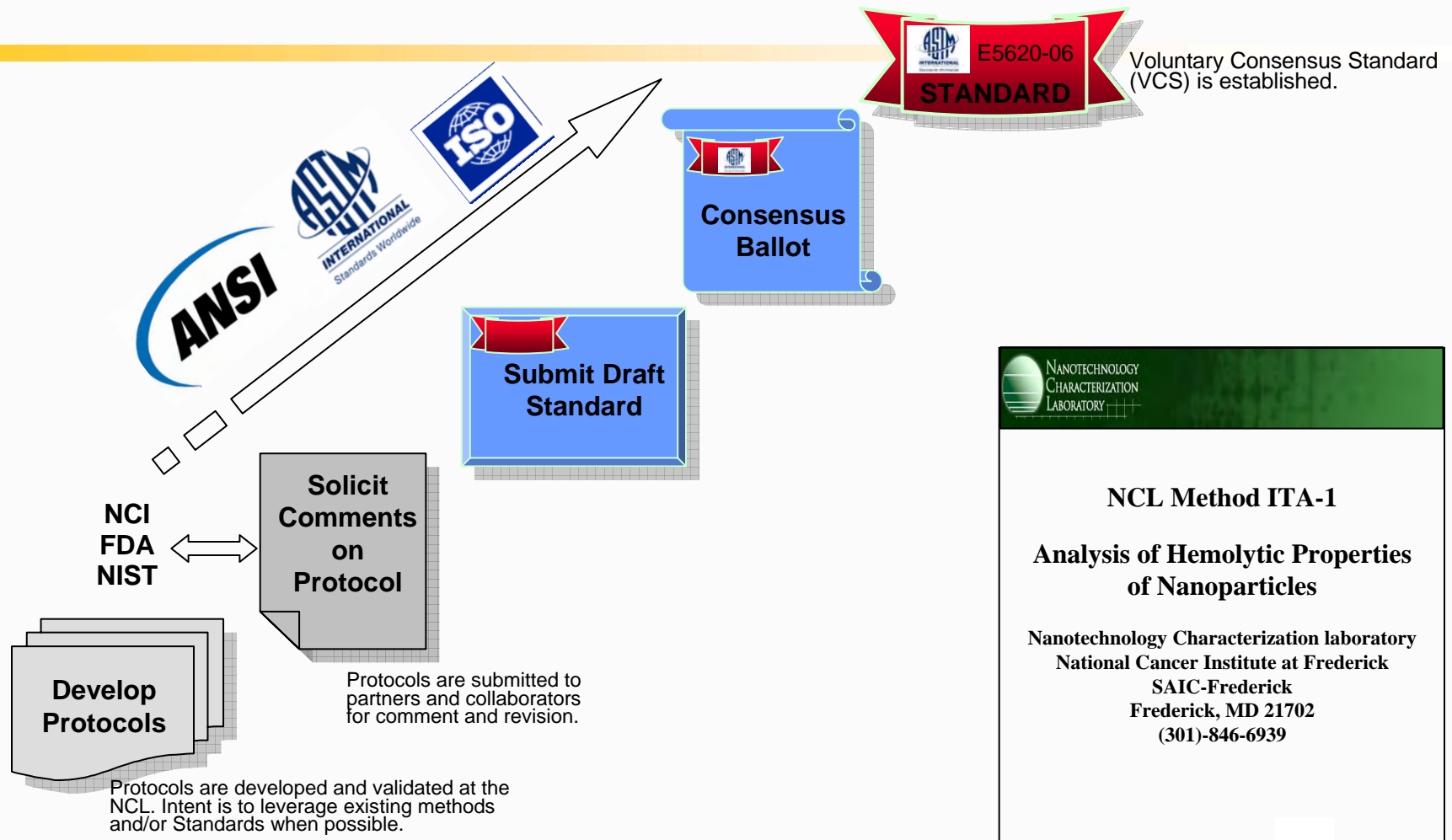
http://ncl.cancer.gov/working_assay-cascade.asp



Voluntary Consensus Standards

Industry, Academia, Government

VCS informs regulatory agencies and promotes commercialization of nanotechnology for medical applications



NANOTECHNOLOGY CHARACTERIZATION LABORATORY

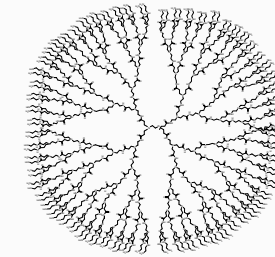
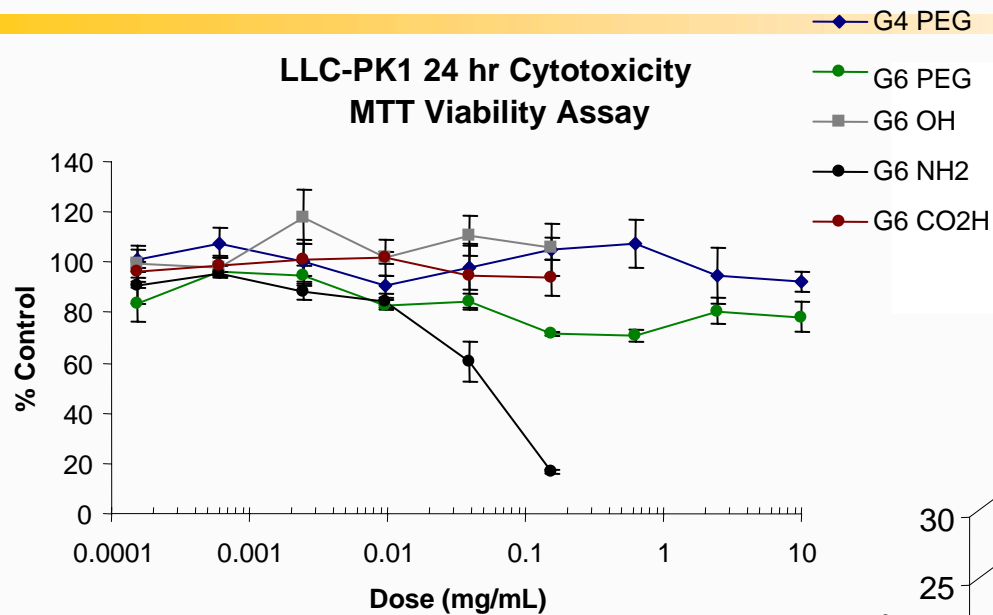
NCL Method ITA-1

Analysis of Hemolytic Properties of Nanoparticles

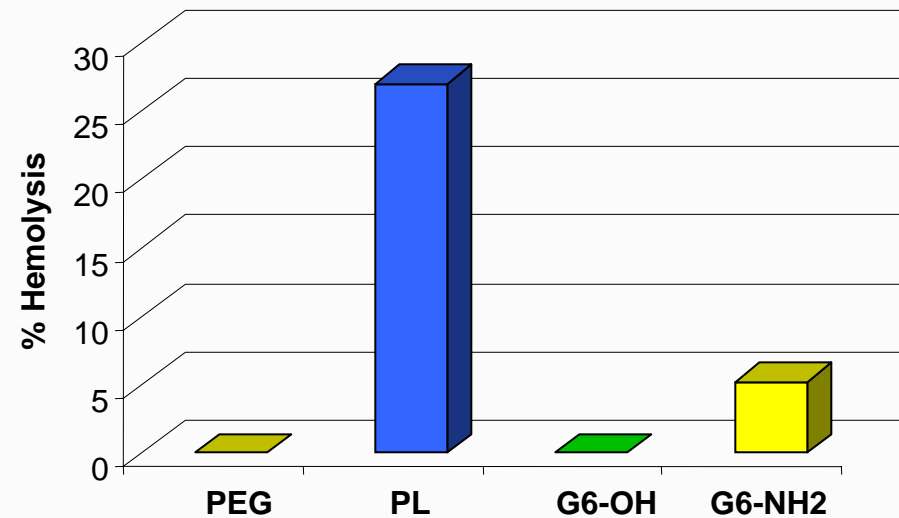
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Structure Activity Relationships

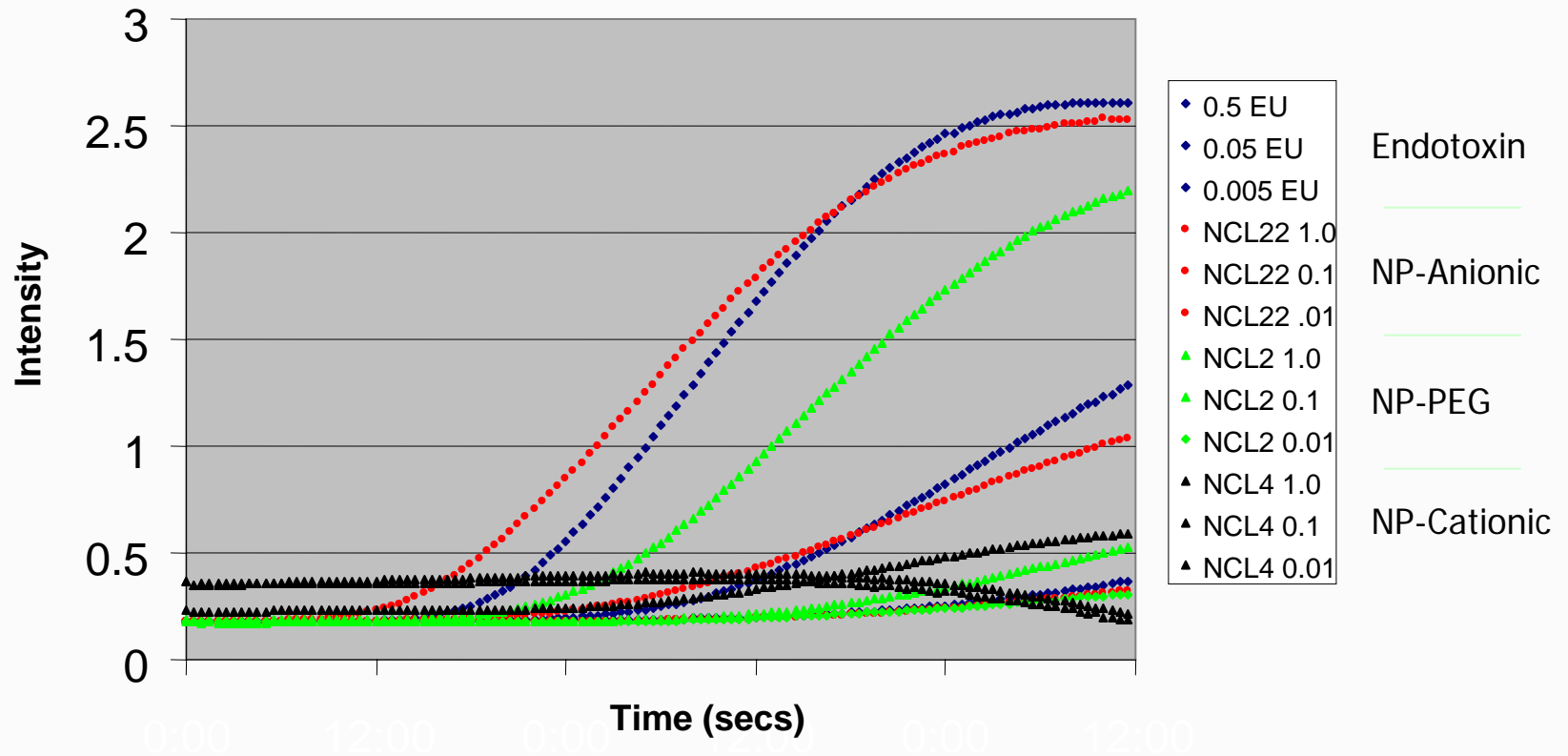
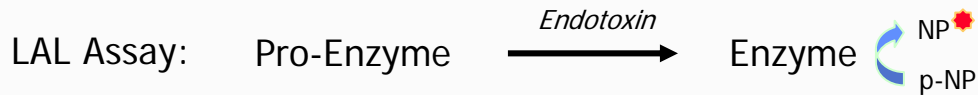


G6 Dendrimer



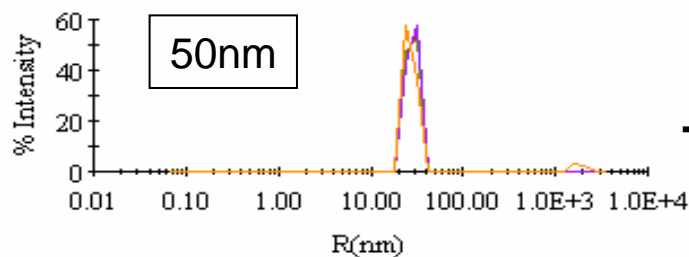
Legacy Methods vs. Nanomaterials

Nanoparticles often have properties that interfere with off-the-shelf kits and methods



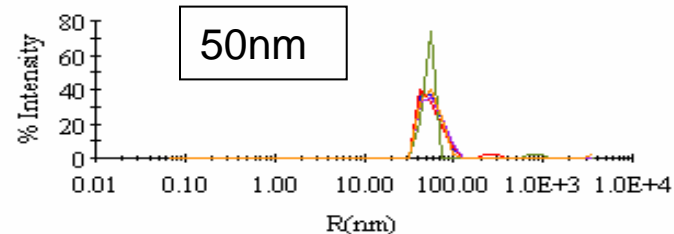
Particle Size in a Biological Context

No Incubation

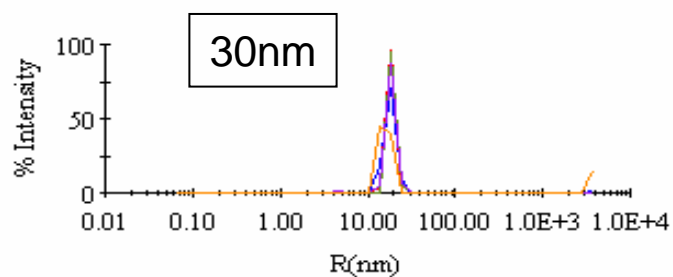


R (nm)	Diam (nm)	%Pd
27.8	55.6	26.7

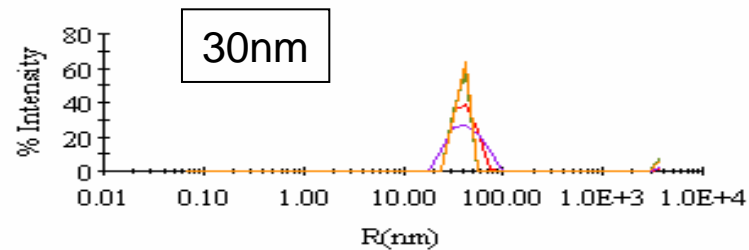
+ Serum



R (nm)	Diam (nm)	%Pd
56.4	112.8	23.0



R (nm)	Diam (nm)	%Pd
17.8	35.7	22.5



R (nm)	Diam (nm)	%Pd
41.0	82.0	34.5



Acknowledgements

NCL

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