Cell-Based Toxicity Assay-on-Chip for the Next-Generation CMOS Technology

(Task Number: 425.037)

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Cost Share (other than core ERC funding):

- **25% cost-share (in cash) from Joint School of Nanoscience and Nanoengineering (collaboration between NCA&T and UNC-Greensboro)**

Year 2 Summary

- Comprehensive physical and chemical characterization of four model slurries and CNTs, along with undispersed/dried micro and nanoparticles of comparable size and method of synthesis
- Conducted NP pathway or lifecycle on interaction with a mammalian cell
  - **Surface interaction** - Cell viability and membrane integrity (MTT and LDH assays)
  - **Cellular uptake and internalization** (using ICP-OES, microscopy, Confocal Raman, ECIS and ROS assays)
  - **Interaction with nucleus** (NP-induced DNA damage, Comet assay)
- Results indicate cellular uptake for all NPs and toxic potential (at least for silica slurry) at higher NP concentration, however minimal to no toxicity due to NP alone (dried/undispersed NPs)
- Trace element studies did not explain silica slurry toxicity; more analysis of slurry constituents is required to understand source of silica toxicity
- Preliminary CMP on interaction of colloidal silica slurries with GaAs

Objectives

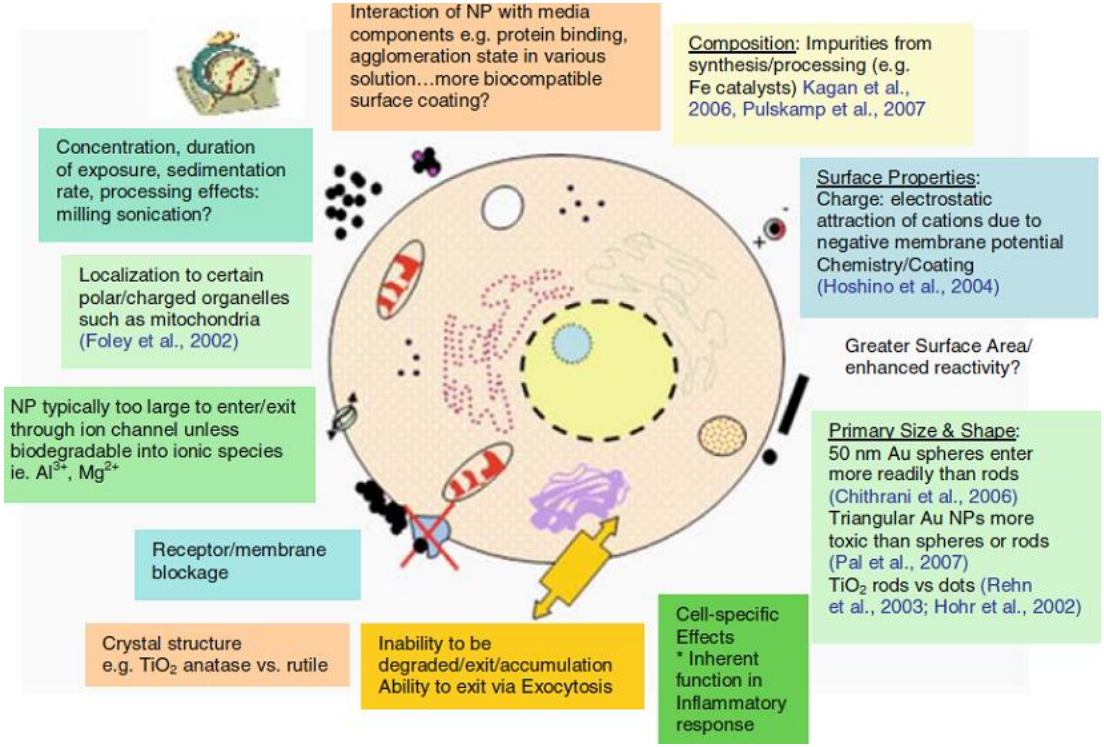
- **Long-term objectives**
  - Understand ESH of Engineered Nanomaterials (ENs) used/to be used in semiconductor industry, particularly NP slurries and CNTs/BNNTs
  - Develop high-content assays-on-chip and analytical/microscopic methods to rapidly assess influence of physiochemistry on ESH
- **Year 3 goals**
  - Completion of cellular uptake and internalization studies with Model CMP slurries and A549 human alveolar basal epithelial cells (lung)
  - Use validated toxicity and longitudinal methods (ECIS, HRTEM, ICP-OES and Confocal Raman) to conduct time- and dose-dependent cell response
  - Conduct preliminary studies with post-CMP slurries and wastes, along with other bound NPs – CNTs and BNNTs to be used in semiconductor packaging

ESH Metrics and Impact

1. **Reduction in the use or replacement of ESH-problematic materials (CMP NP slurries)**
   - Conducted comprehensive physicochemical characterization of four model and few "real" slurries and identified relationship between slurry NP properties and toxic potential using toxicity and uptake assays
2. **Reduction in emission of ESH-problematic material to environment**
   - Conducted preliminary CMP of HDP oxide and III-V (GaAs) using given model and "real" slurries; analyze physicochemical and toxic potential of slurry waste after dilution or neutralization
3. **Reduction in the use of natural resources (water and energy)**
   - Results from Metric 2 will inform us on the efficient use of water for dilution and neutralization processes
4. **Reduction in the use of chemicals**

Understanding influence of Physicochemical Properties on Toxicity

- Number of physicochemical properties and mechanisms occur at the surface of nanomaterial, on its interaction with and inside a cell, thus affecting toxicity (see figure)
- Variability is huge due to different properties, cell types, processing and assay conditions
- Studies with characterized ENs exposed to same cell type/conditions are ideal
- Goal - establish dose-response relationships for predictive nanotoxicity and safe design of EN



Schematic representation of some possible interactions of nanomaterials with a cell in culture media (Schrand et al., 2009. Ch. in Safety of Nanoparticles, T.J. Webster (ed.))

Critical Questions to be Addressed

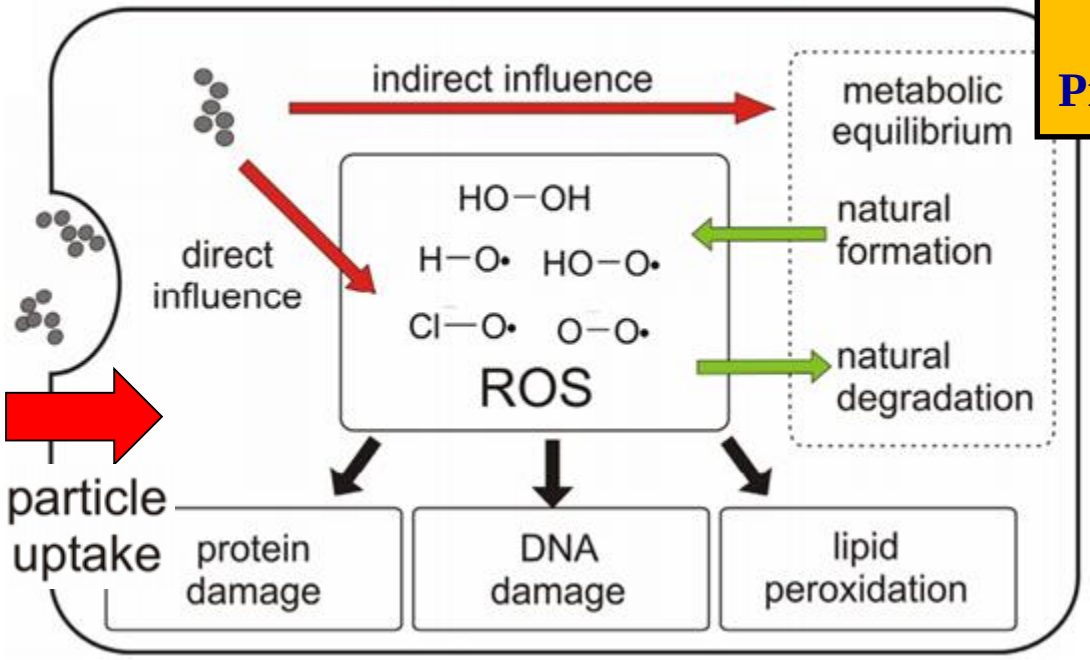
- **Focusing the research efforts, Schrurs et al. Nature Nanotechnology, 2012**
  - Are ENs more cytotoxic than their larger counterparts?
  - Does EN aggregation influence the cytotoxic activity?
  - Which properties of ENs drive their cytotoxic activity? Physiochemical properties such as size, distribution, aggregation, shape, composition, area, morphology, surface charge, chemistry, protein corona
  - Does cytotoxicity of ENs vary with cell type?
  - Do ENs penetrate into cells and how does intracellular trafficking of ENs occur?
  - Address technical interferences and positive control

Experimental Pathway

I **Comprehensive Characterization of ENs**
(DLS, Zeta potential, BET, FTIR, XRD, Raman, ICP-OES, HRSEM, TEM)

High-Content Assays/Longitudinal Methods

II **Acute/delayed cytotoxicity (cell viability and membrane integrity) using MTT and LDH assays**



III **Acute/delayed cellular uptake and internalization**
(ICP-OES, Confocal Raman, ECIS, HRTEM and ROS)

Safe EN design and use; Predictive toxicity

IV **Delayed genotoxicity studies – Comet assays**

Experimental Methods and Approach

- **Materials tested**
  - Model CMP NP slurries and dried/undispersed NPs
  - "Real" CMP slurries - relevant commercial slurries of colloidal and fumed silica, ceria and alumina NPs

Sample	Composition	pH	Size(nm)
Colloidal Silica (NS-0813-01, Slurry 1)	3% precipitated Silica, adjusted with acetic acid	2.5-4.5	50-60
Fumed silica (NS-0813-02, Slurry 2)	5% silica, adjusted with KOH	10	120-140
Ceria (NS-0813-03, Slurry 3)	1% ceria	3-4	60-100
Alumina (NS-0813-04, Slurry 4)	3% Alumina, adjusted with nitric acid	4.5-5	80-100

Dried/undispersed Particles	Size
Colloidal Silica (PS1)	80 nm
Colloidal Silica (PS3)	1-3 µm
Fumed Silica (FS1)	7 nm
Fumed Silica (FS2)	200-300 nm
Ceria (PC1)	50-105 nm
Ceria (PC2)	1-2 µm
Alumina (PA1)	80
Alumina (PA2)	<10 µm

- **Cells studied**
  - **A549 adenocarcinomic human alveolar basal (lung) epithelial cells**

Model CMP NP Slurries

I. Characterization of Nanomaterials

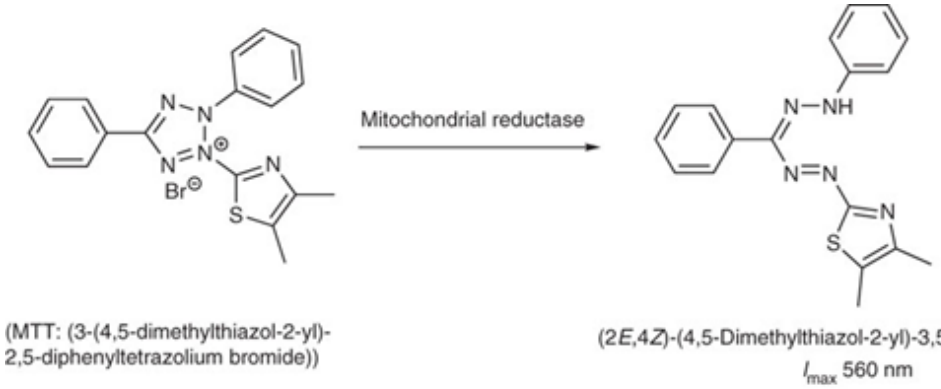
- **Previously reported physical and chemical characterization of model CMP slurries and dried NPs**
  - Size (DLS) and zeta potential
  - Main and trace elemental analysis – ICP-OES, EDS
  - Structure and morphology – HRSEM, TEM
  - BET surface area analysis
  - X-ray diffraction, FTIR, Raman spectroscopic analysis

- **Highlights of physiochemical analysis of "real" CMP NP slurries-colloidal/fumed silica, ceria, alumina (shown later in the presentation)**

II. Cytotoxicity – Cell Viability and Integrity

- **Dose and time-dependent end-point cytotoxicity assays to assess the plasma membrane integrity and cell viability**
- **Address one key question -** Is cytotoxicity driven by composition, dose and time – acute or delayed response?
- **MTT ((3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) colorimetric assay**
  - Based on the conversion of MTT into formazan crystals (purple color) by living cells, which determines its mitochondrial activity. For most cells the total mitochondrial activity is a indicator of number of viable cells, a measure of in-vitro cytotoxicity
- **Lactate Dehydrogenase (LDH) assay**
  - Assessment of membrane integrity - by monitoring the passage of substances that are normally sequestered inside cells to outside.
- **Positive (H_2O_2 or lysis buffer) and negative (healthy cells in media) controls were incorporated to ensure the assays can detect cytotoxic activity**

II. Cytotoxicity – Cell Viability and Integrity



MTT ((3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) colorimetric assay

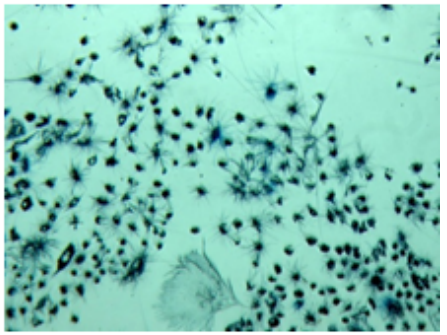
Cells were seeded (density of 10,000 cells/cm^2) in 96 well plate allowed to adhere for 24 hours

Media was replaced and cells were exposed to slurries/nanoparticles for different time points (6,12,24,48,72 hours)

Cells were washed and phenol-red free media was added to the cells and absorbance was obtained at 570 nm, used as baseline.

MTT assay: 10 µl of the MTT solution and incubated for 4 hours for formazan crystal formation. 100 µl of solubilizing solution (SDS) to dissolve formazan crystals

Absorbance at 570 nm after 4-16 hours. Cell viability was evaluated as percent negative control after baseline negation



Formazan crystals in cells

II. Cytotoxicity – Cell Viability and Integrity

Lactate Dehydrogenase (LDH) assay

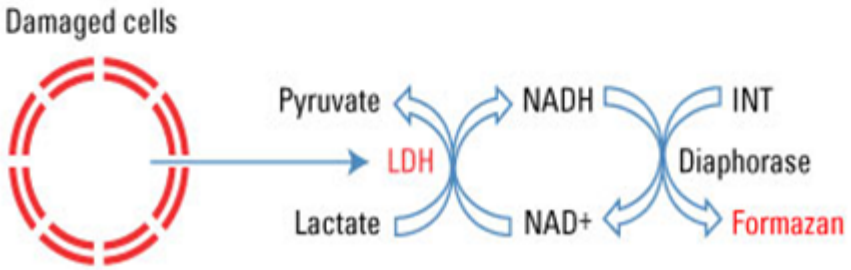
Cells were seeded (density of 10,000 cells/cm^2) in 96 well plate allowed to adhere for 24 hours

Media was replaced and cells were exposed to slurries/nanoparticles for 48 hours

Reaction mixture:0.6 ml of assay buffer in 11.4 ml of substrate mix (lysophilizate)

50 µl of the supernatant transferred to another 96 well plate and 50 µl of the reaction mixture was added, incubated for 30 minutes at RT

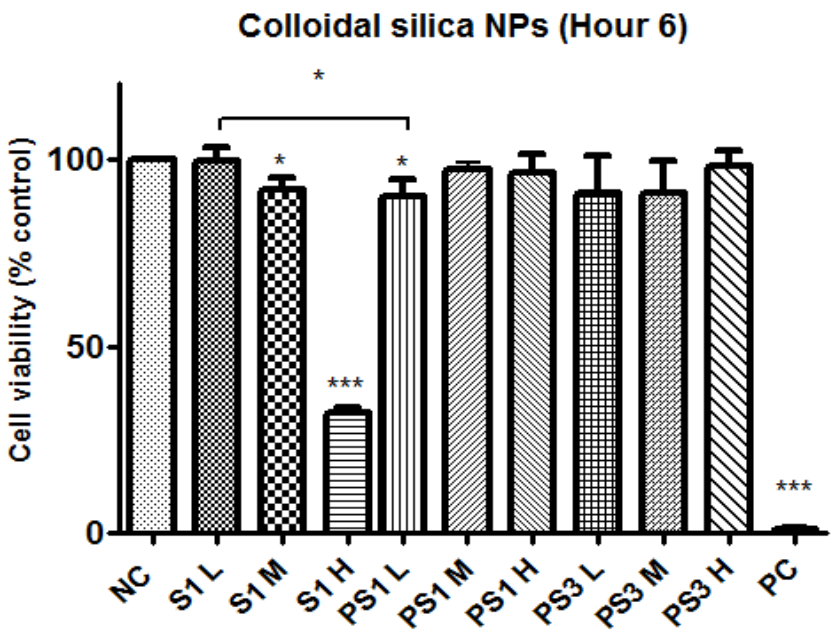
50 ul of the stop solution was added to stop the reaction and absorbance was measured at 490 and 680 nm

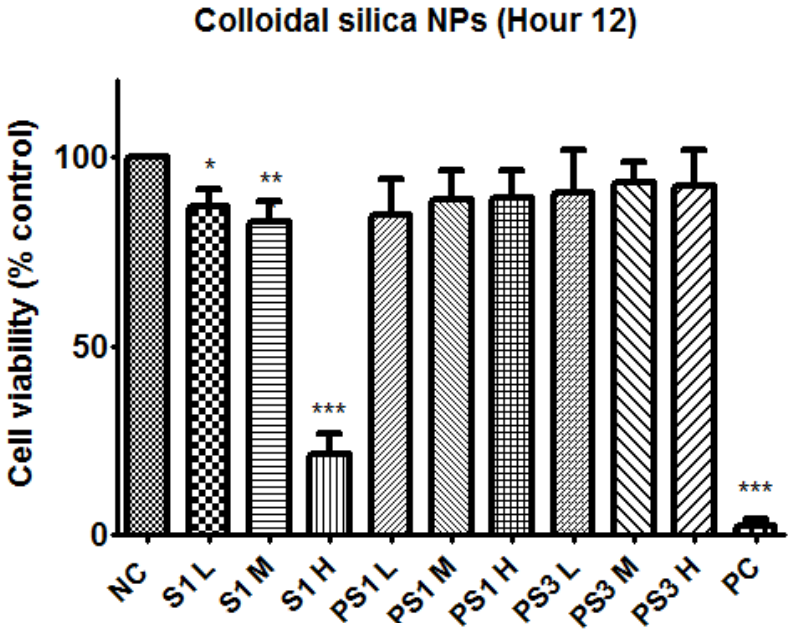


II. Cytotoxicity – Cell Viability and Integrity

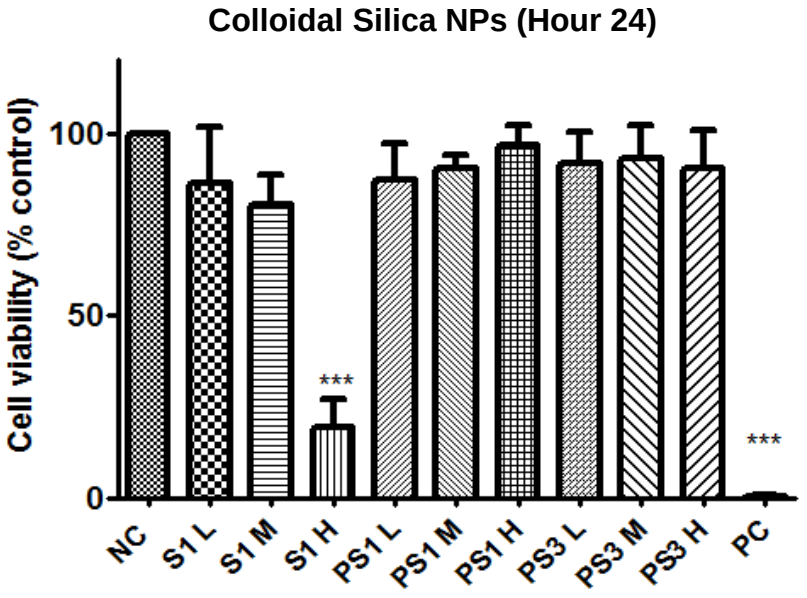
Sample		Volume of slurry (in µL)	Concentration (mg/mL)	pH
Slurry 1	High (H)	10	2.03	7.55
	Medium (M)	1	0.203	7.74
	Low (L)	0.1	0.0203	7.78
Slurry 2	High (H)	10	3.34	8.2
	Medium (M)	1	0.334	7.83
	Low (L)	0.1	0.0334	7.76
Slurry 3	High (H)	10	0.52	7.7
	Medium (M)	1	0.052	7.74
	Low (L)	0.1	0.0052	7.73
Slurry 4	High (M)	10	2.01	7.72
	Medium (M)	1	0.201	7.81
	Low (L)	0.1	0.0201	7.85

II. Cytotoxicity – Cell Viability and Integrity

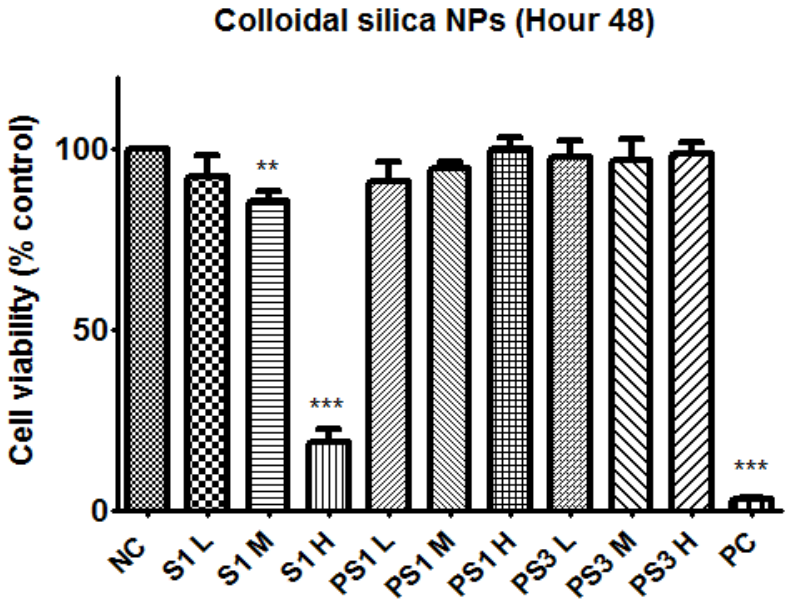


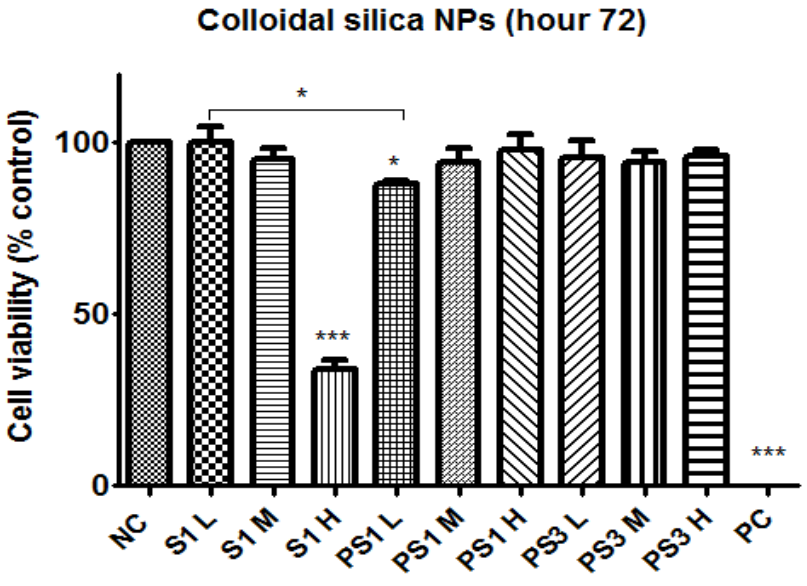


S1: Colloidal silica CMP slurry NPs
PS1: Dried colloidal silica NPs (80 nm)
PS3: Dried colloidal silica MPs (1-3 microns)
PC: Positive control (H_2O_2)
NC: Negative control (media)



II. Cytotoxicity – Cell Viability and Integrity





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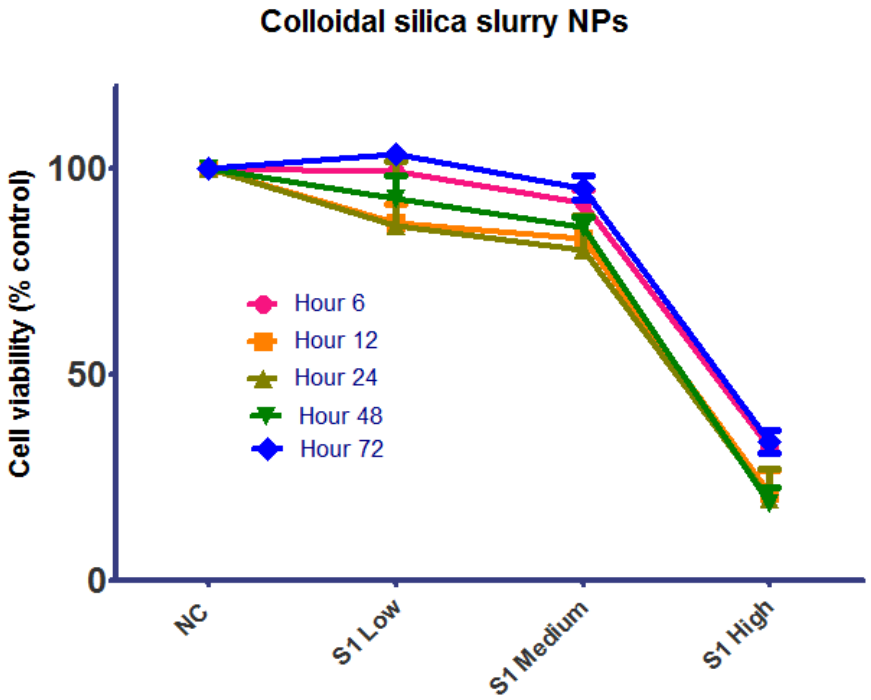
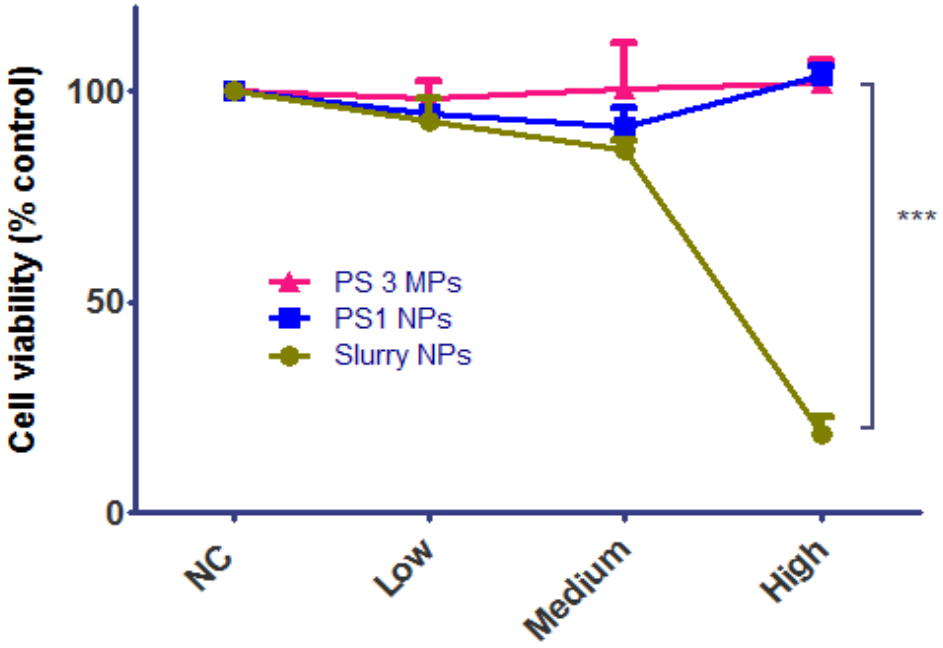
- ANOVA (Analysis of Variance) - "one-way ANOVA" using a significance level of 0.05 (95% confidence intervals); *** - 99.9% confidence interval; ** - 99% confidence and * - 95% confidence interval

II. Cytotoxicity – Cell Viability and Integrity





Exposure time	Cell viability compared to control		
	Low (0.02303 mg/ml)	Medium (0.2303 mg/ml)	High (2.303 mg/ml)
6 hours	99%	91%	32%
12 hours	86%	83%	21%
24 hours	86%	80%	19.7%
48 hours	92%	85%	18%
72 hours	100%	95%	34%

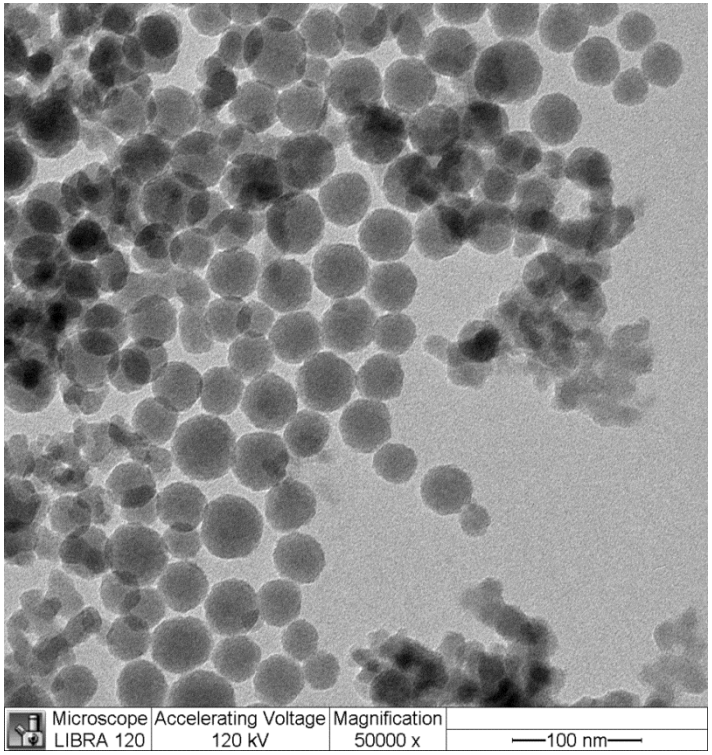
P value 0.0001

P value 0.0009

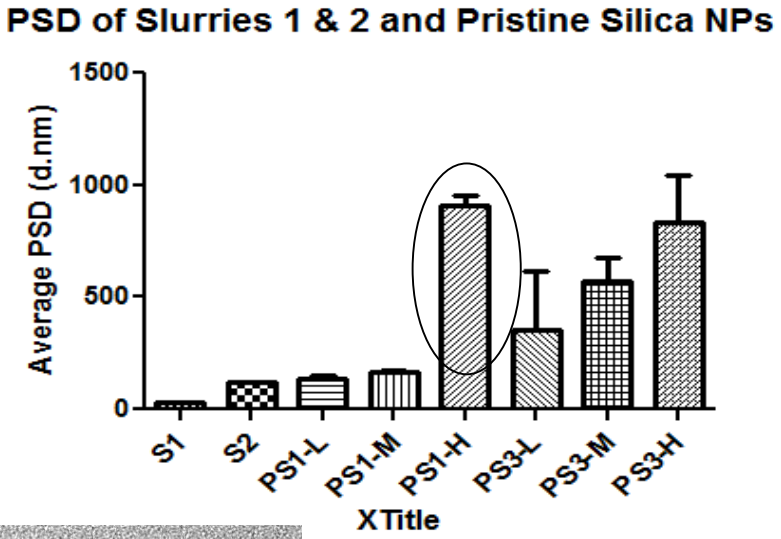
- Significant difference in cell viability was observed for cells exposed to NPs, MPs
- At higher concentration, dried NPs behaved as microparticles

II. Cytotoxicity – Cell Viability and Integrity

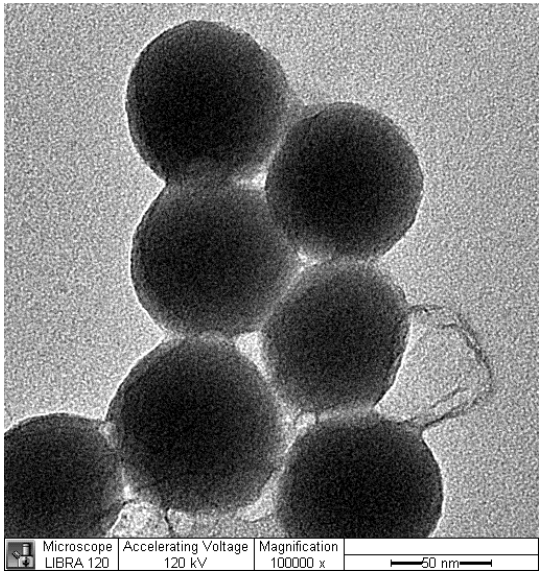
- **Aggregation of colloidal silica NPs in slurries and dried colloidal silica NPs**



TEM of Colloidal Silica NPs in Slurry 1

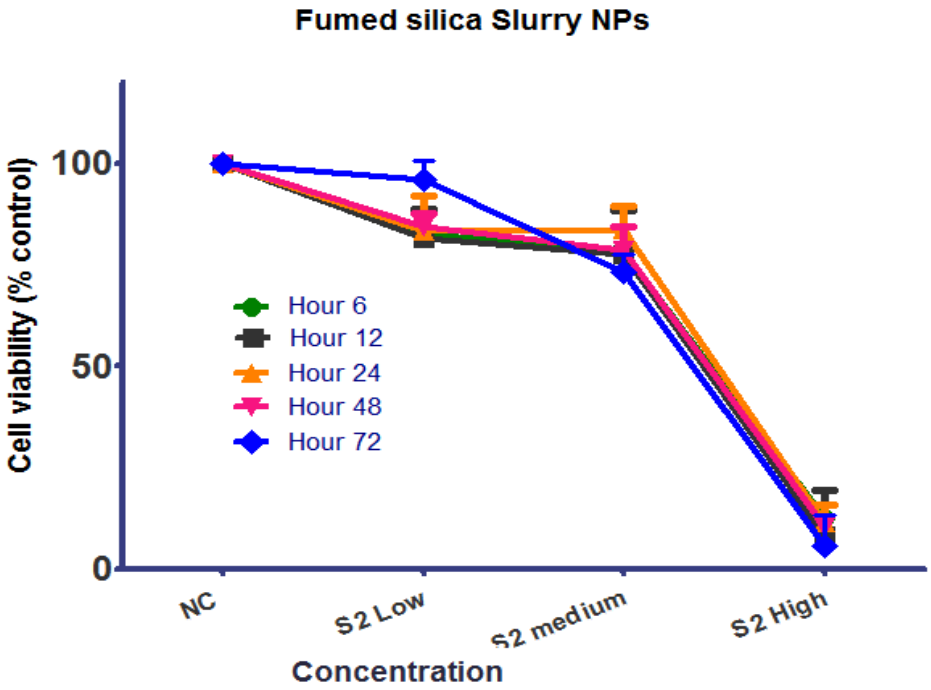


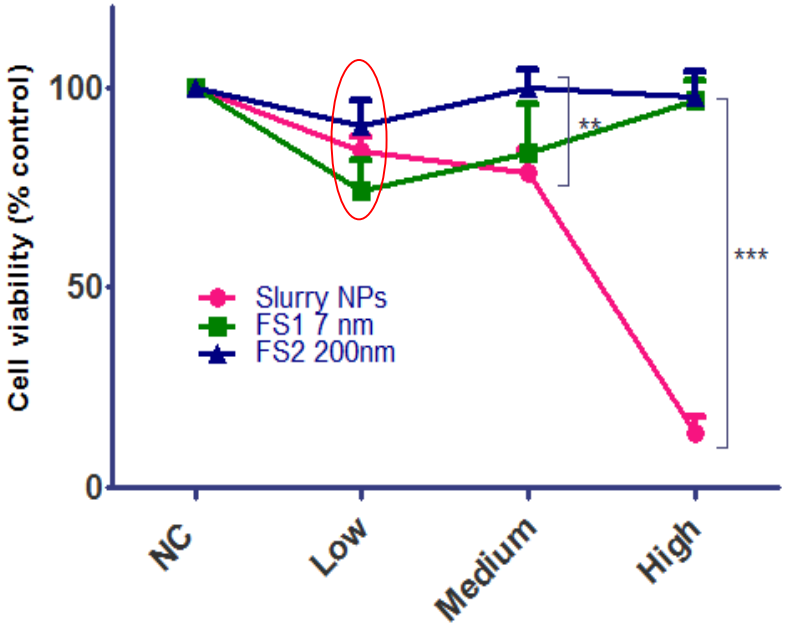
PS1 – dried colloidal silica (80 nm)
PS3 – dried colloidal silica (200 nm)



TEM of dried colloidal Silica NPs of same size as silica in slurry 1

II. Cytotoxicity – Cell Viability and Integrity

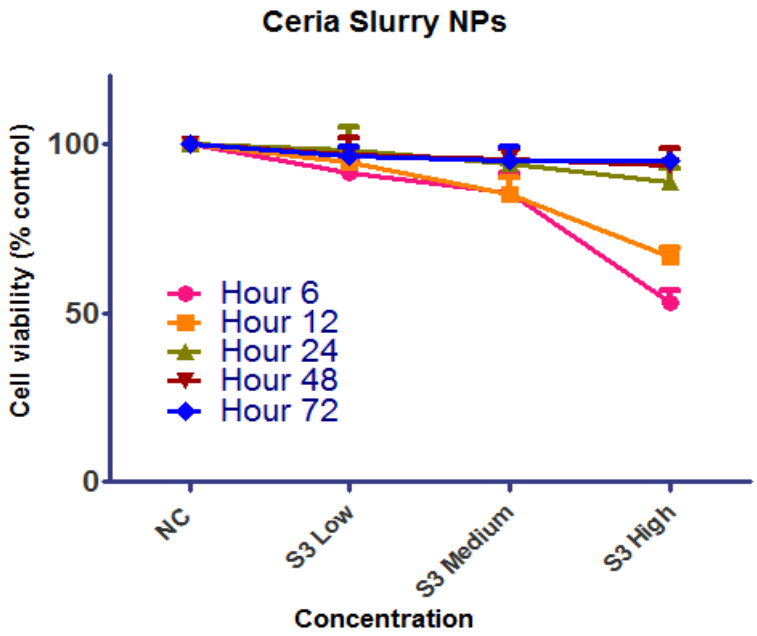


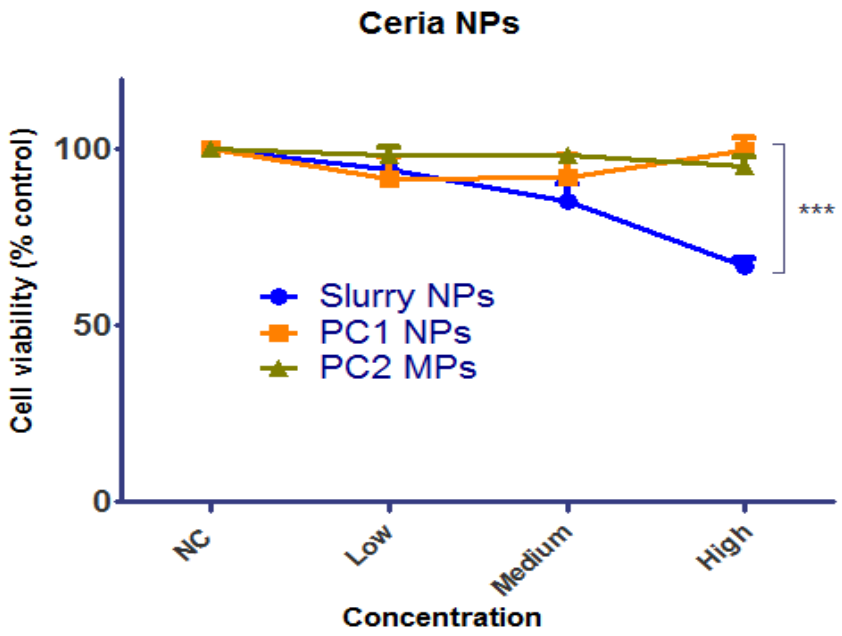


Exposure time	Cell Viability compared to control				
	Fumed Silica Slurry NPs			FS1 (7 nm)	FS 2(200-300nm)
	Low (0.0334 mg/ml)	Medium (0.334 mg/ml)	High (3.34 mg/ml)	Low (0.0334 mg/ml)	Low (0.0334 mg/ml)
6 hours	83	78%	12.5%	80%	NS
12 hours	81.6%	P value 77.4% 0.0001	8%	72.5%	72%
24 hours	83%	83.7%	11.4%	64%	77.7%
48 hours	84%	78%	10%	73%	NS
72 hours	95%	73%	12.5%	77%	NS

S2: Fumed silica CMP slurry NPs
FS1: Dried fumed silica NPs (7 nm)
FS2: Dried fumed silica NPs (200-300 nm)
PC: Positive control
NC: Negative control

II. Cytotoxicity – Cell Viability and Integrity

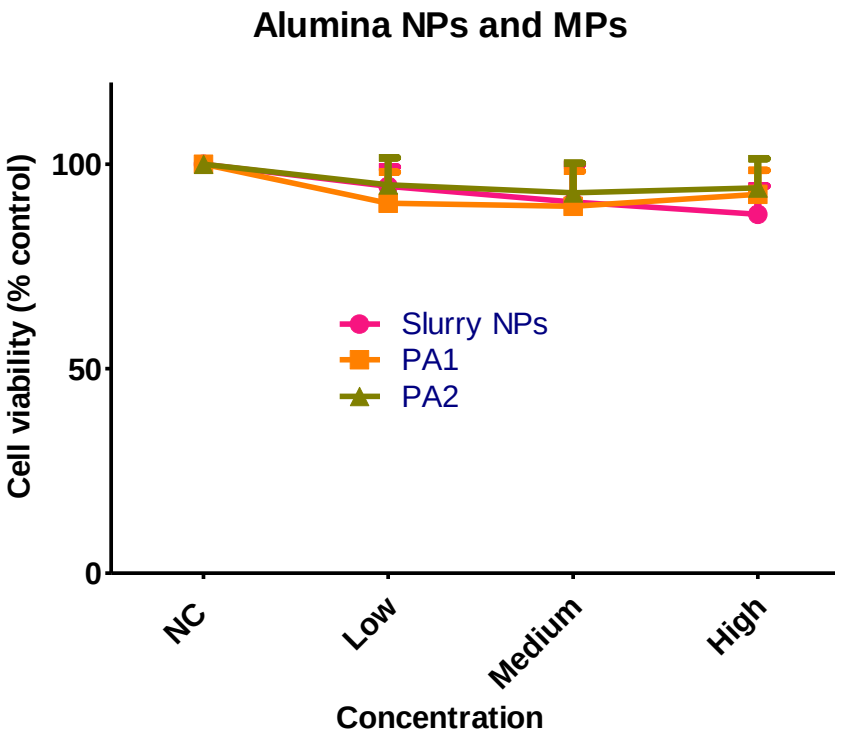


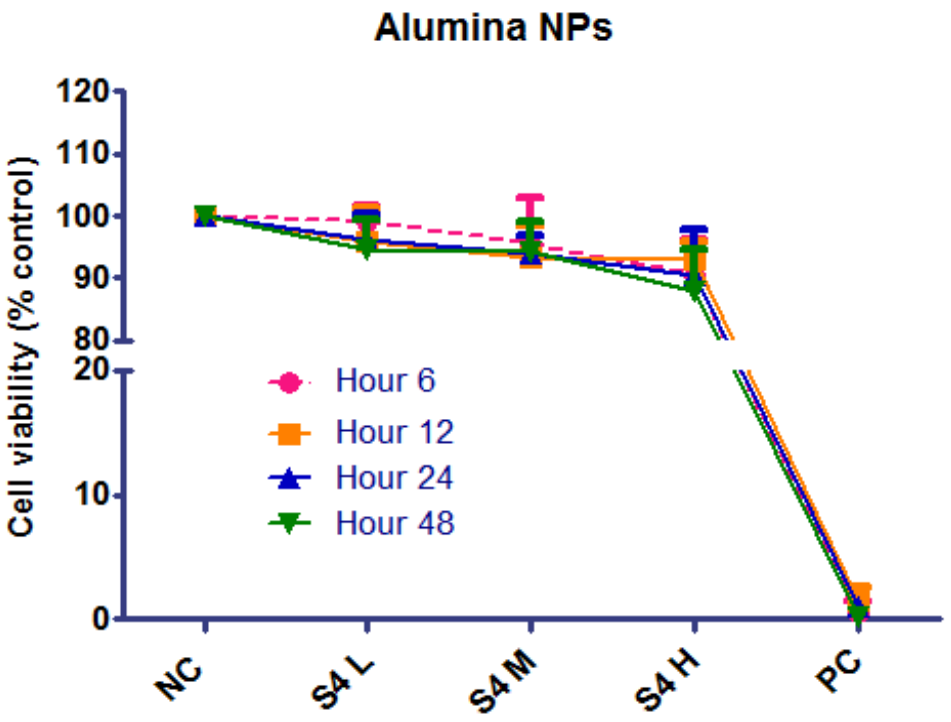


Exposure time	Cell viability compared to control exposed to Ceria NPs		
	Low (0.0052 mg/ml)	Medium (0.052 mg/ml)	High (0.52 mg/ml)
6 hours	NS	78%	53%
12 hours	NS	77.4%	66.5%
24 hours	NS	NS	88%
48 hours	NS	NS	93%
72 hours	NS	NS	NS

S3: Ceria CMP slurry NPs
PC1: Dried ceria NPs (50-105 nm)
PC2: Dried ceria MPs (1-2 μm)
PC: Positive control
NC: Negative control

II. Cytotoxicity – Cell Viability and Integrity





S4 – Alumina CMP slurry NPs
PA1 – Dried alumina NPs (50-105 nm)
PA2: Dried alumina MPs (1-2 μm)

- There was no significant change in the cell viability when exposed to alumina slurry NPs or dried NPs and MPs

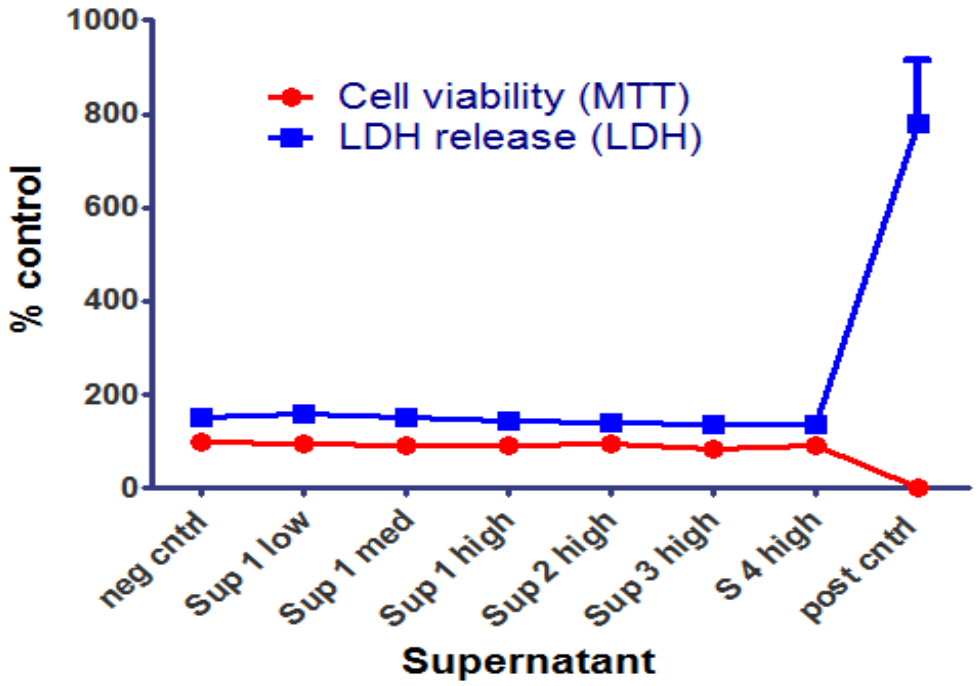
II. Cytotoxicity – Cell Viability and Integrity

- IC-50- Half maximal inhibitory concentration is a measure of effective of a substance in inhibiting a specific biological or biochemical function

Exposure Time	IC50 (mg/mL)		
	c-silica	f-silica	ceria
6 hours	1.679247	1.599972	0.557932
12 hours	1.310647	1.4896	0.898468
24 hours	1.261406	1.649783	NS
48 hours	1.315033	1.562016	NS
72 hours	1.755825	1.677886	NS

II. Cytotoxicity – Cell Viability and Integrity

- **Effect of slurry supernatants on A549 cell viability**
- **Supernatants were prepared by UTD by removing nanoparticles by centrifugation at 200,000g**
- **As stated earlier, the same MTT and LDH cell viability procedures were followed**
- **Supernatants of slurries showed no to minimal cytotoxicity, compared to control cells**



Sup1- supernatant of slurry 1
Sup2- supernatant of slurry 2
Sup3- supernatant of slurry 3
Sup4- supernatant of slurry 4

III. Cellular Uptake and Internalization

- **Do ENs penetrate into cells? If so, where do they accumulate or internalize? What about Reactive Oxygen Species (ROS)?**
- **Studied cell uptake and internalization**
  - Inductively coupled plasma optical emission spectrometry (ICP-OES)
  - Confocal Raman Microscopy
  - Ultrastructural characterization using HRTEM and Helium Ion Microscopy (HeIM)
  - Electrochemical Cell Impedance Spectroscopy (ECIS)
- **Oxidative stress defined as disturbance in the prooxidant-antioxidant balance that is in favor of Pro-oxidant leading to potential damage**
- **Hierarchical oxidative stress hypothesis (A. Nel, Science 2006)**
  - Antioxidant and detoxification enzymes
  - Pro-inflammatory responses
  - Cellular apoptosis and cytotoxicity

III. Cellular Uptake and Internalization

Intracellular ROS production analysis

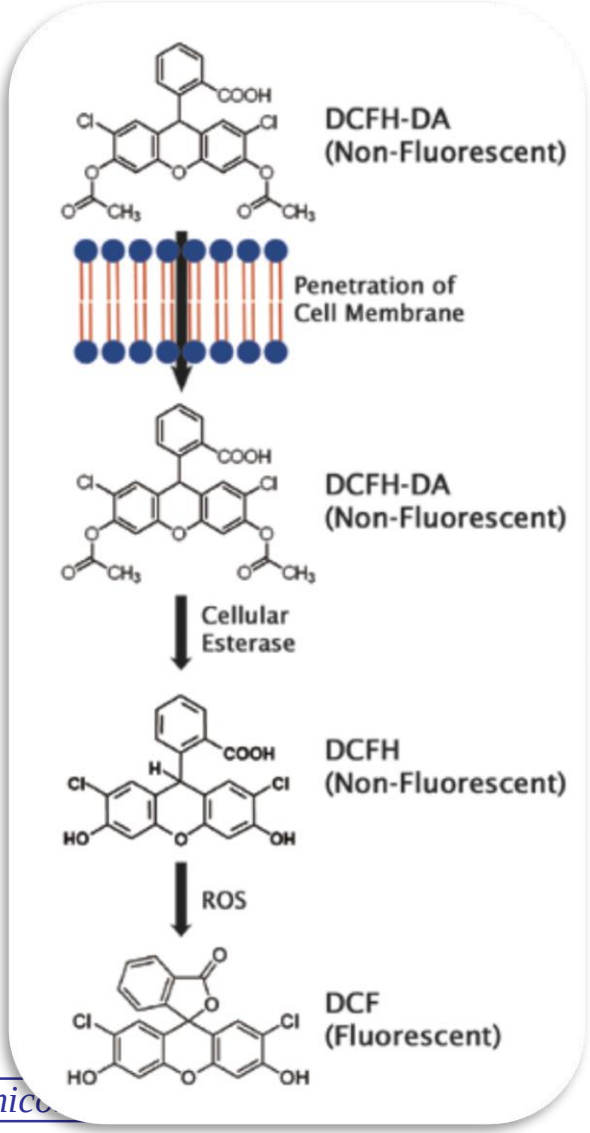
Cells were seeded in 24 well plate at a density of 10,000 cells/cm^2 and allowed to adhere for 24 hours

Media was replaced with fresh media and cells were exposed to slurry NPs at different concentration in triplicates and incubated for 24 and 48 hours

After the incubation, cells were washed and incubated in the DCFDA solution at a final concentration of 20 µM for 30 minutes

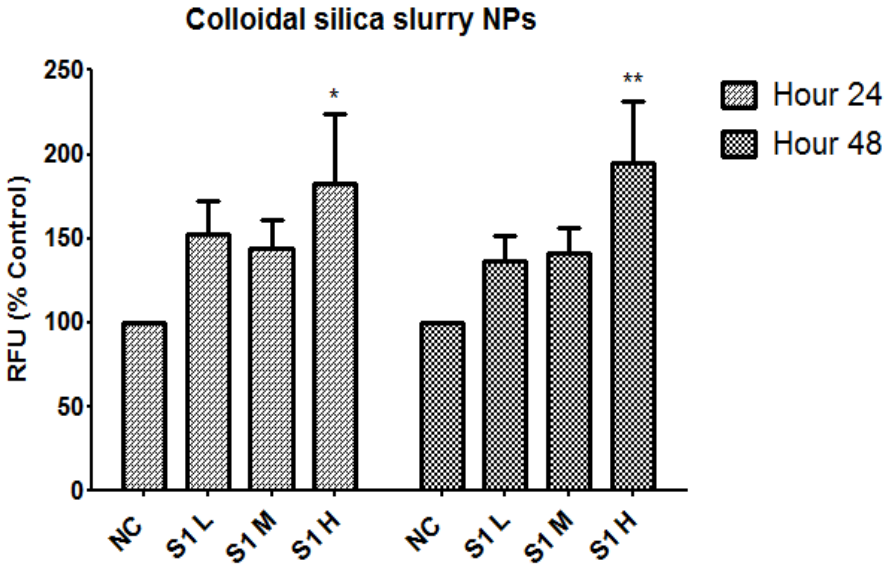
Cells were washed twice to remove the excess dye and fluorescence was measured at 480/520 nm as Ex/Em

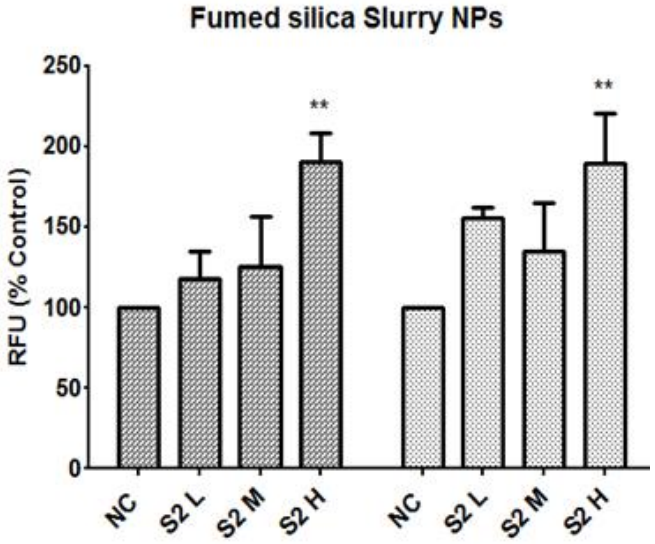
Cell count was performed immediately by Trypan Blue method, DCF-Fluorescence was normalized per 10,000 cells

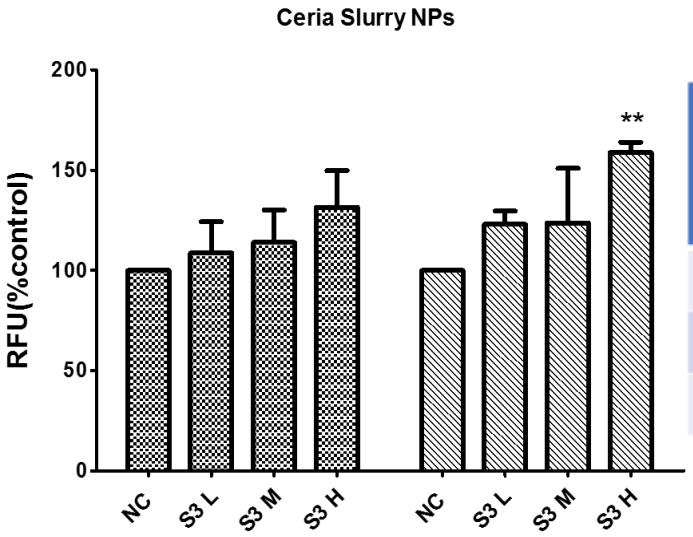


III. Cellular Uptake and Internalization

Intracellular ROS production analysis



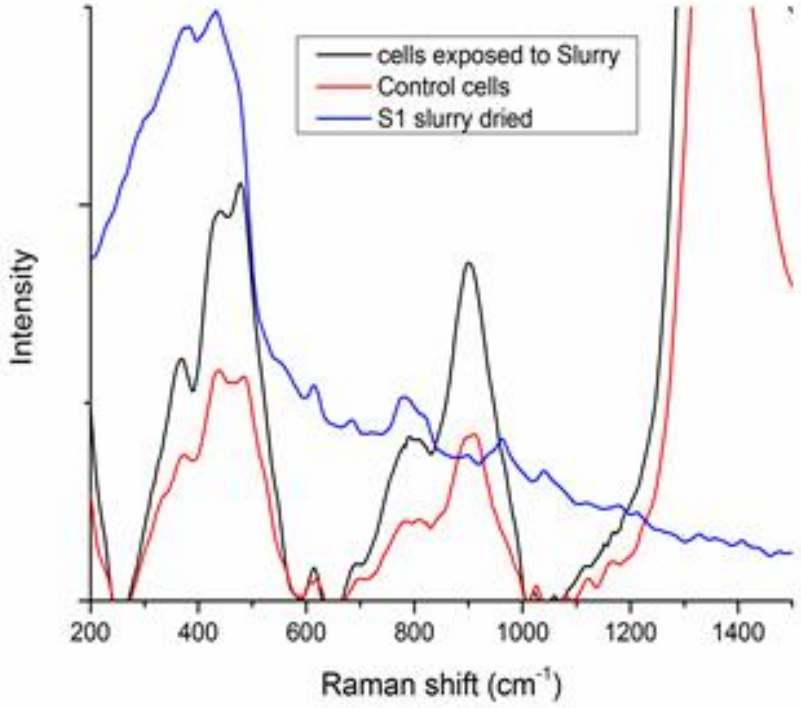


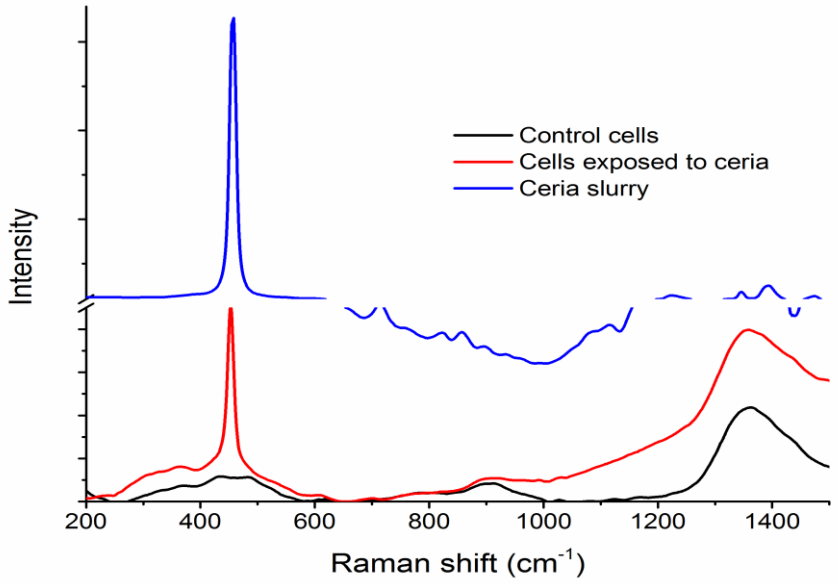


Concentration	Colloidal silica slurry NPs		Fumed silica Slurry NPs		Ceria slurry NPs	
	24 hour	48 hour	24 Hour	48 Hour	24 Hour	48 Hour
Low	52%	37%	18%	55.8%	8%	22%
Medium	43.7%	42%	25.7%	34.8%	13.9%	23%
High	82.3%	94%	90%	89.5%	31.5%	58%

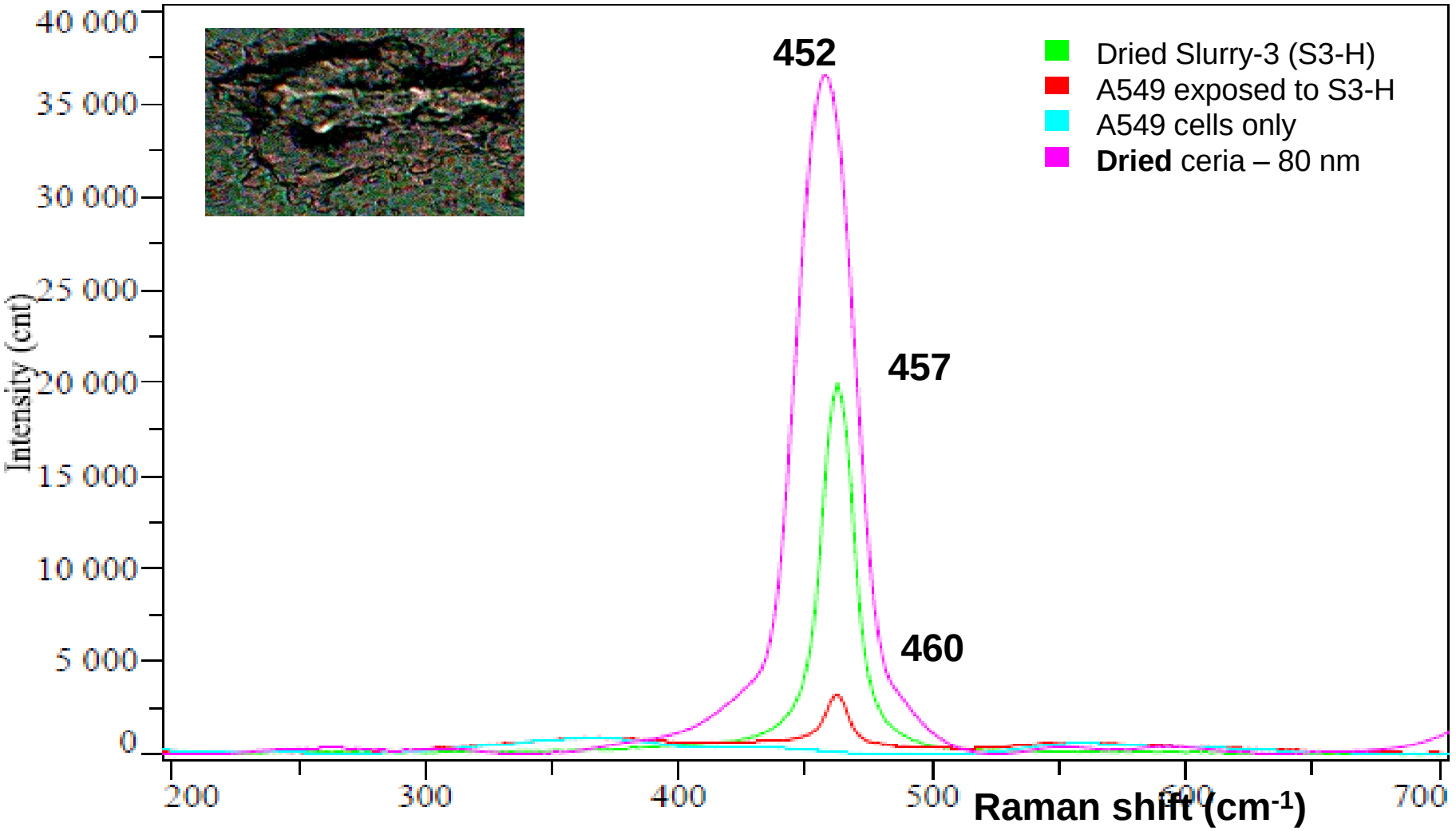
III. Cellular Uptake and Internalization

- Confocal Raman, a non-invasive, non-destructive and label-free technique, was employed to study uptake and localization of NPs
- Horiba XploRA Raman Confocal Microscope System; Spot size – 1.12 µm
- NPs show Raman active vibration modes
- Before analysis, cells were thoroughly washed to remove surface bound NPs



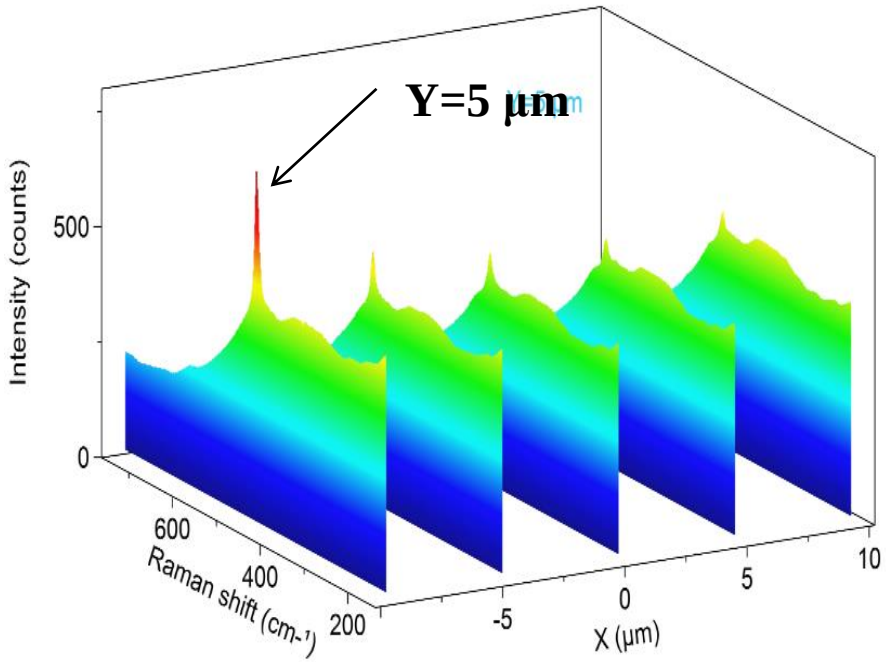


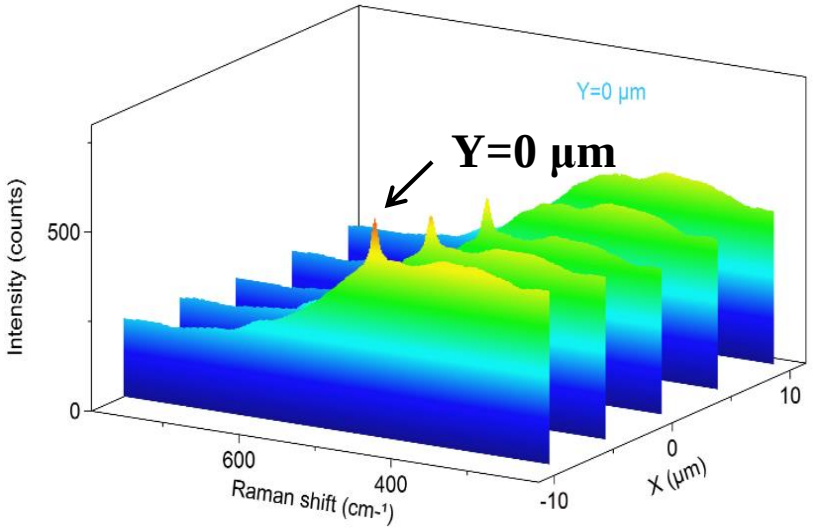
III. Cellular Uptake and Internalization

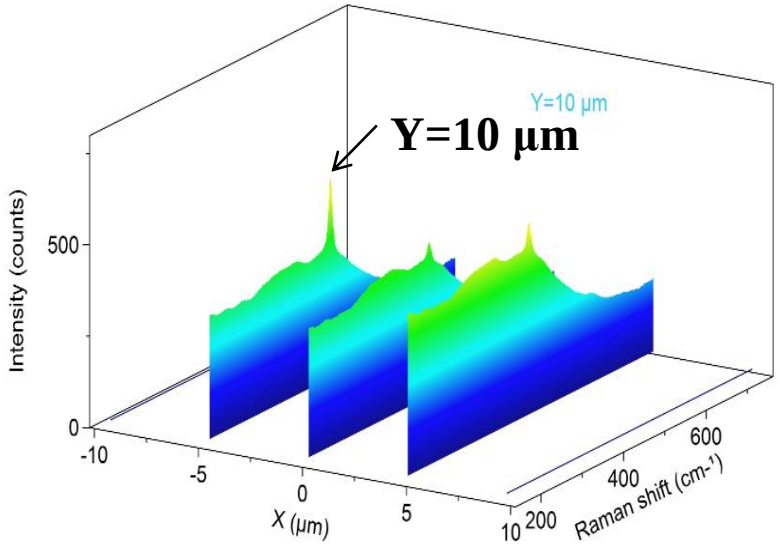


- **Clear evidence of Ceria NP localization within A549 cells**

III. Cellular Uptake and Internalization

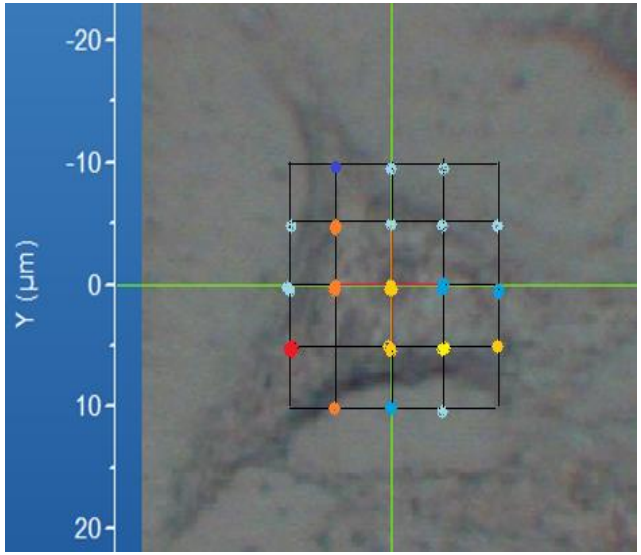




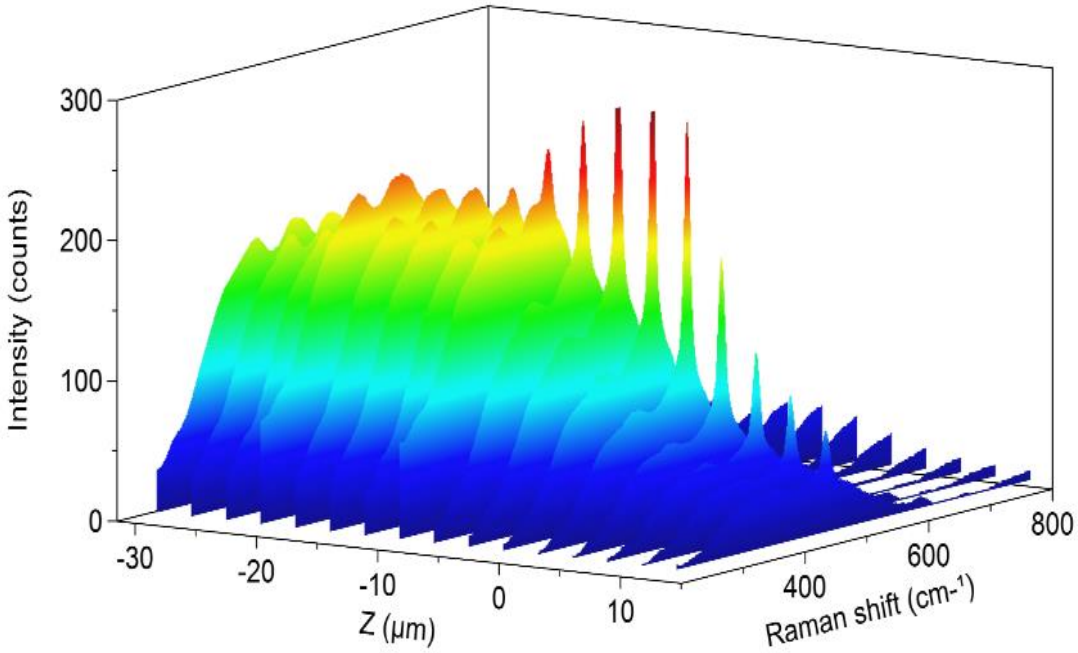


Raman Spectral stacking on cells exposed to ceria Slurry NPs

III. Cellular Uptake and Internalization



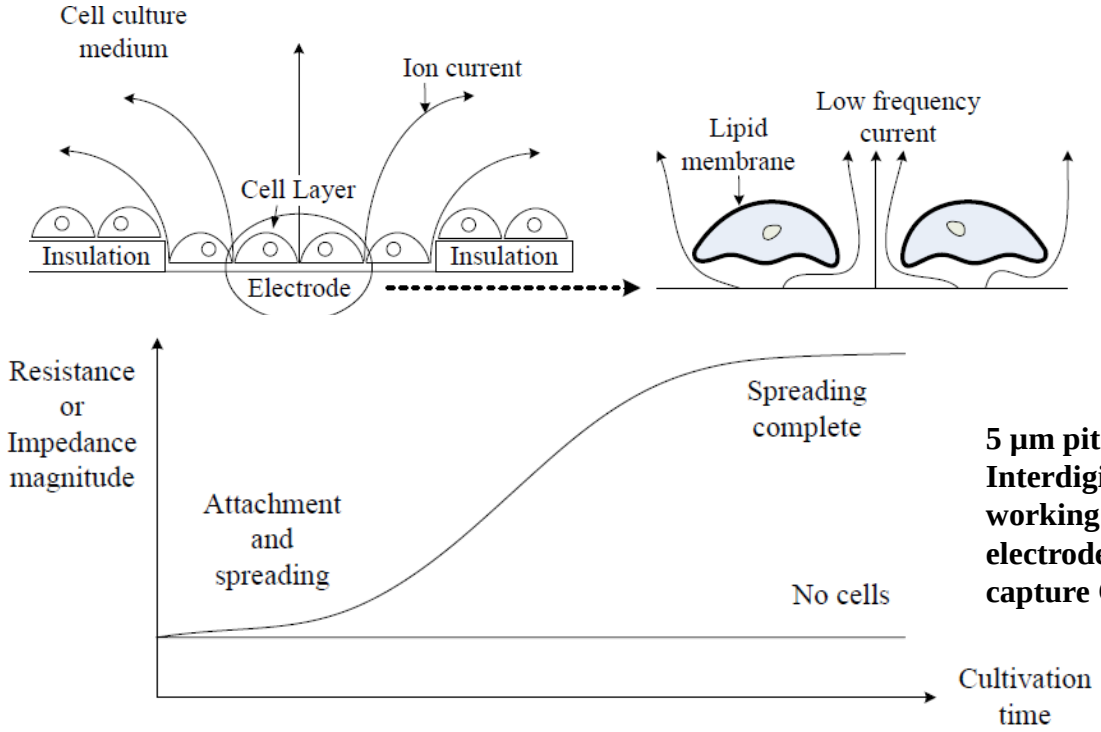
XY Map of cell selected, overlay with the intensities at different spots



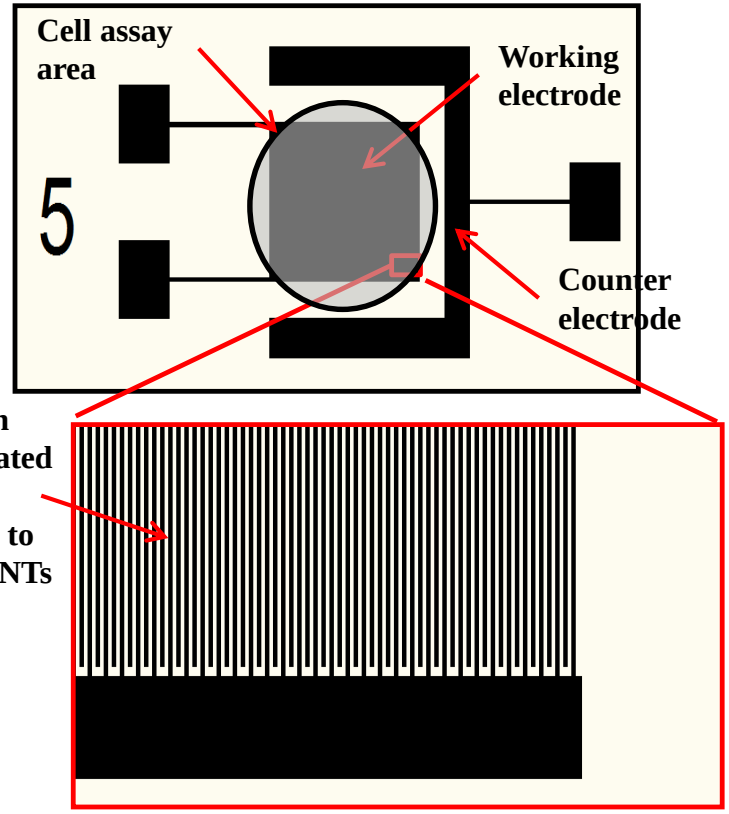
Z plane scanning of cells exposed to ceria slurry NPs

III. Cellular Uptake and Internalization

- **Development and optimization of a high-content screening/monitor method – Electrochemical Cell Impedance Spectroscopy (ECIS)**



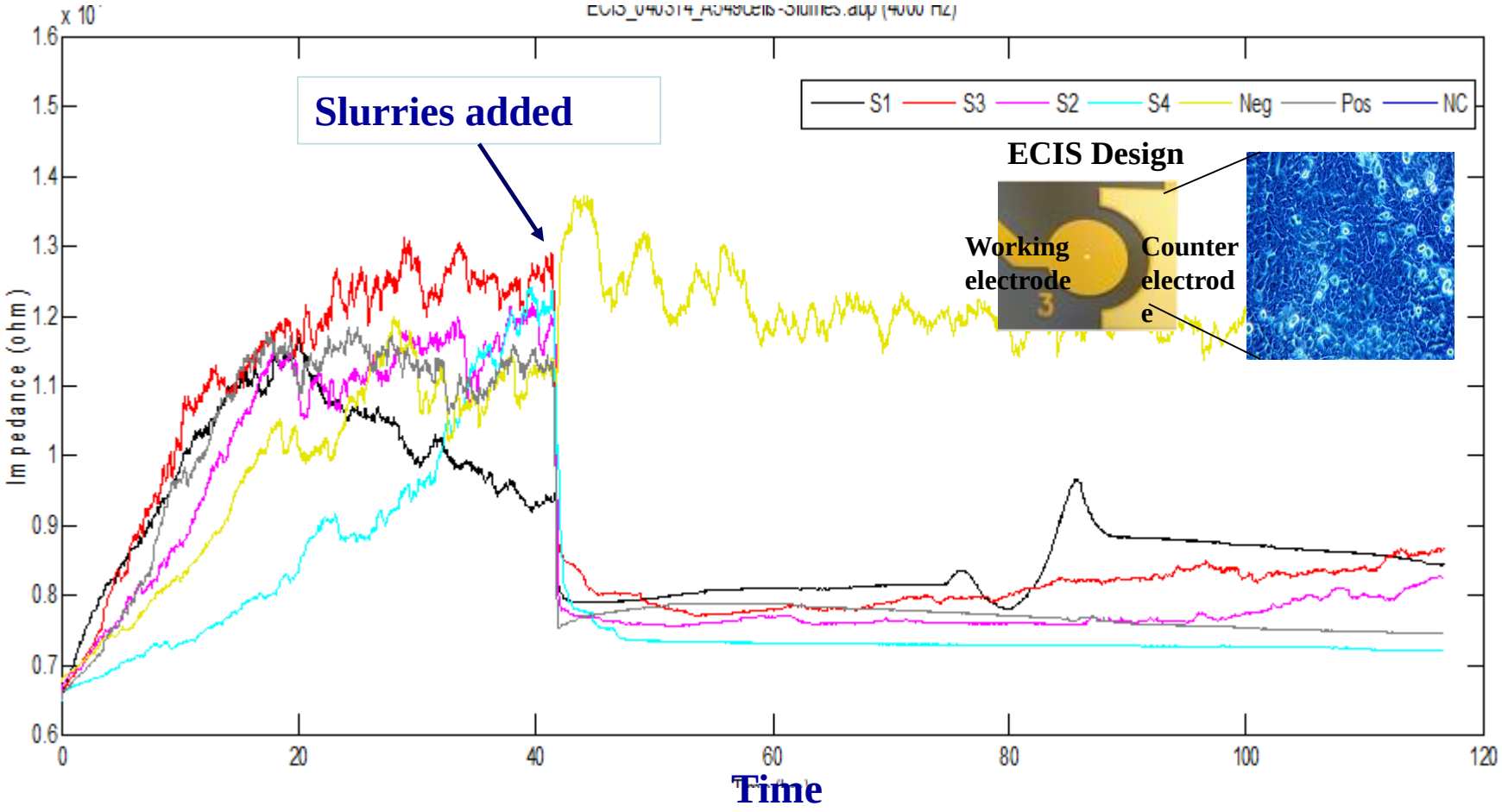
Schematic of microelectrode-based cell chip, below: impedance recorded at the frequency of 4 kHz during the cell growth on the electrode (Giaever and Keese 1993)



ECIS Design I to monitor cell impedance

III. Cellular Uptake and Internalization

- Electrochemical Cell Impedance Spectroscopy (ECIS) of A549 cells
- Cells density: 10, 000 cells/cm^2; single circular 250 µm electrode with area of 0.8 cm^2
- Concentrations : Slurry 1- 2.03 mg/mL, Slurry 2 - 3.34 mg/mL, Slurry 3 - 0.52 mg/mL and Slurry 4 - 2.01 mg/mL



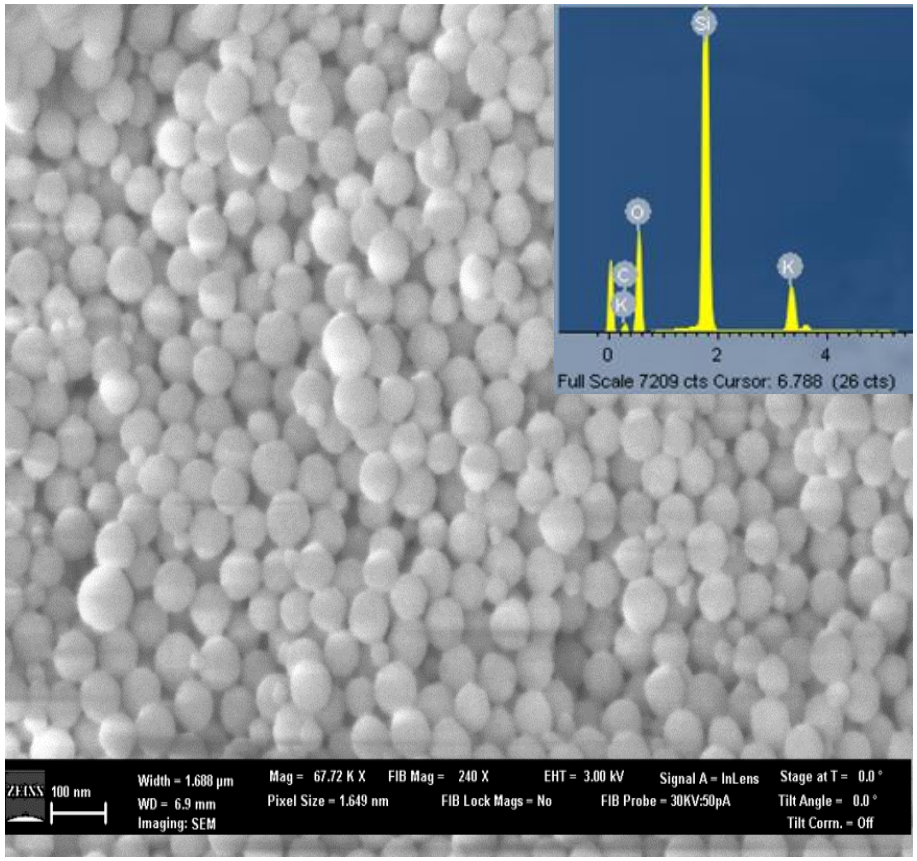
“Real” CMP NP Slurries

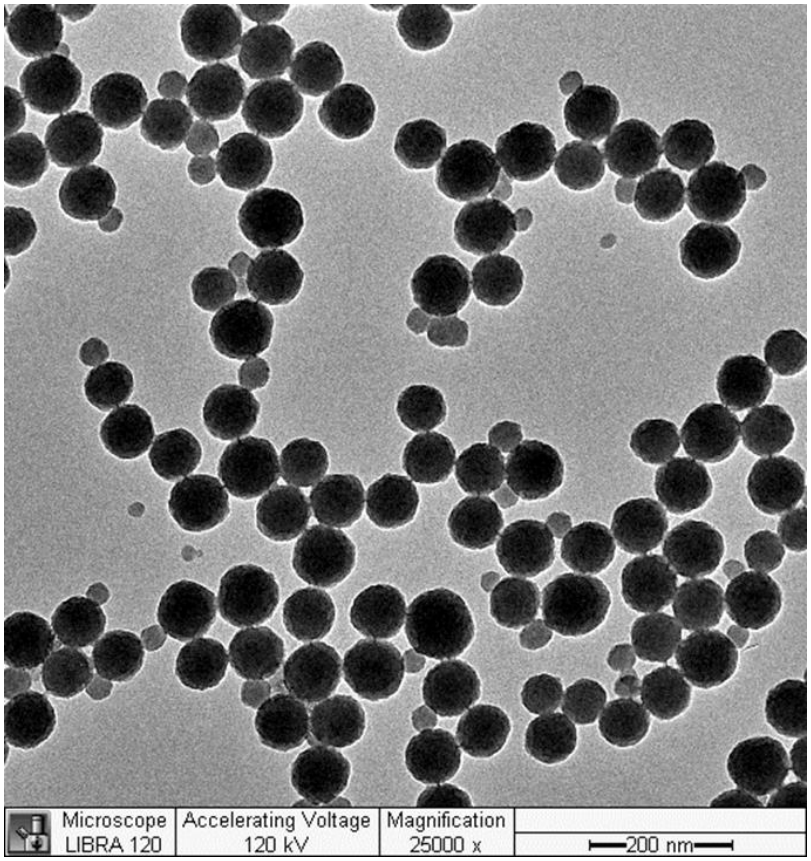
Experimental Methods and Approach

#	Name	Applications	pH	Size (nm)	Solid %	DLS (nm)	Measured pH	Zeta
C1	Ultrasol 200S; Colloidal Silica	Si, GaAs, InP, Ge other IR materials	9.5	30	24	23.96	9.06	
C2	Dow Klebosol 1501-50; Colloidal silica	ILD, STI	10.9	50	30	65.43	10.5	37.8
C3	Dow Klebosol 30 H50; Colloidal silica	W, Cu	2.0	50	30			
C4	Ultrasol 3005; Ceria	STI, ILD, BK7, Fused Silica, Glass	8.8	550	10	319.9	8.56	-89.3
C5	Ultrasol 200A; Alumina	Al, CdZn, Te, GaAs, InP, Ni, Spinel, ZnSe Chalcogenides	4.0	100	20	281	3.19	54
C6	Cabot Semi-Sperse® 12E Fumed Silica	ILD, PMD, polysilicon, STI	10.9	140	10	158.7	8.57	-63.2

- Selection criteria (a) applications, (b) pH and (c) close to model slurries

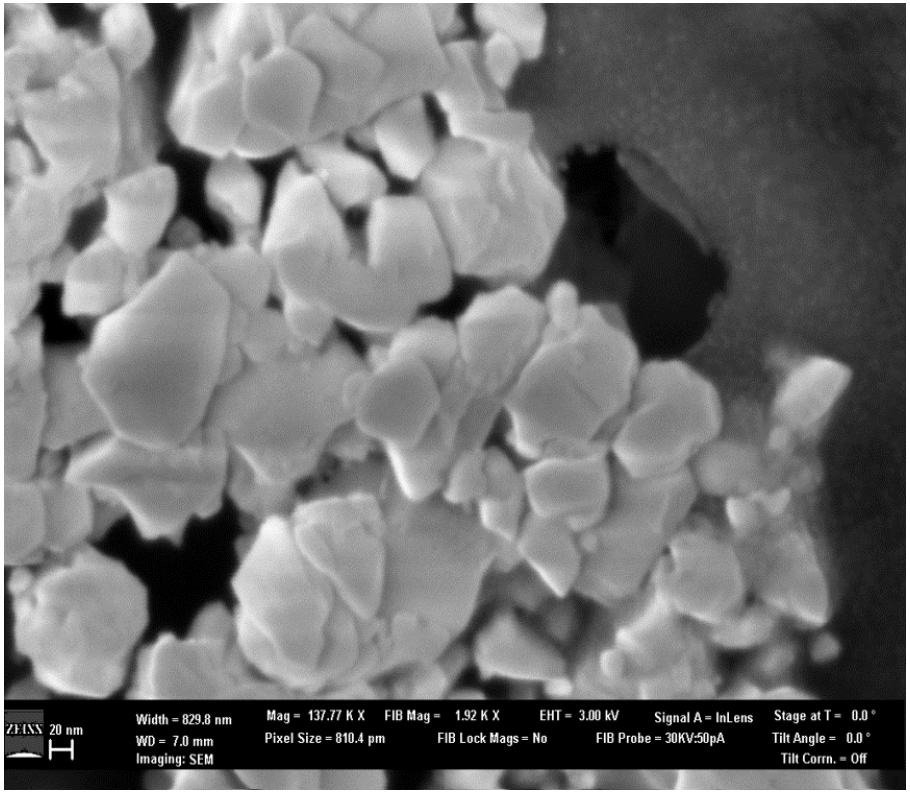
I. Characterization of Nanomaterials

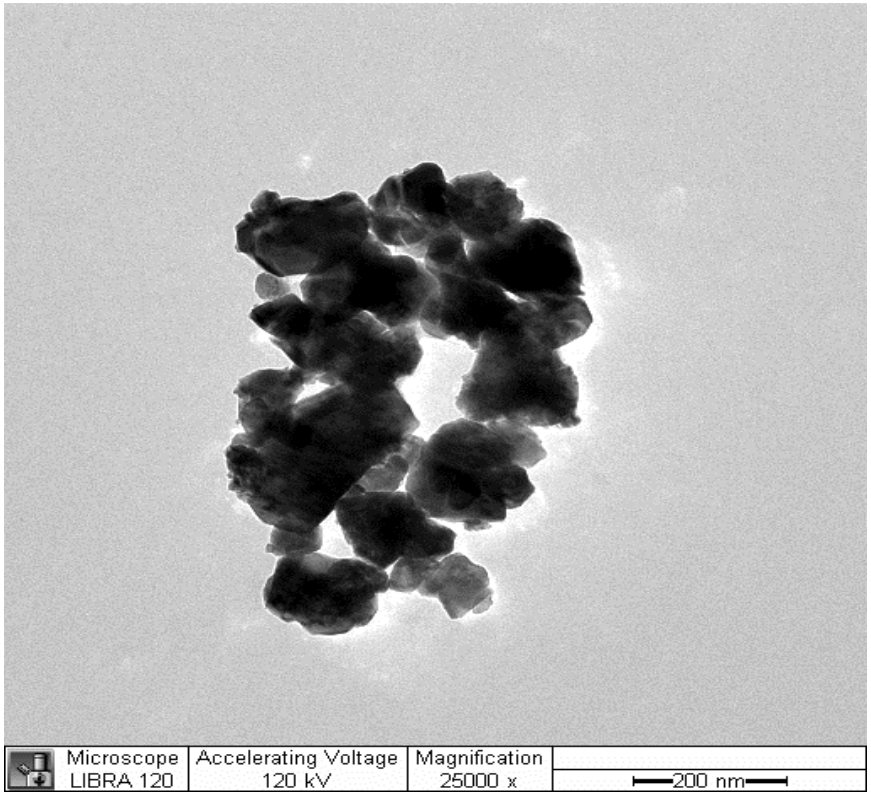




HRSEM and TEM of Slurry C2, colloidal silica, 50 nm

I. Characterization of Nanomaterials

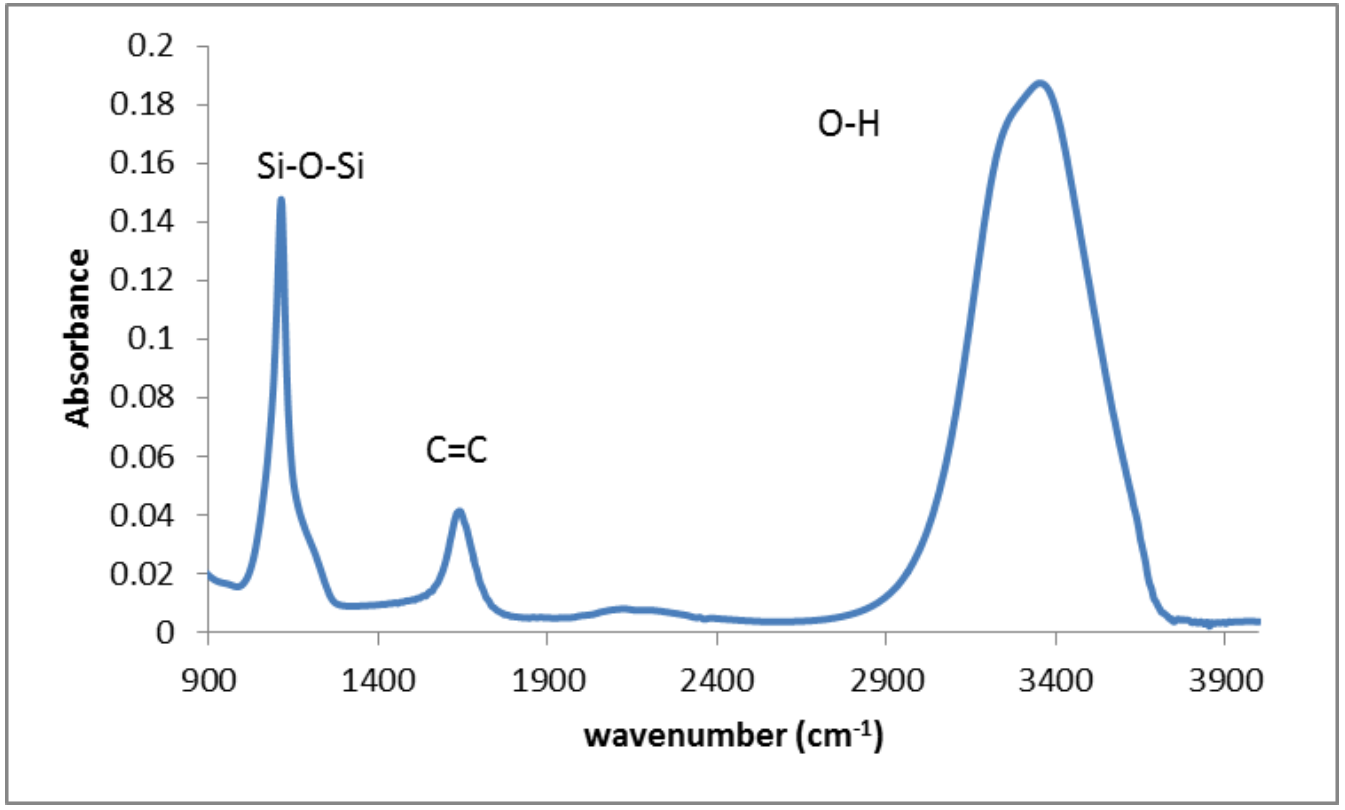




HRSEM and TEM of Slurry C4, ceria, 300-500 nm

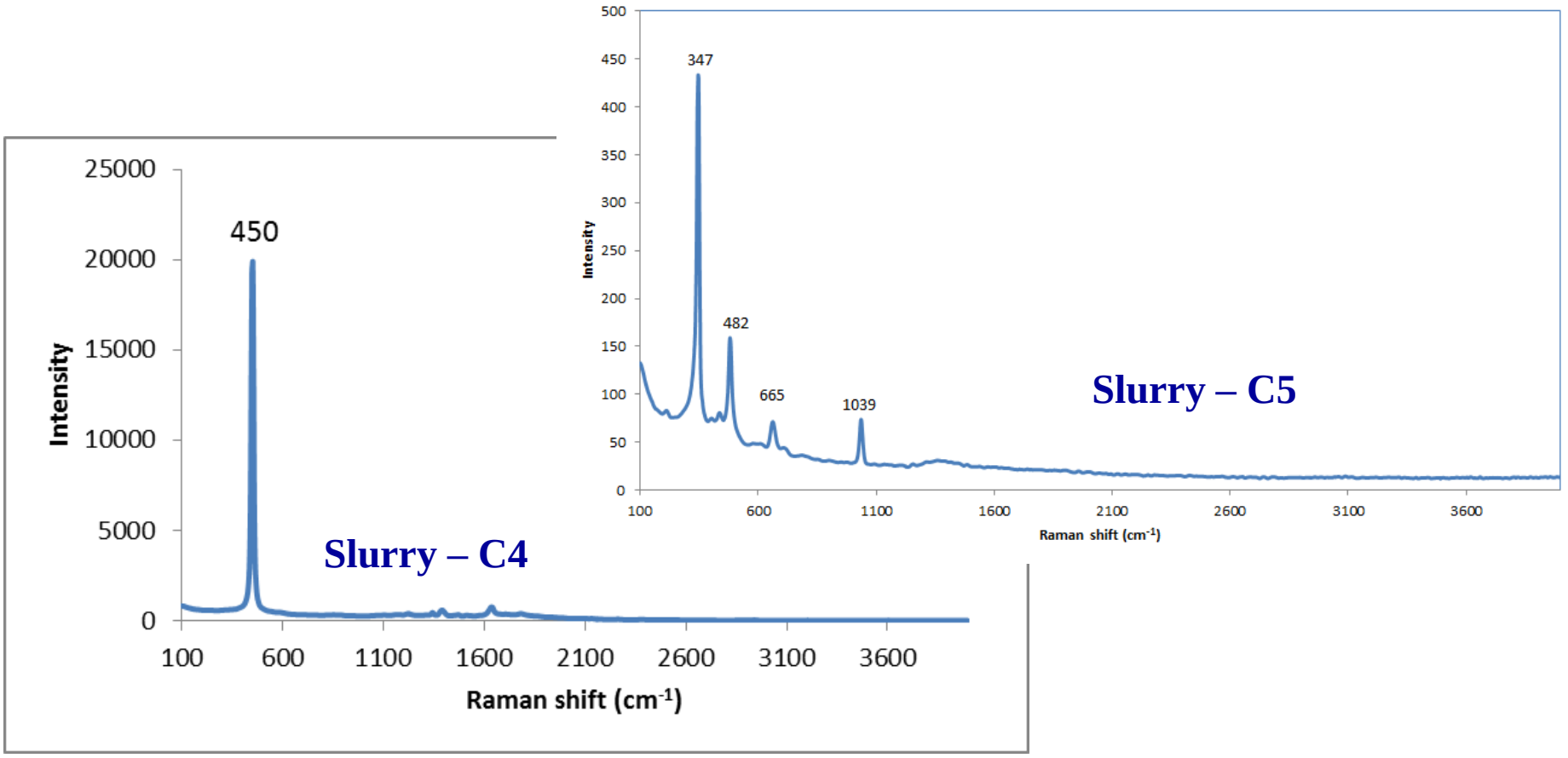
I. Characterization of Nanomaterials

- **FT-IR spectroscopy – ATR on Varian 600 FT-IR spectrophotometer**



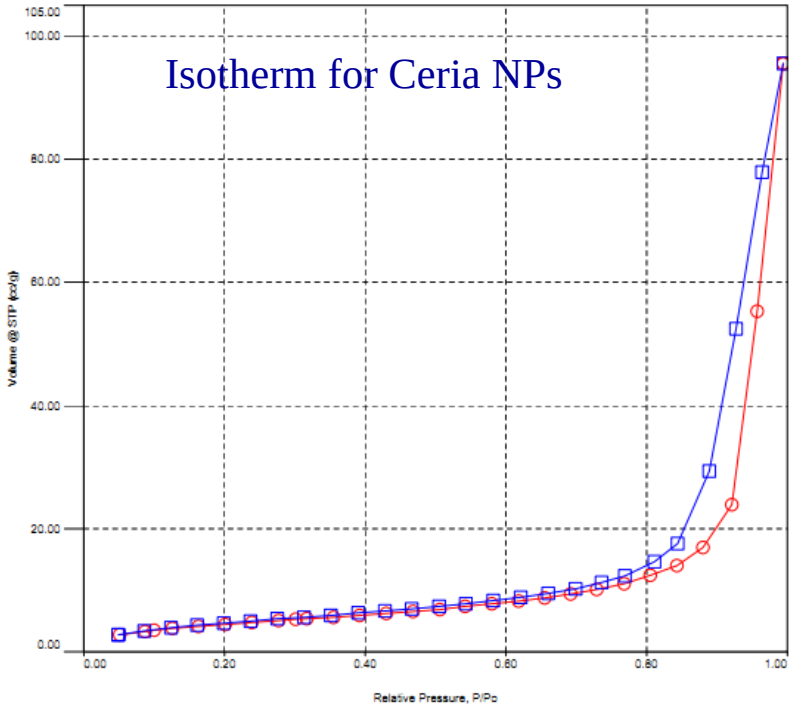
I. Characterization of Nanomaterials

- **Raman spectra of Slurry – C4 and C5**



I. Characterization of Nanomaterials

- NOVA quantachrome 2200e BET surface area analyzer
- Dried slurries were degassed for 4 hours after which nitrogen adsorption and desorption curves were obtained.
- Surface area was calculated using an extension of Langmuir Theory



Slurry	Surface Area (m^2/g)
NS-0813-1 (S1)	99.509
NS-0813-2 (S2)	50.997
NS-0813-3 (S3)	16.979
NS-0813-4 (S4)	50.37

Sample	BET surface area, m^2/g	Langmuir surface area, m^2/g
Dow Kklebsol 1501-50; colloidal silica	37.99	54.19
Dow Klebosol 30N 50; Colloidal silica	53.93	78.83

Preliminary CMP Results

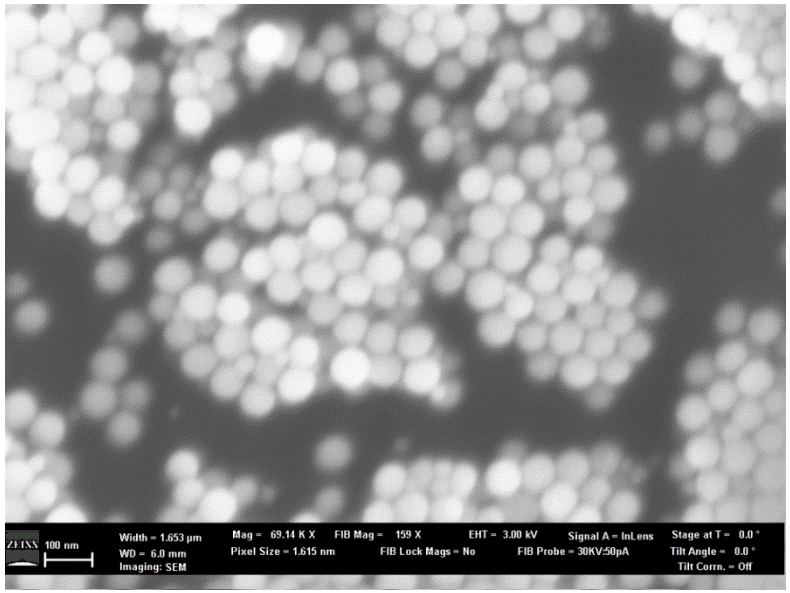
- Previously presented CMP of 6” GaAs substrates on IPEC Avanti 472 CMP
- CMP slurry used – Colloidal silica NP slurry (CS2) and ceria NP slurry (CS4)
- Conditions – Carrier/platen speed- 60/30 rpm, Down pressure – 2.0.psi; Back pressure – 4.5 psi, slurry rate – 200 ml/min, Dow® IC1000™ perforated polishing pad, pad conditioner (diamond), conditioner - 2 lbs, 30 rpm, continuous sweep, Time – 4 minutes
- Blanket 200 mm wafers of 1 µm HDP CVD oxide film
- Post-CMP characterization, toxicity and uptake post-CMP slurry/waste

IPEC Avanti 472 CMP. Inset shows polishing pad/surface

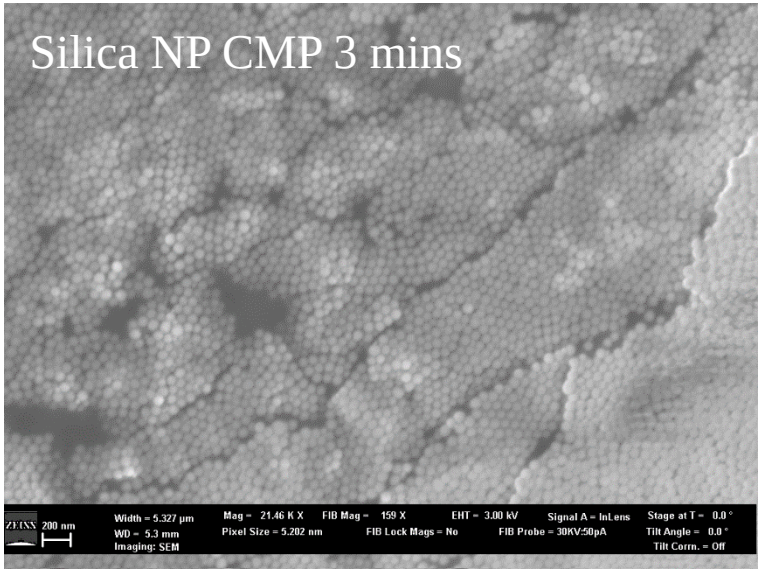
Lam DSS-200 Series II Brush Cleaner

CMP Results with Colloidal Si NPs

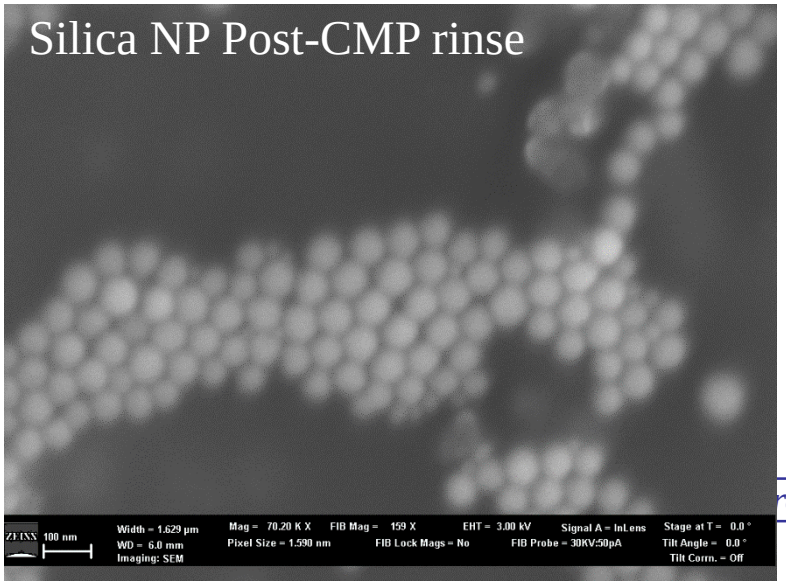
Silica NP CMP 0 mins



Silica NP CMP 3 mins



Silica NP Post-CMP rinse

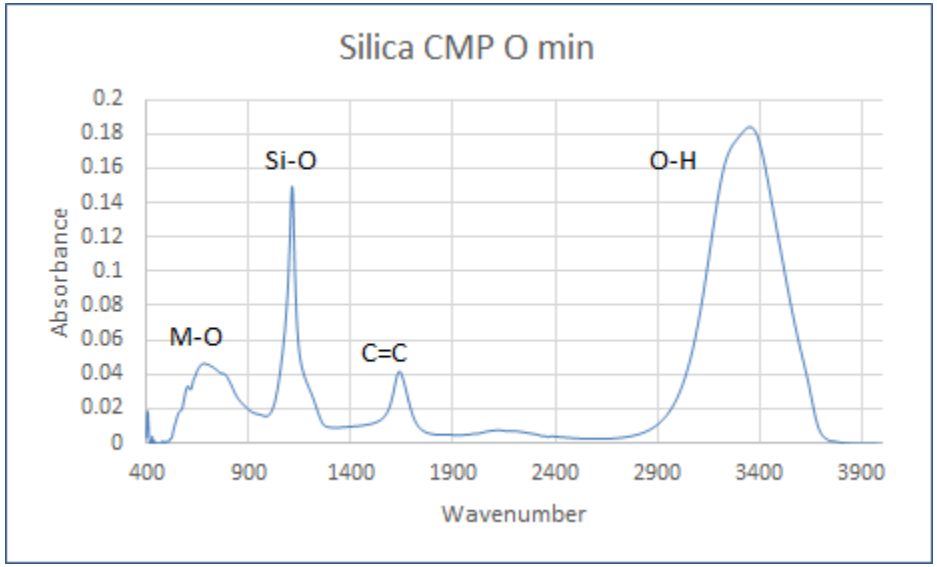


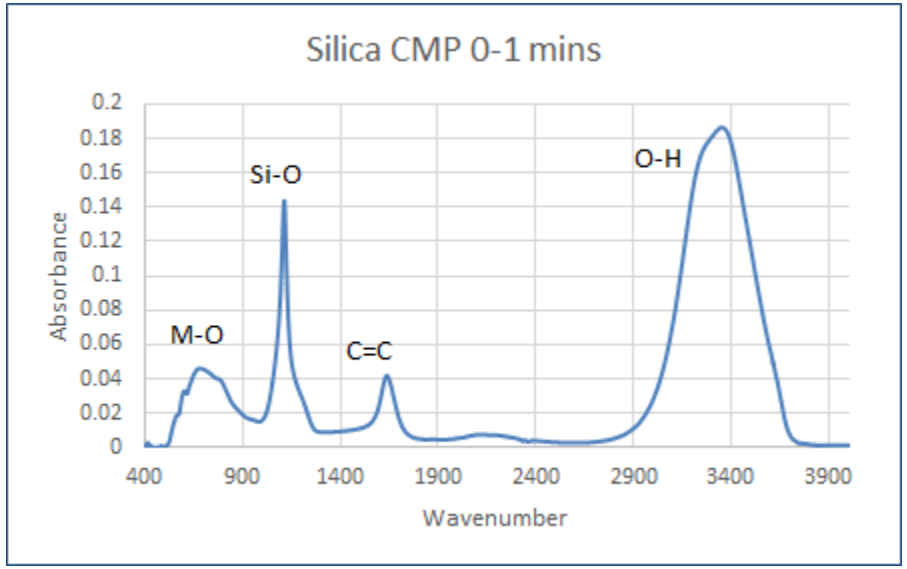
pH, PSD and zeta potential of post-CMP silica

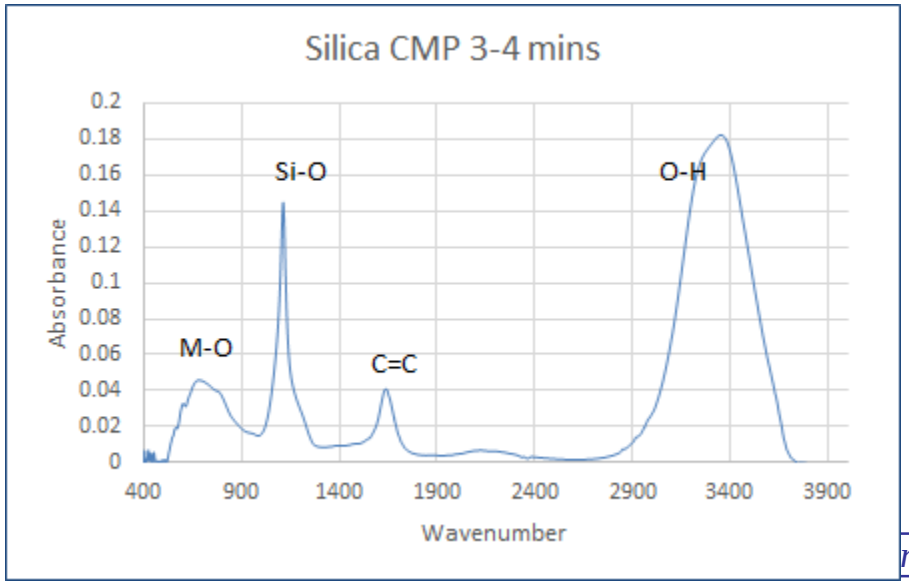
CMP time (min)	pH of post-CMP samples	PSD (d.nm)	Zeta potential
0	10.38	75.95	-36.7
1	10.42	74.11	-15.8
3	10.37	71.89	-24.3
Rinse	7.74	82.83	-0.042

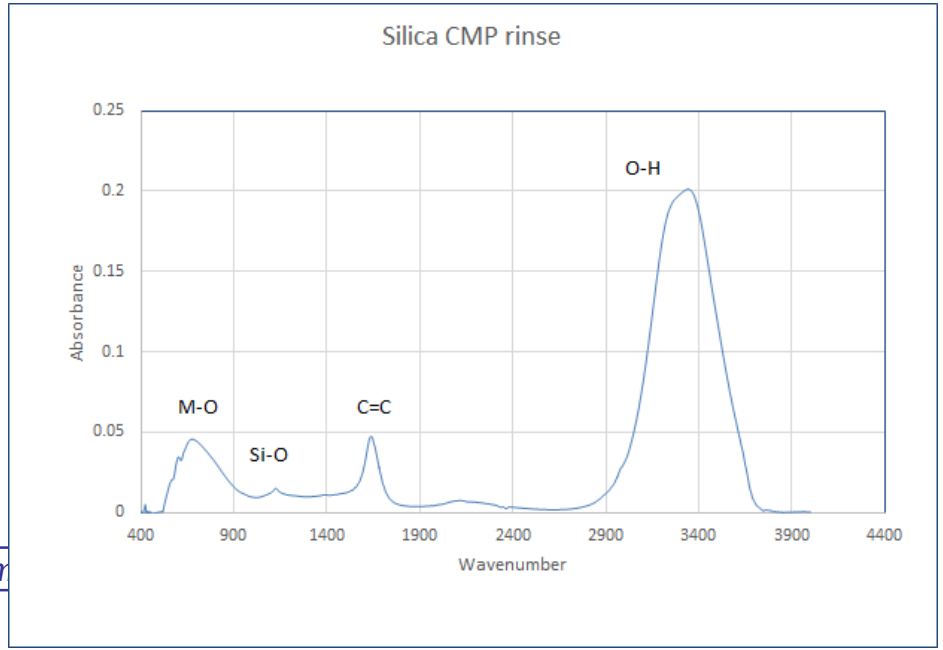
Post-CMP, silica NPs surface area did not change

Preliminary CMP Results

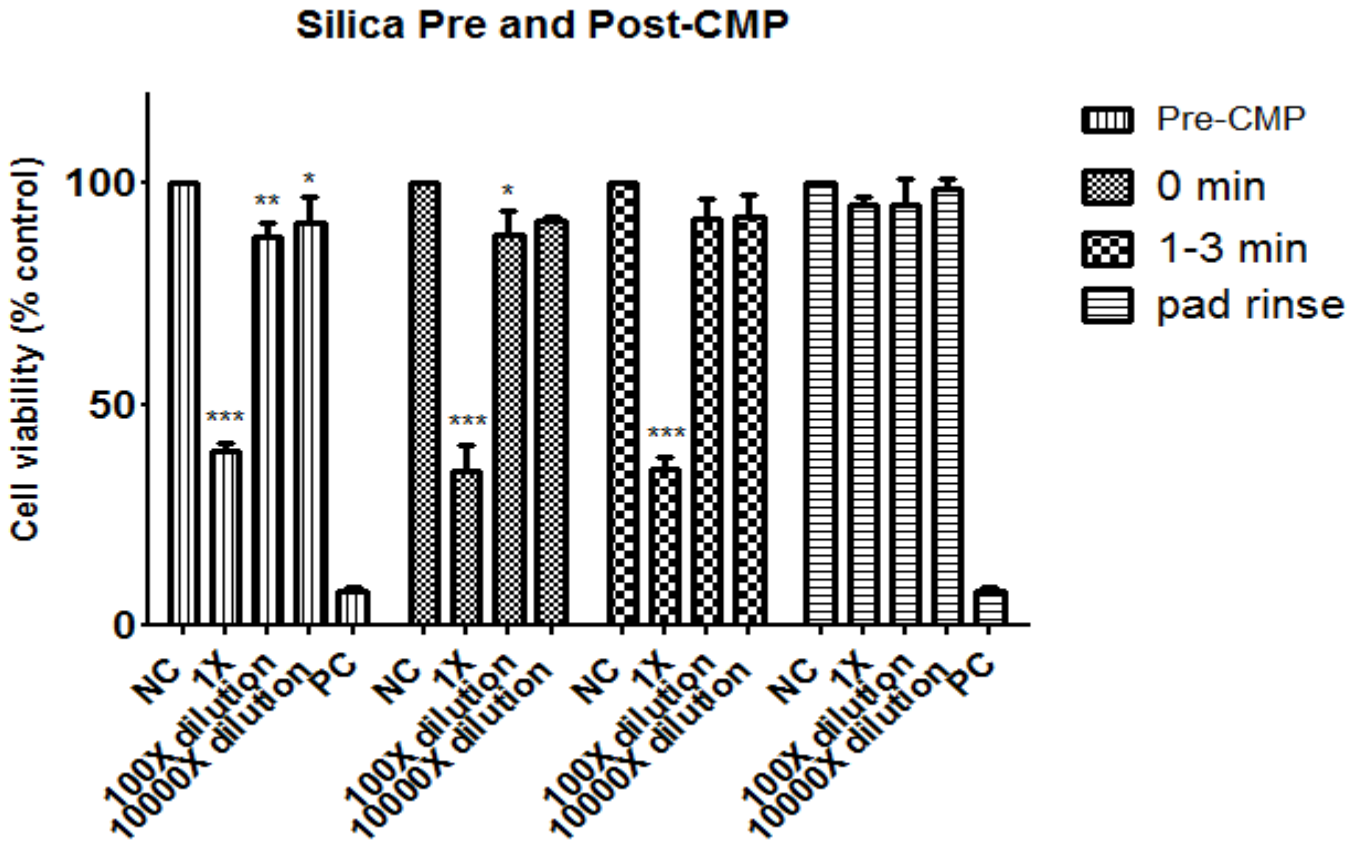




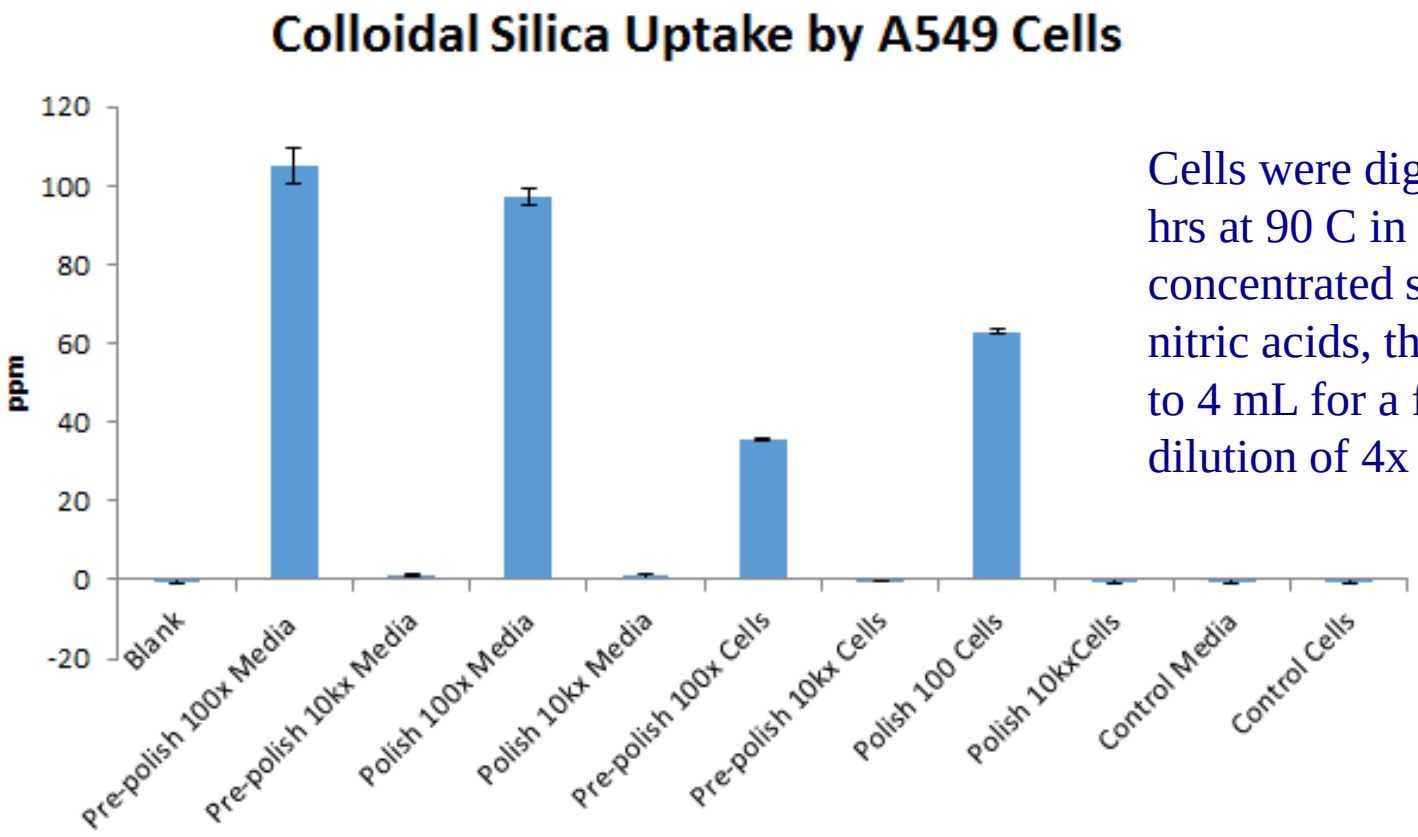




Cell viability of A549 cells exposed to post-CMP silica



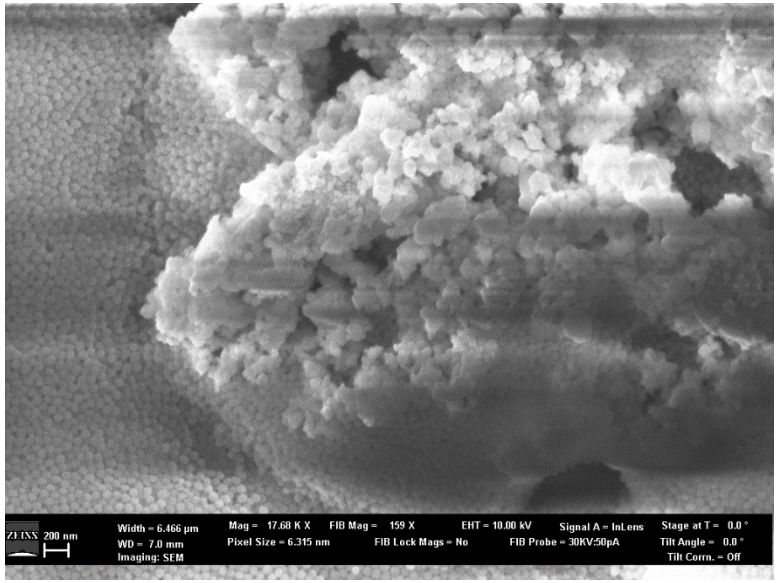
Post-CMP colloidal silica uptake by A549 cells

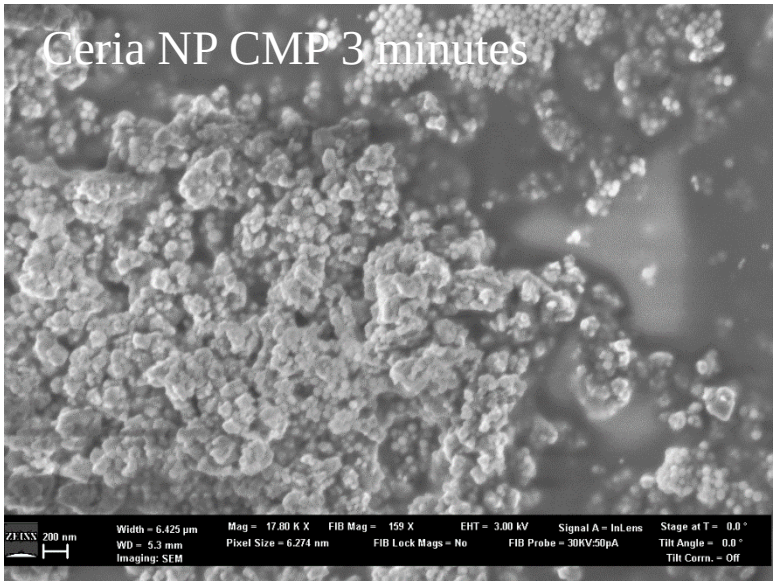


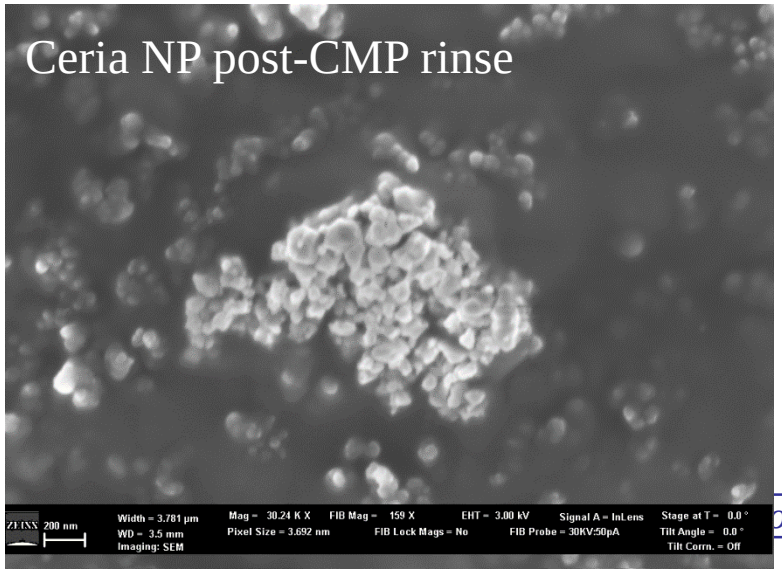
Cells were digested for 3 hrs at 90 C in concentrated sulfuric and nitric acids, then diluted to 4 mL for a final dilution of 4x

Preliminary CMP Results with Ceria NPs

Ceria NP CMP 0 minutes



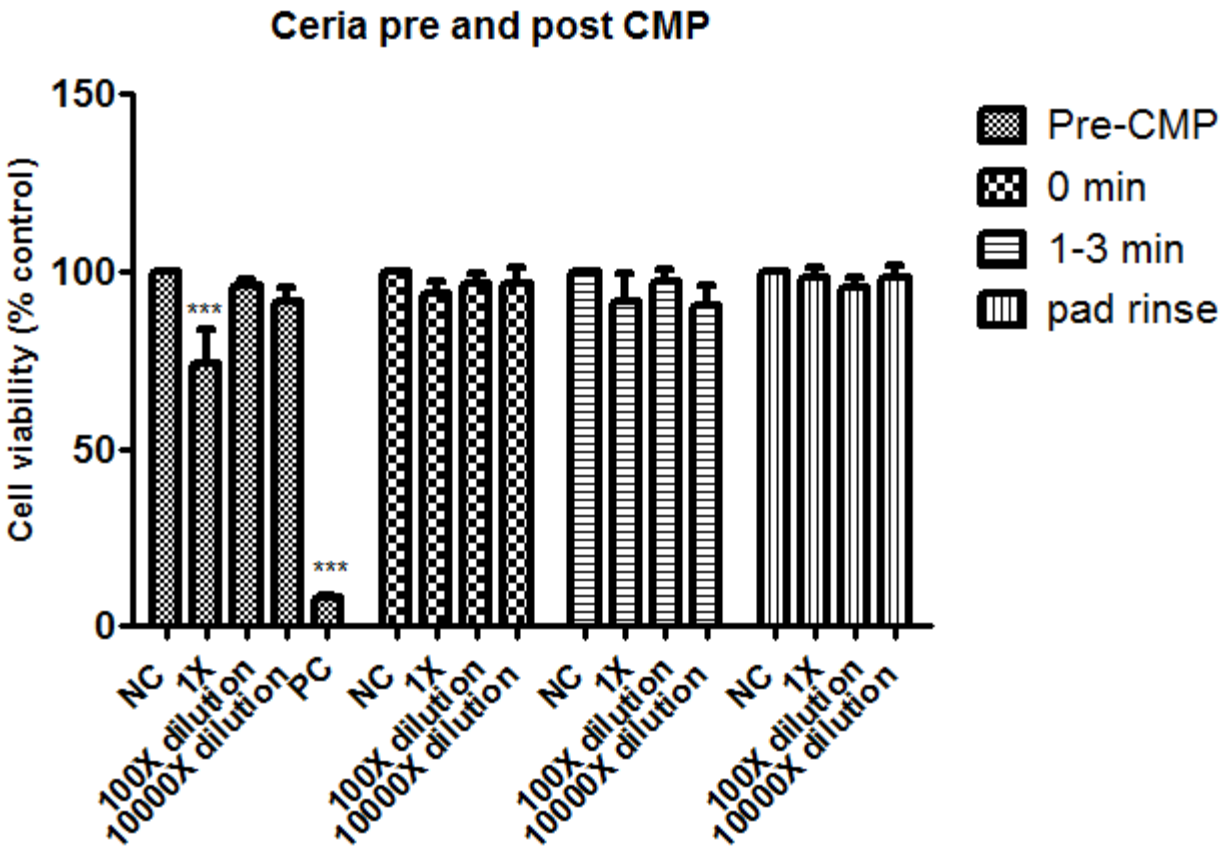




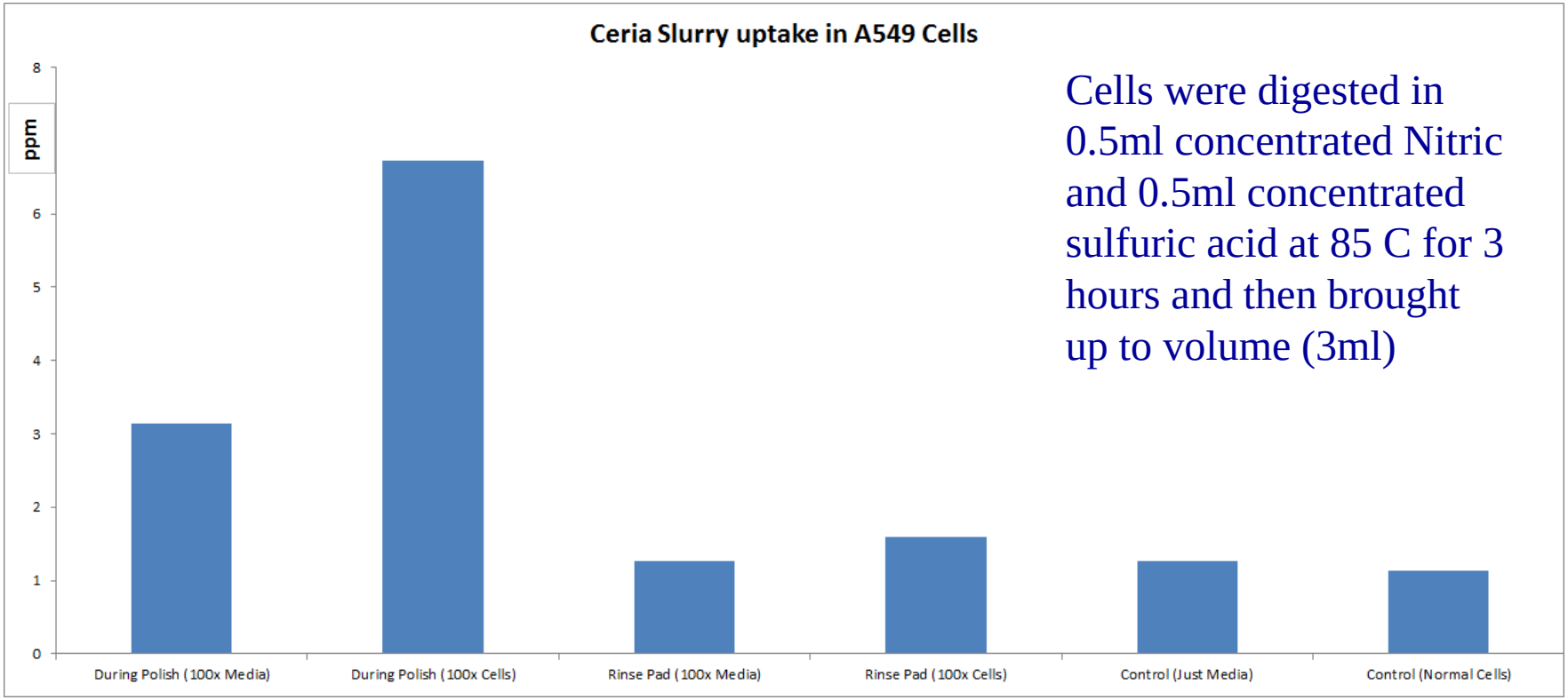
pH, PSD and zeta potential of post-CMP ceria

CMP time (min)	pH of post-CMP samples	PSD (d.nm)	Zeta potential
0	9.74	99.95	-88.7
1	9.02	4427	-96.6
3	8.32	4855	-90
Rinse	7.94	2078	-78.4

Cell viability of A549 cells exposed to post-CMP ceria



Post-CMP colloidal ceria uptake by A549 cells



Cells were digested in 0.5ml concentrated Nitric and 0.5ml concentrated sulfuric acid at 85 C for 3 hours and then brought up to volume (3ml)

Summary of Results

- Conducted comprehensive physical and chemical characterization of four model slurries, bound ENs and few "real" slurries along with dried micro and NPs of comparable size and method of synthesis
- Investigated NP interaction with a mammalian cell
  - Surface Interaction, cellular uptake and internalization, interaction with nucleus (NP-induced DNA damage, Comet assay)
- With model slurries
  - Silica NP slurries NPs showed dose and time - dependent toxicity (both colloidal and fumed silica NPs), NP aggregation major factor in toxicity
  - Acute toxicity observed in case of Ceria slurry NPs and Alumina slurry NPs showed no significant toxicity.
  - Significant increase in production of intracellular ROS, indicating that silica NPs cause cellular toxicity via oxidative stress.
  - Raman Spectroscopy of cellular uptake was used and showed the internalization and inhomogeneous distribution of ceria NPs in cells
- With "real" slurries – preliminary physiochemical, toxicity and uptake data

Industrial Interactions and Technology Transfer

- Acknowledgements to SRC technical liaisons – Chris Lee (TI) and Reed Content (Global Foundries) for valuable comments and suggestions

- SRC/ERC Nanotoxicity consortium with academic researchers and industry liaisons
  - Conducted round-robin studies with other consortium members on these slurries
  - Joint consortium paper on model slurry characterization

- Hosted teleseminars for SRC/ERC for Environmentally Benign Semiconductor Manufacturing during 2014

Publications, Presentations, and Recognitions/Awards

- K. Kosaraju, M. Tarannum, S. Crawford, S. Aravamudhan, "Effect of aggregation on the toxicity of silica nanoparticles", Environ. Sci. Tech. (submitted)
- K. Kosaraju, M. Tarannum, S. Crawford, S. Aravamudhan, "Cellular uptake of ceria nanoparticles..", Chem. Res. Toxicicol.(in preparation)
- Consortium paper - D. Speed et. al., Physical, Chemical and In Vitro Toxicological Characterization of Nanoparticles in ….Environmental Science: Nano (under review)
- J.M. Starobin, S. Aravamudhan, K. Kosaraju, et al., Analysis of cardiac repolarization ..Sustainable Nanoteechnology Organization Conference, Boston, MA, Nov 2-4, 2014.
- K. Kosaraju, K. Garde, S. Crawford, S. Aravamudhan, "Examining the Cellular Uptake of Engineered Nanomaterials," ECS Trans. 61(36), 15-21, 2014
- K. Garde, K. Kosaraju, S. B. Ravari, S. Aravamudhan, "Towards Understanding Toxicity of Engineered Nanomaterials," Ch. in Nanoscience and Nanoengineering: Advances and Applications, CRC Press, ISBN 9781482231199, 2014.
- K. Kosaraju et al. , "Examining the Cellular Uptake of Engineered Nanomaterials," 225th ECS Meeting, Orlando, FL, May 11-16, 2014.
- K. Kosaraju, M. Tarannum, S. Crawford, K. Garde, S. Aravamudhan, "Examining Cellular Uptake of CMP Nanoparticles," TECHCON 2014, Sep 7-9, 2014.

Thank You