rial displayed a characteristic ability to preferentially bind various proteins. Differential binding of proteins, however, could not be explained simply by the surface charge of the nanoparticles which underscores the need for expanded studies to identify the relevant surface properties.

1395 QUALITATIVE AND QUANTITATIVE UPTAKE OF SIO2-COATED FLUOROPHORE NANOPARTICLES.

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In this research, the uptake of nanoparticle-based luminescent probes was examined for biological and environmental imaging and detection applications. Organic fluorophores currently used in cell imaging decompose during imaging, resulting in photobleaching. However, rare earth ions doped inside of silica nanoparticles are stable and do not photobleach, still emitting fluorescence with intensities comparable to single organic fluorophores. Silica-coated FITC (SiO2-FITC) and rhodamine (SiO2-RB) nanoparticles were measured using transmission electron microscopy (TEM). Both nanoparticles are close to 100 nm in diameter and possess similar spherical morphology. Cell viability was determined using MTT assay, and results showed that the SiO2-FITC particles significantly decrease cell viability at 100 ug/mL, while SiO2-RB nanoparticles are not toxic at the concentrations tested (0-100 ug/mL). Fluorescence microscope images show particles agglomerated within cells and verify that washing procedures are successful in removing particles not taken up into cells. A protocol to quantify the uptake of particles into cells using this washing procedure was developed using a fluorescence microplate reader. This method allows for the determination of the critical concentration of particle uptake into the cell, in order to relate this information to cell size and toxicity.

1396 PHOSPHATIDYLSERINE ENHANCES RECOGNITION AND UPTAKE OF SINGLE-WALLED CARBON NANOTUBES BY RAT BRAIN MICROGLIAL CELLS.

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Single-walled carbon nanotubes (SWCNT) are a class of nanosized materials with wide applications in industry and medicine. Inhaled SWCNT have been shown to cause a robust inflammatory and oxidative stress response in the lung and cardiovascular system. Interactions with phagocytozing cells determine SWCNT elimination or spreading into different tissues. The challenge is how to make nanotubes delivered specifically to the target site. We established that macrophages do not effectively recognize non-functionalized SWCNT but readily engulf SWCNT coated with phosphatidylserine (PS), an "eat-me" signal for phagocytes. In the brain, important immunological functions are associated with the ability of microglial cells to exert phagocytic activity. As inhaled nanoparticles have been detected in the brain we were interested to study interactions of SWCNT with microglial cells. Microglial cells were isolated from postnatal rat brains and identified with CD11 antibody. Primary cultures were obtained with 70% microglial cell population which could be activated by lipopolysacharide (LPS) to produce NO revealed by labeling of cells with a specific fluorogenic reagent, DAF-2DA. Further we studied phagocytosis of SWCNT by microglial cells. Cells were incubated with SWCNT coated with either fluorescently labeled nitrobenzoxadiazole (NBD)-PS or NBD-phosphatidylcholine (PC) for 2h. Fluorescent microscopy was applied and revealed that NBD-PS-SWCNT were a more preferred target of recognition and uptake by microlgial cells than NBD-PC-SWCNT. Control experiments were performed to confirm that NBD-phospholipids remained bound to SWCNT. Thus, similar to macrophages, microglial cells utilize PS as a signal for effective recognition and engulfment of SWCNT. Supported by NIOSH OH008282, NIH HL70755, HL70809, AHA0535365N, Human Frontier Science Program.

1397 EVALUATION OF *IN VITRO* PENETRATION OF QUANTUM DOT NANOPARTICLES INTO HUMAN SKIN.

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Topical exposure to nanoparticles is becoming more of an issue due to the increased use of nanosized ingredients in consumer products and because of possible occupational and environmental exposure. Because of their small size, there is concern about the ability of these particles to penetrate through the barrier layer of skin. In vitro skin absorption studies were conducted using cadmium selenide quantum dots (Qdots) as a model nanoparticle because of their relative stability and intense fluorescence. Qdots (PEG coating, maximum emission 621 nm, hydrodynamic diameter 37 nm) were synthesized and formulated into an oil-in-water emulsion, and applied to human cadaver skin assembled in diffusion cells. Initial absorption studies were conducted for 24 hr followed by examination of sections from paraffin embedded skin using a fluorescence microscope. Fluorescence from Qdots appeared to be on or in the surface layer of skin (the stratum corneum), in the opening of hair follicles or in the folds (furrows) of the skin surface. Subsequent studies with Qdot emulsion formulations were conducted for 3, 8, and 24 hr. Frozen skin sections were evaluated for location of fluorescence with a laser scanning confocal microscope (LSCM). Fluorescence in the skin appeared to be found predominately in the stratum corneum with small amounts possibly penetrating further into the upper region of the viable epidermis. Spectral analysis of the fluorescence detected by LSCM showed that most fluorescence observed in the viable epidermis and all fluorescence in the dermis was due to autofluorescence. No significant elevation of cadmium (Qdots) was observed in receptor fluid samples taken beneath the skin. It therefore appears that absorbed Qdots were found predominately in the stratum corneum and they did not penetrate through the skin.

1398 ACCUMULATION OF NANOSCALE QUANTUM DOTS IN MULTIPLE ORGANS IN VIVO, FOLLOWING DERMAL EXPOSURE TO DERMABRADED, BUT NOT TAPE STRIPPED OR INTACT SKH-1 MOUSE SKIN.

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There are currently many cosmetics and sunscreens that contain nanoscale materials such as titanium dioxide and zinc oxide. To date the possible long-term toxicological effects of percutaneous absorption of nanoparticles have not been determined. We used nanoscale polyethylene glycol coated cadmium selenide (CdSe) core quantum dots (QD) as surrogate nanoparticles, and evaluated (a) tissue Cd distribution following intradermal administration and (b) penetration into intact, tape stripped or dermabraded in mouse skin. Female SKH-1 mice were intradermally injected with 5 µL of 19 µM QD, and following sacrifice at 24 hr, tissues were removed and analyzed for Cd content using inductively coupled plasma mass spectrometry (ICP-MS). Approximately 6% and 1% of the administered Cd dose were found in the liver and regional lymph nodes, respectively, with lesser amounts detected in the kidney, spleen, and heart. QD were visualized in the skin and lymph nodes using fluorescence microscopy. These results support the use of liver and regional draining lymph nodes as sentinel organs for assessment of the distribution after dermal exposure of QD. QD were suspended in an oil-in-water emulsion at approximately 9 µM and applied at 2 mg/cm^2 to the dorsal skin of mice pretreated as follows: untreated; tape-stripped to remove the stratum corneum; dermabraded. Cd was not detected by ICP-MS in sentinel organs of untreated or tape-stripped mice 24-48 hr post application; however, in dermabraded mice, approximately 1% and 0.01% of the applied QD were detected in liver and lymph nodes, respectively. These results suggest that percutaneous absorption of nanoscale materials depends on skin barrier integrity, and hence the potential hazard of topically applied nanoscale materials needs further evaluation.

1399 CELLULAR MECHANISMS OF QUANTUM DOT NANOPARTICLE UPTAKE IN PRIMARY HUMAN EPIDERMAL KERATINOCYTES.

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The pathway of nanomaterial uptake into cells may be an important determinant of cytotoxic potential and effects. Quantum dots (QD) 655 with cationic (PEG-amine, NH_2), anionic (carboxylic acid, COOH), and neutral (PEG) surface coatings are non-selectively taken up by primary neonatal human epidermal keratinocytes (HEK) at low concentrations, but the mechanisms of cellular uptake are unknown. The global hypothesis tested herein is that QD surface coating is the primary determinant of the magnitude and mechanisms of cellular uptake by HEK. A fluorescence microplate screen was used to quantitatively determine differences in the magnitude of uptake of 10 nM QD 655 by HEK after 24 h at 37°C. Statistical comparison revealed significant differences among all coatings, with COOH > NH_2 > PEG. Also, we investigated the temperature dependence of QD uptake by performing similar experiments at a temperature of 4°C. Uptake of all three QD

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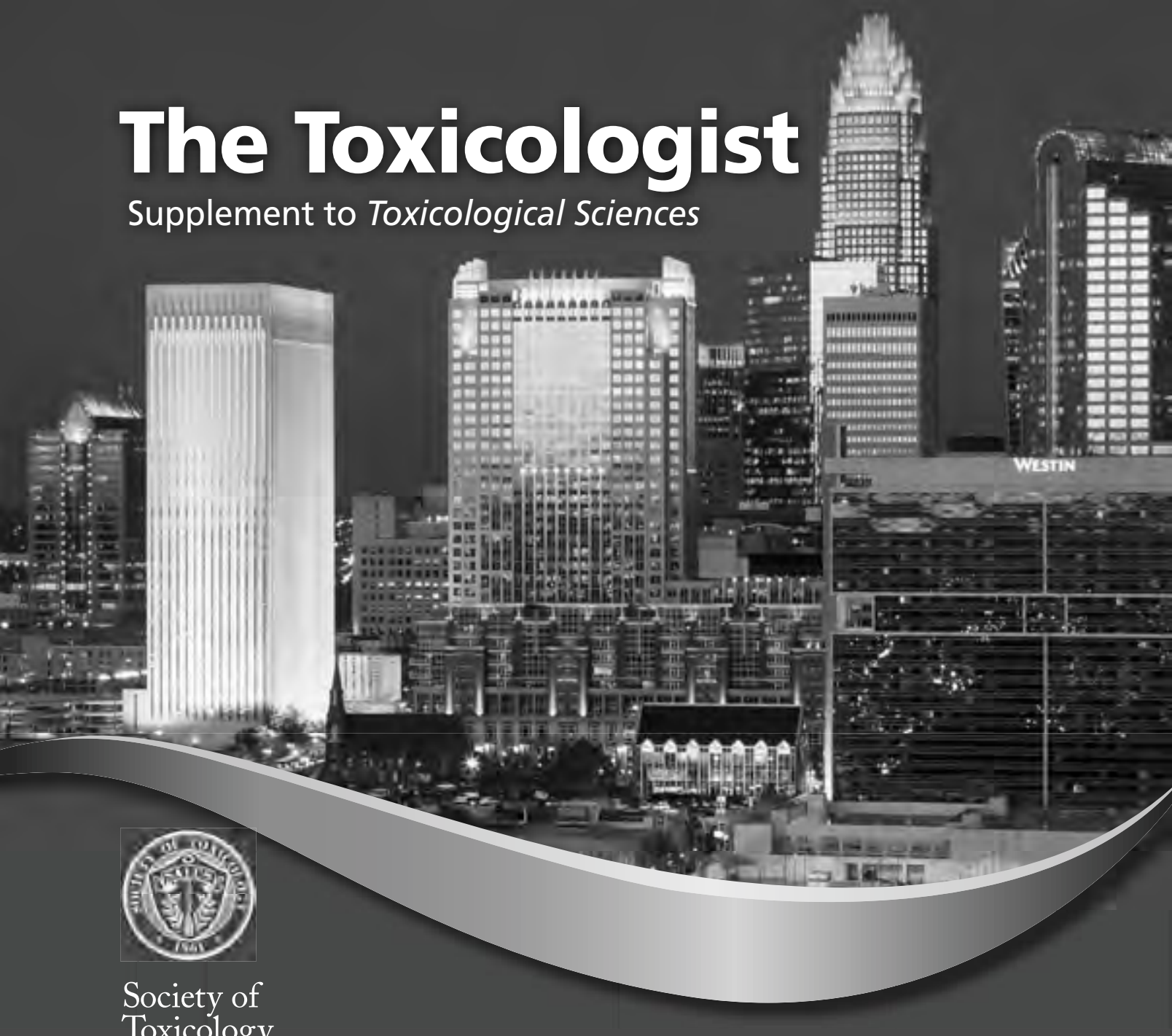

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster discussion, workshop, and poster sessions of the 46th Annual Meeting of the Society of Toxicology, held at the Charlotte Convention Center, Charlotte, March 25–29, 2007.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 449.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 480.

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