corresponding media controls. Preliminary data indicates that the surfactant Pluronic® F127 does reduce MWCNT aggregates in the aqueous medium without causing a significant decrease in HEK viability.

2185 LOCALIZATION OF INTRADERMALLY INJECTED QUANTUM DOT NANOPARTICLES IN REGIONAL LYMPH NODES.

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The *in vivo* disposition of nanoscale materials is of interest due to their potential inclusion in a large number of products. As part of a project to determine the dermal penetration of nanoscale material, we examined the disposition of nanoscale material injected in the dermis of mice. Quantum dots (QD) consisting of CdSe nanocrystals, encased in a ZnS shell and PEG outer coating were injected intradermally (ID) in female SKH-1 hairless mice and their disappearance from the injection site and disposition were determined using digital macrophotography and fluorescence microscopy. Mice were injected in each flank with 5 µl of 5.5 µM red QD (655 nm emission; 6 x 12 nm rods) and 7.5 µM yellow QD (565 nm emission; 6 nm spheres), or sterile saline, imaged under UV illumination, and sacrificed at 0, 6, 12, 18, 24, and 48 hrs. Under UV illumination, the highly fluorescent QD could be observed and digitally imaged moving from the injection sites via subcutaneous lymphatic ducts to regional lymph nodes. The tracking of fluorescence in subcutaneous lymphatic ducts with accumulation in lymph nodes occurred minutes after injection in some animals and was no longer apparent after 6 hrs. Residual fluorescent QD remained at the site of injection until necropsy. Lymph nodes from QD injected animals exhibited fluorescence that was localized in subcapsular and trabecular lymphatic sinuses. QD fluorescence in lymph nodes was most abundant at 0 hr and 6 hr, but was detected at all time points. In conclusion, intradermally injected nanoscaled QD remained as a depot in skin, penetrated the surrounding viable subcutis and were visibly distributed to draining lymph nodes via subcutaneous lymphatics. These results are consistent with the previously reported use of near infrared emitting nanoscale particles for imaging sentinel lymph nodes.

2186 IMAGING THE PENETRATION OF RUBPY-DOPED SILICA NANOPARTICLES INTO HUMAN AND MOUSE SKIN WITH FLUORESCENT MICROSCOPY.

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Nano-sized particles have the potential to enter body through routes that are inaccessible to larger particulates. One such route is dermal absorption. To study the penetration of nano-particulates into mammalian skin, we exposed whole-thickness mouse and dermatomed (600 µm) human skin *in vitro* to suspensions of RubPy doped 50-nm silica particles under static and dynamic conditions. For static samples, 100 x 300 mm skin sections were placed flat with the epidermis side up and a 5 µL aliquot of a 20 mg/mL suspension of the dye doped silica particles was placed on the center of a section. Static samples were left undisturbed for 2 h. Dynamic samples were treated similarly, but placed upon a single-hinged flexing device, which flexed the upper half of the section between 0 and 45° above horizontal 30x/min for two hours. After the 2-h incubation, the skin sections were rinsed with PBS and gently blotted to remove excess particles. After fixing in formaldehyde, samples were cut from dermis side out in 20-µm sections and examined by fluorescent microscopy. The silica particles were found to penetrate into the stratum corneum and epidermis of both skin types and under both treatments with a higher concentration of particles occurring the tissues of flexed samples. Particle count in the epidermis was low compared to the stratum corneum and higher in the mouse than the human; presumably a result of the thinner stratum corneum of the mouse.

2187 MODULATORY EFFECTS OF SUBCHRONIC EXPOSURE TO SIMULATED SOLAR LIGHT ON TATTOOED SKIN IN SKH-1 MICE.

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Tattooing is the process of depositing pigment into the dermis of the skin with a needle producing an indelible decorative pattern. In an attempt to determine the phototoxicity of tattoo pigments, we have shown that tattooing induces an acute inflammatory response in the skin with recovery within 13 days. The present study examines the effect of subchronic exposure of tattooed mice to simulated solar light (SSL). Female SKH-1(*hr*$^-$/*hr*$^-$) hairless mice were tattooed longitudinally on the dorsal side. The test mixtures consisted of vehicle (10% glycerol in water) or vehicle containing cadmium sulfide (CdS) or Pigment Red 22 (PR22). After 2 weeks to allow skin recovery, half of the mice were exposed to 1.4 Standard Erythemal Dose/day SSL for 13 weeks and then euthanized. Minimal dermal inflammation was present in one-third of the non-tattooed and vehicle-tattooed skin not exposed to SSL. The incidence of dermal inflammation increased to 67% and 56%, respectively, upon exposure to SSL. In contrast, exposure to SSL did not increase the incidence of dermal inflammation in the CdS (100%) and PR22 (67%) tattooed skin. Acanthosis was present in all SSL-exposed animals except the CdS-tattooed group. Dermal necrosis and fibrosis, and epidermal hyperplasia were present exclusively in CdS-tattooed animals (100%) with or without SSL. Dermal histiocytic infiltration was noted only in the PR22-tattooed skin and increased in incidence from 33% to 100% in the presence of SSL. Western blotting and immunohistochemistry showed cutaneous COX-1, COX-2 and ODC proteins were significantly different in animals exposed to SSL when compared to non-exposed mice, notably in the CdS group. Real time PCR demonstrated differential expression of cyclin D1, HIF-1α and cMyc in response to SSL in tattooed and non-tattooed mice. The results demonstrate the modulatory effects of subchronic exposure to SSL in the skin of tattooed mice.

2188 ROLE OF VITAMIN E IN THE ANTIOXIDANT DEFENSE SYSTEM OF SKIN IN YOUNG AND OLD MICE EXPOSED TO CUMENE HYDROPEROXIDE.

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The skin is exposed to numerous environmental, chemical, and physical stressors (UV-irradiation) whose injurious action is often associated with the development of oxidative stress. While the skin possesses an elaborate antioxidant (AO) defense system to prevent oxidative stress, excessive exposure to occupational and environmental insults can overwhelm the cutaneous AO capacity. Age-related decline of AO protection may further enhance sensitivity of skin to chemically induced oxidative damage. To evaluate whether aging affected the AO capabilities of the skin, we studied changes in vitamin E, glutathione (GSH), ascorbate, and total AO reserve levels in the skin of female mice from 4 to 32 weeks of age. Among studied AO, we observed the most significant and rapid reduction occurred in the vitamin E content. To study how topical exposure to cumene hydroperoxide (Cum-OOH) affected the AO status of the skin of young/old mice, two models were used: 1) mice given a diet deficient in vitamin E and 2) mice with a genetic deletion of the tocopherol transporter protein (Ttpa knockout). We found that oxidative DNA damage (8-oxo-2′-deoxyguanosine) in skin of old mice (32 weeks) occurred independently of vitamin E status while DNA damage in skin of young animals (13 weeks) exposed to Cum-OOH was dependent upon vitamin E. Cum-OOH induced oxidative stress in old mice as assessed by depletion of GSH, ascorbate, and total AO reserve. Cum-OOH induced morphological changes to a greater extent in the skin of old vitamin E deficient animals compared to young mice. Similar results were found in the Ttpa knockout mice exposed to Cum-OOH; however, the mice only had a 40% reduction in their vitamin E levels and the resulting changes were not as profound as in the mice given the vitamin E deficient diet. In conclusion, AO, in particular vitamin E, play a prominent role in the protection of skin against oxidative injury induced by Cum-OOH exposure *in vivo*.

2189 DETECTION OF BENZO(A)PYRENE-INDUCED DNA DAMAGE IN THE SKIN OF CD-1 MICE USING THE COMET ASSAY.

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The single cell gel electrophoresis assay (SCGE or "comet" assay) is a rapid, sensitive method used to detect DNA damage *in vivo* and *in vitro*. The principle of the assay is based on the ability of denatured, cleaved and unwound DNA to migrate out of the nucleus when an electric current is applied to the cell, whereas intact, undamaged DNA remains within the confines of the nucleus. While this assay has been successful in studies to predict potential clastogenic agents, there is little data published on the use of the comet assay to analyze these agents in intact mammalian skin. Since DNA strand breaks result in the formation of micronuclei, we hypothesized that the comet assay would provide a sensitive method for detecting DNA damage in the skin of CD-1 mice challenged topically with benzo(a)pyrene (BaP), a prototypical carcinogen and potent electrophilic agent. To test this hypothesis, BaP (2mg/ml), or acetone (vehicle), was painted onto the shaved back of CD-1 mice daily for 3, 6, and 10 days. At each time point, two mice were sacrificed

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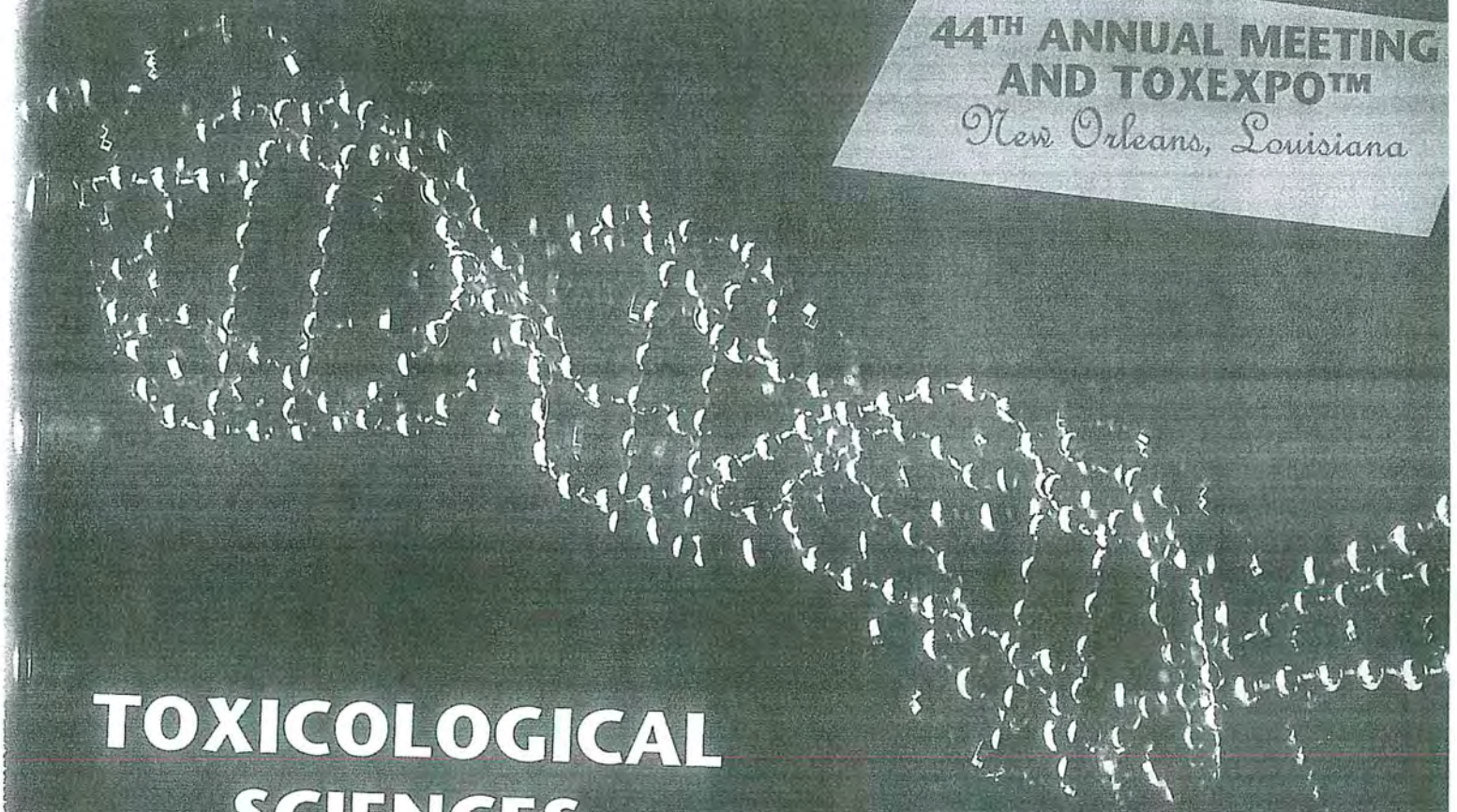

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