(click on page numbers for links)

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	н аг		1 1

Temporary and Permanent Auditory Effects Associated with

Epigenome-wide association studies of occupational exposure to

Occupational Coexposure to Low Levels of Noise and Solvents ......10

benzene and formaldehyde ......11

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#### **CHEMICAL EFFECTS**

## Assessing the Cytotoxicity of TiO 2-x Nanoparticles with a Different Ti 3+(Ti 2+)/Ti 4+ Ratio

2022-08-27

Titanium dioxide (TiO2) nanoparticles are promising biomedical agents characterized by good biocompatibility. In this study, we explored the cytotoxicity of TiO2-x nanoparticles with a different Ti3+(Ti2+)/ Ti4+ ratio and analyzed the efficiency of eryptosis indices as a tool in nanotoxicology. Two types of TiO2-x nanoparticles (NPs) were synthesized by the hydrolysis of titanium alkoxide varying the nitric acid content in the hydrolysis mixture. Transmission electron microscopy (TEM) images show that 1-TiO2-x and 2-TiO2-x NPs are 5 nm in size, whereas X-ray photoelectron spectroscopy (XPS) reveals different Ti3+ (Ti2+)/Ti4+ ratios in the crystal lattices of synthesized NPs. 1-TiO2-x nanoparticles contained 54% Ti4+, 38% Ti3+, and 8% Ti2+, while the relative amount of Ti4+ and Ti3+ in the crystal lattice of 2-TiO2-x nanoparticles was 63% and 37%, respectively. Cell viability and cell motility induced by TiO2-x nanoparticles were investigated on primary fibroblast cultures. Eryptosis modulation by the nanoparticles along with cell death mechanisms was studied on rat erythrocytes. We report that both TiO2-x nanoparticles do not decrease the viability of fibroblasts simultaneously stimulating cell migration. Data from in vitro studies on erythrocytes indicate that TiO2-x nanoparticles trigger eryptosis via ROS- (1-TiO2-x) and Ca2+-mediated mechanisms (both TiO2-x nanoparticles) suggesting that evaluation of eryptosis parameters is a more sensitive nanotoxicological approach for TiO2-x nanoparticles than cultured fibroblast assays. TiO2-x nanoparticles are characterized by low toxicity against fibroblasts, but they induce eryptosis, which is shown to be a promising tool for nanotoxicity screening. The Ti3+ (Ti2+)/Ti4+ ratio at least partly determines the cytotoxicity mechanisms for TiO2-x nanoparticles.

Authors: Volodymyr Prokopiuk, Svetlana Yefimova, Anatolii Onishchenko, Valeriy Kapustnik, Valeriy Myasoedov, Pavel Maksimchuk, Dmytro Butov, Irina Bespalova, Anton Tkachenko

Full Source: Biological trace element research 2022 Aug 27. doi: 10.1007/s12011-022-03403-3.

Titanium dioxide (TiO2) nanoparticles are promising biomedical agents characterized by good biocompatibility.

# Technical Amphibian toxicity testing for identification of thyroid

**Bulletin Board** 

2022-08-20

disrupting chemicals

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Both amphibian metamorphosis assay (AMA) and larval amphibian growth and development assay (LAGDA) can detect thyroid-mediated modality and adversity on the basis of morphological changes during the thyroid hormone-dependent metamorphosis. They are used for identification of thyroid hormone system disrupting chemicals (TDCs) for non-target organisms or the environment. The EU Guidance recommends that the AMA and the LAGDA should be used to address sufficient investigation of the thyroid-mediated modality and adversity, respectively. In the EU discussions over identification of TDCs, the necessity of using LAGDA as a follow-up of positive results of the AMA has been questioned because of the overlap between the endpoints and the exposure of both tests. This study analyzed similarities, differences, and sensitivity of these two assays in detection of TDCs. For agonists and most of antagonists of the hypothalamic-pituitary-thyroid (HPT) axis, both AMA and LAGDA can detect the thyroid-mediated modality and adversity. The LAGDA, as a follow-up of the positive results of the AMA, may not be needed because the results of AMA are considered enough for identification of TDCs. For chemicals like inhibitors of iodotyrosine deiodinase, the LAGDA is considered necessary for identification of TDCs because the thyroid-mediated adversity cannot be detected until Nieuwkoop and Faber (NF) stage 62. Incorporation of mechanistic endpoints into existing test guidelines and the use of Xenopus Eleutheroembryo Thyroid Assay (XETA), extended amphibian metamorphosis assay (EAMA) and adverse outcome pathways (AOPs) for testing and identification of TDCs are further discussed.

Authors: ZhiChao Dang

Full Source: Environmental pollution (Barking, Essex: 1987) 2022 Aug 20;311:120006. doi: 10.1016/j.envpol.2022.120006.

## Perfluorooctanoic acid-induced developmental cardiotoxicity in chicken embryo: Roles of miR-490-5p

2022-08-23

Perfluorooctanoic acid (PFOA) could induce developmental toxicities, affecting various organs, including the heart. Although peroxisome-proliferation activated receptor alpha (PPARα) had been identified as a major target of PFOA, PPARα-independent effects are frequently reported. To further elucidate the mechanism of toxicity in PFOA-

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in hatchling chicken hearts developmentally exposed to vehicle or 2 mg/kg (egg weight) PFOA. RT-PCR and western blotting were then performed to confirm the identified potential targets. Furthermore, lentivirus was designed to overexpress and silence identified target miRNA in developing chicken embryo, and the resulting phenotypes were investigated. 21 miRNAs and 1142 mRNAs were identified to be affected by developmental exposure to PFOA in chicken embryo hearts. Among the identified differentially expressed miRNAs, miR-490-5p was confirmed to be significantly affected by PFOA exposure, along with its downstream targets, Synaptosome associated protein 91 (SNAP91) and LY6/PLAUR domain containing 6 (LYPD6), as indicated by RT-PCR and western blotting results. Lentivirus overexpressing miR-490-5p mimicked the phenotype induced by PFOA exposure, while lentivirus silencing miR-490-5p alleviated PFOA-induced changes. Similar patterns were also observed in the expression of downstream target genes, SNAP91 and LYPD6. In summary, miR-490-5p and its downstream genes, SNAP91 and LYPD6 are associated with PFOA-induced developmental cardiotoxicity in chicken embryo, which might help to further elucidate the mechanism of PFOAinduced developmental cardiotoxicity.

induced developmental cardiotoxicity, RNA-seq analysis was performed

Authors: Yajie Guo, Junhua Yuan, Hao Ni, Jing Ji, Shuping Zhong, Yuxin Zheng, Qixiao Jiang

Full Source: Environmental pollution (Barking, Essex : 1987) 2022 Aug 23;312:120022. doi: 10.1016/j.envpol.2022.120022.

#### **ENVIRONMENTAL RESEARCH**

## A decade of monitoring micropollutants in urban wetweather flows: What did we learn?

2022-08-09

Urban wet-weather discharges from combined sewer overflows (CSO) and stormwater outlets (SWO) are a potential pathway for micropollutants (trace contaminants) to surface waters, posing a threat to the environment and possible water reuse applications. Despite large efforts to monitor micropollutants in the last decade, the gained information is still limited and scattered. In a metastudy we performed a data-driven analysis of measurements collected at 77 sites (683 events, 297 detected micropollutants) over the last decade to investigate which micropollutants are most relevant in terms of 1) occurrence and 2) potential risk for the aquatic environment, 3) estimate the minimum number of data to be collected in monitoring studies to reliably obtain concentration estimates,

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Bulletin Board

**Technical** 

CHEMWATCH

SEP. 02, 2022

and 4) provide recommendations for future monitoring campaigns. We highlight micropollutants to be prioritized due to their high occurrence and critical concentration levels compared to environmental quality standards. These top-listed micropollutants include contaminants from all chemical classes (pesticides, heavy metals, polycyclic aromatic hydrocarbons, personal care products, pharmaceuticals, and industrial and household chemicals). Analysis of over 30,000 event mean concentrations shows a large fraction of measurements (> 50%) were below the limit of quantification, stressing the need for reliable, standard monitoring procedures. High variability was observed among events and sites, with differences between micropollutant classes. The number of events required for a reliable estimate of site mean concentrations (error bandwidth of 1 around the "true" value) depends on the individual micropollutant. The median minimum number of events is 7 for CSO (2 to 31, 80%-interquantile) and 6 for SWO (1 to 25 events, 80%-interquantile). Our analysis indicates the minimum number of sites needed to assess global pollution levels and our data collection and analysis can be used to estimate the required number of sites for an urban catchment. Our data-driven analysis demonstrates how future wet-weather monitoring programs will be more effective if the consequences of high variability inherent in urban wet-weather discharges are considered.

Authors: Lena Mutzner, Viviane Furrer, Hélène Castebrunet, Ulrich Dittmer, Stephan Fuchs, Wolfgang Gernjak, Marie-Christine Gromaire, Andreas Matzinger, Peter Steen Mikkelsen, William R Selbig, Luca Vezzaro Full Source: Water research 2022 Aug 9;223:118968. doi: 10.1016/j. watres.2022.118968.

## The need for environmental regulation of tires: Challenges and recommendations

2022-08-19

The interest in tire wear particles (TWPs), generated from abrasion of tires, have gained traction over the past few years, both in regards to quantifying particulate emissions, leaching of different compounds, toxicity, and analytical methods. The life of a tire, from cradle to end-of-life, crosses over different scenarios during its lifetime and transcends environmental compartments and legislative areas, underlining the need for a collective approach. Sustainability for a tire encompasses the use of raw materials, recycling of raw materials, circular economy and material sourcing. The tire industry is currently making significant efforts towards a greener and more sustainable production considering reduction of CO2-emissions, recycling, material sources and implementing the use of

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# Bulletin Board Technical SEP. 02, 2022

biomass from plants rather than oil-derived alternatives. In this paper, we aim to analyze and discuss the need for environmental regulation of tires in order to provide a series of targeted recommendations for future legislation. Our study shows that the numerous regulations related to tires focus on chemicals, manufacturing, raw materials, use of tires on roads, waste handling, safety and polycyclic aromatic hydrocarbons (PAHs) in different life cycle stages of a tire. However, none directly addresses the contribution of TWPs to the environment. Despite the overall good intentions of the existing regulations, there is a lack of focus on the compounds that partition from the tire and disperse in the environment, their mixture effects, and the transformative products from the parent compounds in the environment. Therefore, a renewed focus is needed on risk assessment of complex mixtures like TWPs. Thus, transparency in regard to use of chemicals in TWP, mixtures, minimization of emissions, and capture of particulate pollution should be a priority.

Authors: Louise Lynn Trudsø, Maria Bille Nielsen, Steffen Foss Hansen, Kristian Syberg, Kristoffer Kampmann, Farhan R Khan, Annemette Palmqvist

Full Source: Environmental pollution (Barking, Essex : 1987) 2022 Aug 19;311:119974. doi: 10.1016/j.envpol.2022.119974.

#### Beach showers as sources of contamination for sunscreen pollution in marine protected areas and areas of intensive beach tourism in Hawaii, USA

2022-09-15

In 2019, sands in nearby runoff streams from public beach showers were sampled on three islands in the State of Hawaii and tested for over 18 different petrochemical UV filters. Beach sands that are directly in the plume discharge of beach showers on three of the islands of Hawaii (Maui, Oahu, Hawai'i) were found to be contaminated with a wide array of petrochemical-based UV-filters that are found in sunscreens. Sands from beach showers across all three islands had a mean concentration of 5619 ng/g of oxybenzone with the highest concentration of 34,518 ng/g of oxybenzone at a beach shower in the Waikiki area of Honolulu. Octocrylene was detected at a majority of the beach shower locations, with a mean concentration of 296.3 ng/g across 13 sampling sites with the highest concentration of 1075 ng/g at the beach shower in Waikiki. Avobenzone, octinoxate, 4-methylbenzylidene camphor and benzophenone-2 were detected, as well as breakdown products of oxybenzone, including benzophenone-1, 2,2'-dihydroxy-4methoxybenzophenone, and 4-hydroxybenzophenone. Dioxybenzone

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Technical

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(DHMB) presented the highest concentration in water (75.4 ng/mL), whereas octocrylene was detected in all water samples. Some of these same target analytes were detected in water samples on coral reefs that are adjacent to the beach showers. Risk assessments for both sand and water samples at a majority of the sampling sites had a Risk Quotient > 1, indicating that these chemicals could pose a serious threat to beach zones and coral reef habitats. There are almost a dozen mitigation options that could be employed to quickly reduce contaminant loads associated with discharges from these beach showers, like those currently being employed (post-study sampling and analysis) in the State of Hawaii, including banning the use of sunscreens using petrochemical-based UV filters or educating tourists before they arrive on the beach.

**Bulletin Board** 

Authors: C A Downs, M Silvia Diaz-Cruz, William T White, Marc Rice, Laura Jim, Cindi Punihaole, Mendy Dant, Krishna Gautam, Cheryl M Woodley, Kahelelani O Walsh, Jenna Perry, Evelyn M Downs, Lisa Bishop, Achal Garg, Kelly King, Tamara Paltin, Ellen B McKinley, Axel I Beers, Sadasivam Anbumani, Jeff Bagshaw

Full Source: Journal of hazardous materials 2022 Sep 15;438:129546. doi: 10.1016/j.jhazmat.2022.129546.

#### PHARMACEUTICAL/TOXICOLOGY

Association of hairdressing with cancer and reproductive diseases: A systematic review

2022-01

Objectives: To review recent epidemiological studies investigating carcinogenic or reprotoxic effects among hairdressers who seem to be at greater risk for systemic adverse effects of chemicals released from hair care products than consumers.

Methods: A systematic review according to the PRISMA-P guidelines was performed and included studies published from 2000 to August 2021, in which cancer or adverse reproductive effects were diagnosed in 1995 and onward. Data were synthetized qualitatively due to the small number of studies, heterogeneity of study designs, outcomes, and methods. Results: Four studies investigating cancer frequencies and six studies investigating effects on reproduction among hairdressers were identified. All were of good quality and with low risk of bias. Only one of the four studies found an increased risk of cancer reporting nine times higher odds for bladder cancer in hairdressers than the population-based controls. Three other studies investigating bladder and lung cancer, and non-Hodgins lymphoma did not find an increased risk in hairdressers.

Objectives: To review recent epidemiological studies investigating carcinogenic or reprotoxic effects among hairdressers who seem to be at greater risk for systemic adverse effects of chemicals released from hair care products than consumers.



Regarding reprotoxic effects, numerous outcomes were investigated including menstrual disorders, congenital malformations, fetal loss, small-for-gestational age newborns, preterm delivery, and infertility. Increased risk was found for ventricular septal defect in newborns of fathers working as hairdressers. Furthermore, several indices of poor neonatal or maternal health were significantly associated with mothers working as hairdresser. Conclusions: Despite the scarce evidence that hairdressers are at increased risk of carcinogenic or reprotoxic effects related to their trade, such health risks cannot be ruled out. Therefore, preventive efforts to diminish occupational exposures to hairdressing chemicals should be targeted.

Authors: Željka Babić, Marija Macan, Zrinka Franić, Sarah Hallmann, Martin S Havmose, Jeanne D Johansen, Swen M John, Cara Symanzik, Wolfgang Uter, Patricia Weinert, Henk F van der Molen, Sanja Kezic, Rajka Turk, Jelena Macan

Full Source: Journal of occupational health 2022 Jan;64(1):e12351. doi: 10.1002/1348-9585.12351.

## The associations of prenatal exposure to PM 2.5 and its constituents with fetal growth: A prospective birth cohort in Beijing, China

2022-08-25

Background: Limited studies investigated the association of prenatal exposure to PM2.5 and fetal growth measured by ultrasound with inconsistent results. No study evaluated the effect of PM2.5 constituents on fetal growth in utero. We aimed to investigated whether prenatal exposure to PM2.5 and its constituents was associated with fetal growth measured by ultrasound.

Methods: A total of 4319 eligible pregnant women in Peking University Birth Cohort in Tongzhou (PKUBC-T) were included in the study. Based on mothers' residential addresses, we estimated prenatal PM2.5 concentrations with a satellite-based spatiotemporal model and PM2.5 constituents concentrations with a modified Community Multiscale Air Quality model. Fetal growth parameters of abdominal circumference (AC), head circumference (HC), and femur length (FL) were measured by ultrasound and then estimated fetal weight (EFW) was calculated. We calculated sex and gestational age-specific fetal growth Z-score and then defined the corresponding fetal undergrowth. Generalized estimating

Background:
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**Bulletin Board** 

**Technical** 

**CHEMWATCH** 

SEP. 02, 2022

equation was used to investigate the association of PM2.5 and its constituents with fetal growth Z-score and fetal undergrowth. Results: Prenatal exposure to PM2.5, OC, EC, SO42-, NH4+, or NO3-was consistently associated with decreased Z-scores of fetal growth parameters (AC, HC, FL, EFW). One IQR increase of PM2.5, OC, EC, SO42-, NH4+, or NO3- was associated with -0.183 [95% confident interval (CI): -0.225, -0.141], -0.144 (95%CI: -0.181, -0.107), -0.123 (95%CI: -0.160, -0.085), -0.035 (95%CI: -0.055, -0.015), -0.095 (95%CI: -0.126, -0.064), and -0.124 (95%CI: -0.159, -0.088) decrease in EFW Z-score, respectively. Prenatal exposure to PM2.5, OC, EC, SO42-, NH4+, or NO3- was also associated with higher risk of fetal AC, HC, FL or EFW undergrowth.

Conclusion: The study identified that prenatal exposure to PM2.5 or its constituents was associated with impaired fetal growth. The findings provided evidence that control measures for PM2.5 constituents should be implemented for further promoting fetal growth.

Authors: Shuang Zhou, Tiantian Li, Na Han, Yi Zhang, Gongbo Chen, Yuelong Ji, Qin Li, Jue Liu, Hui Wang, Jianlin Hu, Ting Liu, Yuming Guo, Hai-Jun Wang

Full Source: Environmental research 2022 Aug 25;214(Pt 4):114196. doi: 10.1016/j.envres.2022.114196.

### **OCCUPATIONAL**

Temporary and Permanent Auditory Effects Associated with Occupational Coexposure to Low Levels of Noise and Solvents

2022-08-11

This study aimed to assess temporary and permanent auditory effects associated with occupational coexposure to low levels of noise and solvents. Cross-sectional study with 25 printing industry workers simultaneously exposed to low noise (<80 dBA TWA) and low levels of solvents. The control group consisted of 29 industry workers without the selected exposures. Participants answered a questionnaire and underwent auditory tests. Auditory fatigue was measured by comparing the acoustic reflex threshold before and after the workday. Workers coexposed to solvents and noise showed significantly worse results in auditory tests in comparison with the participants in the control group. Auditory brainstem response results showed differences in III-V interpeak intervals (p = 0.046 in right ear; p = 0.039 in left ear). Mean dichotic digits scores (exposed = 89.5  $\pm$  13.33; controls = 96.40  $\pm$  4.46) were only different in the left

This study aimed to assess temporary and permanent auditory effects associated with occupational coexposure to low levels of noise and solvents.



ear (p = 0.054). The comparison of pre and postacoustic reflex testing indicated mean differences (p = 0.032) between the exposed (4.58  $\pm$  6.8) and controls (0  $\pm$  4.62) groups. This study provides evidence of a possible temporary effect (hearing fatigue) at the level of the acoustic reflex of the stapedius muscle. The permanent effects were identified mainly at the level of the high brainstem and in the auditory ability of binaural integration.

Authors: Vanessa Bohn, Thais C Morata, Simone Roggia, Fernanda Zucki, Benoît Pouyatos, Thomas Venet, Edward Krieg, Maria Renata José, Adriana B M de Lacerda

Full Source: International journal of environmental research and public health 2022 Aug 11;19(16):9894. doi: 10.3390/ijerph19169894.

## Epigenome-wide association studies of occupational exposure to benzene and formaldehyde

2022-08-25

Relationship between certain myeloid neoplasms and exposure to benzene or formaldehyde. DNA methylation could underlie benzeneand formaldehyde-induced health outcomes, but data in exposed human populations are limited. We conducted two cross-sectional epigenome-wide association studies (EWAS), one in workers exposed to benzene and another in workers exposed to formaldehyde. Using HumanMethylation450 BeadChips, we investigated differences in blood cell DNA methylation among 50 benzene-exposed subjects and 48 controls, and among 31 formaldehyde-exposed subjects and 40 controls. We performed CpG-level and regional-level analyses. In the benzene EWAS, we found genome-wide significant alterations, i.e., FWER-controlled P-values < 0.05, in the mean and variance of methylation at 22 and 318 CpG sites, respectively, and in mean methylation of a large genomic region. Pathway analysis of genes corresponding to benzene-associated differential methylation sites revealed an impact on the AMPK signalling pathway. In formaldehyde-exposed subjects compared to controls, 9 CpGs in the DUSP22 gene promoter had genome-wide significant decreased methylation variability and a large region of the HOXA5 promoter with 44 CpGs was hypomethylated. Our findings suggest that DNA methylation may contribute to the pathogenesis of diseases related to benzene and formaldehyde exposure. Aberrant expression and methylation of HOXA5 previously has been shown to be clinically significant in myeloid leukaemias. The tumour suppressor gene DUSP22 is a potential biomarker

Relationship between certain myeloid neoplasms and exposure to benzene or formaldehyde. Bulletin Board

Technical

SEP. 02, 2022

of exposure to formaldehyde, and irregularities have been associated with multiple exposures and diseases.

Authors: Rachael V Phillips, Linqing Wei, Andres Cardenas, Alan E Hubbard, Cliona M McHale, Roel Vermeulen, Hu Wei, Martyn T Smith, Luoping Zhang, Qing Lan, Nathaniel Rothman Full Source: Epigenetics 2022 Aug 25;1-19. doi: 10.1080/15592294.2022.2115604.