

REFERENCE

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Nano-captured OP-Hydrolyzing Enzymes in OP Antagonism: Cholinesterase Inhibition as Indicator of OP Intoxication

Dendritic poly(2-alkyloxazoline) based polymer, a hyperbranched poly(2-ethyloxazoline) with a $\text{CH}_3(\text{CH}_2)_{17}$ modified surface, was studied as a new carrier system for the organophosphorus (OP)-hydrolyzing recombinant enzymes, organophosphorus acid anhydrolase (OPAA) and organophosphorus hydrolase (OPH). Paraoxon and diisopropylfluorophosphate (DFP) were used as model compounds for organophosphorous agricultural pesticides and chemical warfare agents, such as sarin and soman.

This study suggests that acetylcholinesterase (AChE) activity can serve as an indicator of in vivo antidotal protection. Reactivation of the OP-inhibited AChE was proportional to the pralidoxime (2-PAM) concentration, and the AChE level was proportional to the concentrations of DFP or paraoxon and the nano-captured OPAA (DP-OPAA) or OPH (DP-OPH), respectively. These studies also compare the in vivo efficacy expressed as "Antidotal Potency Ratio" (LD_{50} of paraoxon or DFP with the antagonists/ LD_{50} of paraoxon or DFP without the antagonists) of the two nano-captured enzymes as antidotal systems. The studies demonstrate a synergistic enhancement of the antagonistic therapies, since the antidotal protection of 2-PAM + atropine against DFP and paraoxon is approximately 8 and 60 x LD_{50} , respectively. These studies represent a practical application of polymeric nano-capsules as enzyme carriers in drug antidotal therapy.

REFERENCE

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Changes in lipid raft composition as early events in nanoparticle-induced proliferative signaling

Carbon nanoparticles (CNP) have been shown to trigger pathogenic signaling pathways via MAP-kinases on the level of the membrane receptors EGF-R and $\beta 1$ -integrins. CNP-dependent ROS formation appears to be a critical step in these processes. In the current study, initial events of nanoparticle-cell interaction were investigated on the level of membrane microdomains (lipid rafts) as signaling platforms as well as membrane-located src kinases (SFK). Lipid rafts from rat lung epithelial cells (RLE-6TN), treated with carbon nanoparticles (Printex 90) were analysed for specific changes in protein as well as in lipid composition. Using inhibitor strategies, SFK were identified as integral parts of the described signaling cascade.

Lipid analyses of membrane fractions revealed a nanoparticle-dependent increase of ceramides in these domains, which was accompanied by a decrease of cholesterol and sphingomyelin levels. Furthermore, CNP induced a depletion of EGF-R and SFK which are present in raft fractions in untreated cells. The causal link between lipid changes and initial effects on signaling proteins was investigated by adding external ceramide. This strategy, mimicking CNP-induced lipid changes, resulted in a reduction of EGF-R and SFK in the lipid raft fraction. Moreover, external ceramide induced an activation of SFK and Erk1/2. Pretreatment with α -tocopherol which has antioxidative properties, was able to inhibit the CNP-induced protein depletion in raft fractions and the activation of SFK and Erk1/2.

Altogether, these results support the hypothesis that ROS-dependent generation of ceramide within microdomains is an initial event of CNP-specific pathogenic signaling.

REFERENCE

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An integrated program of characterisation and effects evaluation of nanoparticles in the aquatic environment

Society is facing a new paradigm once nanomaterials do not behave in a predictable way. Understanding the role of nanoparticles on the human health and the environment is a challenge and new knowledge is needed. The project "Integrated evaluation of nanomaterials: Characterisation and Assessment of Environmental Toxicity-NanoTox", supported by the Portuguese Foundation on Science and Technology (2010-2013) is based on the need to characterise nanomaterials and nanoparticle suspensions and to evaluate their effects on several organisms. Nanodiamond, titanium and silicon dioxides were selected as materials for the study. The characterisation is complex and needs an effort to gather different research groups with different expertise and high-tech equipment. The following techniques will be used: Laser Induced Breakdown Detection; Atomic Force Microscopy; X-Ray diffraction; Scanning Electron Microscopy / EDX; Transmission Electron Microscopy; Infrared spectroscopy. The visualization and study of particles distribution in the exposed organisms as well as the evaluation of effects at different levels constitutes important pillars in the overall study. The following methods will be used as "classical" bioassays: *Pseudomonas* test, Microtox® test, Algal test, *Daphnia* tests, Lemna test and Zebra fish test. This work will be complemented with studies on histology and ultrastructure observations and studies on the protein expression profiling in selected species.

The formed consortium that aggregates partners with different skills in the area of science materials, biology and environment, will contribute with new knowledge supporting the European strategy for nanotechnology and also the revision of the European regulation on chemicals - REACH.

REFERENCE

P106

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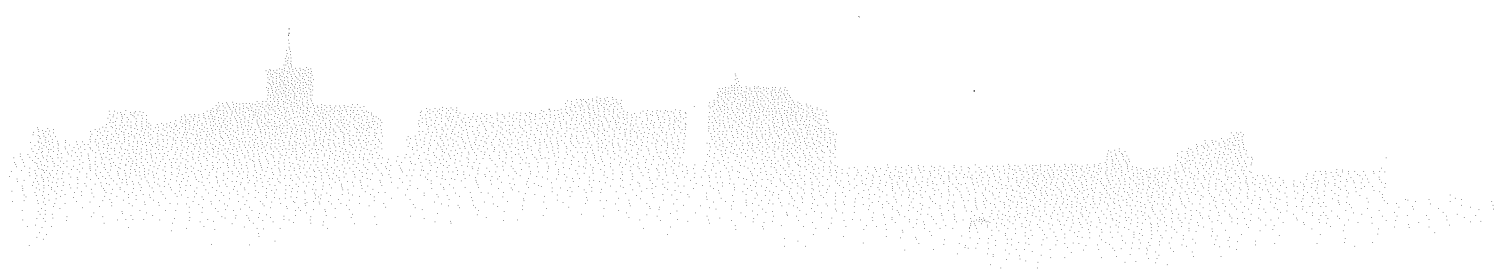
Carboxylic acid functionalized and non-functionalized single wall carbon nanotubes induce cytotoxic effects on human endothelial cells (HUVEC)

Nanotechnology is rapidly advancing, with more than 300 nanoproducts already on the market. In this nanotechnological development, carbon nanotubes (CNTs) have attracted a great deal of attention as they have shown many applications in materials science, electronics, etc. Thus, it is predicted that tons of CNTs will be produced worldwide every year. Several studies have revealed that the same properties that make nanoparticles so unique could also be responsible for their potential toxicity. Considering that unavoidable exposure is expected, in vitro studies become extremely relevant, as they could provide rapid information on how nanoparticles interact with human cells. In this regard, the aim of the present work was to investigate the cytotoxicity of single wall carbon nanotubes (SWCNT) on human endothelial cells (HUVEC) evaluating the influence of acid carboxylic functionalization and also the exposure time (24 and 48h). Biomarkers assessed were neutral red uptake (NR), protein content (PT), a tetrazolium salt (MTS) metabolism and cell viability by means of the trypan blue exclusion test (TBET). Overall, results indicated time and concentration -dependent cytotoxic effects on the HUVEC cells with no clear influence of carboxylic acid functionalization.

Acknowledgments: authors thank Consejería de Salud de la Junta de Andalucía (Project PI-00192/2007) the financial support of this study.

Nanotoxicology 2010 **EDINBURGH**

MEETING PROGRAMME & ABSTRACTS



2ND - 4TH JUNE 2010, EDINBURGH UK