# Thursday, December 12th

**Session: NANOSAFER BY DESIGN**

**14h00 – 16h30**

**Keynote speaker: Sébastien ARTOUS**
*SafeTiPaint project: towards the eco-design of a photocatalytic paint*

*Givry - Savigny room*

# Abstracts

**Thematic Session: Nanosafer by design**
**Keywords: quantum dots, core/shell structure, toxicity, primary keratinocyte**

# Toxicological impact of safer-by-design In-based quantum dots

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Semiconductor nanocrystals also known as quantum dots (QDs) possess unique optical properties, which make them attractive for their utilization in optoelectronic devices and for biomedical applications. During their life cycle, the aging of quantum dots can lead to dissolution and induce high toxicity due to the release of toxic chemical compounds. In this context, InP-based QDs show a lower intrinsic toxicity in comparison to the more popular heavy metal containing Cd-based QDs. However, studies focusing on the InP core material and the influence of different shell designs on the toxicity potential are still limited. Our laboratory synthetizes different indium-based QDs (composed of a core of In, P and Zn, which is covered with a single or a double shell) following a safer by design approach with the aim of producing QDs that are less toxic.

In this study, we investigated the photophysical characterization and toxicity of InZnP QDs covered with a single shell composed of ZnSe/ZnS, and QDs with double shells, where this first shell was further covered with a layer of ZnS. Primary human keratinocytes were exposed to these QDs, either pristine or after aging in a weathering chamber.

Our results show a transformation and a dissolution of QDs after aging. QDs modify zinc homeostasis genes expression in cells and transformed QDs are much more toxic than pristine QDs.

Conclusively, these results confirm that a careful shell design of QDs can reduce their toxicity but does not totally prevent them from dissolving and releasing potentially toxic In ions.

**Thematic Session:** Nanosafer by design
**Keywords:** Nanoparticles, Drug delivery, nanotoxicity, immunotoxicity, surface properties

# Immunotoxicity of poly(lactic-co-glycolic acid) nanoparticles: influence of surface properties on dendritic cell activation

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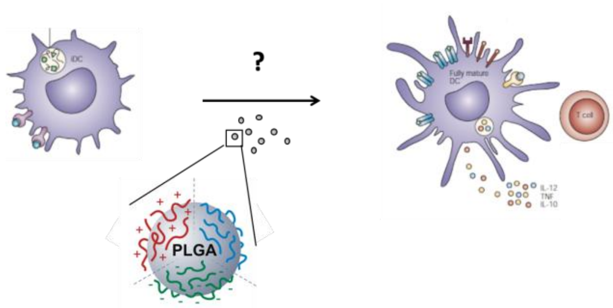
Nanoparticles (NPs) can interact with the immune system by causing its activation to fight tumors or for vaccination. During this activation, dendritic cells (DCs) are effective in generating robust immune response. However, the effect of nanomaterials on dendritic cell (DC) maturation, and the associated adjuvant effect, should be assessed as a novel biocompatibility criteria for biomaterials since immune consequences may constitute potential complications in nanomedicine. Among emerging biomaterials, poly(lactic-co-glycolic acid) (PLGA) NPs are widely explored for various applications in which the degree of desired adjuvant effect may vary. As contradictory results are reported regarding their effects on DCs, we aimed at clarifying this point with particular emphasis on the relative impact of particle surface properties. To that end, NP uptake and effects on the viability, phenotype, and secretory activity of DC primary cultures. Intracellular signaling pathways were explored and evaluated. Immature human and murine DCs were exposed to cationic, neutral, or anionic PLGA NPs. Particle uptake was assessed by both confocal microscopy and flow cytometry. Cell viability was then evaluated prior to the study of maturation by examination of both surface marker expression and cytokine release. Our results demonstrate that PLGA NPs are rapidly engulfed by DCs and do not exert cytotoxic effects. However, upon exposure to PLGA NPs, DCs showed phenotypes and cytokine secretion profiles consistent with maturation which resulted, at least in part, from the transient intracellular activation of mitogen-activated protein kinases (MAPKs). Interestingly, NP-specific stimulation patterns were observed since NP surface properties had a sensible influence on the various parameters measured.



**Thematic Session:** Nanomaterials
**Keywords:** Organometallic nanoparticles, cellulose nanocrystals, hybrid materials

# Organometallic hybrid nanoparticles for safer materials: preparation and physico-chemical characterization

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Regarding environmental awareness, there is a crucial need to think a voluntary guidance on health & safety for nanotechnology development. In this context, the use of biopolymers with environmental sustainability, low cost, low energy consumption, together with high biodegradability is therefore ideally positioned for innovative strategy. Nanoparticles such as metal oxide can exhibit a large range of metallic, semiconductor or insulator characteristics. In a near future these properties will be combined to thermal, mechanical, energy reduction and other physico-chemical properties of engineered nanomaterials. A new type of hybrid nanomatrices is developed that can decrease the impact of such hazard, or potentially hazard, nanoparticles (e.g., Ag, Cu, TiO2) associating them to bio-based nanoparticles for high performance greener materials. We present the various physico-chemical technics that allow a fine characterization of such hybrid systems by different techniques such as UV-VIS, electron microscopy, atomic absorption spectroscopy and X-ray spectroscopy (XANES-EXAFS).

**Thematic Session:** Nanosafer by design

**Keywords:** silver nanoparticles, thiolate, biocide, self-assembly, bio-inspired

# Safer-by-Design Biocide Made of Tri-thiol Bridged Silver Nanoparticle Assemblies

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Silver nanoparticles (AgNPs) are efficient biocide increasingly used in consumer products and medical devices. Their activity is due to their capacity to release Ag(I) ions making them a long-lasting biocide but AgNPs themselves are usually easily released from the product. Besides, AgNPs are highly sensitive to various chemical environment that triggers their transformation, decreasing their activity[1]. Altogether, AgNPs widespread use leads to bacterial resistance and safety concerns. There is thus a crucial need for improvements.

The behavior of AgNPs in presence of thiol molecules is highly versatile either inducing dissolution into ions[2] or forming a coating that protects the NP[3,4]. These phenomena depend on the architecture of the molecules and the number of thiols but remains unpredictable to date. Using a bio-inspired symmetric tri-thiol molecule, we observed a novel behavior, the assembly of AgNPs together[5]. This process leads to the formation of a stable nanomaterial, less sensitive to chemical environment with AgNPs completely covered by organic molecules tightly bound *via* their thiol functions[5]. Very interestingly, these AgNP assemblies are not toxic for human cells, while they deliver sufficient Ag(I) amount for biocidal activity with no release of AgNPs, which are insensitive to transformations within the nanomaterial. Therefore, AgNP assemblies can be considered as safer-by-design and innovative biocides.

1- Marchioni et al., Coord Chem Rev, 2018, 118-136.
2- Marchioni et al., Environ. Sci. Nano, 2018, 1911–1920.
3- Liu et al., ACS Nano, 2010, 6903–6913.
4- Porcaro et al., Materials, 2016, 1028.
5- Marchioni et al., Nanoscale horizons, in press.

**Thematic Session:** (Surface & interface at the nanoscale, Nanosafer by design)
**Keywords:** (Silver nano wires- Printed paper electronic-AFM-Force)

## Safe design of recycling Ag-nanowire on printed paper electronic

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Abstract

Silver nanowires (Ag-NW) have in recent years attracted considerable attention due to their interesting fundamental properties and the exciting prospects for producing printed circuits on a variety of supports, including paper, enabling complex electronic devices to be fabricated in unconventional materials such as creative paper products.

Compared to the conventional printed circuit board (PCB) technology, paper offers important advantages. For example, paper is inexpensive and can decompose easily, it can be folded and unfolded easily, electronics based on paper can be stored in smaller spaces or made to form 3D self-standing structures. Finally, with its porous and breathable nature, paper can potentially be applied in disposable components for adhesives and clinical diagnosis, such as being combined with portable analytical devices.

The safe and successful development of paper printed electronics requires careful assessment of the potential negative impacts at all stages of the product lifecycle. In this project we focused on improving our understanding on Ag-NW and nano cellulose fibre interactions at the microscopic level, in order to design more efficient recycling processes, and thus to go towards a circular economy.

Thanks to atomic force microscopy, we apply force for studying adhesion force between Ag-NW and nano cellulose fibers on various substrates. We studied the force required to pull off the wire by applying normal force across a Ag-NW surface by an AFM tip. We observed that the force necessary to drag the wire decreases with interface area, i.e. when the wire is less embedded in CNF. We also observe dragging force increasing with increasing wire diameter.

**Thematic Session:** **NanoSafer by Design**

**Keywords:** (law; due diligence; nanosafety compliance; nanoregulation; preventing liability)

## Title Global Health Impacts of Nanotechnology:

## Laws Governing Nanosafety and Nanomaterials

**Author Dr. Ilise L. Feitshans JD and ScM and DIR [1], Laurent Charlet[1],**

"Nanotechnology is for All": new economic frontiers with wide horizons, promising new cures for ancient diseases, strong packaging to protect goods from contamination, cheaper consumer products and new medicines to fight cancer, and creating objects not yet imagined in food, healthcare, agriculture, communications and national security.

People using these new materials in the workplace or as consumers encounter applied nanotechnology in both: new materials in the worksite with attendant risks and miraculous treatments for worker rehabilitation using nanomedicine. How can the benefits of nanotechnology be realized while reducing risk to public health?

Not surprisingly, new laws have emerged in nations and in the international legal scene to address nanotechnology. This presentation explores uncharted international law of nanotechnology, some national laws and the unprecedented WHO guidelines protecting workers who are exposed to nanomaterials from the standpoint of PPE and compliance with exposure recommendations as applied to nanopesticides nanofertilizers and nanosilver. This presentation concludes by moving from the theory behind nanoregulation to the practical:

How do we do this? Due diligence is your best friend. Therefore this presentation describes the key components of World Health Organization (WHO) guidelines about workplace exposure to nanomaterials, USA NIOSH Recommended Exposure Limits (RELs) for titanium dioxide and nanosilver, EU REACh USA toxic Substances Control Act (TSCA) and international initiatives designed to address nanotechnology.

**These Comments are *BASED ON THE BOOK Global Health Impacts of Nanotechnology Law: A Tool for Stakeholder Engagement***

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