Smart Multifunctional Materials for Nanomedicine Focus Topic

Room 301 - Session SM-WeM

Smart Multifunctional Materials for Nanomedicine and Theranostics

Moderators: Diego La Mendola, University of Pisa, Italy, **François Reniers**, Université Libre de Bruxelles, Belgium, **Cristina Satriano**, University of Catania, Italy

8:40am **SM-WeM-3 Plasma-Enabled Switchable Surfaces: Going from Molecules to Bacteria***, U. Cvelbar,* ***Martina Modic,*** Jozef Stefan Institute, Slovenia **INVITED**

Switchable and smart surfaces have been a goal in the chemistry community for more than a decade. Although much work has been done in converting surface functionalities going from one function to another, like multiple times reported hydrophobic to hydrophilic or reversible, little has been understood beyond surface morphology, surface energies and surface chemistry initiated. The case of switchable surfaces became even more complex when dealing with macromolecules going down to macro objects like viruses or bacteria. Here plasmas offer a unique opportunity to modify surfaces, not only chemically but also on the atomic scale, interfering and modifying or exchanging chemical bonds in materials or their crystal structures. For this reason, this lecture will try to challenge these ideas, address them on a nanoscopic level and present an overview of results ranging from simple surface properties, macromolecule interactions and at the end, effects on viruses and bacteria interacting with these surfaces.

9:20am **SM-WeM-5 Cisplatin-Loaded Pd Nanoparticles as Bimodal Theranostic Nanomedicine in the Tumor Treatment***, A. Bellissima, G. Scivoletto, L. Cucci, V. Sanfilippo,* University of Catania, Italy*; A. De Bonis,* University of Basilicata, Italy*; R. Fiorenza, S. Scirè,* University of Catania, Italy*; V. Notarstefano, E. Giorgini,* Polytechnic University of Marche, Italy*;* ***Cristina Satriano,*** University of Catania, Italy

In this work, we developed a hybrid nano delivery system made of palladium nanoparticles (NPs) and cisplatin (CisPt), an alkylating drug commonly used to treat various types of malignancies. NPs were synthesized via a new green method based on the use of D-glucose and polyvinylpyrrolidone (PVP) as reducing/stabilizing and capping agents, respectively. Plasmonic properties and photocatalytic activity of the Pd NPs, carried out to prove their capability to act as bimodal theranostic nanomedicine, unveiled a plasmon peak at around 274 nm, well matching an optical size of 5 nm for spherical nanoparticles, and significant H_2 evolution. XPS, XRD, and TEM confirmed the chemical composition and morphology of the NPs. The hybrid NP-drug assembly (Pd@CisPt) was characterized by UV-visible spectroscopy to correlate the changes in the plasmonic peak to the interaction of CisPt with the NP surface as by ICP-OES, to quantitatively estimate the drug loading. AFM and DLS measurements confirmed the strong association of the drug to the nanoparticle surface. The SOD-like activity was tested in a cell-free environment to confirm the maintenance in the Pd@CisPt sample of the antioxidant capability of Pd nanoparticles. The Pd@CisPt theranostic nano platform was tested in prostate cancer cells (PC-3 line) in terms of cytotoxicity, to prove the antitumoral action of the developed nanomedicine. Raman microspectroscopy (RMS) with PCA indicated a condition of protein misfolding/unfolding, directly or indirectly due to cisplatin and/or palladium treatment, and DNA damage especially enhanced upon the treatment with PdNPs@CisPt. The MitoSOX assay confirmed an increase in ROS generation, thus proving that oxidative damage is a key factor for the induction of antitumoral action. LSM cell imaging evidenced dynamic processes at the level of subcellular compartments and modulation of intracellular copper ions accumulation. Finally, cell migration studies upon the treatment with Pd@CisPt evidenced an intermediate response between the inhibitory effect by CisPt and the enhanced rate of cell migration for the metal NPs alone, which pointed out the promising potential of the developed theranostic nanomedicine in tissue regeneration.

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9:40am **SM-WeM-6 Old Drugs for a Golden Future: Clinically Established Au-Based Complexes…from Repurposing to Potential Application in Nanomedicine***,* ***Tiziano Marzo****, L. Chiaverini, D. La Mendola,* University of Pisa, Department of Pharmacy, Italy

Inorganic compounds played a key role in the pioneering times of modern pharmacology starting from the late 19th century. Gold, Bismuth, Antimony, but also Mercury compounds were widely used to treat a variety of diseases, mostly infectious, such as tuberculosis and syphilis, and a variety of parasitic diseases.[1,2] Their use in recent time underwent a rapid decline mainly because of concerns on their systemic toxicity. However, some Gold, Platinum or Arsenic compound is still widely used for clinical applications. Among them, antiarthritic compounds such as Auranofin (AF) or Aurothiomalate (ATM) found important role as repurposed drugs for treating cancer or infections.[3] Interestingly, the medicinal properties of gold(I) compounds might be even improved using biocompatible nanostructures for their delivery.[4] In this frame, we proceeded with the preparation of a nanoformulation of Et_3PAuCl, this latter being an AF analogue endowed with promising anticancer properties. The well-known PLGA-PEG nanoparticles (NPs) were chosen for the encapsulation process and functionalized with a biocompatible fluorescent probe for their tracking in cell. After the characterization of the NPs, we performed a few biological tests on the Et_3PAuCl loaded nanoparticles in comparison to the free Et_3PAuCl drug in 2D and 3D (HCT-116) colorectal cancer models. The biological activity and the mechanistic aspects for the anticancer effects of the loaded NPs are comparatively and critically discussed.

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2- D. Cirri, F. Bartoli, A. Pratesi, E. Baglini, E. Barresi, T. Marzo, Biomedicines, 2021, 9(5), 504.

3- T. Marzo, D. La Mendola, Inorganics, 2021, 9, 46.

4- A. Menconi, T. Marzo, L. Massai, A. Pratesi, M. Severi, G. Petroni, L. Antonuzzo, L. Messori, S. Pillozzi, D. Cirri, Biometals, 2021, 34, 867–879.

11:00am **SM-WeM-10 Plasmonic Tuning of Go-Based Nanosheets by Plasmonic Noble Metal Nanorods for Self-Cleaning Photothermal Surfaces to Fight Surface Contamination***,* ***Vanessa Sanfilippo****, T. Pascal, A. Foti,* University of Catania, Department of Chemical Sciences, Italy*; A. Fraix, S. Petralia, G. Forte,* University of Catania, Department of Drug and Health Sciences, Italy*; C. Fortuna,* University of Catania, Department of Chemical Sciences , Italy*; A. Giuffrida, C. Satriano,* University of Catania, Department of Chemical Sciences, Italy

In this study, we propose a novel hybrid 2D nanomaterial based on thiolated reduced graphene oxide (rGOSH) sheets and silver (Ag) or gold (Au) nanorods (NRs). The goal is to integrate the enhanced self-cleaning properties (super-hydrophobicity) and the plasmonic tuning of photothermal response of the hybrid nanoplatform (GO-NR), to the intrinsic antibacterial properties of each component (GO, Ag, Au), to inhibit surface contamination. Both experimental and theoretical studies were focused on the design, the synthesis, and the physicochemical/biochemical/cellular characterization of the hybrids. A multitechnique approach by UV-visible spectroscopy (UV-VIS), dynamic light scattering (DLS), Zeta potential (ZP), atomic force microscopy (AFM), and water contact angle (WCA) measurements was used to scrutinize the plasmonic features (including the optical size), the hydrodynamic size and the surface charge, the topography and the surface free energy, respectively. The photothermal properties of the hybrids were examined in solution following the increase of temperature under irradiation with CW laser using a FLIR C3 thermal imaging camera. Proof-of-work *in vitro* cellular experiments on human prostate cancer cells (PC-3 line) and murine fibroblasts (L929 line) were carried out to test the nanotoxicity of the hybrids as well as their capability to induce oxidative stress by the production of reactive oxygen species (ROS). Intracellular imaging using confocal laser scanning microscopy (LSM) was performed to evaluate the mechanism of interaction and internalization of hybrid systems on the studied cell lines.

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11:20am **SM-WeM-11 Green Synthesis of Metal Nanoparticles for Wound Healing Applications**, ***Alice Foti,*** *V. Sanfilippo,* University of Catania, Italy*; V. Caruso, R. Inturri, P. Amico, S. Vaccaro,* Fidia Farmaceutici S.p.A., Italy*; C. Satriano,* University of Catania, Italy

Wound healing is a complex process involving multiple cell strains and the related products trying to regenerate and repair the damaged tissue. The multidisciplinary field of nanotechnology that includes, among others, interface and colloid science, molecular biology, and engineering, offers a huge range of applications, including nanomedicine. Metallic nanoparticles (NPs), 1-100 nanometers (nm) in size, have unique physicochemical, optical, and biological properties that gives them a great potential in treating several diseases. Indeed, it is essential to find controlled and reproducible synthetic methods to achieve biocompatibility and the desired therapeutic properties, giving a ground-breaking approach towards the promotion of wound healing. This work focuses on a green synthesis approach to synthesize gold (Au), silver (Ag), and palladium (Pd) NPs, aiming to promote the proliferation of cells in wound healing. Moreover, NPs surface, is capped with hyaluronic acid (HA), known to improve their biocompatibility and promote endothelial regeneration. Physicochemical and biological characterization of the synthesized NPs was assessed with a multi-technique approach. Optical properties were studied with UV-vis spectroscopy; the increase of the hydrodynamic diameter after the conjugation with HA was investigated with dynamic light scattering (DLS) experiments; and the measurement of viscosity was performed with a viscosimeter. Biological tests were assessed on fibroblast (L-929) cells. Particularly, cytotoxicity was inspected via MTT assay; wound healing potential was investigated by *in vitro* wound scratch assay; sub-cellular interactions were analyzed with confocal microscopy.

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11:40am **SM-WeM-12 Nanoparticles Loaded with Histidine Rich Peptides for Wound Healing**, ***Diego La Mendola,*** Università di Pisa, Italy*; L. Chiaverini, T. Marzo,* University of Pisa, Italy

The histidine-proline-rich glycoprotein (HPRG) is a single polypeptide chain protein of 70–75 kDa, with a multidomain structure. In humans, the protein is synthesized in the liver and is present in plasma at relatively high concentrations of 100–150 μg/mL (1.5 μM) [1]. HPRG ability to simultaneously interact with a large number of protein ligands and has been implicated in the regulation of various physiological and pathological processes including the formation of immune complexes, apoptotic/necrotic and pathogen clearance, cell adhesion, antimicrobial activity, anti-/pro-angiogenic activity, coagulation and fibrinolysis. Interestingly, these processes are often associated with sites of tissue injury or tumour growth, where the concentration and distribution of copper and zinc ions is known to vary.

In this work, we tackled the assembling of hybrid platforms made of gold or silver nanoparticles (NPs) functionalized with the peptides belonging to HPRG protein, and rich in histidine residues, in order to achieve a modulation of the angiogenic process in the wound healing treatment in presence/absence of divalent metal ions.

These new systems exploit the synergic effects of different components in the regeneration of damaged tissues.

Nanoparticles were characterized by UV-visible spectroscopy, to scrutinise the peptide binding to Au, by monitoring the changes in the plasmonic peak (AuNP). Atomic force microscopy and dynamic light scattering analyses confirmed a strong association of the peptides to the plasmonic nanoparticles.

Cellular experiments on human foreskin fibroblasts demonstrated the low cytotoxicity of the hybrid assemblies and their high ability to promote wound closure and fibroblasts migration. The activity of Au-GO-ANG were also tested in the presence of copper and/or zinc ions. Besides, cell imaging by confocal microscopy revealed synergic dynamic processes modulated by the different sub-cellular structures (lysosomes, mitochondria, cell cytoskeleton). The obtained results evidence the promising applications of the synthesized nanoparticles for wound care treatment and tissue regeneration.

The authors thank the University of Pisa, “PRA – Progetti di Ricerca di Ateneo” Institutional Research Grants – Project no. PRA_2020_58) and Rating Ateneo 2019-2020 for financial support.

[1] K.M. Priebatsch, M. Kvansakul, I.K.H. Poon, M.D. Hulett, Biomolecules, 2017, 7, 22.

Author Index

Bold page numbers indicate presenter

— A —
Amico, P.: SM-WeM-11, 2
— B —
Bellissima, A.: SM-WeM-5, 1
— C —
Caruso, V.: SM-WeM-11, 2
Chiaverini, L.: SM-WeM-12, 2; SM-WeM-6, 1
Cucci, L.: SM-WeM-5, 1
Cvelbar, U.: SM-WeM-3, 1
— D —
De Bonis, A.: SM-WeM-5, 1
— F —
Fiorenza, R.: SM-WeM-5, 1
Forte, G.: SM-WeM-10, 1
Fortuna, C.: SM-WeM-10, 1
Foti, A.: SM-WeM-10, 1; SM-WeM-11, **2**
Fraix, A.: SM-WeM-10, 1
— G —
Giorgini, E.: SM-WeM-5, 1
Giuffrida, A.: SM-WeM-10, 1
— I —
Inturri, R.: SM-WeM-11, 2
— L —
La Mendola, D.: SM-WeM-12, **2**; SM-WeM-6, 1
— M —
Marzo, T.: SM-WeM-12, 2; SM-WeM-6, **1**
Modic, M.: SM-WeM-3, **1**
— N —
Notarstefano, V.: SM-WeM-5, 1
— P —
Pascal, T.: SM-WeM-10, 1
Petralia, S.: SM-WeM-10, 1
— S —
Sanfilippo, V.: SM-WeM-10, **1**; SM-WeM-11, 2; SM-WeM-5, 1
Satriano, C.: SM-WeM-10, 1; SM-WeM-11, 2; SM-WeM-5, **1**
Scirè, S.: SM-WeM-5, 1
Scivoletto, G.: SM-WeM-5, 1
— V —
Vaccaro, S.: SM-WeM-11, 2