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Smart Multifunctional Materials for Nanomedicine Focus Topic

Room On Demand - Session SM-On Demand

Smart Multifunctional Materials for Nanomedicine Contributed On Demand Session

SM-On Demand-1 Cisplatin-Loaded Palladium Nanoparticles for Cancer Nanomedicine, *L. Cucci, A. Bellissima,* University of Catania, Italy*; T. Marzo, D. La Mendola,* University of Pisa, Italy*; V. Notarstefano, E. Giorgini,* Polytechnic University of Marche, Italy*;* ***Cristina Satriano****,* University of Catania, Italy

In this work, a PdNP@CisPt hybrid based on palladium nanoparticles and cisplatin was developed. Nanoparticles were synthetized via a modified redox chemistry green method, based on D-glucose and PVP as reducing and capping agents, respectively. The CisPtwas immobilized by a physisorption protocol. The characterization of the new hybrid was carried out by UV-visible spectroscopy, to correlate the changes in the plasmonic peak to the interaction of the drug with the PdNP surface, and by AFM and DLS measurements, to get insight into the morphology and size of the functionalized nanoparticles. Additionally, an ICP-AES investigation was carried out to assess the precise Pd to Pt ratio. Results confirmed the strong association of the drug to the nanoparticle surface.Noteworthy, the CisPt activity is often associated with the appearance of several side effects due to its non-specific action, including neurotoxicity, nephrotoxicity and ototoxicity [1]. On the other hand, nanomaterials have a demonstrated capability to overcome the inherent limitations of conventional drug, improving the solubility of hydrophobic molecules, increasing their half-life and selectively, thereby enhancing the therapeutic effects and diminishing the side effects [2-3]. Our cellular experiments on prostate cancer cells (PC-3 line) demonstrated that the developed systems significantly reduced cell migration (scratch test), with a synergistic action of PdNP and CisPt in the PdNP@CisPtagainst PC-3 cells. Moreover, the PdNP@CisPt showed an effective antitumour action (cell viability tests). In cell micro-Raman analyses confirmed the PdNP and PdNP@CisPt cellular internalization at the nuclear level, with a deep alteration in nucleic acids and proteins conformation and relative amount. To scrutinize the antitumor mode of action of PdNP, known to involve the interactions of the nanoparticles with the functional groups of proteins and the phosphate groups of DNA, the leakage of lactate dehydrogenase and the generation of reactive oxygen species (ROS), the xanthine oxidase assay was performed. Results confirmed an increase of ROS species generation. Cell imaging by confocal microscopy showed perturbation in mitochondrial staining, related to oxidative damage, as well as in the intracellular copper accumulation.

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[1] Bortot B, et al., Int J Nanomed 2020; 15: 4793

[2] Di Pietro P. et al., Curr Top Med Chem 2020; 16: 3069

[3] Cucci L. et al., Nanomater. 2021; 11: 201

SM-On Demand-4 A Multifunctional Plasmonic Nanoplatform of Hyaluronan-Decorated Nanoparticles Fabricated by Atmospheric Plasma for Angiogenic and Antibacterial Applications*, V. Caruso,* University of Catania, Italy*; D. Merche, J. Baneton, A. Ozkan,* Université libre de Bruxelles, Belgium*; L. Cucci,* University of Catania, Italy*; R. Inturri, G. Galizia,* Fidia Farmaceutici S.p.A, Italy*; S. Godet, L. Malet, F. Reniers,* Université libre de Bruxelles, Belgium*; S. Vaccaro,* Fidia Farmaceutici S.p.A., Italy*;* ***Cristina Satriano****,* University of Catania, Italy

Plasmas at atmospheric pressure is a simple, fast and versatile method for the synthesis of noble metal nanoparticles (NPs), such as nanosilver (Ag NP) and nanogold (Au NP) [1]. Biomolecules and natural polymers are often used as stabilizer and capping agent during the nanoparticle synthesis, to enhance their biocompatibility as well as targeting capability. In this study, hybrid systems made of an Au or Ag NP metal core capped by a soft shell of hyaluronan (HA) polymer were fabricated by the microplasma method, with reduction of the metal precursor salts in HA aqueous solution. Hyaluronan has excellent properties of water solubility, biocompatibility, biodegradation, non-toxicity, and non-immunogenicity [2]. The multifunctional character of the HA@NP nanoplatforms resulted from the combination of the optical features of the plasmonic nanoparticles as well as their intrinsic biological properties (i.e., angiogenic regulation for Au NP and antibacterial activity for Ag NP, respectively [3]) with the properties of HA, used in the MW range from 200 to 1200 kDa (low-MW HA is angiogenic and high-MW HA is anti-angiogenic [4]). The HA@NP systems were characterized, in the comparison with both bare NPs and the analogous hybrids synthetized via a chemical route, by UV-visible spectroscopy and dynamic light scattering to study the plasmonic properties of hyaluronic acid hybrids with metallic nanoparticles as well as their stability during the aging time. The cytotoxicity of the nanoplatforms was evaluated by MTT assay on the HUVEC cell line. Furthermore, their influence on the wound healing process was examined by microbiological studies on pathogenic bacteria strains of *E. coli* and *S. aureus*.

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(3) Di Pietro, P.; Strano, G.; Zuccarello, L.; Satriano, C., *Gold and Silver Nanoparticles for Applications in Theranostics*. Curr Top Med Chem 2016, 16, (27), 3069-3102.

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SM-On Demand-7 Angiogenin-Functionalized Gold Nanoparticles-Graphene Oxide Nanohybrids for Wound Care Application*, L. Cucci, L. Riela,* University of Catania, Italy*; O. Hansson,* University of Gothenburg, Sweden*; T. Marzo,* University of Pisa, Italy*; C. Satriano,* University of Catania, Italy*;* ***Diego La Mendola****,* University of Pisa, Italy

In this work, we tackled the controlled assembling of gold nanoparticles (AuNP) and graphene oxide (GO) nanosheets at different C/O ratio, followed by their surface tailoring with the angiogenin (ANG) protein.

The Au-GO-ANG nanocomposite, by exploiting the synergic effects of antioxidant and antiangiogenic AuNP [1], antimicrobial GO [2] and angiogenic ANG [3], is a very promising platform to achieve a modulation of the angiogenic process in the wound healing treatment. The Au-GO-ANG hybrids were characterized by UV-visible spectroscopy, to scrutinise the ANG binding to Au-GO, by monitoring the changes in the nanogold plasmonic peak, as well as in the graphene pàp* transition electronic band, respectively. Atomic force microscopy and dynamic light scattering analyses confirmed a strong association of the protein to both the plasmonic nanoparticles and the nanosheets.The interaction of Au-GO-ANG at the biointerface with supported lipid bilayers, inspected by means of the acoustic sensing technique of quartz crystal microbalance with dissipation monitoring, pointed to a strong perturbation of model cell membranes compared to what found with the reference nanosystems without the protein. Cellular experiments on fibroblasts and endothelial cells demonstrated the low cytotoxicity of the hybrid assemblies and their high ability to promote wound closure and cell migration. The activity of Au-GO-ANG were also tested in the presence of copper ions, that can modulate protein signaling pathways. 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 multifunctional biomaterials Au-GO-ANG for wound care treatment and tissue regeneration.

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SM-On Demand-10 Hyaluronan-Metal Gold Nanoparticle Hybrids for Targeted Tumour Cell Therapy and Antibacterial Applications*, **Vanessa Sanfilippo**, L. Cucci, V. Caruso,* University of Catania, Italy*; R. Inturri, L. Messina, S. Vaccaro,* Fidia Farmaceutici S.p.A., Italy*; T. Fontaine, A. Demaude, F. Reniers,* Université libre de Bruxelles, Belgium*; C. Satriano,* University of Catania, Italy

In this work, a multifunctional nanoplatform based on core-shell nanoparticles of antiangiogenic gold nanoparticles (AuNP) [1] capped with low molecular weight (200 kDa) hyaluronic acid (HA) was assembled at room temperature via a green, one-pot redox synthesis method [2]. HA, the main component of the extracellular matrix, is utilised to bioengineer nanoparticles for active targeting, owing to its high affinity in binding the CD44 cell receptor. A dielectric barrier discharge (DBD) plasma at atmospheric pressure [3]was used to obtain plasma-activated hyaluronic acid (p_HA), either in the presence or in the absence of Cu^{2+} (copper is also a known bactericidal agent). Different plasma parameters, including the plasma power and the carrier gas were varied.The HA- and p_HA-conjugated gold nanoparticles were scrutinised by UV-visible spectroscopy, dynamic light scattering and atomic force microscopy, which all pointed to the effective 'surface decoration' of the gold nanoparticles by hyaluronan chains. The CD44-targeting capability of HA-functionalized gold nanoparticles was tested in terms of both cytotoxicity and antibacterial activity. Cell viability assays were performed on two CD44-positive cell models, namely prostate tumour (PC-3) cells and normal human umbilical vein endothelial (HUVEC) in comparison with neuroblastoma cells (SH-SY5Y), which do not express the CD44 receptor. Results demonstrated, upon the cellular treatments by the hyaluronan-functionalized nanoparticles, an increased cytotoxicity in neuroblastoma than in prostate cancer cells compared to the bare, glucose-capped AuNP. A receptor-dependent perturbation effect on both cytoskeleton actin and lysosomal organelles was detected by scanning confocal microscopy. Cell migration studies (scratch test) on PC-3 and HUVEC confirmed the promising potentialities of the plasma technique to modulate the hybrid biointerface between the bioengineered nanoparticles and the cells. On the other hand, an enhanced inhibitory activity was found for HA-capped AuNP against both Gram-negative *Escherichia coli*and Gram-positive *Staphylococcus aureus*. These findings demonstrated the very promising potential of HA–AuNP systems for selective cytotoxicity in cancer therapy with an anti-angiogenic effect tuned by a controlled perturbation of cell migration processes in cancer metastases.

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