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Marilena Carbone

University of Rome Tor Vergata, Italy

Gold nanoparticles for exogenously induced intracellular manipulation

Magnetic nanoparticles are key building blocks for numerous innovative functional maGold nanoparticles (AuNPs) are extensively used in biomedicine as therapeutic agent, since they can be drug carriers, imaging agents, gene-regulating agents and photoresponsive therapeutics. On the other hand, especially when dealing with intracellular activity, fundamental parameters such as the pH must be taken into account and can be conveniently used to direct the action of the AuNPs. Cancer and normal cells, among other things are characterized by different pH in several intracellular compartments, a difference that can be conveniently used to modulate the action inside the cells of AuNPs. In a reversed perspective, extensive intracellular acidification may be induced by exogenous agents to cause a decrease of pH beyond the tolerance level of cancer cells. This is being implemented by designing tailored molecules which can provide protons release upon light irradiation and are also capable of cell internalization. The outcome is a system that can act as acidifying agent "on command". The monitoring is typically carried out in a non-invasive way, i.e. by infrared spectroscopy. The protons released by irradiation bind the hydrogencarbonate abundant in the cells, to yield the carbonic acid which readily dissociates in H_2O and CO_2 according to the equilibrium:

$HCO_3^- + H^+ - H_2CO_3 H_2O + CO_2$. This has the advantage of an easy monitoring, as the asymmetric stretching of the CO_2 falls in a region free from other absorptions. This method becomes even more effective, when AuNPs are coupled to photoacids, since they possibly provide a more efficient permeation of the cell membrane and a localized concentration of protons, with a consequent local swift decrease of pH. This offers the additional advantage of a carrier for cancer cell recognition. A scheme of the photosensitive compounds conjugated to the AuNPs and the effects on the cells (HEK-293) is reported in Figure1. More complex systems are under investigation, with photoacids coupled to AuNPs, which provide selectivity towards cancer cells as an effect of the irradiation.

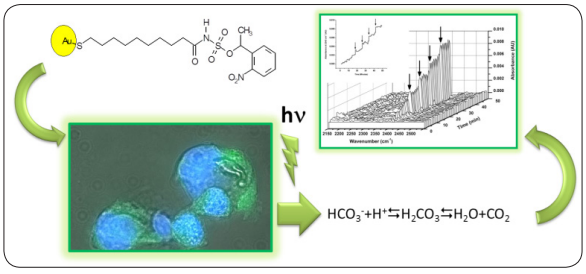

Figure 1: A scheme of the photoacid conjugated to the AuNPs. The nanoparticles were additionally functionalized with a fluorescent agent and dosed to HEK-293. Once the cells are irradiated with UV-light, protons are relesed, decreasing the pH and increasing the yield of CO_2. This effect is 400 times larger for photoacids coupled to AuNPs as compared to non-conjugated ones

Recent Publications

1. Carbone M (2017) Bi-verse relationship between gold nanoparticles and intracellular pH. J. King Saud Univ - Sci. 29(3):284-290.

2. Carbone M et al. (2016) Modulating intracellular acidification by regulating the incubation time of proton caged compounds. Eur. Biophys. J. 45(6):565-571.
3. Carbone M et al. (2015) Exogenous control over intracellular acidification: enhancement via proton caged compounds coupled to gold nanoparticles. Biochim. Biophys. Acta. 1850(11):2304-2307.
4. Sabbatella G et al. (2015) Synthesis of proton caged disulphide compounds for gold nanoparticle functionalization. New J. Chem. 39(4):2489-2496.
5. Carbone M, Zlateva T and Quaroni L (2013) Monitoring and manipulation of the pH of single cells using infrared spectromicroscopy and a molecular switch. Biophys. Acta. 1830(4):2989-2993.

Biography

Marilena Carbone graduated in Chemistry with Honor, holds a PhD in Materials Science, gained experience in several labs Europe-wide (Sweden, France, Germany, UK, Switzerland), especially synchrotron radiation facilities and currently is the Chair of Inorganic Chemistry at the University of Rome Tor Vergata, Italy. She has her expertise in designed synthesis and functionalization of nanoparticles and their application to nanobiomedicine and electrochemistry. She has developed a method of evaluating the intracellular pH, which is currently being implemented for selectivity towards cancer cells. Other streamlines include the engineering of metal oxide nanoparticles with structural and morphological dependent optical and electrochemical properties and the bespoken synthesis of metal mixed oxides with antibacterial properties in aqueous environment for water remediation and sanitation. She covered the position of Guest-Editor-In-Chief of the *Journal of King Saud University – Science,* hosted by Elsevier.

carbone@uniroma2.it

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