Antifolate functionalizated SERS-active nanovector: from cell targeting to theranostics

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Nowadays, early diagnosis of cancer is one of the main biomedical proposes that involve physics, chemistry, biology and nanotechnology. Over the last few years, several methods have been tested and developed from standard assays to really innovative techniques. One of the most exploited technologies for the early detection of cancer involves the well-known, molecular based SERS-active nanovectors [1,2] for selective bio-recognition of cancer cells. A SERS-active nanovector consists in a metallic nanoparticle (Np) core functionalized with a suitable molecular layer. Due to the excitation of the electron cloud inside the metal nanostructure, when the Np is illuminated by a light beam (visible/IR), the localization of extremely intense electromagnetic fields occurs at the metal surface [3]. This field can be exploited as a spectroscopic probe for Surface Enhanced Raman Scattering (SERS) experiments. Beside specific bio-recognition, the advantages of SERS in biomaterials investigations are the possibility of tracing Nps across sample, to produce imaging and, if necessary, to perform photothermal effect therapy. Nanovectors are often functionalized with antibodies or other small molecules, which are chosen based on specific properties of cancer cells (e.g. overexpression of certain receptors or membrane protein, differences in the cell cycle, etc.) [2,4].
In our recent work, we proved high sensitivity and selectivity of folate-conjugated Nps and suggested the possibility to add theranostic features by substituting folate with antifolate drugs [2]. We are here presenting our result in the characterization of different theranostic nanovectors (functionalized with folate and with antifolates, as aminopterine and methotrexate) performed through SERS, UV-visible and Z-potential measurements. We proved the successful functionalization of the Nps and we investigated the different spectroscopic features of these nanovectors (Fig.1). Moreover, through a titration experiment, we are able to predict how many molecules are covalently bound with the Nps.

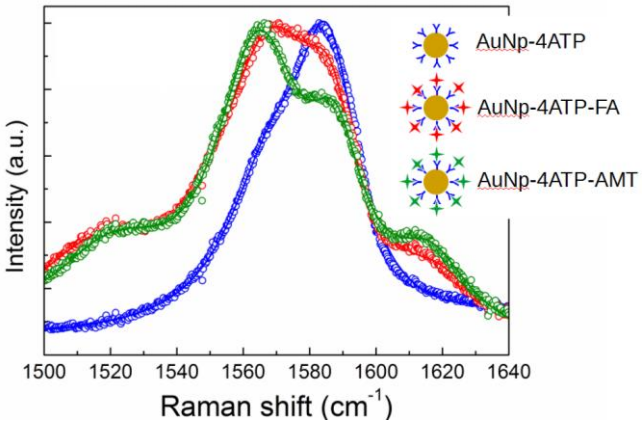

Fig.1: SERS comparison of the three nanovectors in the region of 1585 cm^{-1}: in blue the first step of functionalization of gold nanopartiles with 4-aminothiophenol (4-ATP); in red the second step of functionalization with folic acid (FA) and in green the antifolate coniugation with aminotpetrine (AMT).

[1] Salvati et al., Nanomedicine 10.23 (2015): 3495-3512.
[2] Fasolato et al., submitted to Biomaterials (2016).
[3] Fan et al., Science 328.5982 (2010): 1135-1138.
[4] Pallaoro et al. Proceedings of the National Academy of Sciences 108.40 (2011): 16559-16564.