Surface Enhanced Raman Microimaging Allows for Screening Single Cells With Different Folate Binding Capability

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In the last few decades, the development of novel spectroscopic techniques, often combining a very high sensitivity with huge spatial resolution, allowed the possibility of investigating down-scaled phenomena, as for example biochemical and biophysical processes in living systems. Among these, Surface Enhanced Raman Spectroscopy (SERS) is based on plasmonic excitations in metallic nanostructures \cite{1}. The oscillation of the free electron gas in metallic nanoparticles (Nps) causes the confinement of strong electromagnetic fields, which can be used for spectroscopy, at the Np surface. Moreover, SERS-labelled nanomaterials, such as properly functionalized Nps, paved the way for applications in the emerging field of nanomedicine \cite{2}, e.g. in the early detection of cancer. Addressing this problem, we designed a biocompatible system based on SERS-labelled gold Nps conjugated with folic acid, a biomolecule essential in cell reproduction. Folic acid receptors are overexpressed in many types of cancer cells, as these reproduce more frequently than ordinary ones \cite{3}. The presence of folate receptors on the membrane strongly depends on the physiology of the cell line considered. In this presentation, after briefly exposing the system characterization, we will illustrate the interaction of our nanobiovector with different cell cultures. SERS mapping, performed on different cells, allowed us to detect our nanovector bound to the cell membrane and, therefore, to map the presence of the folate receptors even at subcellular level. A SERS screening protocol used to measure wide cell populations allowed us not only to discriminate between healthy and cancer cells, but also to distinguish two types of cancer cells showing differential folate-receptor expression (see Fig. 1) \cite{4}. These results suggest the possibility to combine the nanovector plasmonic properties with opportune chemical conjugations, aiming at SERS-based biophysical investigations, e.g. mapping the molecular receptors on cell membranes. Preliminary results on the functionalization of the nanovector with antifolate drugs will also witness the potential theranostic application of this nanovector.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig1.png}
\caption{Sketch of the experiment, which consists in the treatment of three different cell lines (one healthy, two cancerous) with the folate-functionalized nanovector. By measuring the average SERS signal on the cells, it is possible to discriminate between healthy and cancer cells and to distinguish three different populations, namely HaCaT (human keratinocytes, “healthy”), PC-3 (prostatic cancer cells, “cancer 1”) and HeLa (cervical cancer cells, “cancer 2”).}
\end{figure}

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