

SERS intracellular monitoring of Galunisertib release from porous diatomite nanoparticles in colorectal cancer cells.

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Nanoscale delivery systems have been investigated for disease treatment due to their well-recognized advantages, including the sustained delivery of drugs to cells, enhanced therapeutic efficacy and reduction of undesired effects compared to conventional treatments. The application of nanocarriers in medicine is still hampered by significant experimental challenges, such as the investigation of the drug release profile in living cells rather than in cell medium. Here, we describe a hybrid nanoplatform for monitoring the drug release in colorectal cancer (CRC) cells at a femtogram scale by Surface-Enhanced Raman Scattering (SERS). Specifically, the anticancer drug Galunisertib was encapsulated in porous diatomite nanoparticles (DNPs) decorated by 25 nm gold nanoparticles (AuNPs) and capped by a layer of gelatin¹. The combination of the drug-loading capacity of DNPs with the strong Raman enhancement of molecules close to AuNPs enabled combining therapeutic purposes with label-free intracellular drug monitoring. The hybrid nanoplatform integrated bio-imaging and drug delivery goals without the use of any fluorophore or marker, avoiding fluorescence-quenching issues. Thanks to the strong enhancement provided by the AuNPs, the drug release profile was monitored and quantified by SERS with a femtogram scale resolution. When the gelatin layer was digested by proteases, Galunisertib was released and the SERS spectrum of the drug decreased as well, allowing to quantify the amount of drug released in CRC cells within 48 hours (Fig. 1). The results were compared to *in vitro* investigations performed with spectroscopic techniques, revealing that the gelatin layer caused both a sustained and pH-sensitive release of Galunisertib. The drug release was faster in the acidic microenvironment and slower in the physiological medium. The therapeutic outcomes of the nanoplatform were finally tested in the CRC cell line, revealing that the Galunisertib delivery system improved drug efficacy, reduced its toxicity, offering an alternative administration route for cancer treatment.

Tramontano, C.; Chianese, G.; Terracciano, M.; de Stefano, L.; Rea, I. Nanostructured Biosilica of Diatoms: From Water World to Biomedical Applications. *Appl. Sci.* **2020**, *10*, 6811. <https://doi.org/10.3390/app10196811>

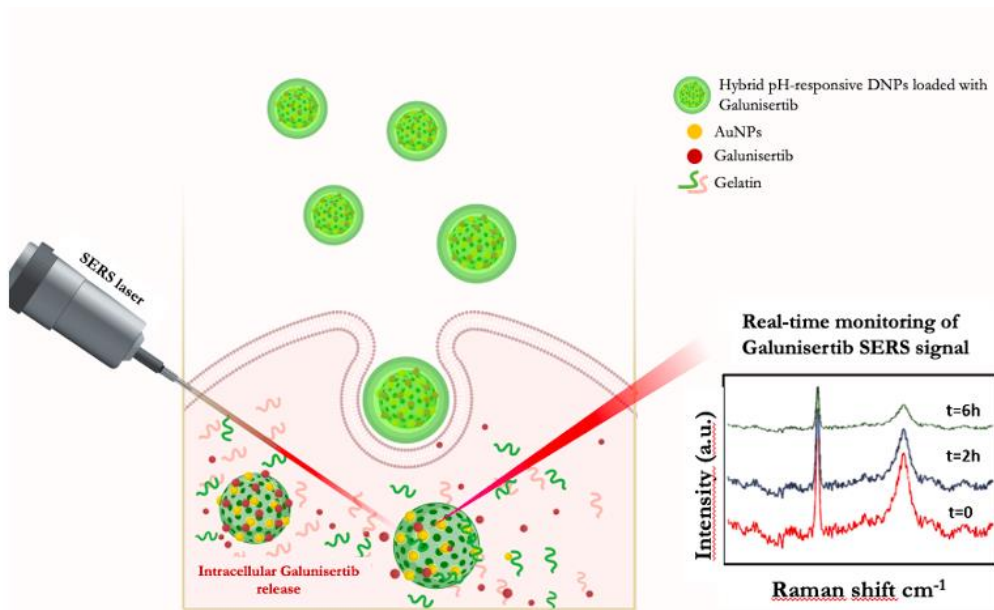


Figure 1 Scheme of the nanoplateform uptake in CRC cells. After internalization, the acidic tumor environment degrades the gelatin layer and triggers the release of Galunisertib from the platform. The drug release can be real-time monitored by SERS