ITALY - CHINA
SCIENCE, TECHNOLOGY & INNOVATION WEEK
25-27 OTTOBRE 2016
BERGAMO 25/10 · BOLOGNA 26/10 · NAPOLI 26-27/10

In vitro, in silico and live-cell monitoring of protein interactions with anticancer drugs and metal nanoparticles

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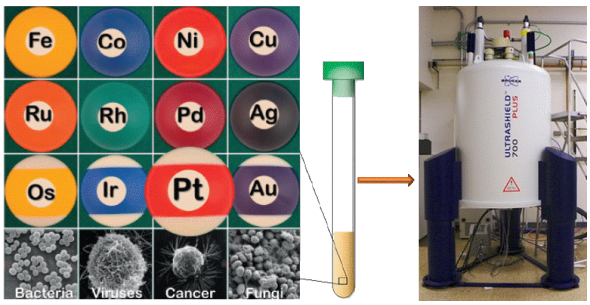
Abstract

The extensive use of inorganic drugs and nanomaterials for biomedical applications requires an in-depth molecular characterization of associated resistance mechanisms.
The cellular uptake and efficacy of the clinically approved platinum anticancer drugs relies, at least in part, on copper transporters [1].
Combining spectroscopic data and hybrid QM/MM simulations, we have worked out at the atomic level the structural determinants in solution of platinated copper transport proteins [2-4]. Atomic scale investigations were also carried out in a physiological environment via a tandem NMR-MS approach, aimed at monitoring the encounter of platinum drugs with biomolecular targets in living cells [5].
The in-cell spectroscopic approach proved to be valuable also to probe the fate and toxicity of antimicrobial silver nanoparticles. Again, copper transporters are involved in the binding of Ag(I) ions released by the nanoparticles and, moreover, they can interact with nanoparticles that reach the appropriate cellular compartment [6].
The elucidation of protein interactions with inorganic drugs and nanoparticles provides a way for unraveling the biological effects of these materials and avoiding resistance mechanisms in cancer and bacterial cells.



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