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Nanocages for self-triggered nuclear delivery of Doxorubicin at cancer cells

Mazzucchelli Serena[1], **Bellini Michela**[1], **Fiandra Luisa**[1], **Marta Truffi**[2], **Tortora Paolo**[2], **Prosperi Davide**[2] and **Corsi Fabio**[1,2]
[1]Luigi Sacco University Hospital, Italy
[2]University of Milan-Bicocca, Italy

Engineered apoferritin nanoparticle (HFn) was developed to achieve a cumulative self-triggered nuclear delivery of antitumor drugs in cancer cells (CC) with subcellular precision. The rationale of our approach is based on exploiting the natural arsenal of defense of CC to stimulate them to recruit large amounts of HFn loaded with doxorubicin (DOX) inside their nucleus in response to a noxious stimuli, which leads to decrease of viability and cell death. After demonstrating the selectivity of HFn for representative cancer cells compared to healthy fibroblasts, DOX-loaded HFn were used in CC treatment. Our results proved that loading of DOX in HFn increased the nuclear delivery of the drug, thus enhancing DOX efficacy. DOX-loaded HFn acts as a "Trojan Horse": HFn were internalized in CC more efficiently compared to free DOX, then promptly translocated into the nucleus following to the DNA damage caused by the partial release in the cytoplasm of encapsulated DOX. This self-triggered translocation allowed the drug release directly in the nuclear compartment, where it exerted its toxic action probably bypassing the action of the Glycoprotein-P. This approach was reliable and straightforward providing an antiproliferative effect with high reproducibility. The particular self-assembling nature of HFn nanocage makes it a versatile and tunable nanovector for a broad range of molecules suitable both for detection and treatment of CC.

Biography

Serena Mazzucchelli is a Post-doc fellow at Centro di Microscopia Elettronica per lo sviluppo delle Nanotecnologie applicate alla medicina in University of Milano, Italy. Her work is focused on biochemical and cellular applications of nanotechnology. She current scientific interests concern: expression and purification of recombinant protein in E. coli in order to functionalize various typologies of hybrid nanoparticles for biomedical applications.

serena.mazzucchelli@gmail.com