

# Ultrasound responsive hybrid nanoconstruct as targeted therapy against cancer

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During the last decade, nanotechnology has increasingly gained attention for its beneficial role in several scientific areas, among which nanomedicine is one of the most studied. Nanomedicine can be defined as the application of nanotechnologies for medical purposes, as diagnosis, monitoring, prevention, and therapy, or even the simultaneous combination of them, named nanotheranostic.

Nanomedicine results to be particularly appealing for cancer applications, which is today a leading cause of death worldwide, even superior to Covid-19 related deaths. This is due to the ability of nanomaterials to deliver drugs, be tools for diagnosis and imaging, create nano medical devices and even be therapeutic agents themselves. In particular, nanoparticles (NPs) have been widely studied, trying to address various medical challenges faced with conventional medicine, as poor target specificity, systemic and organic toxicity and lack of efficiency. The unique nano-dimension of particles provides them with specific physical and chemical properties, related to their size, shape, crystalline structure and surface-to-volume ratio. They can be excellent carriers for different types of therapeutic molecules, their surface reactivity can be exploited for bio mimicking and targeting purposes, or they can be considered the therapy itself taking advantage of the chemical nature of NPs or their effects under external stimuli.

Whitin this frame of reference, zinc oxide nanocrystals (ZnO NCs) are particularly interesting and versatile nanomaterials, as they can be doped with transition metals, their surface can be modified with chemical and biological entities, and show intriguing properties (semiconducting, piezoelectric, and even magnetic properties). In this lecture, the role zinc oxide nanocrystals, will be thoroughly discussed proposing strategies to render zinc oxide nanoparticles efficiently biomimetic, site-selective, and stimuli-responsive, and finally theranostic weapons against cancer.

The design, construction and characterization of biomimetic nanoconstructs based on ZnO NCs will be shown: chemically synthesized nanocrystals can be coupled with a lipidic bilayer shell made by commercially available lipids and/or extracellular vesicles (EVs), and further equipped with synthetic targeting peptides or monoclonal antibodies. The biomimetic nanoconstructs are rationally made to fulfill multimodal properties for diagnostic and therapeutic purposes adequate to fight against different cancers, focusing on Burkitt's lymphoma and acute myeloma.

Intracellular delivery of the biomimetic nanoconstructs is proved to be enhanced in the presence of the targeting ligand, the therapeutic activity is provided by a combination of chemical and physical stimulations, remotely controlled, while the diagnostic capabilities allow bio-imaging functions in real-time and at high resolution. The challenging purpose of the presented work is eventually of shedding light on future treatments out of the currently followed well-worn paths, being able to meet the specific needs of each tumor in question and developing high precision and personalized treatments.

## References

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