Magnetic navigation of swarms of enzyme-powered nanomotors with photothermal properties for immunogenic cell death

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Immunogenic cell death (ICD) is a process where damage-associated molecular patterns (DAMPs), such as ATP and calreticulin (CLRT), are released or exposed at the cell's surface. ICD has emerged as a promising strategy for enhancing the efficacy of cancer immunotherapy. Recent studies have demonstrated that ICD can be induced by means of light-triggered effects without the need for chemotherapeutics with potential side effects.1 Light-responsive nanomaterials could improve ICD induction further if they could collectively displace and penetrate more efficiently into tumors. Advanced nanomaterials able to convert chemical energy into motion or nanomotors (NMs) are being actively explored due to their ability to overcome different biological barriers and their capability to collectively displace in the form of swarms.2 Among these, urease-powered nanomotors have gained significant attention due to their biocompatibility, biodegradability, and the possibility of using urea as fuel at physiological concentrations to power their motion.3 In addition, the use of iron oxide as chassis of these motors allows to combine the motion capabilities with photothermal and magnetic properties to offer an additional advantage for therapies.4

In this work we investigated the magnetic navigation capabilities of swarms of urease-powered iron oxide nanomotors (IONMs), guided by external magnetic fields, for enhanced and selective displacement and accumulation in desired regions of 3D-printed phantom models. In addition to their navigational abilities, we evaluated the photothermal properties of the iron oxide nanoparticles for induction of vapor nanobubbles (VNBs) formation upon irradiation with a pulsed laser to induce selective cell killing. As light-triggered cell death by means of VNBs holds the potential for generating DAMPs crucial to activating anti-tumor immune responses, we proceed to characterize the release of ATP and CLRT exposure in treated samples.
The combination of magnetic navigation and photothermal properties of IONMs proved to have clear potential for the selective displacement and accumulation of NMs and to induce the release and exposure of ICD hallmarks upon irradiation.

References

[1] Ramon, J.; et al. J. Control. Release 2023, 1–45.
[2] Hortelao, A. C.; et al. Sci. Robot. 2021, 6 (52), eabd2823.
[3] Arqué, X.; et al. Chem. Sci. 2022, 13 (32), 9128–9146.
[4] Fraire, J. C.; et al. ACS Nano 2023, 17 (8), 7180–7193.