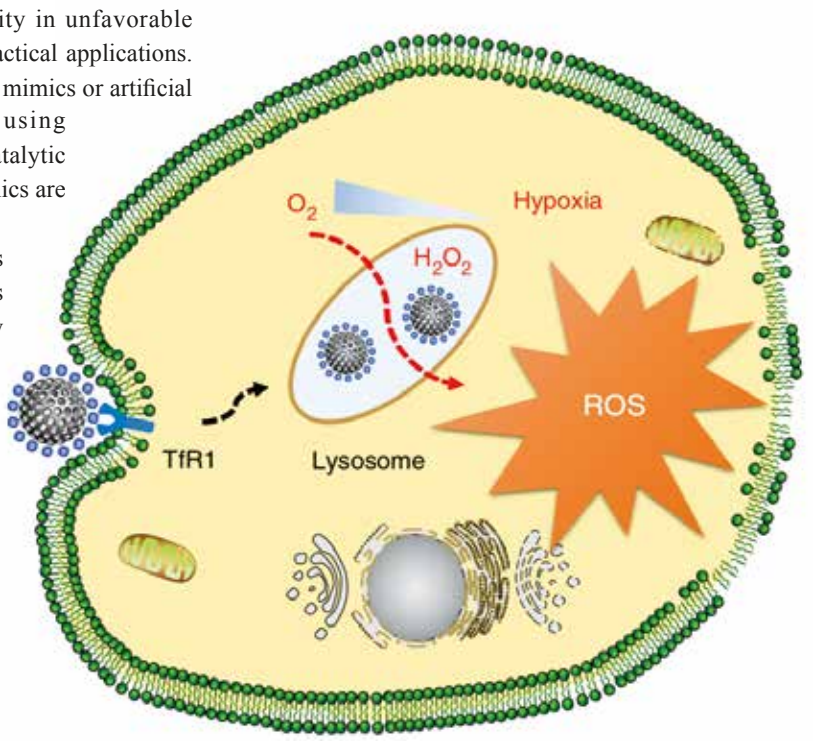
Tumor Catalytic Therapy with Nanozymes

High amounts of abnormal metabolic products are produced during tumor growth and development. For instance, elevated level of hydrogen peroxide (H_2O_2) is often exhibited in solid tumors, which renders tumor cells more resistant to therapeutic treatment. However, if the accumulated H_2O_2 can be converted instead to something damaging tumor cellsthemselves, more effective results of tumor therapy may be then expected, with a mindset of "Give tumor a taste of its own medicine." Natural enzymes with peroxidase activity can be used to convert H_2O_2 into toxic reactive oxygen radicals (ROS) which effectively kills tumor cells. However, most natural enzymes are not suitable for *in vivo* applications due to their sensitivity and low stability in unfavorable environments, which limits their practical applications. To overcome its limitations, enzyme mimics or artificial enzymes have been developed using chemical synthesis, although the catalytic efficiency of traditional enzyme mimics are often not sufficient.

In recent years, nanomaterials with intrinsic enzyme-like properties (Nanozymes) emerged as a new generation of enzyme mimics which features high activity, stability and low cost, showing great potential in biomedical applications from *in vitro* detection to *in vivo* therapy. With nanozymes having multiple different activities, controlling the *in vivo* behavior of them has become an urgent, challenging issue.

In the paper entitled "In vivo Guiding Nitrogen-doped Carbon Nanozyme for Tumor Catalytic Therapy", published in *Nature Communications* on April 12, 2018, Prof. YAN Xiyun from the Institute of Biophysics (IBP), CAS and Prof. GAO Lizeng from THE Institute of translational Medicine, School of Medicine, Yangzhou University, China, reported a novel tumor catalytic therapy using nanozymes to convert O_2 and H_2O_2 to toxic ROS for tumor destruction. In their previous studies, they discovered that iron oxide nanoparticles exhibited intrinsic peroxidase-like activity (*Nature Nanotechnology*, 2007) and, if encapsulated in ferritin, can be used for *in vitro* tumor diagnosis (*Nature Nanotechnology*, 2012).



A nitrogen-doped porous carbon nanosphere (N-PCNS) is shown performing four enzyme-like activities for tumor catalytic therapy via human H-ferritin (HFn) guided delivery.

In the current work, the authors developed a novel nanozyme using nitrogen-doped porous carbon nanospheres (N-PCNSs) to mimic four enzyme-like activities (oxidase, peroxidase, catalase, superoxide dismutase). They found that these nanozymes were able to regulate intracellular ROS and boost ROS generation by oxidase and peroxidase activities under acidic microenvironment. To utilize the enzymatic performance for tumor therapy, ferritin was introduced to target tumors and deliver N-PCNSs to lysosome to control ROS generation. In vivo tests demonstrated that ferritin-N-PCNSs specifically suppress tumors in animal model, indicating that the nanozymes activities are controllable to perform the desired purpose. Meanwhile, ferritinylation ensured the nanozymes' specificity and delivery to the tumor. This work has demonstrated the feasibility of using nanozymes for tumor catalytic therapy.

Importantly, as a nanomaterial, N-PCNSs possess excellent biocompatibility. They are biodegradable under physiological conditions. In addition, N-PCNSs can be made at large scale with low cost. These properties make them superior to natural enzymes in biomedical applications.

"If decorated with the right surface modifications, nanoparticles can function as Trojan horses, transporting cell death-facilitating compounds to tumour cells. Here, the authors prepare a particle with four enzyme-like activities and show that ferritin can direct nanoparticles to tumour cells," commented the Editor of *Nature Communications*.

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For full-text, please see: https://www.nature.com/articles/s41467-018-03903-8

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