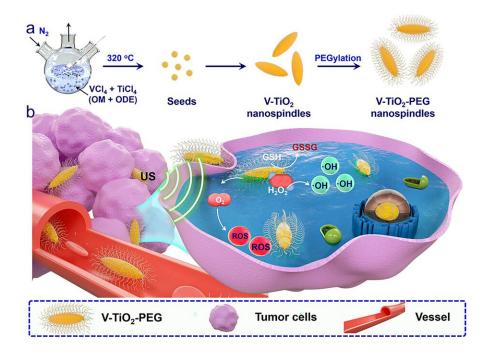


Tiny nanospindles enhance use of ultrasound to fight cancer

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Vanadium-doped titanium dioxide nanospindles encased in polyethylene glycol (PEG) and used in combination with ultrasound waves can kill cancer cells. Credit: Liang Cheng

Ultrasound can be used to treat cancer when used in combination with molecules that sensitize the system to sound waves. These sonosensitizers generate toxic reactive oxygen species that attack and kill tumor cells.



In *Applied Physics Reviews*, scientists from Soochow University in China report a new type of sonosensitizer based on a vanadium-doped titanium dioxide, V-TiO2, that enhances the amount of damage ultrasound inflicts on tumors. Studies in mice showed that tumor growth was markedly suppressed when compared to a <u>control group</u>.

Organic molecules have been used in the past as sensitizers, but these are unstable and can lead to phototoxicity, where exposure to light can produce rashes or extreme sunburn. Inorganic sensitizers based on TiO₂ nanomaterials are also used, but these do not work well and can remain in the body for long periods.

TiO₂ does not work well as a sensitizer, because it has a wide band gap in its electronic structure. Even when the ultrasound strips electrons away from the TiO₂ nanoparticles, the electrons rapidly recombine with the nanoparticles, preventing the generation of reactive oxygen species that could attack tumor cells.

The investigators realized they could avoid this effect by doping TiO₂ nanoparticles with the metal vanadium to form nano-sized spindles.

"The band gap of V-TiO₂ nanospindles is reduced, increasing the efficiency of ultrasound-triggered reactive oxygen species production compared to that of pure TiO₂ nanoparticles," said author Liang Cheng.

The microenvironment around the tumor is key to cancer metastasizing and invading other tissue, and important for the way chemotherapy and other treatments work. The tumor microenvironment has an acidic pH but also contains a lot of hydrogen peroxide and a substance known as glutathione.

The investigators realized the V-TiO₂ spindles act like tiny enzymes that catalyze chemical processes in the microenvironment. In the presence of



ultrasound waves, the spindles allow a two-pronged attack on the tumor: one involving sound waves, the other a type of chemotherapy that degrades hydrogen peroxide and consumes glutathione. Both effects kill tumor cells without harming healthy tissue.

The investigators carried out a careful study using controls on both breast cancer <u>tumor cells</u> and on mice infected with these cancerous cells. In addition to direct measurements about <u>tumor growth</u>, they employed fluorescent probes to visualize reactive oxygen species and glutathione during the process.

"It is worth noting that V-TiO₂ nanospindles are rapidly excreted from the body," said Cheng. "This helps prevent any possible long-term toxicity effects."

The scientists were also able to observe V-TiO₂ nanospindles in the spleen and liver of the mice and, later, in the feces and urine. No obvious signs of organ inflammation or damage were observed, showing that these sensitizers are both safe and effective.

More information: "V-TiO2 nanospindles with regulating tumor microenvironment performance for enhanced sonodynamic cancer therapy," *Applied Physics Reviews*, aip.scitation.org/doi/10.1063/5.0027606.

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