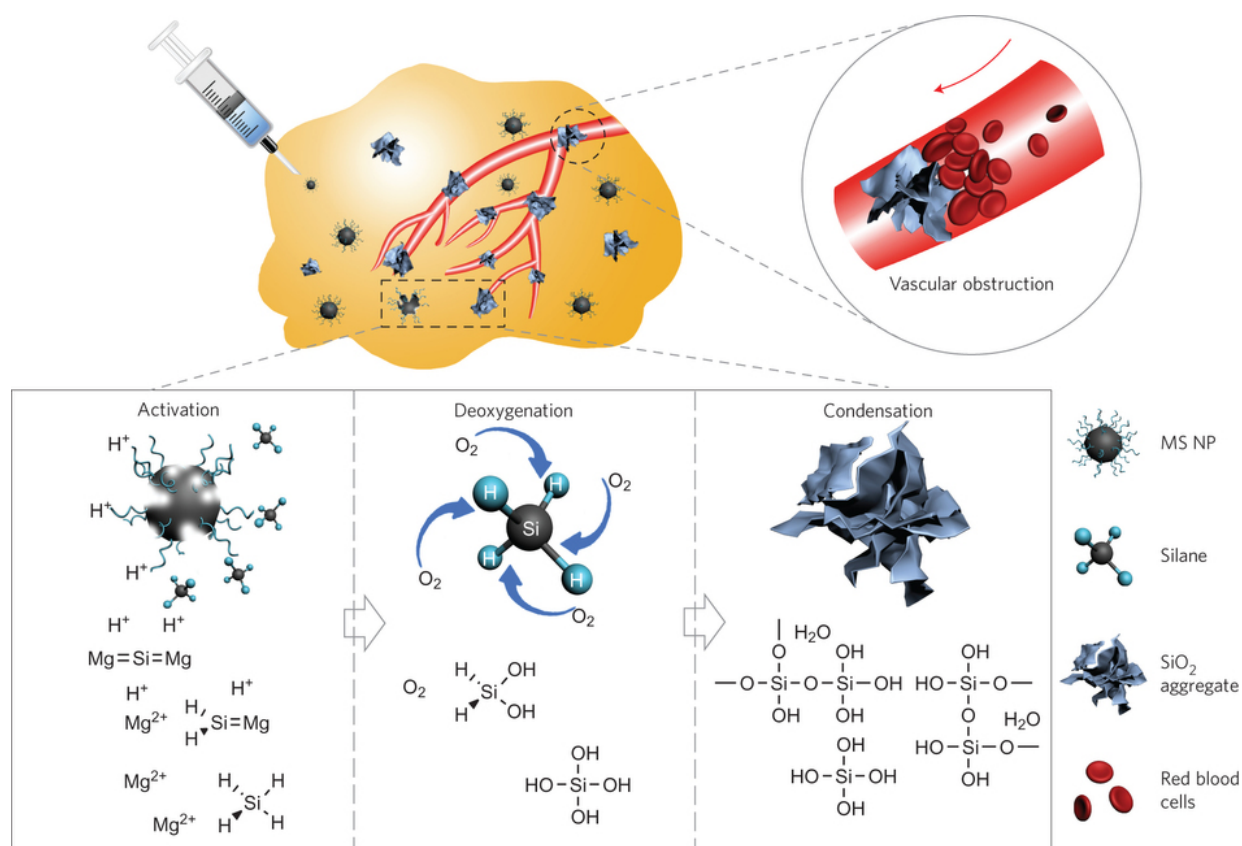


# Study shows that nanoparticles serve as a good tumor deoxygenation agent

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Schematic diagram of MS NPs serving as an intratumoral DOA for specific cancer-starving therapy. Activated by the acidic tumour microenvironment, the MS NPs produce reactive silane to give rise to an efficient deoxygenation effect and produce in situ SiO<sub>2</sub> blockers in tumour blood capillaries, which subsequently prevent undesired reoxygenation. The deoxygenated tumour with no further oxygen supply will suffocate in the absence of the necessary energy metabolism. MS NP here is the PVP-modified Mg<sub>2</sub>Si nanoparticles.

(Phys.org)—One target therapy in cancer research is to suffocate the tumor. Cells need oxygen to survive so researchers have focused on methods for cutting off the blood supply to the tumor. Very little research has involved the direct removal of oxygen within the tumor.

To this end, a group of researchers from the Shanghai Institute of Ceramics, Chinese Academy of Sciences and the East China Normal University have developed a deoxygenation agent using polyvinyl pyrrolidone modified  $\text{Mg}_2\text{Si}$  [nanoparticles](#). This agent is pH sensitive, efficiently consumes [oxygen](#), and one of the products of [oxygen consumption](#) also forms aggregates that could potentially block blood vessels. Preliminary mouse studies show [tumor hypoxia](#) and good biocompatibility. Their work appears in *Nature Nanotechnology*.

There are several important qualities for a good [tumor](#)-starving agent. For one, the agent must be biocompatible which negates the use of heavy metals for oxygen absorption. Additionally, the agent must be efficient at deoxygenation and serve as a long-term oxygen scavenger including preventing re-oxygenation of deoxygenated tumors through undamaged blood vessels. And, as always, any cancer treatment needs to target tumors without damaging healthy tissue, and the agent should be easily injectable by syringe.

In the current research, Zhang et al. developed polyvinyl pyrrolidone (PVP)-modified  $\text{Mg}_2\text{Si}$  nanoparticles that have several of the qualities for a good tumor-starving agent. Importantly, the main components, magnesium, silicon dioxide, and water are biocompatible. Additionally, the reaction mechanism forms a highly reactive  $\text{O}_2$  scavenger,  $\text{SiH}_4$ , which serves to make these nanoparticles highly efficient at scavenging oxygen.

In order to make injectable nanoparticles, Zhang et al. developed a self-propagating high-temperature synthesis in an oxygen-argon atmosphere.

This allows the nanoparticles to remain dispersed in the liquid, rather than form clusters, so that they are injectable into tissue. This synthesis takes advantage of the formation of MgO by-product that halts the continual formation of  $\text{Mg}_2\text{Si}$  aggregates.

Part of the reaction mechanism involves the formation of  $\text{Si}^{4-}$ , which is highly sensitive to acid. This is important because the tumor environment tends to be acidic compared to normal tissue (pH~6.4), and pH sensitivity may help with tissue specificity. To investigate the pH sensitivity of their deoxygenation agent, Zhang et al. placed their nanoparticles in a dialysis bag, which were then immersed in buffer solutions of varied pH values within closed tubes. In acidic conditions, the nanoparticles irreversibly decreased the level of oxygen, but were unreactive in neutral pH. Furthermore,  $\text{SiO}_2$  aggregates formed in situ that served to block a simulated capillary.

Additional studies demonstrated that the  $\text{MgSi}_2$  nanoparticles demonstrated very little cytotoxicity until they encountered the acidic environment of the cancer cell. Using MCF-7 human breast adenocarcinoma cells, Zhang et al. observed that the combination of acid and nanoparticles led to cell efficient hypoxia. Furthermore, cell proliferation decreased, which is likely due to mitochondrial damage from deoxygenation.

In vivo studies involving bilateral 4T1 xenotumor-bearing mice demonstrated that  $\text{Mg}_2\text{Si}$  nanoparticles served as efficient deoxygenation agents. Each mouse was injected with the nanoparticle deoxygenation agent in the right tumor and with saline solution as a control in the left tumor. Measurements of [blood oxygen saturation](#) levels after ten minutes showed little change in the control tumor and a drastic reduction in oxygen in the test tumor. Oxygen reduction continued for three hours in the tested tumor until tests on both the hemoglobin-bound oxygen and blood oxygen showed complete depletion within the tumor. Notably,

PET/CT images show that hypoxia occurred within the tumor and not in the surrounding tissues.

Additional observations from the in vivo study showed that the tumors that received  $\text{Mg}_2\text{Si}$  nanoparticles demonstrated a slower growth rate compared to controls and after twenty-four hours, although cell proliferation was not slowed down as significantly as in the in vitro studies. These cells showed evidence of fibrosis, necrosis, and apoptosis. Additionally, magnesium was quickly eliminated from the body while silicon was eventually eliminated.

Overall, this research provides a compelling proof-of-concept for the use of PVP-modified  $\text{Mg}_2\text{Si}$  nanoparticles as potential candidates for use as a tumor-targeted deoxygenating agent. The authors point out that future research would involve exploring surface modifications of the nanoparticles to tailor the length of time the nanoparticles can travel through the blood stream.

**More information:** Chen Zhang et al. Magnesium silicide nanoparticles as a deoxygenation agent for cancer starvation therapy, *Nature Nanotechnology* (2017). [DOI: 10.1038/nnano.2016.280](https://doi.org/10.1038/nnano.2016.280)

## **Abstract**

A material that rapidly absorbs molecular oxygen (known as an oxygen scavenger or deoxygenation agent (DOA)) has various industrial applications, such as in food preservation, anticorrosion of metal and coal deoxidation. Given that oxygen is vital to cancer growth, to starve tumours through the consumption of intratumoral oxygen is a potentially useful strategy in fighting cancer. Here we show that an injectable polymer-modified magnesium silicide ( $\text{Mg}_2\text{Si}$ ) nanoparticle can act as a DOA by scavenging oxygen in tumours and form by-products that block tumour capillaries from being reoxygenated. The nanoparticles are prepared by a self-propagating high-temperature synthesis strategy. In

the acidic tumour microenvironment, the  $\text{Mg}_2\text{Si}$  releases silane, which efficiently reacts with both tissue-dissolved and haemoglobin-bound oxygen to form silicon oxide ( $\text{SiO}_2$ ) aggregates. This in situ formation of  $\text{SiO}_2$  blocks the tumour blood capillaries and prevents tumours from receiving new supplies of oxygen and nutrients.

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