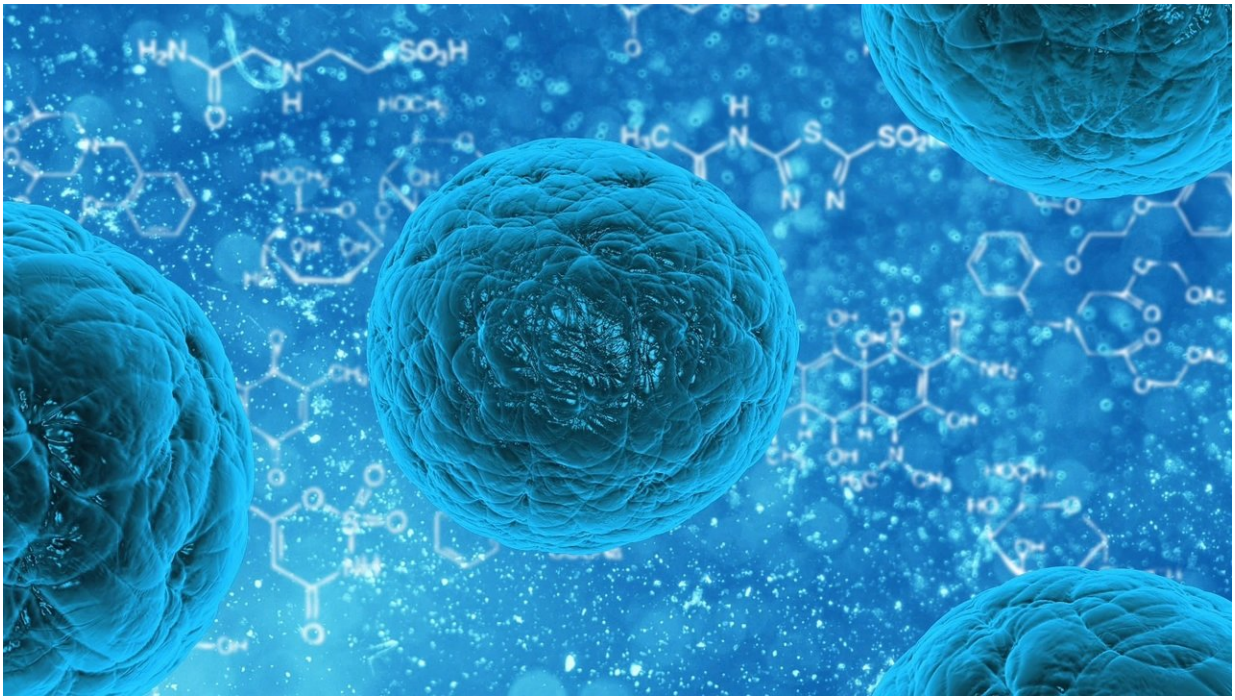
Acidity-activatable dynamic nanoparticles boost cancer immunotherapy

July 16 2021, by Liu Jia



Credit: CC0 Public Domain

Immunotherapy has great potential in clinical cancer treatment due to systematic activation of antitumor immunity. However, low immunogenicity, or negative feedback on immunotherapy, greatly hinders the efficacy of currently used cancer immunotherapy.

In a study published in *Advanced Materials*, a research team led by Yu

Haijun from Shanghai Institute of Materia Medica of the Chinese Academy of Sciences proposed acidity-activatable dynamic nanoparticles to boost ferroptosis and immunogenic death (ICD) of tumor cells for cancer immunotherapy.

Ferroptosis is a new type of cell death caused by lipid peroxidation (lip-ROS). The repairment axis of lip-ROS contains glutamate–cystine antiporter for synthesis of intracellular glutathione (System XC-) and Glutathione Peroxidase 4 (GPX4), both of which play important roles to fight against lip-ROS. Those produced lip-ROS were reported to act as "find-me" signals to promote the phagocytosis of antigen-presenting cells and to further activate cytotoxic T lymphocytes to enhance tumor immunotherapy.

The researchers firstly synthesized amphiphilic acid-sensitive block copolymer coupled with photosensitizer (pyrochloric acid, PPA) and phenylboric acid through hydrophobic interaction and π-π conjugation to encapsulate insoluble GPX4 inhibitor (RSL-3).

Then they found nanoparticles with external light can induce obvious ICD as well as cytotoxic T lymphocytes which secrete IFN-γ. IFN-γ and RSL-3 presented synergistically inhibition on the repairment axis and SystemXC—GPX4, while increased the accumulation of lipid-ROS in tumor cells, thus revealing the interaction between ferroptosis and immunotherapy.

Additionally, the researchers found that the nanoparticles combined with immune checkpoint therapy (ICB) dramatically reduced the tumor-infiltration of dedifferentiated tumor cells in a manner of ferroptosis.

The study offered a new way to improve ferroptosis-mediated tumor immunotherapy.

More information: Rundi Song et al, Acidity-Activatable Dynamic Nanoparticles Boosting Ferroptotic Cell Death for Immunotherapy of Cancer, *Advanced Materials* (2021). DOI: 10.1002/adma.202101155

Provided by Chinese Academy of Sciences