Novel Nanotechnology Found to Enhance Fight Against Colorectal Cancer and Melanoma

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researchers recently completed a study that has the potential to improve cancer treatment for colorectal cancer and melanoma by using nanotechnology to deliver chemotherapy in a way that makes it more effective against aggressive tumors. The findings were published in Nature Nanotechnology.

“I’ve always been interested in harnessing the intrinsic immunity to fight against cancer,” said JIANQIN LU, BPHARM, PHD, assistant professor of pharmaceutics and pharmacokinetics in the UArizona COLLEGE OF PHARMACY’s Department of Pharmacology and Toxicology and associate member of the UArizona Cancer Center. “To do this in a safe and effective way, nanotechnology comes into play because of its ability to improve drug movement and therapeutic efficacy, as well as the potential to reduce systemic toxicities. My hope is that these innovative nanotherapeutics and therapeutic regimens eventually will help cancer patients combat cancers more effectively and safely.”

Immunotherapies help boost the immune system’s ability to fight off cancer cells. Immune checkpoints are regulators of the immune system, which are pivotal in preventing the body from attacking healthy cells indiscriminately. Some types of cancer circumvent these checkpoints, allowing cancerous cells to avoid detection and continue to spread. Immune checkpoint blockade (ICB) is a newer therapy that can essentially "release the brakes" on the immune system and help the body fight back.

ICB therapies are effective for some types of cancer, but they don’t work for every patient. For example, only approximately 4% of patients with colorectal cancer, the second leading cause of cancer-related deaths in U.S., will respond to ICB therapy, Dr. Lu said.

Recent research has focused on ways to enhance the power of ICB therapies by combining them with chemotherapeutic agents such as camptothecin. Though camptothecin is potent, it is also unstable, has poor solubility in water and can have serious side effects for healthy

cells.

Dr. Lu and the research team created the first nanotherapeutic platform of its kind to overcome these hurdles. Using a nanotechnology delivery method, researchers enhanced camptothecin's ability to synergize with ICB therapies, making them more effective against aggressive tumors.

"To render a more effective ICB therapy, we have developed a nanotherapeutic platform that can switch the tumors from 'immune-cold' to 'immune-hot,'" said Dr. Lu, who is also a member of the BIO5 Institute and The Southwest Environmental Health Sciences Center (SWEHSC). "As a result, this nanotherapeutic platform was able to increase the effectiveness of the ICB therapy to eradicate a large portion of early-stage colorectal cancer tumors while concurrently activating the body's memory immunity, preventing tumor recurrence."

The team attached camptothecin to sphingomyelin, a naturally occuring lipid found on the surface of cells. The combination of the two molecules into a nanovesicle called camptothesome stabilized camptothecin, improving its efficacy and diminishing systemic toxicities. The nanotech delivery method also improved the tumor uptake of the camptothesome in a rodent model, where it deeply penetrated the tumour with efficient release of the chemotherapy.

Dr. Lu and the research team then created a way to load an immune checkpoint inhibitor targeting one of the key checkpoints, indoleamine 2,3-dioxygenase (IDO1), inside of the camptothesomes. When combined with inhibitors targeting other immune checkpoints known as PD-L1 and PD-1, this nanotherapeutic strategy eliminated a significant portion of clinically difficult-to-treat late-stage metastatic colorectal cancer and melanoma tumors, paving the pathway for further studies.

The researchers note that their nanotechnology platform can be used to deliver a range of cancer therapeutics, and it has a significant head start in the drug development pipeline as it is derived from sphingomyelin, a lipid that is already approved by the U.S. Food and Drug Administration.

Dr. Lu hopes to collaborate with oncologists at the UArizona Cancer Center to further optimize the nanotherapeutic system to make it suitable for an early phase clinical trial.

Read the original article on University of Arizona.