Statins inhibit spread of some cancers in laboratory tests

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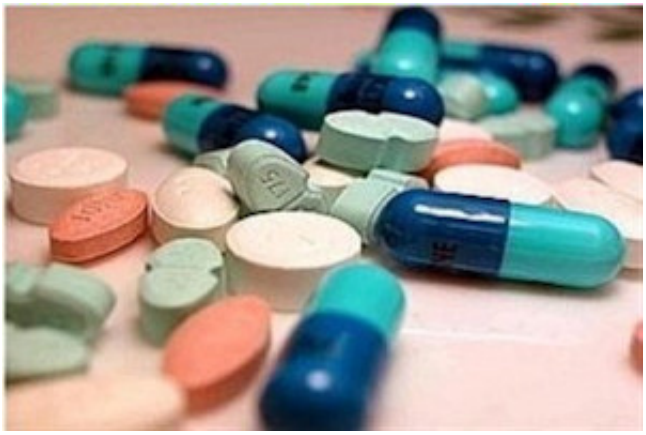

Various pills. Credit: Wikipedia

Cholesterol-lowering drugs appear to be a promising, cost-effective way to reduce the risk of metastases in some cancers, according to laboratory research led by the University of Pittsburgh School of Medicine. Metastases, rather than the original tumor, are what usually kill people with cancer.

The discovery, published in the open-access journal *Scientific Reports*, part of the Nature Publishing Group, reveals the mechanism by which statins may impede the process that cancerous tumor cells need in order to split off from the primary tumor and cause cancer elsewhere in the body.

"We didn't plan to discover this – we were actually modeling metabolism of tumor cells and looking at the response of various tumor cells to existing drugs, including statins," said senior author Zoltán Oltvai, M.D., associate professor of pathology at Pitt. "But, sure enough, we were able to show that these cholesterol-lowering drugs interrupt the growth of some cancer cell lines that are very similar to those cancer cells that leave the primary tumor and eventually colonize other organs."

When a tumor metastasizes, it spreads cancer cells through the body using the blood stream. The cells then come to rest at another site in the body, eventually forming new tumors. Sometimes these cells lie dormant, and a person can appear cancer-free after the primary tumor is removed, only to have his or her cancer reappear years later in another organ.

Scientists have known for several years that statins sometimes seem to fight cancer; however, the mechanism wasn't clear, and previous clinical trials have yielded mixed results regarding statins as anti-cancer drugs.

Cancer cells require the synthesis of cholesterol and cholesterol precursor molecules to reprogram themselves from an adherent, or "epithelial" state, to a mobile, or "mesenchymal" state, in order to leave or "shed" from the primary tumor and recolonize elsewhere in the body. Statins, which are routinely used to lower lipid levels, could potentially block cancer cell spread by inhibiting an enzyme that catalyzes a key step in the cholesterol synthesis process, Dr. Oltvai said.

His team found that slower-growing, mesenchymal-like cancer cell lines that contain the protein vimentin inside the cell, but do not display the protein E-cadherin on their surface, are particularly sensitive to statins. Knowing this, doctors eventually may be able to test biopsies from cancerous tumors for these markers to determine if statins may be effective.

"While statins probably aren't going to be effective against a patient's primary tumor, they could work to block the tumor's ability to metastasize," said Dr. Oltvai. "And that is very important because most cancer patients die because of the metastases."

Dr. Oltvai noted that coupling treatment of the primary tumor – which can involve chemotherapy, surgical removal of the tumor and radiation – with

statins might be a way to prevent the primary tumor from shedding cells, and also prevent those cells from surviving their journey through the body or reactivating elsewhere in the body later on.

These are preliminary results, and people should not start taking statins as an anti-cancer drug, Dr. Oltvai stressed. His team tested the cancer cells' reaction to statins in the laboratory, and the process could be different in the human body. The researchers are pursuing funding for additional studies on how exactly statins can interfere with the process that leads to metastases and whether combining statins with other drugs may be even more potent than using statins alone.

More information: "Statin-induced mevalonate pathway inhibition attenuates the growth of mesenchymal-like cancer cells that lack functional E-cadherin mediated cell cohesion." *Scientific Reports* 4, Article number: 7593 DOI: 10.1038/srep07593

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