Selenocompounds kill multidrug resistant cancer cells, block cells' defenses against cancer drugs

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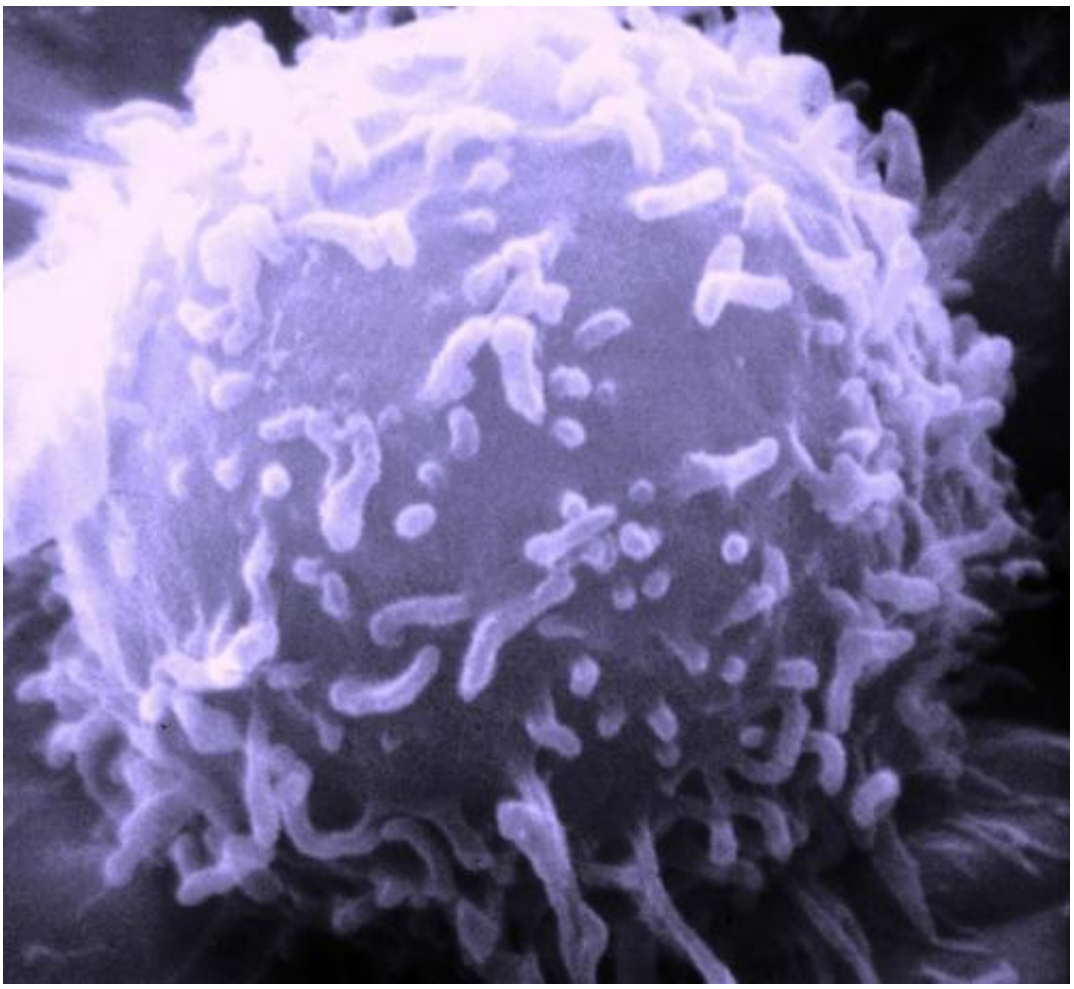

Electron microscopic image of a single human lymphocyte. Credit: Dr. Triche National Cancer Institute

Newly discovered molecules can kill multidrug resistant cancer cells by blocking cells' defenses against cancer drugs, according to a new study published in Bioorganic & Medicinal Chemistry Letters. The lead author of the research, from the University of Navarra in Spain and Jagiellonian University Medical College in Poland, hopes the findings provide an initial step towards more effective treatments in the future against resistant cancers.

Cancer is a leading cause of death worldwide and its incidence and mortality are arising, mainly in developed countries. Treatment is often aggressive and can cause severe side effects, but still many of the deaths can be attributed to cancers that are resistant to chemotherapy drugs. Because of this, scientists are working hard to develop new drugs that can kill cancer cells that have become resistant to multiple treatments.

The first step in this process is to identify molecules that can evade cancer cells' defenses against chemotherapy drugs. In the new study, researchers from the University of Navarra in Spain, Jagiellonian University Medical College in Poland, University of Szeged in Hungary and Saarland State University in Germany show that a newly-discovered class of molecules - called selenocompounds - can kill multidrug resistant mouse cancer cells.

"Our research reports a new way to fight multidrug resistance in cancer," said lead author Dr. Enrique Domínguez-Álvarez from the University of Navarra in Spain and Jagiellonian University Medical College in Poland. "We are realistic and we know that much more research needs to be done, but we are excited about these promising results that open new and unexplored possibilities."

In previous studies, Dr. Domínguez-Álvarez and his colleagues discovered 57 new molecules that prevented the growth of, and even killed, cancer cells. While reading up on similar compounds, they found

that some could enhance the potency of chemotherapy drugs, so they decided to investigate.

When faced with aggressive treatment, cancer cells can sometimes develop a defense mechanism called an efflux pump: a protein in the cell membrane that can push the drug back out of the cancer cell to protect it. One such protein is called ABCB1.

The researchers tested the selenocompounds to see if they stopped this mechanism from working. They found that the compounds block these efflux pumps, effectively shutting down the defense mechanism. In fact, the most active molecule worked almost four times better than the reference - the original molecule that does the same job.

They also found that the selenocompounds can induce the process of cell suicide, or apoptosis, in cancer cells, with a similar potency to an existing drug. The most active compound killed about 80 percent of the mouse cancer cells.

Dr. Domínguez-Álvarez will continue this work in his new role at the Spanish National Research Council. The next step will be to synthesize similar compounds to determine the most promising derivatives. Dependent on funding, Dr. Domínguez-Álvarez and his colleagues will consider further steps like testing the compounds in vivo.

"The ultimate aim of cancer research is to give more chances to people whose lives are at risk due to this disease. The development of pharmaceutical drugs requires a lot of effort and time, and the results our group presents are just preliminary. But contributing my effort to this fight, even in these starting steps, fulfills me. I hope that in the future our work will serve as the basis to develop new drugs against cancer that reach the patients who need them."

More information: Enrique Domínguez-Álvarez et al. Identification of selenocompounds with promising properties to reverse cancer multidrug resistance, *Bioorganic & Medicinal Chemistry Letters* (2016). DOI: 10.1016/j.bmcl.2016.04.064