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Molecule that provides cellular energy found key to aggressive thyroid cancer

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Cancer researchers at Mayo Clinic's campus in Jacksonville, Florida, have identified a molecule they say is important to survival of anaplastic thyroid carcinoma (ATC)—a lethal tumor with no effective therapies. The molecule also seems to play a role in a wide range of cancers.

In an online issue of *The Journal of Clinical Endocrinology and Metabolism*, they identify Stearoyl-CoA desaturase 1 (SCD1) as an oncogenic enzyme that when inhibited and paired with another targeted drug effectively shuts down ATC cell growth and induces cell death.

Investigators think that ATC relies on SCD1 to provide the fuel the cancer cells need to rapidly duplicate. The molecule provides this energy by promoting the cancer cell's ability to generate certain fatty acids that are important for several biological processes such as cell division, survival, drug resistance and migration.

"We now have some hope for treatment of this cancer, which is arguably the most lethal solid tumor known to medicine," says John Copland, Ph.D., a cancer biologist and the study's senior author. "Although ATC is rare—accounting for only 1 to 2 percent of thyroid cancers, it is responsible for up to 39 percent of all thyroid cancer-related deaths."

"Currently, there are no therapies for ATC that lead to prolonged survival, but I think combining an SCD1 inhibitor with a cocktail of other agents, all of which have dramatically different targets and approaches, may work," says co-author Robert Smallridge, M.D., an

endocrinologist who treats thyroid cancer.

The Mayo researchers have already developed SCD1 inhibitors and are testing the agents in different tumor models.

Cells normally take the fatty acids they need from the bloodstream, instead of making them internally, says lead author Christina von Roemeling, a graduate student and cancer researcher. "But we have found this very unique switch in tumors that makes them very dependent on this method of fatty acid synthesis," she says.

"Given the work we have done in the past several years, it is becoming really clear to us that fatty acid metabolism is quite possibly a crutch used by many cancers," von Roemeling says. "An SCD1 inhibitor might be a therapeutic target that is multipotent for several cancers—not just a one-hit wonder in a single cancer but very useful as a generic therapy."

"We have seen activity of SCD1 in a number of cancer cell lines—everything from melanoma to ovarian and breast cancer to prostate and pancreatic cancer," says Dr. Copland.

"We now have a new area of cancer therapy to explore that has not been looked at yet in anaplastic thyroid cancer," adds Dr. Smallridge.

Provided by Mayo Clinic