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Fighting cancer with cancer: Mayo Clinic finds promising use for thyroid cancer gene

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A mutant gene long thought to accelerate tumor growth in thyroid cancer patients actually inhibits the spread of malignant cells, showing promise for novel cancer therapies, a Mayo Clinic study has found.

Dr. Reddi's discovery could have widespread implications in cancer research and endocrinology. It could help oncologists sharpen the diagnosis of specific types of thyroid cancers, while leading pharmaceutical researchers toward therapeutics derived from a protein once thought to feed tumor growth.

"It's not an oncogene like everyone thought it was," Dr. Reddi says, referring to a gene with the potential to cause cancer. "We all knew what happened in the cell culture, but we said, 'That's not good enough,' so we asked, 'What would it do in mice?'"

Thyroid cancer is the sixth most common cancer in the world, and 15 to 20 percent of all thyroid cancer cases are follicular, a type that is more aggressive. Dr. Reddi's findings could aid this diagnosis and treatment for thousands of patients.

Distinguishing benign from malignant follicular thyroid cancer poses a unique challenge to oncologists. An accurate diagnosis of malignant follicular cancer cannot be made until after cancerous material is removed. That has led to countless unnecessary surgeries in patients with benign thyroid tumors. Patients who now present with non-papillary cancerous growths on thyroid cells must undergo surgery to remove the

tumor — even if the cancer is benign.

Dr. Reddi's research found that the PAX8/PPARγ fusion protein, developed from a mutated fusion gene found in many follicular thyroid carcinomas, functions as a tumor suppressor by upregulating (encourages natural production of) microRNA-122 and PTEN, both naturally occurring anti-tumor agents.

PAX8/PPARγ results from the translocation of genetic material between human chromosomes 2 and 3. Previous in vitro studies of the PAX8/PPARγ protein found rapid acceleration of cell growth, which led researchers to the false interpretation that PAX8/PPARγ functioned as an oncogene, a type of mutated gene that encourages tumor propagation, Dr. Reddi says.

Mayo Clinic's in vivo animal studies show that PAX8/PPARγ upregulates the well-known anti-cancer protein PTEN, as well as microRNA-122, and likely facilitates other cancer-fighting molecules.

PAX8/PPARγ does not boost tumor progression when exposed to cancerous cells, Dr. Reddi says. Rather, its facilitation of other native anti-cancer molecules appears to outweigh the tumor propagation. Tumors grew about four times slower in mice exposed to the PAX8/PPARγ gene than those who were deprived of the protein's cancer-fighting qualities.

Among the team's goals in future research is the identification of other microRNA-like markers, which could identify a benign disease and obviate the need for immediate and unnecessary surgery.

Based on her discussions with clinicians at Mayo Clinic, Dr. Reddi says, "There are many complications from thyroid surgery, and having early detection markers could save thousands of unnecessary surgeries every

year. We're just getting started and look towards a rapid translation from bench to bedside."

Provided by Mayo Clinic