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Researchers identify a protein that may predict who will have thyroid cancer recurrence

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Researchers at the National Institutes of Health (NIH), Bethesda, MD, have taken the first steps to determine if a protein, called Programmed Death Ligand 1 (PD-L1), can help to predict which thyroid cancer patients will most likely have a recurrence of the disease. Study findings were presented today at the 2013 Clinical Congress of the American College of Surgeons.

More than 80 percent of patients diagnosed with thyroid cancer have a type called papillary thyroid cancer, which usually grows on only one side of the thyroid gland, according to the American Cancer Society.[1] Most of these patients are women and some have been exposed to ionizing radiation, reports the Centers for Disease Control and Prevention.[2]

Although the five-year survival rate is 93 percent at stage three,[3] the number of people diagnosed with papillary thyroid cancer each year has more than doubled in the last 25 years to 60,220, the American Cancer Society reports.[4] Although thyroid cancer is not usually aggressive, the National Cancer Institute estimates that 10 to 30 percent of these patients still end up having a recurrence.[5]

Previous research has already shown a connection between papillary thyroid cancer and the immune system through inflammatory thyroid disease, reports study coauthor Ryan J. Ellis, a researcher in the

endocrine oncology branch of the NIH and a fourth-year medical student at the University of Pennsylvania's Perelman School of Medicine.

This NIH study specifically focused on the role of a specific protein, PD-L1, which is normally present in the body's immune system to assist with communication between immune cells and help regulate immune response. PD-L1 is also present in some papillary thyroid cancer cells, and may actually help to protect the tumor from the immune system.

"If the immune system tries to approach the tumor and its immediate surrounding area, PD-L1 will make the immune system take a step back and turn off," Mr. Ellis explained.

This protection may then allow the cancer to grow and eventually spread, often to the lymph nodes.

Focusing on prognosis

For other types of cancer, previous clinical trials have used certain treatments to block PD-L1 on the cancerous tumor, allowing the immune system to infiltrate and attack the cancer, explained Myriem Boufraqech, PhD, study coauthor and researcher in the endocrine oncology branch of the NIH. However,

Dr. Boufraqech, Mr. Ellis, and their colleagues wanted to deter-mine the role that PD-L1 plays in predicting whether patients have a more aggressive form of papillary thyroid cancer.

For this study, the researchers looked at resected tumor samples from more than 200 patients. The tumor samples had been stored at extreme freezing temperatures, about negative 80 degrees Celsius. They then used gene expression microarrays to collect data on more than 30,000 genes in each sample—including the PD-L1 gene.

Next, the investigators were able to confirm these findings by focusing on PD-L1 expression in each sample. The final step was to compare PD-L1 levels with medical records of how the patients fared.

"In this cohort of patients, we found that those with high levels of PD-L1 were about twice as likely to have a recurrence as patients with normal PD-L1 levels," Mr. Ellis reported. Results also showed that higher levels of PD-L1 were associated with a higher tendency of having the cancer spread to the lymph nodes.

Next steps and ultimate goals

Mr. Ellis explained that this study is still too early and the cohort group is too small to say whether PD-L1 is associated with a higher likelihood of dying from papillary thyroid cancer, mainly because the number of people who die from the disease is very low.

"This is the first study to show a specific function of the immune system in the proliferation of thyroid cancer," said Lisa Zhang, PhD, study coauthor and a researcher in the endocrine oncology branch of the NIH.

As the study moves from data analysis into a mouse model and ultimately to clinical trials, Mr. Ellis said the findings could potentially change how surgeons provide care to papillary thyroid cancer patients before and after their cancer operations. "The real potential is being able to differentiate, by the time of surgical treatment, who may have a more aggressive type of thyroid cancer," Mr. Ellis said. "Surgeons could potentially look at the patient's PD-L1 expression following biopsy or immediately after resection to see if the patient is more likely to have a recurrence."

"That approach could change the course of treatment," he added, "and allow surgeons, medical endocrinologists, and oncologists to more

intelligently make postoperative decisions for their patients that would help to reduce the risk of a recurrence." Electron Kebebew, MD, FACS, also participated in this study.

More information: 1 "What is Thyroid Cancer?" American Cancer Society. Available at: American Cancer Society. Accessed: September 10, 2013.

2 "Thyroid Cancer and the Environment." Centers for Disease Control and Prevention. Available at: U.S. Centers for Disease Control and Prevention. Accessed: September 10, 2013.

3 "Thyroid cancer survival by type and stage." American Cancer Society. www.cancer.org/cancer/thyroidc … ancer-survival-rates (.) Accessed: September 10, 2013.

4 "What are the key statistics about thyroid cancer?" American Cancer Society. www.cancer.org/cancer/thyroidc … ancer-key-statistics (.)

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5 " Recurrent Thyroid Cancer." National Cancer Institute. www.cancer.gov/cancertopics/pd … hProfessional/page9(.) Accessed: September 10, 2013.

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