Research finds no correlation between regulatory T cells and survival in glioblastoma

16 April 2015

Using a novel methodology of epigenetic quantitative analysis, Dartmouth-Hitchcock's Norris Cotton Cancer Center's interdisciplinary team of investigators led by Camilo Fadul, MD, found no correlation between regulatory T cells (Tregs) and survival in the tumor microenvironment or blood, even when adjusting for well-known prognostic factors. Titled, "Regulatory T Cells Are Not a Strong Predictor of Survival for Patients with Glioblastoma," the findings were published in *Neuro-Oncology*.

"The traditional methods to quantify Tregs may be subjective and result in variability that may explain, in part, the controversial results found in the past," said Fadul. "We used epigenetic quantitative analysis, a novel methodology that more accurately measures lymphocyte populations including Tregs in tumor tissue and peripheral blood."

Patients with glioblastoma, the most frequent and malignant type of brain cancer, exhibit tumor induced immune suppression. Regulatory T cells are one of the types of cells in charge of controlling the immune system in the healthy recognition of self (tolerance) and non-self (foreign) antigens. Patients with glioblastoma have a higher proportion of Tregs than healthy controls, but how important the Tregs are in suppressing the immune system, and if that correlates with prognosis, has been controversial.

Fadul's team studied the correlation with survival, of the Tregs in the tumor microenvironment as well as in peripheral blood of 25 patients with newly diagnosed glioblastoma. They examined tumor-infiltrating Tregs and CD3+ T cells using quantitative DNA demethylation analysis (epigenetic qPCR) and by immunohistochemistry, and peripheral blood Treg proportions measured by flow cytometry. Further analysis used data from The Cancer Genome Atlas to correlate expression of Treg markers with patient survival and glioblastoma subtypes.

"Our finding of no correlation between Tregs and survival in glioblastoma has implications for the design of future immune therapy clinical trials," said Fadul.

The Dartmouth investigators hypothesize that an immune "net score," which takes into account the proportion of regulatory and effector immune cells as well as the expression of co-stimulatory and inhibitory receptors by both cancer and immune cells, will be a useful indicator of the patient's immune status with prognostic and therapeutic implications.

Looking forward, Fadul is analyzing 100 glioblastoma samples from another medical center and using the same novel methodology to determine a model that may allow neuro-oncologists to prognosticate and personalize the immune therapy approach.

More information: *Neuro Oncol* (2015). DOI: 10.1093/neuonc/nou363

Provided by The Geisel School of Medicine at Dartmouth