T cell repertoire changes predictive of anti-CTLA-4 cancer immunotherapy outcome revealed

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Sequenta, Inc. today announced publication of a study done in collaboration with researchers from UCSF and UCLA that used the company's proprietary LymphoSIGHT immune repertoire sequencing platform to investigate the effects of anti-CTLA-4 antibody on the number and types of T cells present in a patient's blood. The results, which appear in the May 28 issue of *Science Translational Medicine*, shed light on the mechanism of action of this type of cancer immunotherapy and suggest that immune repertoire sequencing could be used to predict which patients will have improved survival in response to treatment.

"Immune repertoire sequencing is a new tool that allows us to assess the totality and complexity of immune responses in ways not previously possible," said Lawrence Fong, M.D., Professor, Division of Hematology/Oncology, Department of Medicine, UCSF. "Our analysis of anti-CTLA-4 antibody treated patients using the LymphoSIGHT platform revealed that this therapy induces profound turnover and large-scale remodeling of the entire human T cell repertoire. These findings have implications for understanding how cancer immunotherapy works, which patients will benefit, and the etiology of side effects, such as autoimmune responses."

The researchers used next-generation sequencing to assess the impact of CTLA-4 blockade on changes to the T cell repertoire in 25 metastatic castration-resistant prostate cancer patients treated with ipilimumab and

GM-CSF, 21 metastatic melanoma patients treated with tremelimumab, and nine untreated control subjects. Results showed that patients with longer survival had significantly lower numbers of T cell clones (sets of T cells that all express the same receptor) that decreased in frequency after treatment compared to patients with shorter survival. This association held for both the prostate cancer patients (p

"By leveraging the power of Sequenta's LymphoSIGHT platform for immune repertoire profiling, we and our collaborators have uncovered new aspects of the mechanism of action of anti-CTLA-4 monoclonal antibodies in human cancers," said Tom Willis, CEO of Sequenta. "We have also demonstrated the potential of next-generation sequencing analysis of the immune repertoire for identification of patterns that may predict clinical benefit of immunotherapies, which will be crucial for optimal use of currently available treatments and efficient development of new ones."

More information: "Improved Survival with T Cell Clonotype Stability After Anti–CTLA-4 Treatment in Cancer Patients," by E. Cha et al. stm.sciencemag.org/lookup/doi/ … scitranslmed.3008211

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