TScan Announces Discovery of Precise T Cell Targets in COVID-19 Convalescent Patients to Inform Development of Next-generation Vaccines and T Cell-based Diagnostics

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Data show T cells recognize a small set of immunodominant epitopes shared among patients and predominantly located outside the spike protein

Targets identified using TScan's high-throughput TCR target discovery platform

Waltham, MA, July 28, 2020 — TScan Therapeutics, a biopharmaceutical company focused on the development of T cell receptor (TCR)-engineered T cell therapies in oncology, today pre-published data on medRxiv.org identifying the precise targets of T cells isolated from COVID-19 convalescent patients. Immunodominant targets were shared among patients with the same human leukocyte antigen (HLA) type and were primarily located outside the spike protein. These findings have been submitted for scientific review and publication with the goal of guiding COVID-19 vaccine development that may confer broad, durable immunity by eliciting a robust T cell response. These discoveries may also enable the development of reliable T cell-based diagnostic tests to determine longer-term immunity and inform the development of therapeutic agents.

"COVID-19 vaccine development efforts have been progressing rapidly, but to date remain largely focused on eliciting a neutralizing antibody response against the virus' spike protein," said Gavin MacBeath, Ph.D., Chief Scientific Officer at TScan. "Because antibodies to SARS-CoV-2 appear to diminish over time, there is growing concern that if vaccines do not also generate a strong T cell response, they may only provide short-term immunity. An increasing body of evidence suggests that the T cell response is important in the defense against COVID-19, and T cells that recognize coronaviruses tend to persist much longer than antibodies. In this study, we identified a short list of the most critical T cell targets that could form the basis of a second-generation vaccine, potentially an important follow-on approach to the spike protein vaccines that are currently being developed."

Leveraging its core T cell target identification technology, TScan mapped the memory CD8+ T cell responses of convalescent COVID-19 patients, with a focus on the six most prevalent HLA types. For each HLA type, patient T cells largely recognized the same three to eight immunodominant epitopes. Importantly, a majority of the identified T cell targets were not found in the spike protein of the virus, the target of most vaccines currently in development.

Additionally, these immunodominant targets were not found in other coronaviruses, limiting the likelihood that prior coronavirus infections may confer immunity to COVID-19.

"When the pandemic began, we realized very quickly that our platform technology was well suited to rapidly identify the dominant T cell targets for COVID-19. We are hopeful these data will aid in the progress of developing vaccines with durable protection, as well as therapeutics and diagnostics," said David Southwell, Chief Executive Officer at TScan. "In a matter of three months we were able to collect patient samples and effectively leverage our platform technology to make these important discoveries. We are in discussions with diagnostic, therapeutic and vaccine developers to advance these discoveries into solutions that help bring an end to this pandemic."

TScan collaborated with two academic partners, Atlantic Health System in Morristown, NJ, and Ochsner Medical Center in New Orleans, LA, to collect blood from convalescent patients. In total, 43 patient samples were analyzed in this study.

The company's core focus remains in applying its unique T cell target ID platform to identify novel, shared antigens targeted by T cells in patients with solid tumors that are responding to immunotherapy, with the goal of developing TCR-T cell therapies. This recent study highlights the potential application of the platform in facilitating discovery efforts beyond oncology, including autoimmunity and infectious diseases.

SARS-CoV and SARS-CoV-2 immunity data

Studies of the closely related coronavirus SARS-CoV that caused the 2003 SARS outbreak showed that virus-specific memory CD8+ T cells persisted for up to six years in individuals who had recovered from SARS, whereas memory B cells and anti-viral antibodies were largely undetectable (Peng et al., 2006; Tang et al., 2011). Mouse studies also showed that immunization with a single immunodominant CD8+ T cell epitope is sufficient to confer protection from lethal SARS-CoV infection (Channappanavar et al., 2014). Recent studies of COVID-19 convalescent patients showed that while antibody responses to SARS-CoV-2 could be detected in most infected individuals 10 – 15 days following symptom onset, these antibody responses declined to baseline in many patients during the study's three month follow up period (Seow et al., 2020).

About TScan Therapeutics

TScan discovers and develops transformative T cell therapies (TCR-T) to treat liquid cancers, solid tumors, and other serious diseases. Our proprietary, high-throughput platform identifies previously uncharacterized, clinically-derived shared T cell antigens and all off-target TCR interactions, to enable the development of highly efficacious TCR-Ts with minimal off-target effects. Lead program TSC-100 is expected to enter clinical development for liquid cancers in 2021, and the Company is advancing additional TCR-Ts for solid cancers. TScan was co-founded by Chair Christoph Westphal (Partner, Longwood Fund) based on pioneering research from the Elledge Lab at Brigham and Women's Hospital. The Company has raised over $80 million to date from leading strategic collaborators and investors including Longwood Fund, Novartis Institutes for Biomedical Research, Astellas Venture Management, Novartis Venture Fund, Bessemer Venture Partners, GV, 6 Dimensions Capital, and Pitango Venture Capital.

For more information, please visit www.tscan.com

Link to Manuscript: https://lnkd.in/diB63tW

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