

EMERGING COMPANY PROFILE

ACHILLES' TRUNCAL NEOANTIGENS

BY MICHAEL LEVITEN, SENIOR WRITER

Achilles Therapeutics Ltd. is developing a personalized T cell therapy that uses “truncal” neoantigens expressed in all tumor cells to drive T cells selected from tumor-infiltrating lymphocytes (TILs).

Neoantigen discovery is fueling a burst of cancer immunotherapy companies taking advantage of the tumor specificity of the antigens, bolstered by evidence that high neoantigen burden correlates with prolonged survival and a positive response to immune therapies (see “[Neo Wave](#)”). Because cancers arise from one mutant founder cell, tumors have a clonal history that generates an evolutionary tree. Truncal (clonal) neoantigens arise in the founder cell at the base of the tree’s “trunk”, whereas other neoantigens occur only in the branches.

Achilles uses its Peleus platform to find truncal neoantigens and expand truncal neoantigen-targeting T cells (cNeTs) to generate a personalized T cell therapy derived from TILs.

CEO Iraj Ali said not all neoantigens are created equal. “We believe we’re targeting the best neoantigens by taking the tumor evolutionary approach. We couple it with adoptive T cell therapy that delivers more T cells than a vaccine approach. So you have exquisite targeting with real therapeutic punch.”

Prior to taking the helm at Achilles, Ali was a partner at Syncona Ltd., a founding investor in Achilles.

Achilles emerged from Charles Swanton’s work at the Francis Crick Institute and Cancer Research UK (CRUK). In a seminal 2016 *Science* paper, Swanton and collaborators used data from the first 100 patients in a longitudinal CRUK-funded study (TRACERx) to train an algorithm to identify neoantigens likely to be presented to T cells in tumor samples.

The company now has data from 600 patients; Ali said the ongoing trial will include 850 in total. “The *Science* paper showed bioinformatics could predict clonal neoantigens in tumors, and we could find intratumoral T cells that were activated by these neoantigens.”

ACHILLES THERAPEUTICS LTD., STEVENAGE, U.K.

Technology: Neoantigen directed adoptive T cell therapy

Disease focus: Cancer

Clinical status: Preclinical

Founded: May 2016 by Charles Swanton, Karl Peggs, Sergio Quezada and Mark Lowdell

University collaborators: University College London, Francis Crick Institute

Corporate partners: None

Number of employees: 50

Funds raised: £28.3 million (\$36.3 million)

Investors: Syncona Ltd., CRT Pioneer Fund and UCL Technology Fund

CEO: Iraj Ali

Patents: None issued

Achilles has exclusive rights to TRACERx data and has filed patents on the Peleus algorithms that evolved from the study.

The company uses Peleus to predict which tumor neoantigens are truncal. Then it feeds neoantigen peptides to dendritic cells from the patient’s blood; mixes the peptide-loaded cells with TILs, which stimulates expansion of cNeTs; and conducts assays to confirm antitumor activity and identify which neoantigens stimulated cNeT growth.

Achilles can go from biopsy to personalized T cell therapy in 10 weeks. CAR therapies take roughly two weeks.

Achilles’ approach is similar to Steven Rosenberg’s latest neoantigen-driven TIL therapy. In a June *Nature Medicine* paper, Rosenberg’s team reported [data](#) showing a complete response in one patient with chemorefractory metastatic breast cancer. NCI has the therapy in an ongoing Phase II for metastatic cancers. Rosenberg is NCI chief of surgery and head of the Tumor Immunology Section.

Ali believes Peleus gives Achilles a leg up on Rosenberg's strategy. In addition, although Achilles and NCI both tap into neoantigens and use TILs, Ali said Peleus' predictive power lets the company test all clonal neoantigens identified by the algorithm and ensure a cNeT therapy is produced.

According to BioCentury's BCIQ database, one company, Persimmune Inc., has a neoantigen-based T cell therapy in the clinic. At least 12 other companies are developing cancer therapies using neoantigens.

Ali said Achilles has filed clinical trial applications with MHRA and expects to submit an IND to FDA this year for its lead therapy, ATL-

001. The company plans to initiate trials of ATL-001 in 2H19 in non-small cell lung carcinoma (NSCLC) and melanoma. ■

COMPANIES AND INSTITUTIONS MENTIONED

Achilles Therapeutics Ltd., Stevenage, U.K.

Cancer Research UK, London, U.K.

Francis Crick Institute, London, U.K.

National Cancer Institute (NCI), Bethesda, Md.

Persimmune Inc., San Diego, Calif.

U.K. Medicines and Healthcare products Regulatory Agency (MHRA), London, U.K.

U.S Food and Drug Administration (FDA), Silver Spring, Md.

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