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EMERGING COMPANY PROFILE | REPRINT FROM JUNE 19, 2023

TRexBio: restoring tissue immune homeostasis via Treg modulation

BY DANIELLE GOLOVIN, BIOPHARMA ANALYST

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TRexBio's high-throughput system for target validation harnesses insights gained from regulatory T cell biology in human tissue to recreate disease-relevant pathways in vitro. The company is putting the platform to work in autoimmune and inflammatory diseases, including through two pharma deals.

Because tissue-resident regulatory T cell (Treg) populations have different behaviors and phenotypes in mice than in humans, rooting drug discovery in human Treg biology is key, TRex Bio Inc. CSO Melanie Kleinschek told BioCentury. "The key for us is to use a systematic approach to study these cells in human tissues and find out how they are different and how we can use these insights to derive novel therapeutics for inflammatory diseases."

TRexBio's "Deep Biology" platform maps the behavior of Tregs in human tissue to disease processes. The process starts by collecting healthy and diseased samples of human skin, gut and lung, and then performing bulk and single-cell sequencing to build a map of Treg phenotypes, gene networks and cell-cell interactions in the different tissues.

The goal is to identify targets that can modulate the immune system to restore human tissue immune homeostasis, and to do so efficiently.

"We really focus on streamlined workflows so that we can derive these insights quickly. Right now, we can turn around five novel target ideas within one month for functional validation," said Kleinschek.

After building a "high-resolution map" of human tissue immune regulation to identify important Treg-selective pathways, Kleinschek said "We then validated their activity in a custom suite of disease-relevant functional assays that we built in-house to establish their therapeutic potential."

The functional readouts include intrinsic signaling, stability, apoptosis, proliferation, suppressive activity and adhesion capacity. "We're plotting these outputs on a radar plot and calling that our functional fingerprint. Dependent on what the functional fingerprint looks like, we can map that to the diseases where those functions are impaired," said Kleinschek.

The company has a database of over 200 patient samples, including 300 million cell profiles, and its in vitro culture system recapitulates about 70% of the Treg pathways found in human tissue, said Kleinschek.

TRexBio's technology attracted multiple strategic investors to the company's $85 million series A in March 2022 and has already yielded deals with two of the pharmas who invested in the round.

In January, TRexBio announced a deal with Eli Lilly and Co. (NYSE:LLY) to develop therapies using the Deep Biology platform to treat immune-mediated diseases that granted the pharma exclusive global rights to develop and commercialize three preclinical therapies: TRB-051, TRB-041 and TRB-031. The biotech received $55 million up front and is eligible to receive more than $1.1 billion in milestones under the deal, which builds on a prior collaboration between the companies.

TRexBio CEO Johnston Erwin, a longtime Lilly veteran who most recently was VP, corporate business development – Lilly New Ventures, said he expects TRexBio's lead candidate TRB-061 to be in the clinic in the next 18 months. The modalities, targets and indications of the company's programs are undisclosed.

In January 2022, TRexBio partnered with the Janssen Pharmaceuticals unit of Johnson & Johnson (NYSE:JNJ) to discover targets in immunology and inflammation, with Janssen gaining an option to an exclusive license to therapeutics directed against targets arising from the deal in exchange for an upfront payment, option fees and potential milestones and royalties. Details are not disclosed.

"We have a long held belief that the brilliance that we bring is the biology and the tissue understanding and what the pharma organizations bring is the downstream applications of indications, clinical utilization, clinical trial activity, and in some cases they bring expertise in manufacturing and the understanding of the various chemical entities we would use for the manipulation of tissue Tregs," said Erwin.

TRexBio's origins partly reside in the lab of Michael Rosenblum at University of California San Francisco.

COMPANY PROFILE
TREX BIO INC.

South San Francisco, Calif.

Technology: Tissue Treg-focused therapeutics for immune-mediated diseases

Origin of technology: University of California San Francisco and in-house

Disease focus: Autoimmune, inflammation

Clinical status: Preclinical

Founded: 2018 by Houman Ashrafian, Michael Rosenblum, Adil Daud, Jim Wells, Drew Pardoll, Alison Simmons, Diane Mathis and Wilson Liao

Academic collaborators: University of California San Francisco, University of Oxford

Corporate partners: Eli Lilly and Co. (NYSE:LLY), Janssen unit of Johnson & Johnson (NYSE:JNJ)

Number of employees: About 65

Funds raised: $85 million

Investors: Eli Lilly and Co., SV Health Investors, Johnson & Johnson Innovation – JJDC, Inc., Pfizer Ventures, Polaris Partners, Alexandria Venture Investments, Laurion Capital Management

CEO: Johnston Erwin

Patents: None issued

Rosenblum's team discovered that Tregs promote hair follicle regeneration by augmenting hair follicle stem cell proliferation and differentiation.

The group performed transcriptional and phenotypic profiling to find Tregs preferentially express high levels of the Notch ligand family member JAG1 and showed in a 2017 Cell paper expression of JAG1 on Tregs facilitated hair follicle regeneration.

The company's co-founders also include Diane Mathis, who published a 2016 review comparing mice and human tissue Tregs, Houman Ashrafian, head, experimental therapeutics and clinical pharmacology at University of Oxford and managing partner at SV Health Investors, among others.

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