Docket #: S19-484

EcoTyper: Tumor microenvironment (TME) profiling for personalized cancer therapy

Stanford researchers have formulated a first in line framework called EcoTyper which systematically profiles the tumor microenvironment (TME) cell states in multiple solid tumor types, providing a platform for effective personalized cancer decisions.

EcoTyper solves a huge unmet medical need to better understand the diversity of the tumor microenvironment. By discovering co-associations and patterns of cells found within a tumor from gene expression data, EcoTyper creates a detailed atlas for these cells, both cancer and immune. This invention uses CIBERSORTx, a computational technique, to analyze the RNA of individual cells taken from tumor tissue samples and to purify their distinct gene expression profiles *in silico*. The inventors first demonstrated the technology by dissecting the TME of diffuse large B cell lymphoma's (DLBCL) and then in later studies the inventors expanded the technique to profile the TMEs of 16 types of human carcinoma, characterizing multicellular communities of thousands of solid tumors at the transcriptional level. Almost all the cell types, both known and novel, were validated in a compilation of small conditional RNA-seq (scRNA-seq) tumor atlases.

This information allows critical insight into the potential development of individualized immunotherapies for DLBCL and several other types of solid tumor. The potential therapeutic discoveries, clinical management improvements, and diagnostic impact of this invention can help guide personalized cancer medicine in a monumental way.

Figure

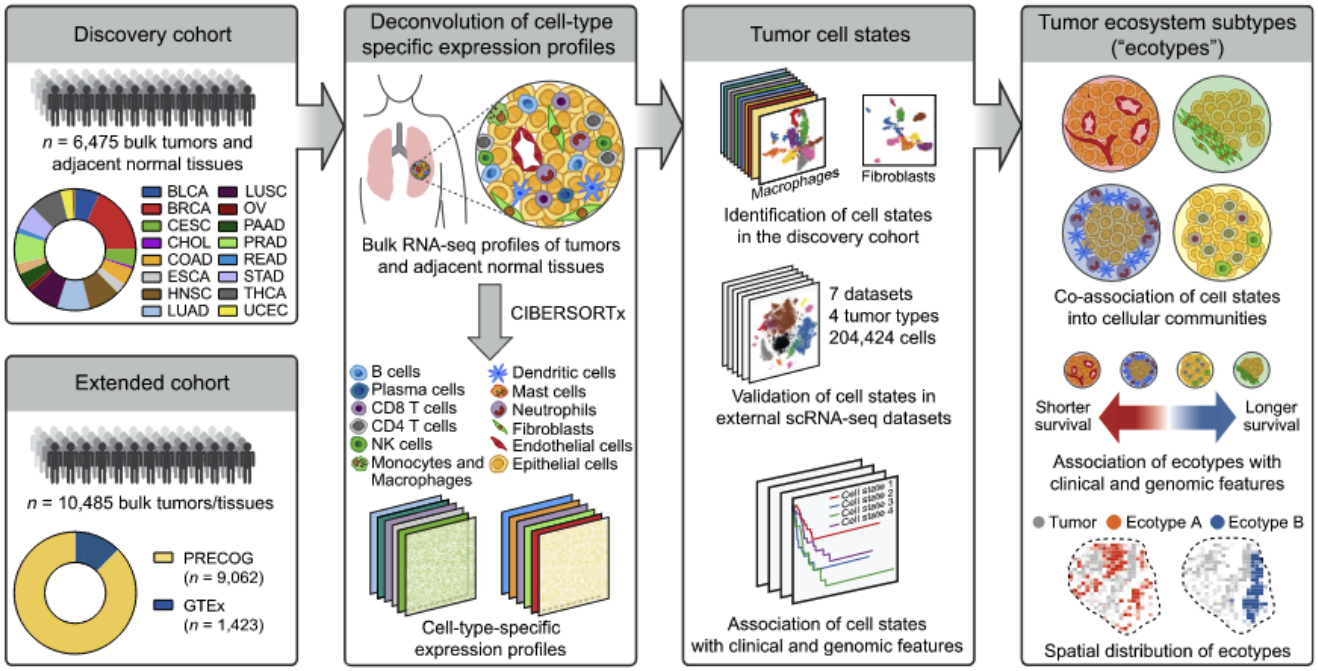

Figure Description: Schematic detailing the discovery and validation of clinically-relevant cell states and cellular ecosystems with EcoTyper. (*Image credit: inventors' publication, Bogdan et al., listed below.*)

Stage of Development:
Inventors analyzed patient biopsy samples from 1,300 DLBCL tumors and defined an atlas of 49 distinct transcriptional states across 13 major cell types. 94% of these states were validated from approximately 200,000 single cell transcriptomes derived from lymphomas, healthy control tonsil tissues and other tissue types. In later studies, inventors further analyzed 16 types of human carcinoma and defined an atlas of 69 cell states for these carcinomas.

Applications

- Personalized **therapeutic target** – For example, several immunologically-active lymphoma therapies rely on the dynamic of TME, such as rituximab, lenalidomide, CART 19, ibrutinib
- Patient selection – for **clinical studies**
- Cancer **monitoring and follow-up**

Advantages

- Potential to create **novel therapeutic and immunotherapeutic targets**
- Predict **clinical outcomes and efficacy**
- Future **drug personalization**
- **Diagnostic tools** for improved disease management
- Potential to aid **earlier cancer diagnosis**
- Enables identification of **new clinically relevant TME in other cancers**
- **First in line** – A vast and comprehensive characterization of cell states in DLBCL and in human carcinomas linking TME to tumor subtypes and genotypes

Publications

- Bogdan A. Luca, Chloé B. Steen, Magdalena Matusiak, Armon Azizi, Sushama Varma, Chunfang Zhu, Joanna Przybyl, Almudena Espín-Pérez, Maximilian Diehn, Ash A. Alizadeh, Mattvan de Rijn, Andrew J. Gentles, Aaron M. Newman. Atlas of clinically distinct cell states and ecosystems across human solid tumors , Cell (published 14 October 2021).
- Barzin Y. Nabet, David M. Kurtz, Chih Long Liu, Farnaz Khameneh, Ranjana H. Advani, Yasodha Natkunam, June H. Myklebust, Maximilian Diehn, Andrew J. Gentles, Aaron M. Newman, Ash A. Alizadeh. The landscape of tumor cell states and ecosystems in diffuse large B cell lymphoma, Cancer Cell (published 30 September 2021).
- Chloé Beate Steen, Bogdan Alexandru Luca, Mohammad Shahrokh Esfahani, Barzin Y. Nabet, Brian Jeffrey Sworder, Farshad Farshidfar, Kiarash Shamardani, David Matthew Kurtz, Yasodha Natkunam, Ranjana Advani, Chih Long Liu, Maximilian Diehn, Andrew J Gentles, Aaron Matthew Newman, and Ash A Alizadeh, An Atlas of Clinically-Distinct Tumor Cellular Ecosystems in Diffuse Large B Cell Lymphoma, Blood (published 13 Nov 2019).

Patents

- Published Application: WO2021092236
- Published Application: 20230027353

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