

Engitix Therapeutics

engitix.com



Engitix Therapeutics: beyond the cells

A novel platform that incorporates the human extracellular matrix is helping to accelerate drug development for diseases including fibrosis and solid tumors.

Only 5% of oncology drugs that enter clinical development ultimately reach the market. Contributing to the high failure rate is that most in vitro target and biomarker identification and validation involves growing mammalian cells on artificial substrates that do not accurately model human physiology. The extracellular matrix (ECM) is a dynamic bioactive acellular environment, but its critical role in driving solid tumor development, immune-cell exclusion and therapy resistance is typically ignored. Although ECM proteins represent promising therapeutic targets, the importance of the ECM in its complexity has largely been overlooked in target and drug discovery efforts.

Addressing this gap is Engitix, with a first-in-class platform aimed at deconvoluting the bioactive role of the tissue-specific and disease-specific acellular microenvironment. By combining its unique understanding of the ECM with world-class technology—including a unique tissue collection, proprietary tissue decellularization protocols, and Engitomix bioinformatic software—Engitix is unlocking insights and developing physiologically realistic in vitro three-dimensional (3D) platforms incorporating the ECM. These platforms enable the generation of new, more relevant therapeutics against fibrosis and solid tumors, and meaningful biomarkers to ensure their delivery to the right patients.

Reshaping target identification, drug discovery and development

The ECM, comprising some 300 proteins, provides structural, biochemical and bioactive support to cells within human tissues and organs. It is constantly being remodeled to control and/or regulate critical biochemical and biomechanical processes required for tissue morphogenesis, differentiation and homeostasis. Changes in the composition and structure of the ECM (or genetic mutations that result in aberrant remodeling) can affect the phenotype of the associated cells, leading to multiple diseases.

Engitix has pioneered a platform to decipher and model the complexity of the ECM. For a particular disease, using samples from its own human tissue biobank and proprietary tissue-decellularization protocols, Engitix conducts proteomic and transcriptomic analysis on ECM from healthy and diseased tissues (Fig. 1). Characterizing the different ECM compositions allows the identification of potential therapeutic targets that locally activate and influence pathology. To decipher the role of ECM in modulating cellular phenotype, disease-relevant cell types are then re-seeded in tissue-specific and disease-specific ECM. Omics analysis is used to understand ECM-driven modulation of cellular phenotypes critical for disease

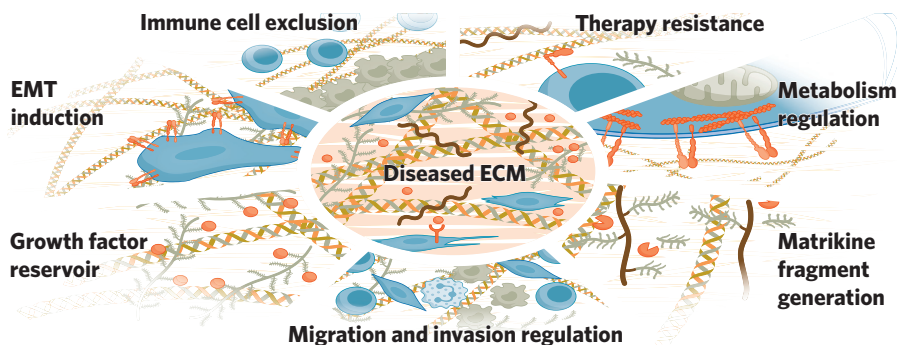


Fig. 1 | The bioactive functions of the extracellular matrix (ECM) in solid tumors.

development, after which Engitix incorporates the human ECM platform within a hydrogel format for target validation using a cell-based high-throughput screening platform.

“Using our technology, we have the unique ability to decode tissue- and disease-specific ECM and create highly clinically relevant models of fibrosis and cancer,” said Mike Burbridge, VP Oncology and IO. “In addition, our platform provides an in vitro 3D ECM pre-clinical and clinical de-risking screening tool to allow rapid prioritization of disease-relevant targets, compounds and biomarkers—testing candidates in the context in which they will ultimately be used, thereby accelerating successful drug discovery.”

Critical role of the extracellular matrix in cancer

Changes in the ECM play a key role in tumor progression. It is thus crucial to develop and rigorously study preclinical models of ECM in different cancer types to successfully progress clinically relevant therapeutic candidates. Engitix is using 3D in vitro models based on tissue-specific ECM to model primary and metastatic tumors, and sensitivity and resistance to drug treatments.

The company is developing a broad portfolio of proprietary and partnered programs in fibrosis and solid tumors, including candidates for pancreatic ductal adenocarcinoma and hepatocellular carcinoma. With partnerships central to its research and development (R&D) strategy, Engitix has already established two discovery and development collaborations with Takeda Pharmaceuticals in advanced fibrotic liver diseases and fibrostenotic inflammatory bowel diseases, and a collaboration with Dompé Farmaceutici combining the Engitix ECM platform with Dompé’s Exscalate artificial intelligence platform to further accelerate drug discovery and development in fibrosis and solid tumors.

The extracellular matrix drives immune-cell exclusion

It is often incorrectly assumed that the ECM simply acts as a physical barrier to therapies and immune cells. Engitix has demonstrated that this is not the case, and that antibodies, small molecules and immune cells readily traverse the ECM. Immune-cell exclusion is clearly shown to be a dynamic process, driven by cancer cells in specific ECM environments. This has important implications for understanding and overcoming immune-cold tumors and immunotherapy resistance. “Use of clinically relevant 3D human ECM-based in vitro models enables the interrogation of immune-cell exclusion and modulation of the immune response,” explained Mike Burbridge. “We are driving novelty through providing the right environment to mimic the way cancer cells and immune cells behave in patient tumors.”

Engitix is interested in collaborating with biopharma companies to explore unique ECM protein signals and novel targets in new indications; identify novel targets for second-generation chimeric antigen receptor T cells (CAR-T) immunotherapies for solid tumors; and advance selected pre-clinical programs against Engitix targets through candidate selection and IND-enabling studies.

“Our unique ECM platform is de-risking and re-shaping drug discovery and development processes,” said Giuseppe Mazza, CEO and co-founder. “It is applicable to multiple organs, disease indications and therapeutic modalities, and has considerable potential to improve the lives of patients and their families.”

CONTACT Giuseppe Mazza, Co-founder & CEO
Engitix Therapeutics
London, UK
Email: giuseppe.mazza@engitix.com