Arbele
www.arbelebio.com

Defeating cancer with next-generation immunotherapies

Gastrointestinal cancers present a huge unmet medical need. Arbele is working to bring cutting-edge immunotherapy to these patients.

Gastrointestinal (GI) cancers (including colon, stomach, liver, esophagus and pancreas) account for more than 3.3 million deaths annually worldwide, far exceeding the 1.7 million attributed to the most common cancer, lung cancer. With the exception of colorectal cancer (CRC), the vast majority of patients with GI cancer are diagnosed at an advanced stage when curative or effective treatments are very limited. Poor prognoses result from a lack of treatment options due to inadequate drug development, and most of the current drugs approved by the US Food and Drug Administration (FDA) are line extensions from other cancer indications. There is great need for therapeutics targeting both GI tumor-specific antigens and the immune system, and specifically to address the complexities of the solid tumor microenvironment (TME).

Arbele is a biopharmaceutical company which has established R&D sites in the Seattle area and at the Hong Kong Science and Technology Park. To more effectively treat solid tumors, Arbele is targeting cadherin-17 (CDH17) with new 'combination' treatments that incorporate multiple mechanisms of anti-tumor activity within a single therapeutic. CDH17 was initially identified as an oncogenic driver of liver and stomach cancers by John Luk, founder and CEO of Arbele. In GI cancer where CDH17 is highly expressed, both Wnt-β-catenin and MAPK signaling pathways are activated and its crosstalk with α2β1 integrin signaling further promotes tumor growth and metastasis. Increased expression of CDH17 has been detected in more than 50% of GI cancers, and 90–95% of CRC and gastric adenocarcinomas. These findings present a promising opportunity to treat millions of GI cancer patients worldwide by redirecting the patient's immune cells to target CDH17.

Arbele has developed its proprietary technology mainly on two platforms: next-generation chimeric antigen receptor T (CAR-T) cells and multi-specific T cell engaging antibodies. To effectively address formidable protumor mechanisms within a solid TME, Arbele's non-viral CAR vectors are engineered for multiple antitumor CAR cell activities, such as targeting more than one tumor antigen, reversal of tumor immunosuppression and the recruitment and activation of additional effector cell types and cytotoxic activities (Fig. 1). Certain vector genes are engineered to be expressed only in response to the local TME to ensure greater safety and efficacy. These otherwise quiescent CAR cells are stimulated by tumor cells or other components of the TME to generate an artificially enhanced immune response and in this way function as artificial immunosurveillance CAR cells or 'AI-CAR'. AI-CAR is being further developed as a 'point-of-care' therapy targeting a 3–7 day process from 'needle-to-needle'.

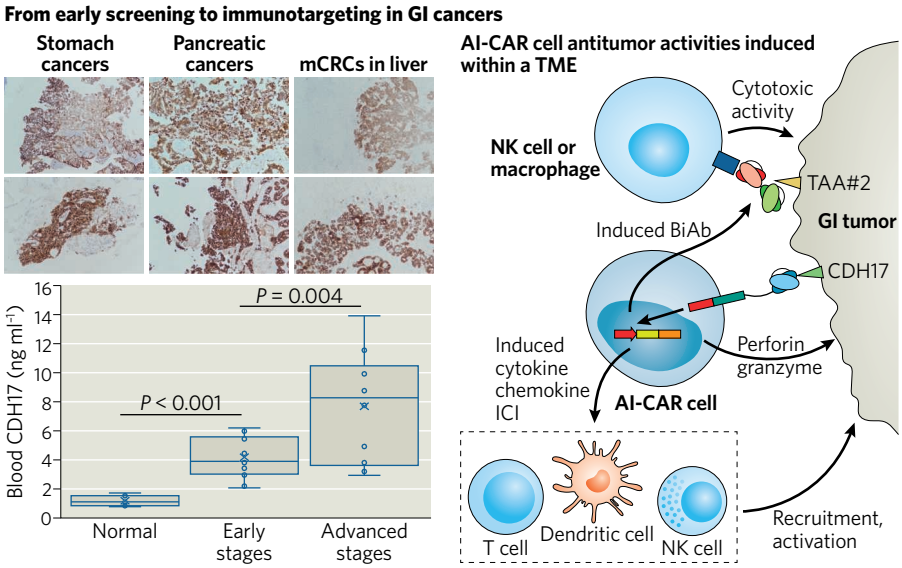

Fig. 1 | Immunotargeting activities in gastrointestinal cancer. Artificial immunosurveillance chimeric antigen receptor (AI-CAR) cell antitumor activities induced within a tumor microenvironment. BiAb, bispecific antibody; GI, gastrointestinal; ICI, immune checkpoint inhibitor; NK, natural killer; TAA, tumor-associated antigen; TME, tumor microenvironment.

TriAx antibodies

Arbele's multi-specific antibodies are also designed for greater efficacy in GI cancer treatment through the combination of multiple antitumor mechanisms. Arbele has developed a family of multispecific antibodies, based around two novel core structures. These TriAx antibodies possess certain characteristic antibody features for stability, desirable pharmacokinetic properties and low antigenicity. For high-yield manufacturing, Arbele is developing a proprietary single-vector expression system. Typically, TriAx antibodies target tumor-associated antigens and engage T cell receptors to redirect T cell cytotoxicity. These heterodimeric antibodies are designed primarily for the generation of tri-specific and tetra-specific antibodies with lower molecular weight and potentially greater tumor penetrance relative to their homodimeric counterparts. These formats with higher-order valency enable the generation of a single antibody that, for example, antagonizes immunosuppression within the TME, targets a second tumor antigen and favours distribution to a tumor relative to lymphoid tissue. Arbele's lead antibody, ARB-202, which binds to CDH17 and the T cell receptor antigen CD3, is set to enter human clinical trials in late 2020.

Looking ahead

Arbele has multiple patent filings around its proprietary cell and antibody therapies, such as AI-CAR and TriAx platforms, in addition to its worldwide patent protection on CDH17 and its utilities in therapeutics and diagnosis (Fig. 1). Although Arbele's immunotherapeutic platforms have initially focused around CDH17 to tackle GI cancers, additional targets and mechanisms of action are being incorporated to generate increasingly potent treatments for specific GI cancers. Arbele welcomes discussions with potential partners who wish to join the company on their path toward developing AI-CAR and TriAx therapies, and those who would like to draw on Arbele's immunotherapeutic expertise to support development of their own candidates.

CONTACT
Don Staunton, Co-Founder and CSO
Arbele
Redmond, WA, USA
Tel: +1-206-602-2282
Email: info@arbele.org