Chiome Bioscience Inc.
www.chiome.co.jp

Diversified antibodies to accelerate drug discovery

With its innovative antibody discovery platform ADLib, Chiome Bioscience is nurturing a pipeline of antibody candidates ready for partnering.

Chiome Bioscience aims to discover and develop therapeutic antibodies for unmet medical needs using its monoclonal antibody platform ADLib (Autonomously Diversifying Library). The company, which floated on the Tokyo Stock Exchange in 2011, has grown from an antibody-generation startup to a biotech focusing on discovery and development with early clinical trial capabilities. As well as conducting contract work for pharma, biotech companies and academia, Chiome has an in-house clinical stage pipeline and candidates undergoing preclinical testing.

"Monoclonal antibodies are our core competence," said Yoshinori Yamashita, Head of R&D Division & Business Development.

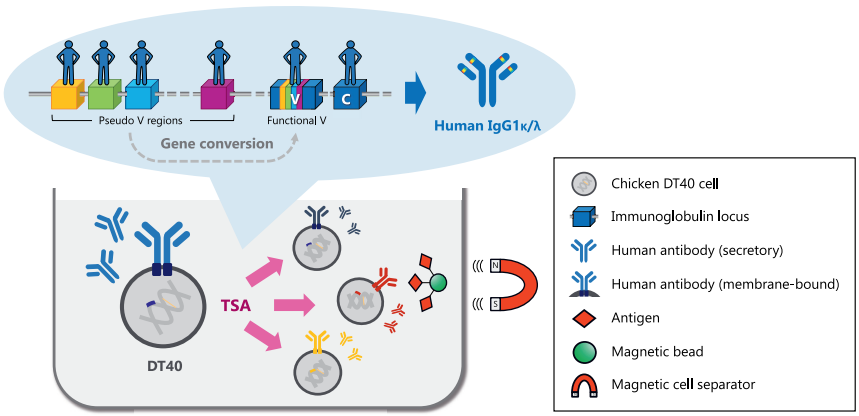

Fig. 1 | The human ADLib system. In DT40 cells, chicken immunoglobulin loci were replaced with human counterparts and a variety of designed human pseudogenes were inserted upstream of functional V gene. Gene conversion of the resulting cells can be enhanced with treatment of trichostatin A (TSA), creating diversified, avian B cell libraries expressing full-length human antibodies for in vitro selection. Antigen specific clones can be enriched by antigen-conjugated magnetic beads and isolated by fluorescence-activated cell sorting. The antibodies are then screened and assayed using culture supernatants. This process can be repeated to streamline antibody generation and affinity maturation.

Building on antibody discovery

Chiome was established in 2005 to commercialize ADLib, an innovative antibody discovery platform invented at RIKEN. ADLib creates diversified libraries of antibodies using DT40 cells, a line of avian B cells. The ADLib system generates diversity in the immunoglobulin gene through gene conversion, enhanced by trichostatin A (TSA) treatment.

"This is a 'copy and paste'-type process, which overwrites existing genes to increase diversity," said Ke-Yi Lin, Principal Scientist and CMC lead.

ADLib also relies on the ability of DT40 cells to express both membrane-bound and secreted antibodies. The cells expressing the clones of interest can be selected based on the membrane bound antibodies, using high-throughput fluorescence-activated cell sorting. The antibodies can be assayed directly or isolated from the supernatant after cell selection, allowing screening and validation without the need to extract antibody genes and express them. This process can be repeated to improve monoclonal antibody affinity, seamlessly building in affinity maturation as part of the process. ADLib allows for constant diversification of antibodies (Fig. 1).

The original ADLib system produced chicken antibodies that were then converted to humanised antibodies. The human ADLib system can create libraries of fully human monoclonal antibodies, bypassing the humanisation process.

"ADLib is a robust and simple method incorporating selection, full-length IgG expression, de novo humanisation, and affinity maturation in one platform, meaning that we can go from antigen to primary hit antibodies in seven days," said Lin. "Our technology uses the power of cells to create unique gene sequences."

Chiome's monoclonal antibody discovery engine also includes technologies to prepare soluble proteins and membrane proteins for research, and create antibody-based multi-specific modalities.

Creating a pipeline

Chiome's lead candidate is CBA-1205, an ADCC-enhanced antibody against DLK1, a first-in-class target. CBA-1205 is in the dose-escalation part of a phase 1 study. The second part of the phase 1 study, in hepatocellular carcinoma patients, is planned for the second half of 2021. Chiome primarily intends to out-license CBA-1205 once phase 1 is complete.

CBA-1535, in development for the treatment of solid tumors, is a Tribody designed to engage T cells and target the 5T4/WAIF1 antigen on the surface of many solid tumors, bringing the cancer cell and T cell together. Preclinical development is underway, with phase 1 planned for early 2022.

Chiome plans to license out its pipeline products at preclinical or early clinical stages and already has some deals in place. In a January 2021 agreement with Shanghai Henlius Biotech for LIV-2008/2008b, an anti-Trop-2 antibody, Henlius gains exclusive development and commercialisation rights in Chinese territories, along with option rights for the rest of the world. The deal is worth up to $122.5 million plus royalties. In May 2021, Chiome signed a collaborative research agreement with UK company Mologic covering antibody discovery and development for use in advanced diagnostic tests. Chiome will receive research fees as well as royalties on any marketed diagnostics.

Other deals include a joint research agreement with partner Trans Chromosomics, and a licensing agreement with ADC Therapeutics for LIV-1205 (ADCT-701), which targets DLK1 for development as an antibody–drug conjugate for cancer therapy. ADC Therapeutics is preparing for clinical trials.

Growing through collaboration

Chiome works with contract clients to support drug discovery. Fee-for-service agreements include Chugai Pharmaceutical, Mitsubishi Tanabe Pharma, Ono Pharmaceutical and Kyowa Kirin. Utilizing Chiome's ADLib, Fujirebio has created several antibodies and launched diagnostic kits for vitamin D (2013) and aldosterone (2019).

Chiome is looking to set up synergistic collaborations with other companies to access technologies that can be integrated into Chiome's core competency in antibody generation and engineering for therapeutic and/or diagnostic use.

"What makes Chiome different is that we have our own proprietary platform. We have capabilities that equip us with the toolkit needed throughout the whole antibody development process, from hit identification to mid-scale production," said Yamashita. "Our aim is to accelerate every step within the antibody development cycle."

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