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Chiome Bioscience Inc

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Fully human antibodies in vitro in 10 days

Chiome Bioscience announces breakthrough technology that generates fully human, highly diversified antibodies in vitro in 10 days, without immunisation.

The speed of fully human antibody generation entirely in vitro in as little as 10 days has major implications for medical science, from tailor-made medications at a patient's bedside to fast and powerful responses to a pandemic or bioterrorism, according to Chiome Bioscience.

The company's innovative technology is based on a gene conversion mechanism in chicken DT40 cells which can generate monoclonal antibodies with huge diversity at very rapid speeds. While some methods using bacteria or yeast claim rapid generation of antibodies, the ADLib® (Autonomously Diversifying Library) system is differentiated by its generation of a full-length antibody.

Chiome Bioscience's original ADLib® system has already proven its potential to generate antibodies for uses including highly conserved proteins, small molecules, toxic compounds, peptides, lipids, glyco-chains and GPCRs (G protein-coupled receptors). Now Chiome has achieved a major milestone in its technology development: the human ADLib® system.

"We believe Chiome is the only biotech company that develops its antibody library using DT40 cells in an in vitro system," said Masa Fujiwara, CEO of Chiome Bioscience. "Using conventional methods, it can take at least two months to generate human antibodies, but we need only 10 days."

A global innovator, Chiome Bioscience is a venture biotech company founded in 2005 to develop and commercialise the ADLib® for industrial use. The technology was originally invented by RIKEN, one of the largest science and technology research institutes in Japan. When the inventor and a venture capitalist decided to commercialise this technology, Dr Fujiwara accepted the position of CEO.

He recognised the potential impact of new antibody discoveries, particularly after watching his mother suffer from the painful side effects of ineffective treatment of Hepatitis C. His vision for the company is to "provide antibody drugs with 100% efficacy and zero side effects to individual patients who have not been satisfactorily treated".

In 2007 Chiome signed a collaboration agreement with Chugai (a member of the Roche Group), a leading company in biologics in Japan. Under this agreement Chiome generates chicken IgM and mouse-chicken IgG antibodies for Chugai's targets. This collaboration has contributed significantly to the ongoing development of the technology, particularly the human ADLib® system.

Early research identified speed and diversity

Early research showed that, when the chicken DT40 B-cell line was undergoing gene conversion, the conversion rate at the immunoglobulin locus was enhanced by treating the cells with TSA (trichostatin A). Enhancement of gene conversion rates results in the generation of huge diversity in the library.

As the DT40 cell displays surface-type and soluble-type antibodies, the target antigen is conjugated with magnetic beads and put into a cell library. Only those specific clones which bind to the antigen are collected. These cells are cultivated in a nutrient medium for about one week, and antibodies recovered.

The ADLib® system's alternative diversity benefits those pharmaceutical companies which are keen to obtain as many antibodies as possible in the discovery stage. It also means they can expect to obtain unique sequences or new epitopes that differ from those obtained by other methods.

"Hybridoma and phage display are two key methods generally employed in antibody generation, however these technologies are not powerful enough to generate antibodies against many tough antigens," Dr Fujiwara said.

"Our strategy is not to compete with these technologies, but to generate antibodies against more challenging targets such as GPCRs, ion channels, transporters and evolutionally conserved proteins."

For example, the ADLib® system successfully generated antibodies for Semaphorin 3A in only nine days for Chiome collaborator Professor Yoshio Goshima of Yokohama City University, who had made many unsuccessful attempts using conventional methods.

Chiome's laboratories maintain huge frozen ADLib® library stocks which can be accessed at any time.

"This system could be a powerful weapon to fight against a pandemic or bioterrorism," Dr Fujiwara said. "Researchers would not have the time to wait months for development of a human antibody."

"It also has the potential to offer a tailor-made solution at a patient's bedside, with the best-matched antibody generated in a few days."

Currently there are three types of ADLib® libraries:

- First generation (IgM): 200 libraries in stock.
- Second generation (mouse – chicken IgG2a): 80 libraries in stock.
- Fully human (IgG): with expanding diversity and a growing library size.

In further developing and commercialising this technology, Chiome Bioscience has three business models:

Collaboration, alliance and partnership in drug discovery

Chiome Bioscience's primary role is to generate antibodies for a partner's antigen, co-develop a lead candidate, then grant a licence to a pharmaceutical or diagnostic partner.

Out-licence lead antibody

Collaboration with academia and institutes to develop first-in-class therapeutic antibodies. A lead antibody is developed up to the preclinical stage, then out-licensed to a pharmaceutical company or developed in-house.

Out-licence AdLib® system

The technology is out-licensed to a company seeking a high throughput antibody generation platform. A licence has been granted to FUJIREBIO INC, one of Japan's leading diagnostic companies, which has developed an antibody for Vitamin D by the ADLib® system and made it into a diagnostic kit. Sales of the kit commenced in Europe in December 2013.

Chiome Bioscience is keen to sign further partnership and out-licensing agreements.