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AdAlta Pty Ltd

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New next generation i-body technology foreshadows major advantages over traditional antibodies

An Australian biotech company is pioneering next generation antibody technology using modified shark antibodies and their human analogue, the i-body, to develop new therapies and diagnostics. A unique binding structure, extreme stability and alternative delivery mechanisms are key advantages.

While the single domain of the shark antibody has led to AdAlta's groundbreaking R&D, it is the development of the i-body as a human scaffold that has enabled this Australian biotech company to attract new collaborations with major global biopharma companies.

"We have identified a human protein that essentially has the same structural properties and behaves in the same way as the single domain of the shark antibody," said Ms Samantha Cobb, CEO of AdAlta Pty Ltd. "We have used this protein as a scaffold to build a library of compounds with unique features similar to the shark antibody.

"There is no one else working on this human scaffold, and we are now at the stage of proving that the i-body platform works in vivo."

As a next-generation discovery platform, the shark antibody and the i-body combine the advantages of conventional antibodies with important features of small molecule drugs. Like conventional antibodies, they have exquisite specificity and high affinity for their target.

But they also have a unique binding structure with a very long loop that human antibodies and other next generation biologics do not possess. Dr Mick Foley, founding scientist and Chief Scientific Officer of AdAlta, said this long binding loop can access epitopes that traditional antibodies and other scaffolds cannot.

Long binding loop penetrates difficult targets

"The loop extends like a finger and is able to penetrate into clefts and grooves on targets which traditional monoclonal antibodies find difficult," said Dr Foley. "The shark antibody and i-body scaffolds have CDR3 binding loops that are between 10-20 amino acids in length. In human antibodies the average CDR3 length is 10-12 amino acids."

AdAlta has established that, like the shark antibody, the i-body is also extremely stable at high temperatures and both high and low pH for extended periods. They can be manufactured in bacterial systems, an inexpensive and easy method compared to traditional antibodies which require human cell culture.

“The stability of the technology is such that we can boil these, put them in acid, and look at extreme pH and extreme temperatures over long periods of time,” Ms Cobb said.

This could mean that the first barrier to oral delivery – stability within the harsh environment of the stomach – could be overcome. Other delivery mechanisms that are not available with traditional antibodies may also be possible.

Therapies could be developed for topical applications, and the small size of the protein could make the i-body an attractive candidate for inhalation. Stability and small size may drive ophthalmology applications such as eye drops, while the high level of stability points to improved product shelf life. As a human protein, the i-body will also be less immunogenic.

Clinical trial timeframes may be cut

The single domain shark antibody technology and the i-body have been developed into phage-displayed libraries that can be used to rapidly screen and identify binders to a particular target. Lead compounds may be identified more quickly, cutting timeframes to reach clinical trials.

This, coupled with the lack of royalty stacking issues through manufacture in *E.Coli* or other bacteria-based systems, could reduce production costs.

Ms Cobb said the new technology also has applications in areas such as GPCRs and ion channels.

“GPCRs are a target class that have been difficult to approach with the traditional antibody or other biologic-based technologies because these targets are complex proteins that span the membrane multiple times. The long binding loop of the i-body scaffold really has an advantage in being able to access the binding pockets, providing antagonist or agonist binders.”

AdAlta last year signed an agreement with Roche to evaluate and identify shark antibody binders. AdAlta is screening its shark antibody library against a target and providing Roche with the identified shark antibody binders for further evaluation.

A newly signed agreement with a major multinational biopharma company is the first to focus specifically on the therapeutic application of the i-body technology, with AdAlta screening its i-body library on one of the company’s therapeutic targets.

AdAlta is keen to discuss further similar partnering opportunities.

“Our technology could be the one to step up and find the right compounds where companies have been having difficulties finding small molecule drugs or antibodies for targets,” Dr Foley said.

In the next three to five years, AdAlta’s goals are to demonstrate the i-body technology and its versatility for a variety of therapeutic interventions and diagnostic reagents, and to progress a lead compound into clinical trials in humans.

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