YUMAB GmbH
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Nature knows best: fully human antibodies take the therapeutic lead

YUMAB, a global provider of fully human monoclonal antibodies, offers ultra-fast discovery and efficient lead development. The company is looking to expand its network of collaborators and clients through flexible licensing options for diagnostics and therapeutics development, as well as the provision of customized fee-for-service solutions.

In little more than five years, German biotechnology company YUMAB (a phonetic play on HUMAB (human monoclonal antibody) in which the "Y" symbolizes the antibody structure) has become a global player in human monoclonal antibody (mAb) discovery and development, and it is now a driver of the general trend in the immunotherapy space toward the use of fully human mAbs for therapeutic applications. Unlike their predecessors—mAbs of animal origin, or humanized or synthetic mAbs—YUMAB's fully human mAbs maximize epitope diversity while minimizing immunogenicity and thus adverse effects.

After the US Food and Drug Administration approval in 2002 of the first ever fully human mAb drug (AbbVie's Humira (adalimumab)), fully human mAbs rapidly became the gold standard of mAb-based immunotherapy. Today, 40% of all marketed mAbs are of human origin, and four of the five mAbs approved in the first quarter of 2017 are fully human mAbs[1]. This shift toward using human mAbs for immunotherapeutic applications has resulted in a need to rethink antibody discovery and development strategies to optimize the process from beginning to end.

YUMAB's versatile platform for ultra-fast mAb discovery and efficient lead development makes it a partner of choice for the generation of novel fully human mAbs tailored to the client's needs in any kind of mAb-development program, at any stage, and with the properties needed for any immunotherapeutic strategy (**Fig. 1**).

"Today, when I look back to the 28 years of scientific research, I dedicated to make antibodies as human as possible, I am really happy to see that the market has finally recognized the advantages of fully human antibodies for immunotherapy," said Stefan Dübel, co-inventor of antibody phage display and co-founder of YUMAB.

The YUMAB platform: fast and reliable

Human mAbs are currently developed via one of three platforms: transgenic animals that express human immunoglobulins, bacteriophage display of human antigen-binding fragments, and yeast display of human immunoglobulins. Of the 23 fully human mAbs approved so far, 17 are derived from transgenic mice and 6 were developed with phage-display technology. Yeast display has generated a clinical pipeline, but no marketed product yet.

On the basis of the clinical success of fully human mAbs and the founders' 28 years of experience with fully human mAb selection from ultra-diverse phage-display libraries of naive antibodies, YUMAB has refined a development platform that delivers the antibodies closest to germline among those on the market.

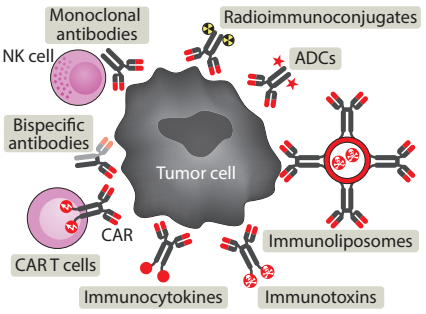

Figure 1: YUMAB's platform for the discovery and development of fully human mAbs. Shown are the various antibody drug formats that can be generated for oncology applications. CAR, chimeric antigen receptor; NK cell, natural killer cell; ADC, antibody–drug conjugate.

YUMAB uses libraries of close to germline origin, but highly diverse antigen-binding fragments that represent the entire natural human antibody repertoire for the initial *in vitro* screening, with a coverage of up to 10^{11} native antibody fragments (next-generation-sequencing-verified diversity).

By performing the whole antibody-discovery process *in vitro* and bypassing animal immunization, YUMAB eliminates potential epitope restriction by the host immune response. The resulting comprehensive coverage of the human antibody repertoire translates into vastly improved success rates in identifying antibodies that target rare or difficult antigens, including multi-spanning transmembrane receptors such as G protein receptors or ion channels.

YUMAB's optimized naturally derived libraries also exhibit consistently broader length distributions in complementarity-determining regions—up to 32 amino acids (aa), compared with a maximum of 17 aa in typical synthetic libraries—thus allowing much deeper exploration of the structural space of the human antibody repertoire. All of the above is provided in an antibody-discovery process that takes only 4–8 weeks to identify candidate antibodies, even to difficult antigens.

The resulting antibodies are maximally de-risked with respect to immunogenicity, because every V region sequence has been expressed in a human body before. This, in combination with the early de-risking of potential development issues through stability and productivity testing, means YUMAB's antibodies can quickly travel the path from basic research to clinical translation. The versatility of the resulting antibodies further allows for any level of manipulation, including functionalization or combination (**Fig. 1**).

Fully human antibodies to jump-start drug development

YUMAB's mission is to accelerate the antibody pipelines of its customers by utilizing its robust antibody-discovery and lead optimization platform. The company's proprietary libraries and technologies have provided human mAb candidates to world-leading pharma companies, and several products are in clinical development already.

YUMAB facilitates all kinds of collaborations in order to maximize the impact of its antibody technology; consequently, it offers three general options for partnering. First, YUMAB offers a contract research organization (CRO)-like option tailored to meet the specific needs of very diverse customers from biotech and pharma. Alternatively, it offers customized deals with low entry costs for academic labs and biotech start-ups with promising targets. Finally, the company has established its internal pipeline of fully human mAbs, mainly in oncology, for out-licensing in the future.

According to Thomas Schirrmann, CEO of YUMAB, "we cannot change biological mechanisms behind the success of antibody drugs, but we can focus on fully human antibodies as early as possible in our R&D programs to accelerate the translation from bench to bedside and mitigate risk of clinical failure. YUMAB supports clients and partners worldwide in this process to save time, improve the biological quality of their lead candidates and ultimately help increase the value of their drug development pipelines."

1. Booth, B. Human antibody discovery: of mice and phage. *Forbes* https://www.forbes.com/sites/brucebooth/2017/05/11/human-antibody-discovery-of-mice-and-phage/ (2017).

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