YUMAB GmbH
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Targeting difficult antigens in immuno-oncology with fully human antibodies

YUMAB's antibody discovery and development platform integrates superior technologies for the development of fully human antibodies against complex or difficult novel targets to generate advanced immuno-oncology biotherapeutics.

The rapid development of novel immuno-oncology (I-O) approaches has fundamentally disrupted the oncology market. I-O has now become a key component of cancer therapy and has quickly reshaped priorities in oncology research and development (R&D) across the industry. Unprecedented clinical success in certain cancer types continues to fuel record investment and partnering activity, and today more than 4,000 I-O agents, including checkpoint inhibitors, oncolytic viruses, cell therapies, and CD3-targeted bispecific antibodies, are in preclinical or clinical development[1,2].

Yet still only a minority of patients benefit from effective and durable I-O treatments. Major challenges to unlocking the full potential of I-O therapies include the development of resistance, the lack or unpredictability of responses due to tumor heterogeneity, a dearth of novel targets, and mounting target complexity, making it increasingly difficult to engage these targets therapeutically. Indeed, most monoclonal antibody (mAb) drug discovery projects in I-O are focused on just a few targets, such as the checkpoint molecule programmed cell death 1 and CD19-specific chimeric antigen receptor (CAR) T cell therapies, but great effort is being channeled into targeting more complex and difficult antigens, such as multimembrane-spanning receptors, receptor complexes, and post-translationally modified proteins.

YUMAB has developed an advanced antibody discovery and development platform covering all technologies from target to lead (**Fig. 1**). "The discovery of mAb drug candidates for I-O is like trying to find a needle in a haystack," said Thomas Schirrmann, CEO of YUMAB. "Our platform provides a uniquely large and comprehensive set of human antibody candidates with a broad range of functional properties that helps to minimize the time to lead identification and to maximize the therapeutic potential of antibody drugs."

> **"The key for better I-O biotherapeutics is a uniquely large and comprehensive set of human antibody candidates**
>
> Thomas Schirrmann, CEO, YUMAB

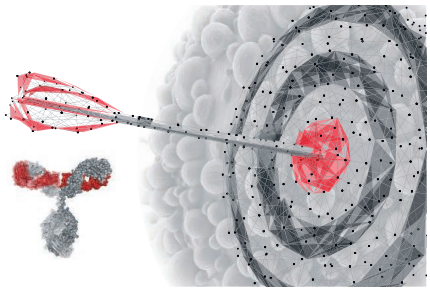

Fig. 1 | YUMAB's integrated platform. YUMAB's platform supports the development of fully human antibodies and offers a unique solution against complex or difficult novel targets in immuno-oncology.

A comprehensive human mAb platform

The YUMAB platform integrates an advanced in vitro antibody discovery process bypassing the need for immunization and thus eliminating issues related to potential epitope restriction by the host immune response. The resulting comprehensive screen of the human antibody repertoire translates into vastly improved success rates in mAb identification, including rare and potentially functional antibody candidates that target difficult antigens such as those of interest to I-O.

YUMAB's in vitro antibody discovery process quickly identifies a huge number of unique candidate antibodies. This process can be combined with patient-derived libraries, which are accessed by YUMAB's clinical collaboration partners.

As an additional source of human antibodies, immune libraries generated from humanized mice can be used to expand the available human antibody repertoire, and combine in vivo antibody generation and maturation with the power of in vitro selection. For nonhuman antibodies, YUMAB provides optimized bioinformatic humanization solutions to generate super-humanized antibody variants mimicking sequence characteristics close to fully human antibodies.

The combination of different discovery technologies is of importance to obtain mAbs targeted against difficult antigens and rare functional epitopes. Advanced antibody lead optimization by bioinformatic modelling and in vitro evolution allows early derisking of potential development issues through stability and productivity optimization of the sequences. This approach enables YUMAB to advance quickly from basic research to clinical translation.

YUMAB's mAbs can be further developed for use as immunomodulatory agents or can be integrated into bispecific antibodies or CAR T cells, for example, to fulfill the needs of I-O therapy.

Setting up next-generation I-O therapeutics

YUMAB has adopted a customized and flexible approach to its partnerships, through contract research, partnered R&D or collaboration. The company offers a solution that integrates its unparalleled expertise along the entire mAb discovery and development process, with a uniquely versatile discovery and protein engineering platform under one roof and flexible business conditions that are tailored to the needs of the individual companies, from small biotech startups to large biopharmaceutical companies.

YUMAB is constantly pushing the boundaries of therapeutic mAb development. Ongoing clinical collaborations, for example, are expanding the company's antibody repertoire to libraries from patients with cancer, opening new avenues for therapeutic development. And later this year, YUMAB will roll out a novel fully humanized mouse system for generating human mAbs against typically immunologically tolerated antigens.

According to André Frenzel, YUMAB's CSO, the company's strategy going forward is "to expand our therapeutic antibody platform by integrating additional discovery technologies, increasing our already huge collection of universal and patient-derived libraries, and soon introducing a novel fully human mouse system. We are constantly improving and expanding our tool box of lead optimization technologies to accelerate and maximally derisk downstream antibody drug development to match the requirements of current and next-generation I-O biotherapeutic development."

1. Yu, J. X., Hubbard-Lucey, V. M. & Tang, J. *Nat. Rev. Drug. Discov.* https://doi.org/10.1038/d41573-019-00090-z (2019).
2. Tang, J., Pearce, L., O'Donnell-Tormey, J. & Hubbard-Lucey, V. M. *Nat. Rev. Drug. Discov.* **17**, 783–784 (2018).

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