

## **DZIF Bridging Topic “Antibody-based Therapies”**

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### **Mission**

The working group aims to facilitate the development, production, and clinical testing of monoclonal antibodies for the prevention and treatment of infectious diseases. To this end, the working group will actively foster the exchange of critical knowledge and build a collaborative network for translating antibody discoveries into clinical application.

### **Background**

The use of passive immunization dates back to the end of the 19<sup>th</sup> century when Emil von Behring and Kitasato Shibasaburō demonstrated the effective use of serum therapy to combat diphtheria and tetanus. Since the advent of recombinant antibody generation technologies, more than 150 therapeutic monoclonal antibodies (mAbs) have been approved for clinical application. While most antibodies are used to treat cancer or autoimmune diseases, indications for antibody treatment have expanded to almost all fields of medicine including infectious diseases. For instance, the antibody Pavilizumab (approved 1998) targets the respiratory syncytial virus (RSV) and was shown to potently prevent pulmonary infections in premature infants. Moreover, the administration of a single or a combination of mAbs (Ansuvimab; Inmazed®) were recently demonstrated to reduce mortality of Ebola virus disease (EVD) of up to 90%. Thus, the use of antibody therapeutics is the first highly effective antiviral for EVD therapy. Finally, with the onset of the SARS-CoV-2 pandemic, identification and clinical development of neutralizing monoclonal antibodies occurred at a remarkable pace. As a result, first emergency use authorization was granted for Bamlanivimab for the treatment of COVID-19 in less than 12 months after the emergence of SARS-CoV-2. Additionally, numerous mAbs received approval to prevent and treat COVID-19 over the last two years. However, challenges remain as illustrated by the frequent emergence of new SARS-CoV-2 variants with immune evasion properties.

While those examples demonstrate the tremendous potential of antibody therapeutics, as of today, only a few infectious diseases benefit from approved antibody-based drugs. Given the current challenges of antimicrobial resistance and emerging viruses, concerted efforts are needed to further exploit antibody-mediated therapeutics to better protect our society from infectious diseases.

### **Current Situation and Challenges**

Today, advanced technologies enable rapid isolation of specific antibodies and various strategies are applied for the clinical application of antibody therapeutics. These include the use of antibody drug conjugates, immunotoxins, or antibodies that permit bi- or trivalent binding. Moreover, antibodies are frequently modified to improve their affinity, pharmacokinetic profiles or effector-functions and new technologies are exploited for antibody expression *in vivo* (e.g., vector- or mRNA-based systems). Despite this progress, numerous obstacles challenge the discovery and clinical development of antibody-mediated therapies. These include insufficient infrastructures for timely production of the drug substance, pre-clinical evaluation, regulatory hurdles, selection of pharmaceutical partners, as well as demanding legal and logistic requirements. Finally, antibody therapies can require a tailored clinical structure that allows, for example, i.v. drug administration of potentially infectious patients. Therefore, logistical, technical, administrative, and regulatory aspects need to be considered for translating antibody therapeutics into clinical practice.

Within the DZIF, numerous research groups provide a broad spectrum of expertise including technologies for high throughput human antibody discovery, functional and structural characterization, and pre-clinical studies. Furthermore, several research groups are highly experienced in conducting early phase clinical trials. The goal of this working group is to foster existing resources for the successful development of antibody-mediated therapies.

### **Specific Aims**

The working group sets out to support researchers by their goal to develop strategies for antibody-mediated prevention and therapy of infectious diseases. This includes:

- Exchange of information and the establishment of an antibody community within the DZIF
- Strengthening collaboration with other networks and interested research groups
- Facilitating access to antibody resources including antibody/nanobody discovery platforms
- Secure funding for constituting an infrastructure that promotes antibody research collaborations as well as antibody workshops
- Initiating discussions with regulatory authorities to path the way towards clinical testing
- Evaluating the establishment of a DZIF GMP facility for rapid antibody production
- Career support of young scientist in antibody research
- Engage with pharmaceutical partners to build alliances between academia and pharmaceutical industry
- Fostering collaboration for successful grant application
- Initiating discussion of founding a German Society of Antibody Research

### **Recent Activities**

The bridging topic “Antibody-based Therapies” has facilitated scientific exchange across the TTUs of the DZIF. Our efforts have led to the development of initial concepts for successfully integrating the topic of therapeutic antibodies within DZIF's future endeavors.

- Kick off meeting Nov 11, 2022. Providing an overview on current DZIF antibody activities and platforms.
- Online workshop Feb 23, 2023. Sharing experiences on developing novel antibody therapeutics.
- One-day F2F symposium June 12, 2023. Strengthening our translational output and fostering strategic discussions.

In addition, the Bridging Topic established a DZIF-Ab-Core platform that aims to support and provide the requirements for a fast and comprehensive evaluation of novel antibody candidates. Using this platform, DZIF members will be able to securely submit antibody sequence information via an online interface and select from a collection of DZIF-Ab-Core resource tools according to the needs of the investigator.

### **Next Steps**

We will bring together the antibody community within DZIF on a F2F Meeting in September 2024 followed by an online Workshop in December 2024. Results and Services of the Ab-Core project will be presented.

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