



## Antibody technology

### Problem to be solved

Antibodies are important tools for medical applications as well as for experimental research. One crucial point is the development of a suitable format in terms of affinity and activity to the antigen but also of intended application strategy and last but not least producibility. Antibodies against various targets are currently in different stages of development. So far mainly full antibodies are used as drugs. Production and application are limited by high costs. There is a need for alternatives. To be applied for a wider range of diseases for large numbers of patients it is necessary to not only produce the appropriate amounts but also to meet compatible prices to make therapeutic antibodies feasible for the application in treatment of diseases and also for prevention.

The majority of antibodies are composed of two heavy chains and two light chains, where both chains contribute to the antigen-binding site. Camelids and sharks produce antibodies consisting only of heavy chains. This unusual format forms an antigen-binding site only by a single domain designated VHH in camelids. As recombinant proteins lacking constant parts they are designated as nanobodies or single domain antibodies. Their small size is thought to confer improved tissue penetration, and they show a reduced tendency to aggregate and/or degrade proteolytically compared to single-chain Fv (scFv) antibody fragments. Nonetheless, the specificity and antigen affinity of VHH antibodies have been shown to be generally comparable to those of IgG antibodies, with dissociation constants (KD) lying in the nanomolar range. Further benefits are their high solubility, high thermal stability and high refolding capacity. As a result, they have been proposed as an alternative drug format.

### New antibody formats

A further improvement of these molecules is achieved by a new antibody format - dimers of variable domains of the heavy chain. These are not only highly specific and compared to the monomers significantly more active they also show an improved neutralizing activity. They can easily be produced in suitable amounts since the provided formats are extremely well expressed in many expression systems but particularly well in plants. Other technologies for selection – a semisynthetic library and conversion of other antibody formats e.g. IgG, scFv or Fab into the new format can be offered. There are also approaches to fuse the antigen binding molecule to appropriate proteins not only allowing an easy purification but also stabilizing the protein thereby increasing the serum half life significantly.

### Applications

The new antibody formats can be developed to be applied for the treatment of diseases in humans as well as in animals.

### Patent situation

A German patent application has been filed, which can be extended to an international patent.

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