CASE STUDY

VHH DISCOVERY FOR BISPECIFICS – COMBINATION OF IN-VIVO IMMUNIZATION AND IN-VITRO DISPLAY

YUMAB

THE NEED

Small antibodies with high tissue penetration and stability

Conventional IgG antibodies are powerful tools for many applications. Despite their flexibility, they also encounter limits of feasibility. With their size of 150 kDa they are limited in tissue penetration and are less stable when it comes to harsh conditions, such as pH stress, temperature stress or protease rich environments, just to name a few.

THE SOLUTION

Single domain VHH antibodies as an elegant add-on tool

In contrast, single domain antibodies (e.g. VHH) possess properties which circumvent some of these limitations. Their simple structures allow for higher stability and producibility. With a size of around 15 kDa single domain antibodies can penetrate deep into tissue and access hidden epitopes on the antigens. Also, for the generation of bispecific antibodies they are a convenient building blocks to avoid light chain mispairing.

YUMAB's VHH discovery platform combines in-vivo immunization of llamas with the power of in-vitro display technologies. The immunization can be carried out with soluble proteins (e.g. ECD of CD3) or with a novel and unique llama immunization cell line that overexpresses any multipass-transmembrane protein of interest on the cell surface (e.g. CD20).

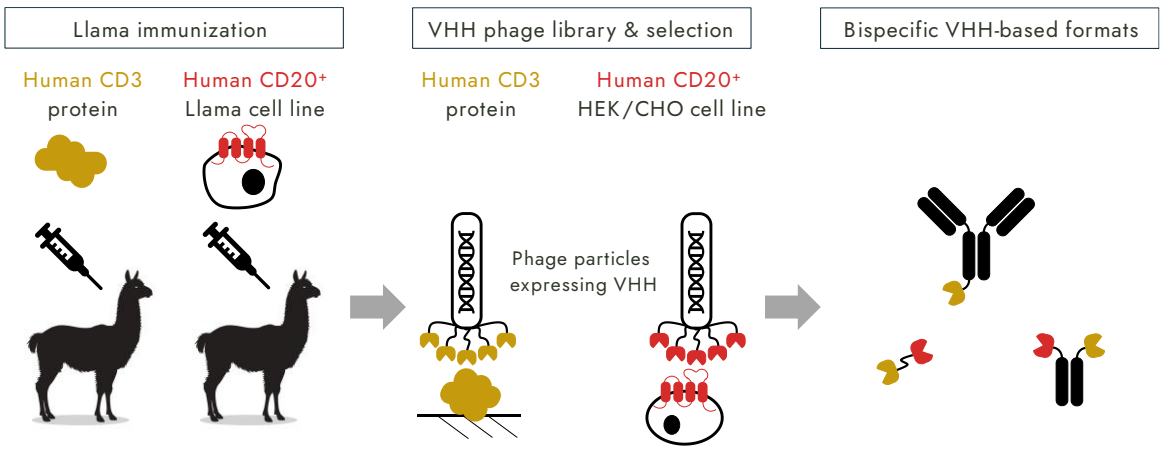

Figure 1. YUMAB's VHH discovery platform generates target-specific VHH's from immunized llamas, that can be easily employed for the generation of bispecific antibodies.

After the immunization, B-cells are collected, and the VHH-coding genes are isolated for the construction of antibody-phage libraries. Antibodies with the desired binding properties are isolated by biopanning on the target protein (e.g. CD3) or on target-expressing cells (e.g. CD20) and converted into any desired mono-, bi- or multispecific antibody format (Figure 1).

THE IMPACT

Naturally matured VHH antibodies with beneficial characteristics

Taking advantage of the natural affinity maturation in-vivo with subsequent stringent antibody selections and screenings in-vitro leads to a high-rate of diverse and target-specific VHH antibodies. The identified antibodies exhibit high binding affinity, specificity and favorable biochemical properties such as low polyreactivity and high stability (Figure 2), which makes them ideal building blocks for the generation of bi- or multispecific antibodies.

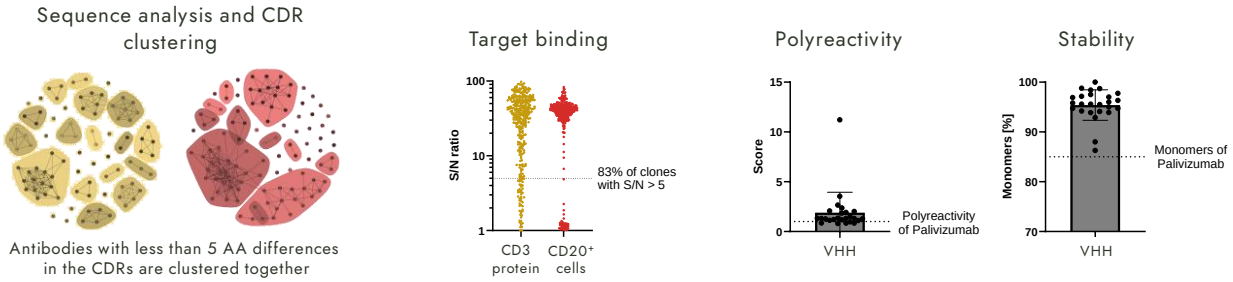

Figure 2. VHH antibodies have a high sequence diversity and a strong target binding with favorable biochemical characteristics.

This data was generated from the YUMAB® platform in an ongoing collaboration with MOLCURE Inc. Kawasaki 212-0032, Japan.