

## State of the Art on Plant-Made Single-Domain Antibodies

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In addition to conventional antibodies (with heavy and light chains), camelids also produce functional antibodies devoid of light chains (HCAbs) without the first constant domain (CH1). Their variable domains (VHH) have binding properties, high stability and solubility, and are considered the smallest available intact antigen-binding fragment derived from a functional immunoglobulin. For their practical utilities VHHs have been expressed in different platforms. This review aims to provide an update in the field of plant-made VHHs, their applications and limitations, and a discussion about the challenges for the near future in this field. Antibodies are secreted by B cells of the adaptive immune system, mostly by differentiated B cells called plasma cells. Antibodies can occur in two physical forms, a soluble form that is secreted from the cell to be free in the blood plasma, and a membrane-bound form that is attached to the surface of a B cell and is referred to as the B-cell receptor (BCR). The BCR is found only on the surface of B cells and facilitates the activation of these cells and their subsequent differentiation into either antibody factories called plasma cells or memory B cells that will survive in the body and remember that same antigen so the B cells can respond faster upon future exposure. In most cases, interaction of the B cell with a T helper cell is necessary to produce full activation of the B cell and, therefore, antibody generation following antigen binding. Soluble antibodies are released into the blood and tissue fluids, as well as

many secretions to continue to survey for invading microorganisms. Antibodies are glycoproteins belonging to the immunoglobulin superfamily. They constitute most of the gamma globulin fraction of the blood proteins. They are typically made of basic structural units—each with two large heavy chains and two small light chains. There are several different types of antibody heavy chains that define the five different types of crystallisable fragments (Fc) that may be attached to the antigen-binding fragments (Fab). The five different types of Fc regions allow antibodies to be grouped into five isotypes. Each Fc region of a particular antibody isotype is able to bind to its specific Fc Receptor (FcR), except for IgD, which is essentially the BCR, thus allowing the antigen-antibody complex to mediate different roles depending on which FcR it binds. The ability of an antibody to bind to its corresponding FcR is further modulated by the structure of the glycan(s) present at conserved sites within its Fc region. The ability of antibodies to bind to FcRs helps to direct the appropriate immune response for each different type of foreign object they encounter. For example, IgE is responsible for an allergic response consisting of mast cell degranulation and histamine release. IgE's Fab paratope binds to allergic antigen, for example house dust mite particles, while its Fc region binds to Fc receptor  $\alpha$ . The allergen-IgE-FcR $\alpha$  interaction mediates allergic signal transduction to induce conditions such as asthma.