Nanobodies

Why in News

An international research team led by the University of Bonn (Germany) has identified and further **developed novel antibody fragments (nanobodies) against SARS-CoV-2,** the virus that causes **Covid-19.**

Key Points

- **Nanobodies Against SARS-CoV-2:**
  - **Produced along with Antibodies:** On injection of surface protein of the coronavirus into an alpaca and a llama, their immune system not only produced antibodies directed against the virus but also a simpler antibody variant that can serve as the basis of nanobodies.
  - **More Effective:**
    - They had also **combined the nanobodies into potentially particularly effective molecules,** which **attack different parts of the virus simultaneously.** This new approach **could prevent the pathogen from evading the effect of antibodies through** mutations.
    - Nanobodies **appear to trigger a structural change** before the virus encounters its target cell - an unexpected and novel mode of action. The change is likely to be irreversible; the virus is therefore no longer able to bind to host cells and infect them.
- **Antibodies:**
  - Antibodies are **an important weapon in the** immune system**'s defense against infections.**
  - They **bind to the surface structures of bacteria or viruses** and **prevent their replication.**
  - One strategy in the fight against disease is therefore to produce effective antibodies in large quantities and inject them into patients. However, **producing antibodies is difficult and time-consuming;** they are, therefore, **probably not suitable for widespread use.**
- **Nanobodies:**
  - Nanobodies are **antibody fragments** that are so simple that they **can be produced by bacteria or yeast,** which is **less expensive.**
  - These are **antibodies with a single variable domain located on a heavy chain,** also known as **VHH antibodies.**
  - These are **often seen as an alternative to conventional antibodies,** and have **significant differences** in both **production** and **use** that influence their suitability.
- **Difference between Nanobodies and Conventional Antibodies:**
  - **Difference in Structure and Domains:**
    - **Conventional antibodies** have **two variable domains, called VH and VL,**

which offer each other stability and binding specificity.

- **Nanobodies have VHH domains** and **lack VL domains,** but are still highly stable. Lacking the VL domain also means nanobodies have a **hydrophilic** (having a tendency to dissolve in a water) side.
    - Hydrophilic side means they **do not have issues with solubility and aggregation** otherwise associated with conventional antibodies.
- Nanobody production follows many of the same protocols as used in traditional antibody production. However, it also has distinct advantages not available with traditional antibodies, such as **improved screening, improved isolation techniques, and no animal sacrifice.**

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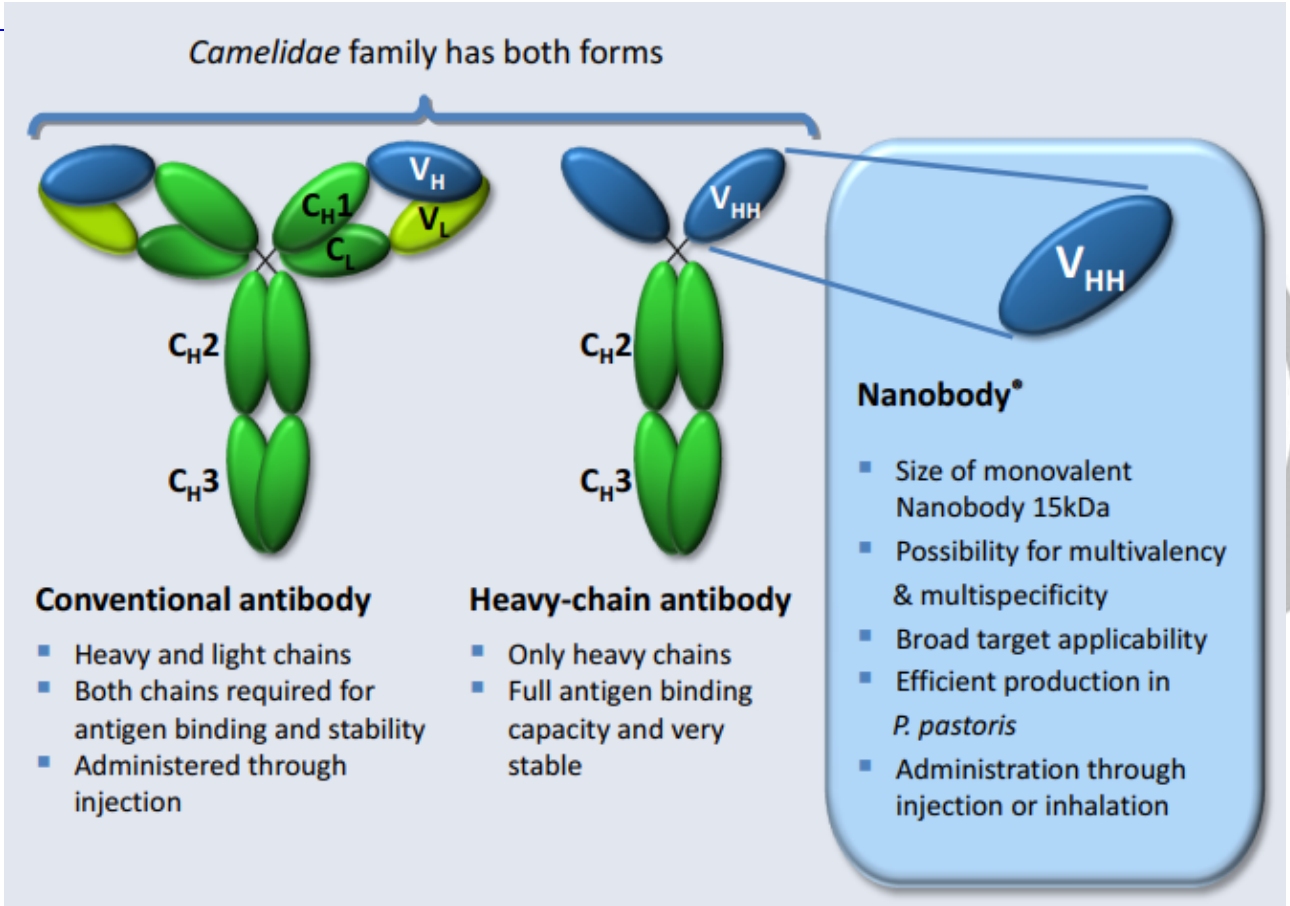

- **Use:**
    - **Nanobodies** are much smaller than classic antibodies and they, therefore, **penetrate the tissue better** and can be produced more easily in **larger quantities.**
    - **Nanobodies** are **stable in a wide range of temperatures,** remaining functional at temperatures as high as 80°C. As an added bonus, **unfolding of the nanobody due to high temperatures** has been shown to be **fully reversible, unlike conventional antibody fragments.**
        - Nanobodies are **also stable at extreme pH levels,** able to survive exposure to gastric fluid.
    - **Nanobodies** are also **compatible with genetic engineering methods,** which allow alteration of amino acids to improve binding.
- **Limitations of Nanobodies:**
    - **Monoclonal and polyclonal antibodies** are slightly **safer to produce than nanobodies,** as there are biohazards involved in nanobody production not present for conventional antibody production.

- The biohazards result mainly from **use of hazardous bacteriophages** (any of a group of viruses that infect bacteria) for selection of nanobodies. Other sources include plasmids, antibiotics, and recombinant DNA. These materials require safe disposal.

    - **Polyclonal antibodies** are made using several different immune cells.
    - **Monoclonal antibodies** are made using identical immune cells that are all clones of a specific parent cell.

Source: IE