



Nanobodies

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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**.

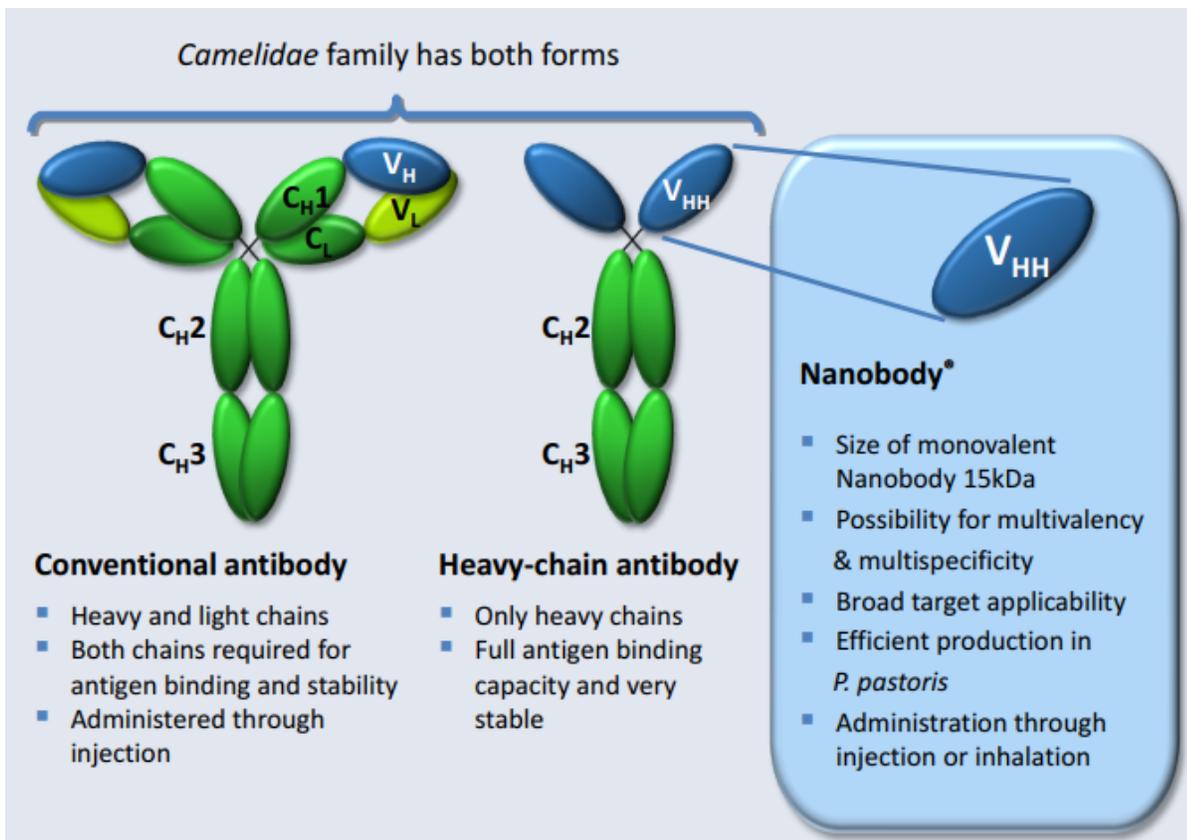
- **Nanobodies:**

- 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**.



- **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