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Nanobodies: A versatile single-domain antibody format from camel heavy chain only immunoglobulins

All camelids (llama and camels) possess unique antibodies comprising a homodimer of heavy chains only. The antigen of these heavy chain-only antibodies is recognized by virtue of one single variable domain, known as VHH. A straightforward technology was developed to immunize a camelid, to clone the repertoire of VHHs, from which the antigen-specific fragments are rapidly identified after phage display selections. The resulting monoclonal, recombinant, antigen-binding single-domain antibody fragments are also referred to as Nanobodies (Nbs) because of their size of 4 nm height by 2.5 nm in diameter.

Nanobodies are well produced in microbial systems, very robust and highly soluble. They bind their cognate antigen with high affinity and specificity. Very often the Nanobody recognizes an epitope that is difficult to target with human or mouse antibodies. The 'humanization' or 'PetizationTM' of Nanobodies is/should be straightforward. Probably, the largest advantages of Nanobodies come from their strict monomeric behavior, the ease to tailor them into larger pluripotent constructs and their functionality when expressed intracellularly.

Such beneficial properties of Nanobodies over other antigen-binding fragments from conventional antibodies inspired many researchers to employ Nanobodies as a versatile tool in various innovative applications in biotechnology and medicine as:

- a research tool to immune-capture the antigen from complex mixtures,
- a potent probe to trace (or eliminate) target antigen within living cells,
- an excellent diagnostic tool for non-invasive in vivo imaging of tumors, or inflammation
- a therapeutic tool to eradicate tumors or infections in animal models,
- an anti-venom to protect animals from scorpion or snake envenoming

Biography

Serge Muyldermans obtained a PhD at the 'Vrije Universiteit Brussel', Brussels, Belgium in 1982. He was a postdoc at this university at the time the functional Heavy-chain only antibodies were discovered in camelids. He developed a streamlined method to identify rapidly the antigen-specific, single-domain antibody fragments derived from the unique Heavy chain antibodies of camelids. This technology was used to found Ablynx NV in December 2001, a Belgian private biotech company actively developing protein therapeutics based on single variable domains or NanobodiesTM and currently employing 300 people. In 2003, he became professor at the 'Vrije Universiteit Brussel' where he is heading the camel-antibody engineering group in the laboratory for Cellular and Molecular Immunology. Apart from using the Nanobodies as a research tool, we are developing some of our Nanobodies for in vivo diagnostics and for therapy.

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