

Production of new llama-heavy chain only antibodies in transgenic mice

The advantages of llama VHH with the genetic versatility of mice

Background & Innovation

The use of **antibodies** for therapeutic and diagnostic purposes is well established.

Nanobodies / llama VHHs offer an attractive solution due to their unique characteristics that **outperform monoclonal antibodies**:

- higher stability and solubility
- easier formatting of bispecifics
- higher expression yields
- better in vivo tissue penetration
- better binding to crevices

Nanobodies are currently produced in camelids, requiring higher **costs** compared to transgenic mice without **genetic engineering possibilities**.

Our technology offers **novel transgenic mouse models to produce llama VHHs**, paired with the vast genetic engineering possibilities of the mouse.

Competitive advantage

Nanobody discovery from our transgenic mice features:

- only VHH, no conventional antibodies
- full VHH repertoire from lymphatic organs
- direct sequence information
- no VH-VL pairing -> better developability
- use of established mouse immunization and hybridoma technologies
- use of target-ko mice to address conserved epitopes.

Technical Description

We present novel genetically engineered mice for the production of nanobodies.

This is the **first available** genetic construct and transgenic animal that comprises: camelid VHH, D, J and constant heavy chain regions, which are **not rearranged**.

This mouse model was generated by insertion of an engineered llama IgH locus into the mouse genome by **BAC-recombineering**.

The usage of transgenic mice allows **flexible and efficient generation** of VHHs by:

- **hybridoma technology**
- **phage display technology**
- direct cloning and sequencing
- high yield production in CHO & HEK cells

Nanobodies can be produced in **mice deficient for the target antigen (knock-out)**.

Summary

Thanks to their **unique features**, nanobodies are becoming more and more important for biomedical applications.

We are presenting a **unique platform** for the production of camelid VHHs in genetically engineered mice with **greater technical flexibility** and **lower costs** than nanobody discovery in camelids.

FOCUS SECTORS

- Therapeutics
- Transgenic mice
- Gene/tumor therapy
- Nanobody production
- Nanobody therapy/diagnostics

PROJECT KEY WORDS

- Llama VHH/Nanobodies
- Transgenic mouse model
- Production of VHH antibodies

DEVELOPMENT STATUS

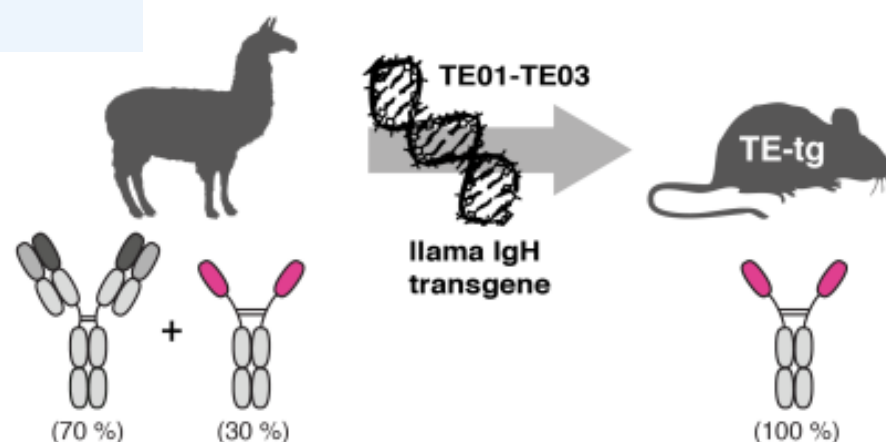
- Immunized mice produce affinity matured, soluble heavy chain antibodies containing the best natural and synthetic VHH frameworks

PATENT PROCEDURE STATUS

- Patent application pending in AU, CA, EP, JP, KR, NZ, US

POTENTIAL FOR COOPERATION

- R&D Cooperation
- Licensing via commercialization partners



Discovery of specific VHH by

- **hybridoma technology**
- **expression in HEK-cells**
- **phage display**



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