

# Case Study

## Nanomouse: Camelid Antibody Expressing Mouse Chimera

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Products  
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# Overarching Technology Transfer Inquiries

## Patentable/Patent Eligible (under U.S. Law)?

- Is this a “product of nature” or “abstract idea”?
- Is the invention useful?
- Is the invention novel and non-obvious?



## On balance, should the *NIH* file a patent on it?

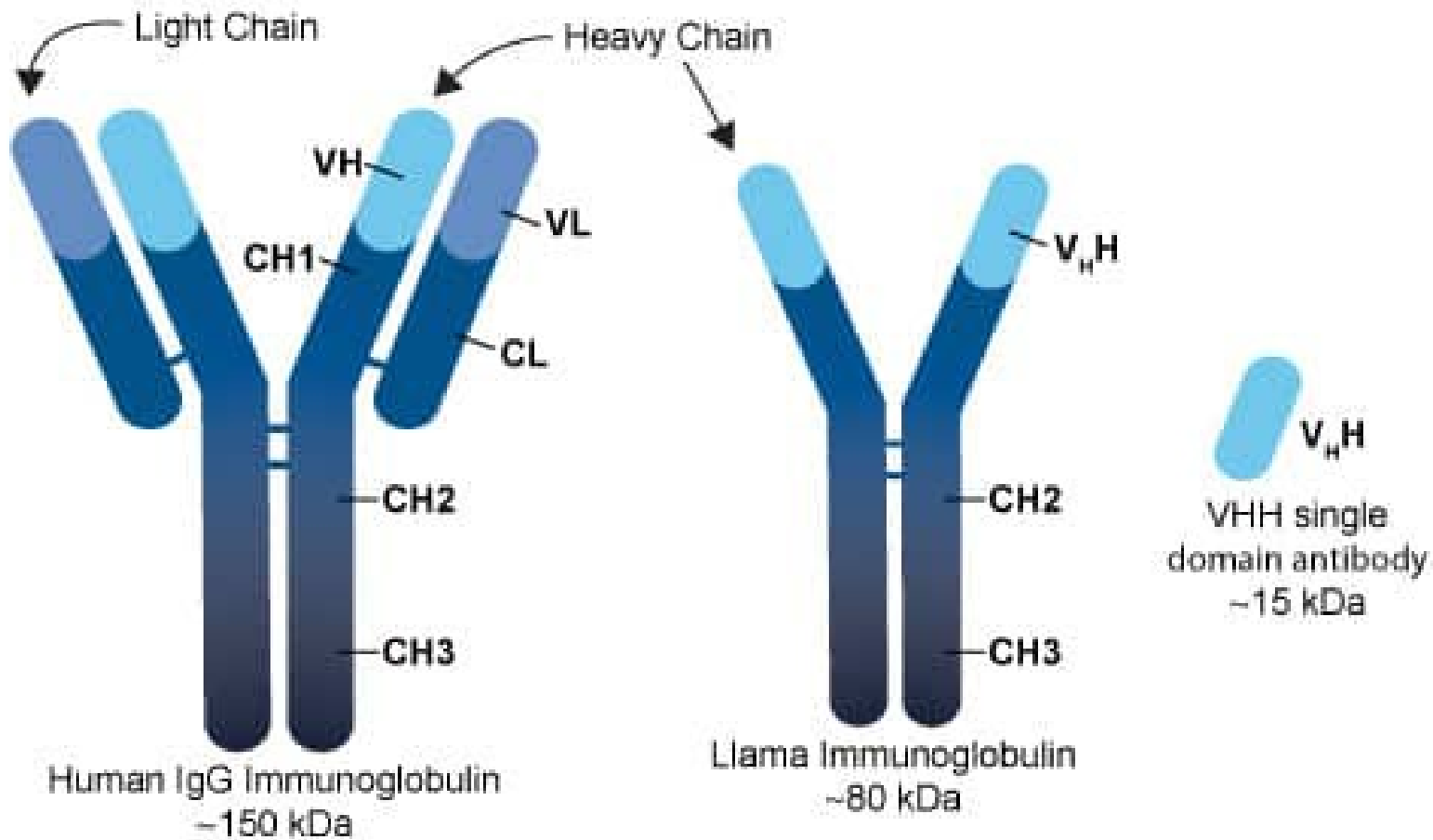
- What is the best way to disseminate the invention?
  - Incentivize innovation (R&D, clinical trials, FDA filings....)
  - Tax payer funding? Public access?
  - Blocking others from using if we file? (exclusivity?)



# Inventions that are Research Tools

- No patenting of research tools
  - To academia under MTAs (royalty free)
  - Nonexclusive
  - Distribute widely
  - To commercial entities under biological materials licenses (royalty bearing)

# Camelid v. Human Antibodies



# Advantages of Camelid nano-antibodies

- Smaller size and extended CDRs
- Bind epitopes not normally accessible to conventional antibodies
  - Better tissue penetrance: deep crevices and concave surfaces.
- Higher expression yields.
- Enhanced solubility.
- Great for therapeutics
- Particularly against human viruses which often mask conserved epitopes with glycan shields.

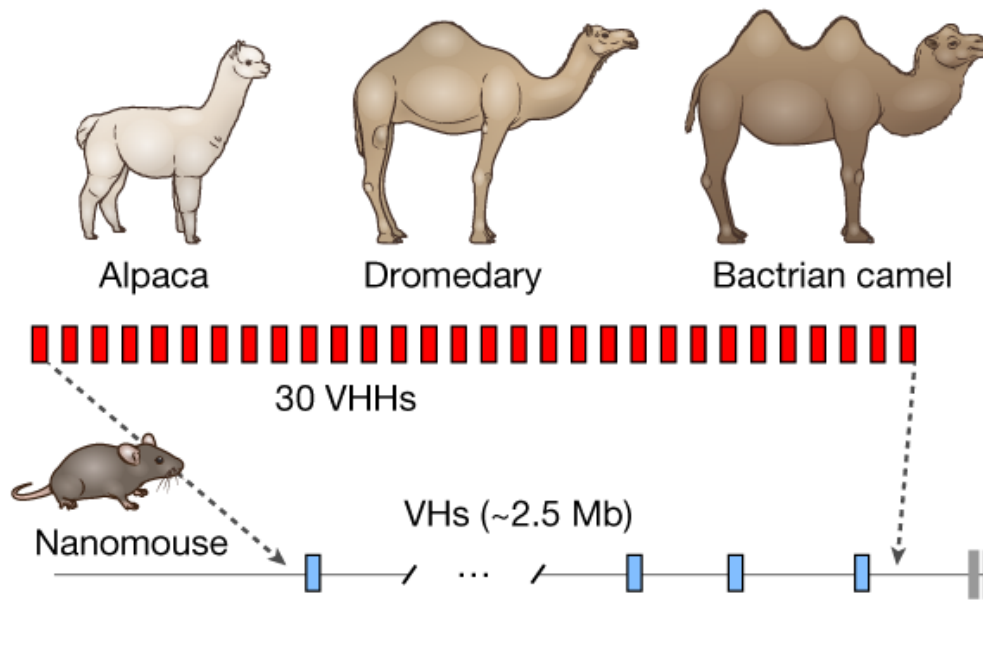


# So.... Why aren't they used more often?

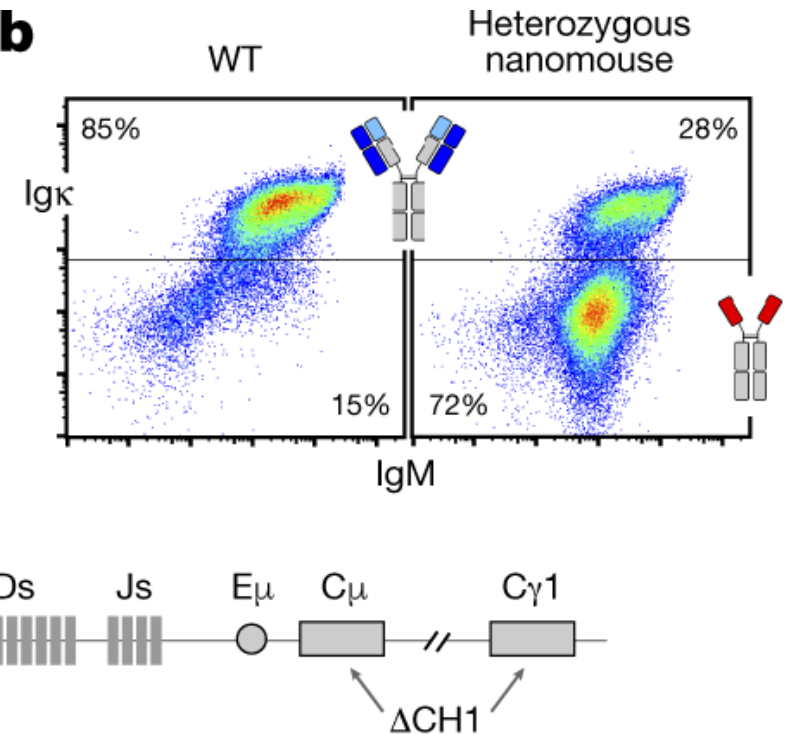
- Hard to ranch llamas, camels, alpacas at academic institutions
- Low Inbreeding
  - Heterogenous immune responses (high variability)
    - Good for herd immunity
    - Bad for research dependent on consistent results
- Cloning VHHs into phage display libraries an option for research
  - Absence of affinity maturation in vivo (germinal centers)
    - High specificity

# Chimeric Mouse

**a**



**b**



# Nanobody generating Mouse Chimera

Patent Eligible?



Novel/Nonobvious?



Does NIH file?



Why? **Research Tool --- patents don't provide incentive**  
**Used to search for new therapeutics**  
**Wide Dissemination**



# But wait...there's more

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

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**Published:**

- without international search report and to be republished upon receipt of that report (Rule 48.2(g))
- with sequence listing part of description (Rule 5.2(a))

## Claims

1. An **isolated single-domain antibody**, or an antigen binding fragment thereof, that **specifically binds to SARS-CoV-2**.

2. The single-domain antibody, or antigen binding fragment thereof, of claim 1, wherein the single-domain antibody, or antigen binding fragment thereof, specifically **binds to a receptor binding domain of SARS-CoV-2 (SARS-CoV-2 RBD)**.

3. The single-domain antibody, or antigen binding fragment thereof, of claim 1 or 2, wherein the SARS-CoV-2 RBD is a polypeptide comprising the amino acid sequence **SEQ ID NO: 124 or SEQ ID NO: 127**.

4. The single-domain antibody, or antigen binding fragment thereof, of any one of claims 1 to 3, wherein the single-domain antibody, or antigen binding fragment thereof, comprises a complementarity determining region 3 (CDR3), wherein the **CDR3** is selected from the group consisting of: a) an amino acid sequence of any one of **SEQ ID NOS: 77 to 91**; b) an amino acid sequence having at least 80% identity to at least one of the amino acid sequences of SEQ ID NOS: 77 to 91; c) an amino acid sequence having 3, 2, or 1 amino acid differences with at least one of the amino acid sequences of SEQ ID NOS: 77 to 91.

... (60 total claims)

# References

- McMahon, C., Baier, A.S., Pascolutti, R., Wegrecki, M., Zheng, S., Ong, J.X., Erlandson, S.C., Hilger, D., Rasmussen, S.G.F., Ring, A.M., *et al.* (2018). Yeast surface display platform for rapid discovery of conformationally selective nanobodies. *Nat Struct Mol Biol* **25**, 289-296.
- Xu, J., Xu, K., Jung, S. *et al.* (2021) Nanobodies from camelid mice and llamas neutralize SARS-CoV-2 variants. *Nature* **595**, 278–282.
- <https://patents.google.com/patent/WO2022178255A2/en?q=PCT%2fUS2022%2f016986>

# Thanks You.

# Questions?



**National Heart  
Lung and Blood Institute**  
People Science Health