IABS-HSI webinar:

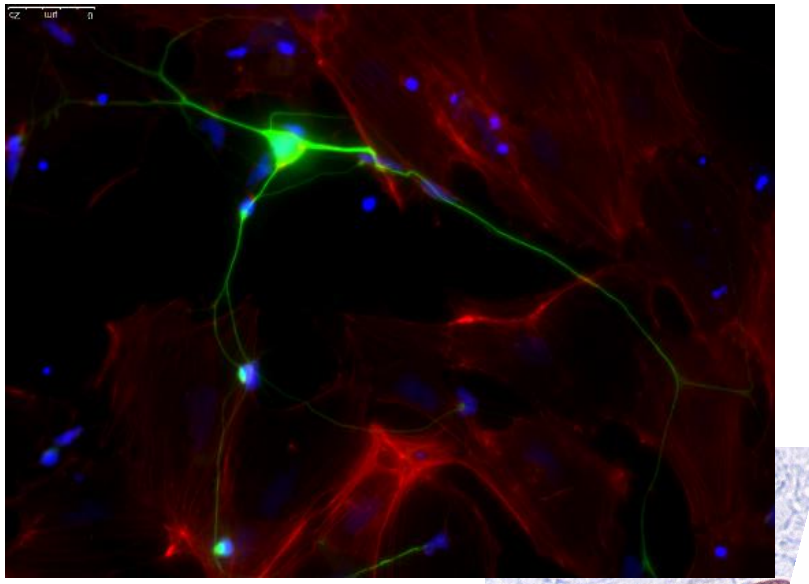
Global availability of critical reagents for biologicals testing. Current status, challenges and possible solutions.

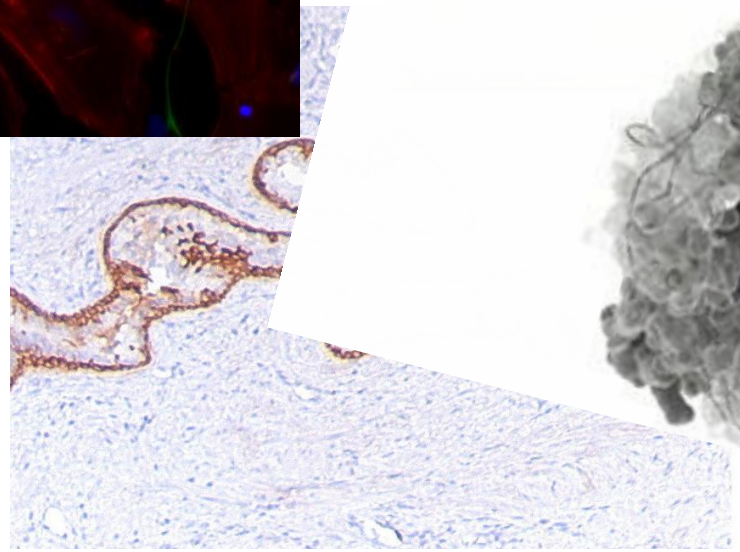
Animal-free recombinant antibodies

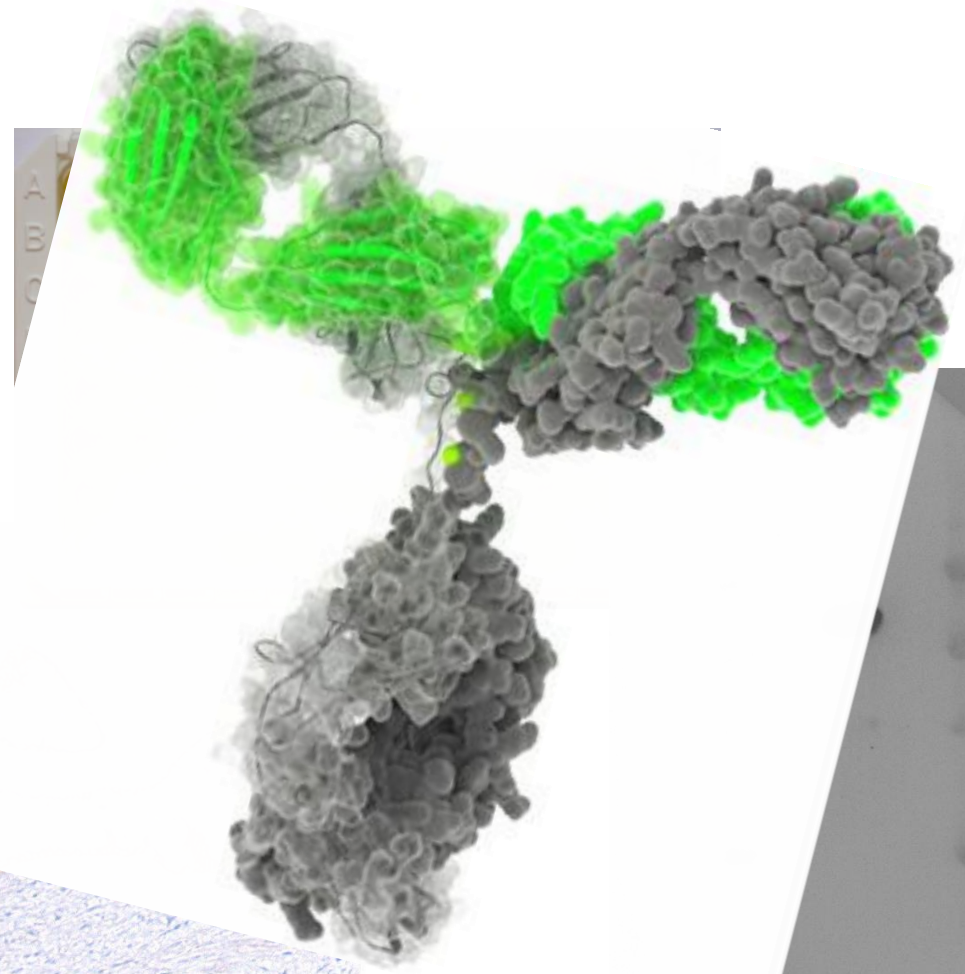
www.abcalis.com

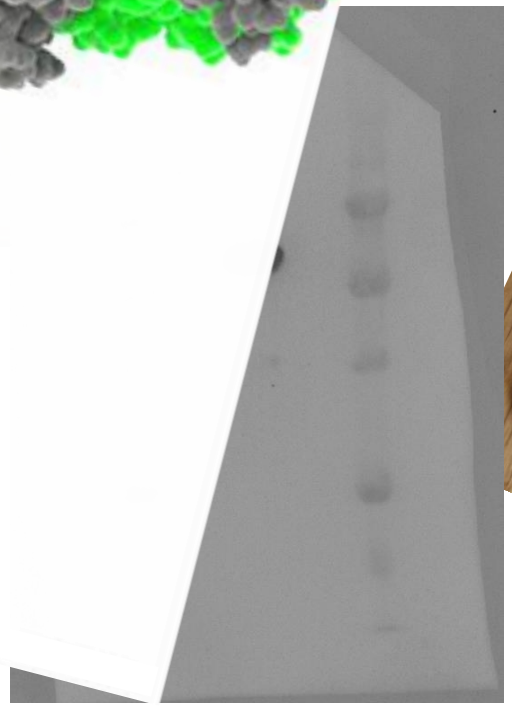
Dr. Esther Wenzel

Daily life of a scientist



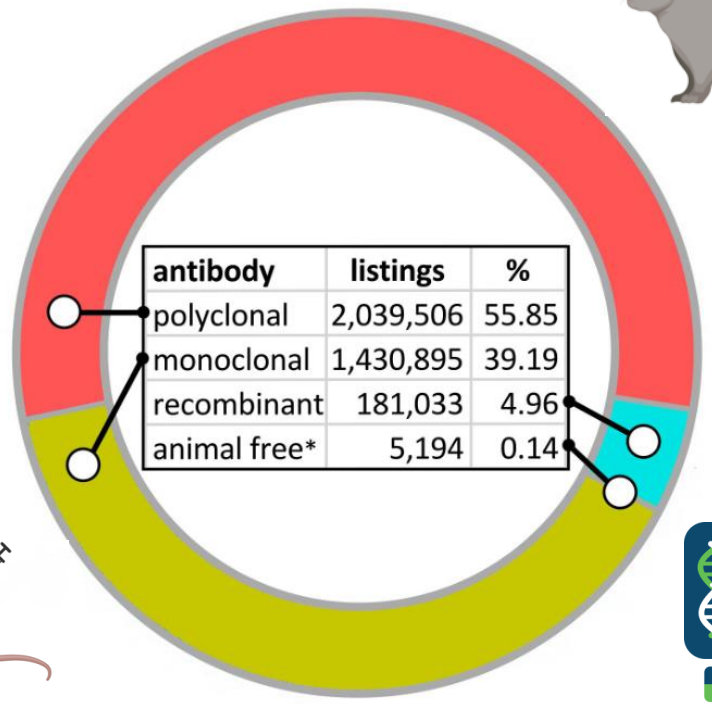






Daily life of a scientist

Products on the market

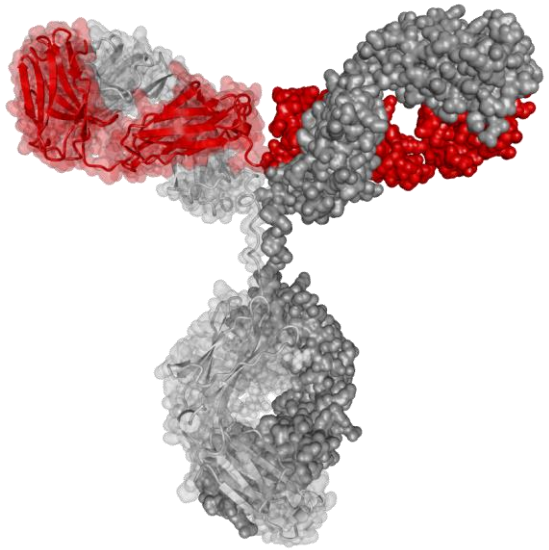


antibody	listings	%
polyclonal	2,039,506	55.85
monoclonal	1,430,895	39.19
recombinant	181,033	4.96
animal free*	5,194	0.14

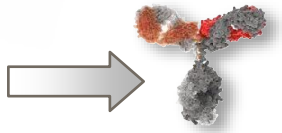
Total: 3,656,628

Source: Dübel, mAbs, 2024

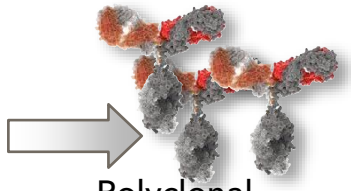
95 %



Immunisation

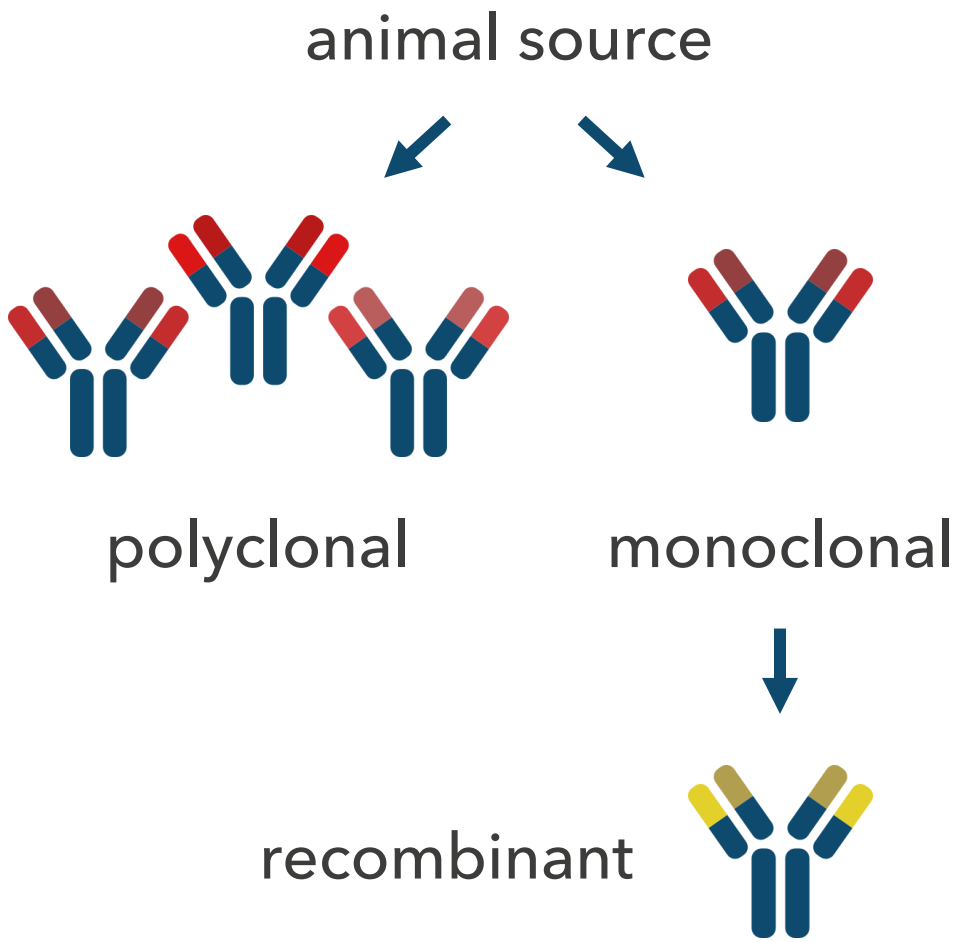


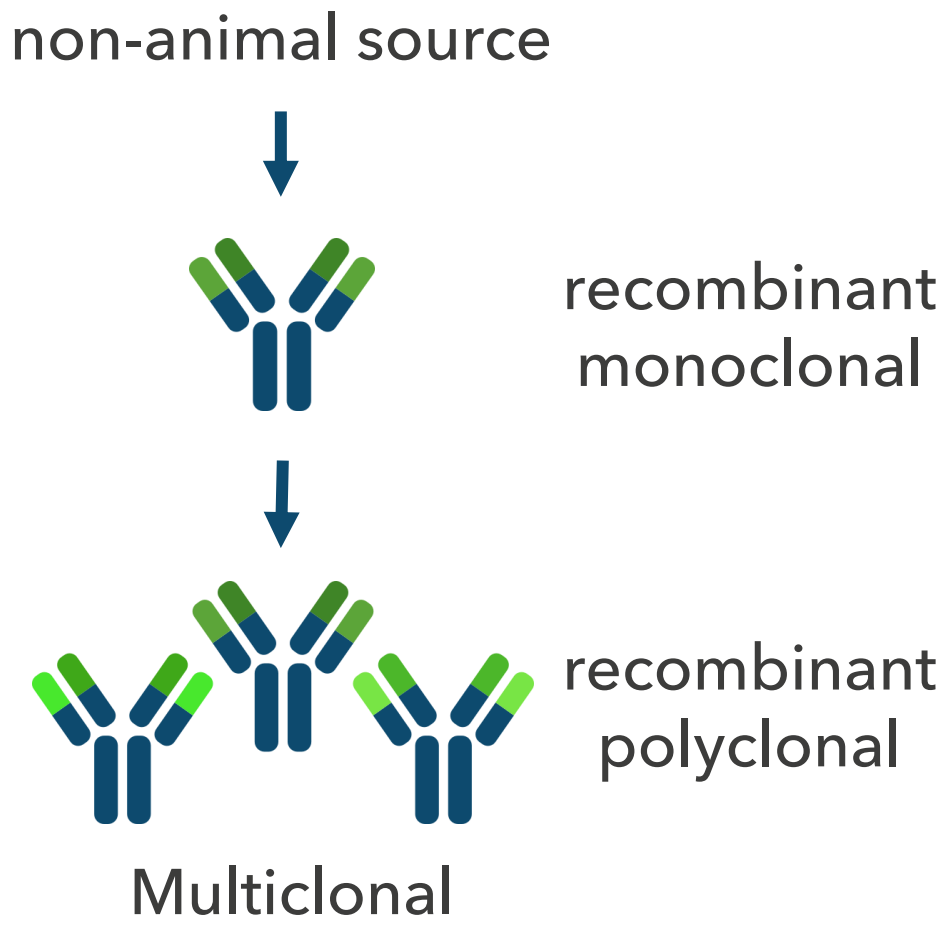
Monoclonal animal antibody



Polyclonal animal antibody

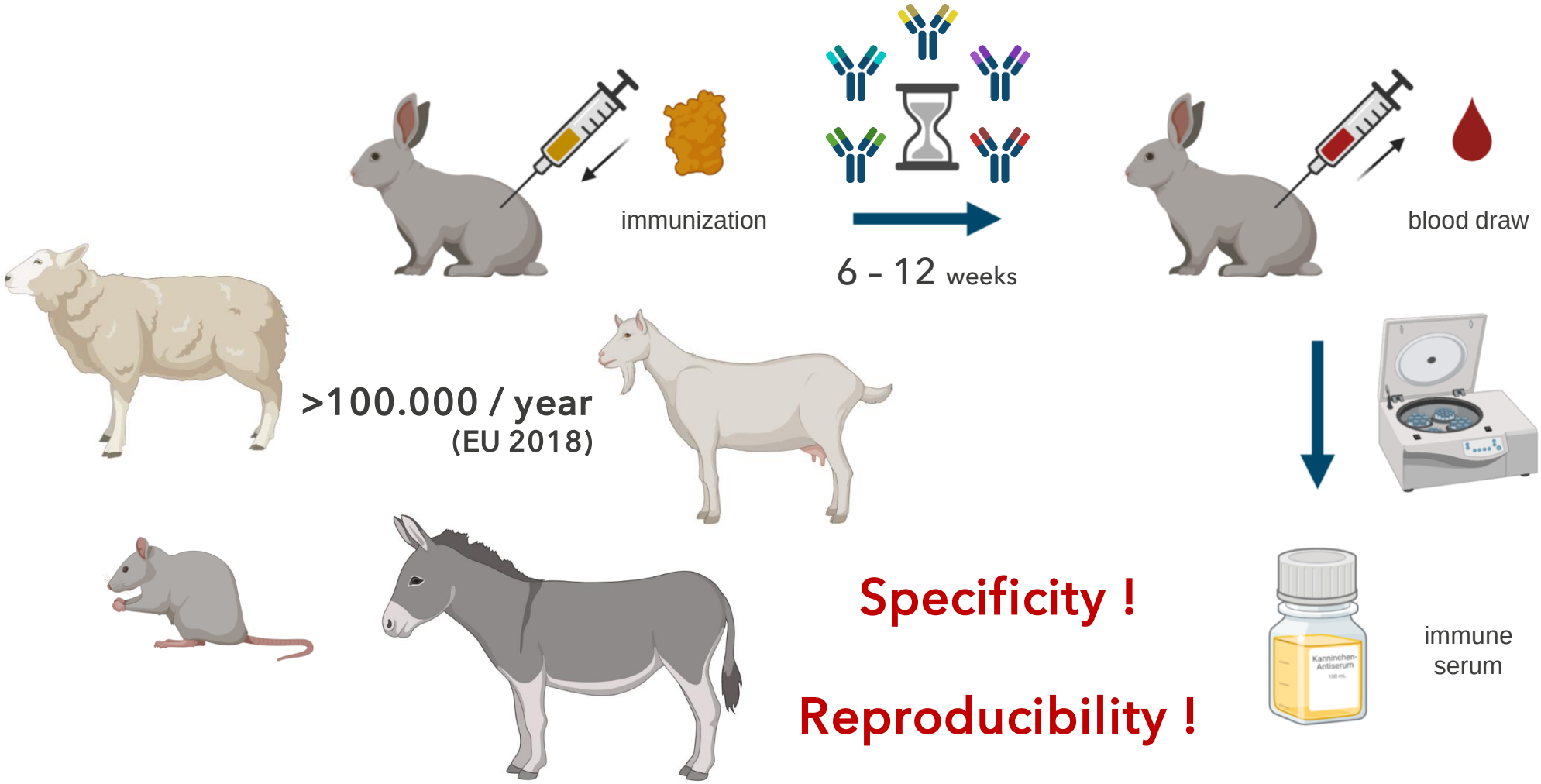
Types of antibodies – recombinant ≠ animal-free





non-animal derived antibodies → **NADA**

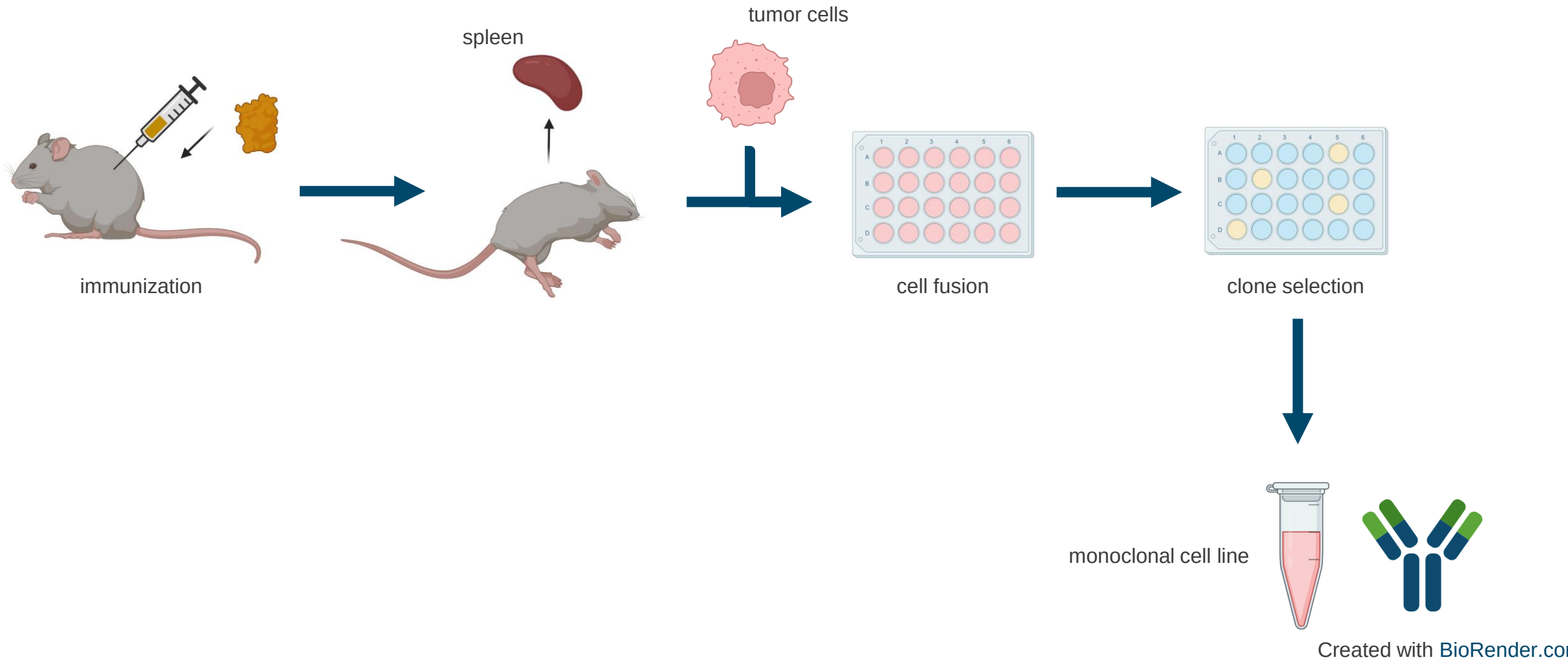
Polyclonal antibody generation



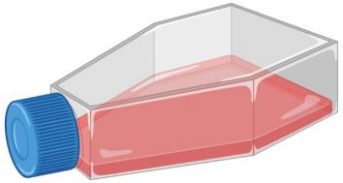
EU Commission (2021): Summary Report on the statistics on the use of animals for scientific purposes in the Member States of the European Union and Norway in 2018

Created with BioRender.com

Monoclonal – Hybridoma generation

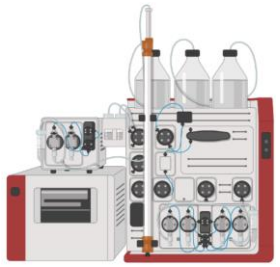


Monoclonal – Hybridoma production

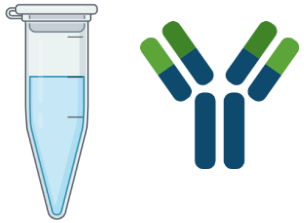


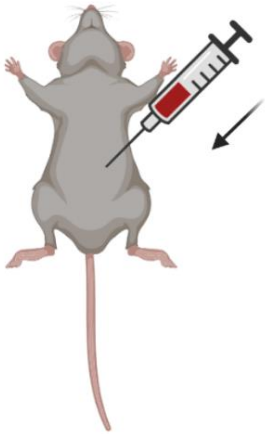
monoclonal cell line

supernatant harvest

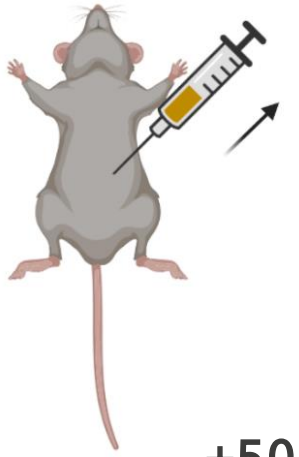


protein A purification

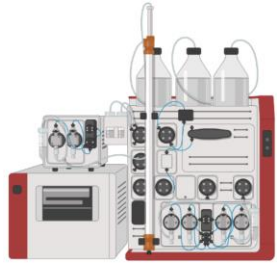




Hybridoma injection



ascites harvest

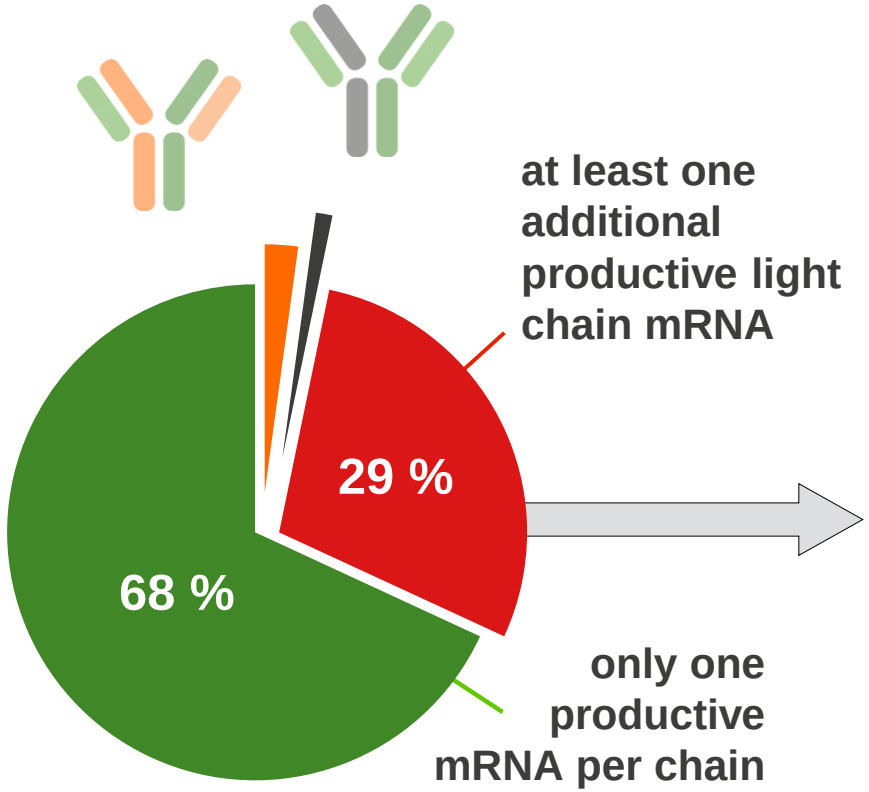


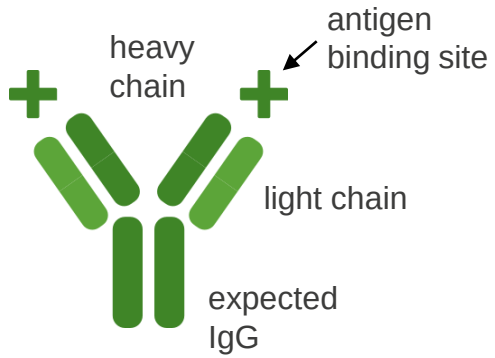
protein A purification

+50.000 mice / year
(EU 2018)

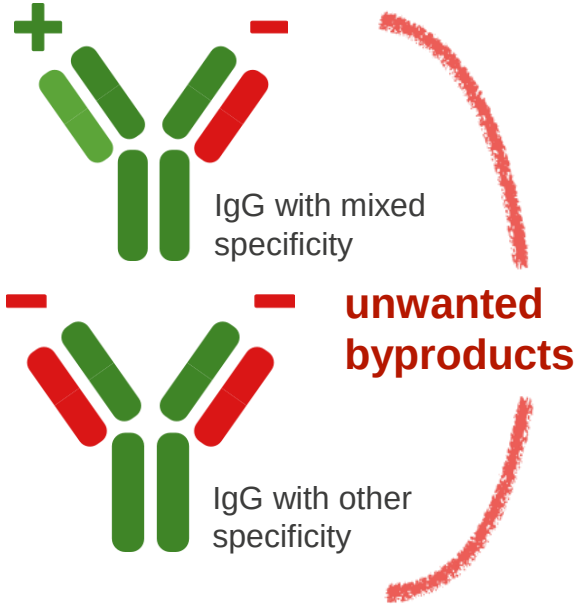
Created with BioRender.com

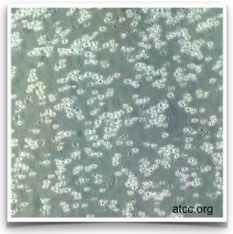
Many Hybridoma monoclonals are not monospecific





Specificity !

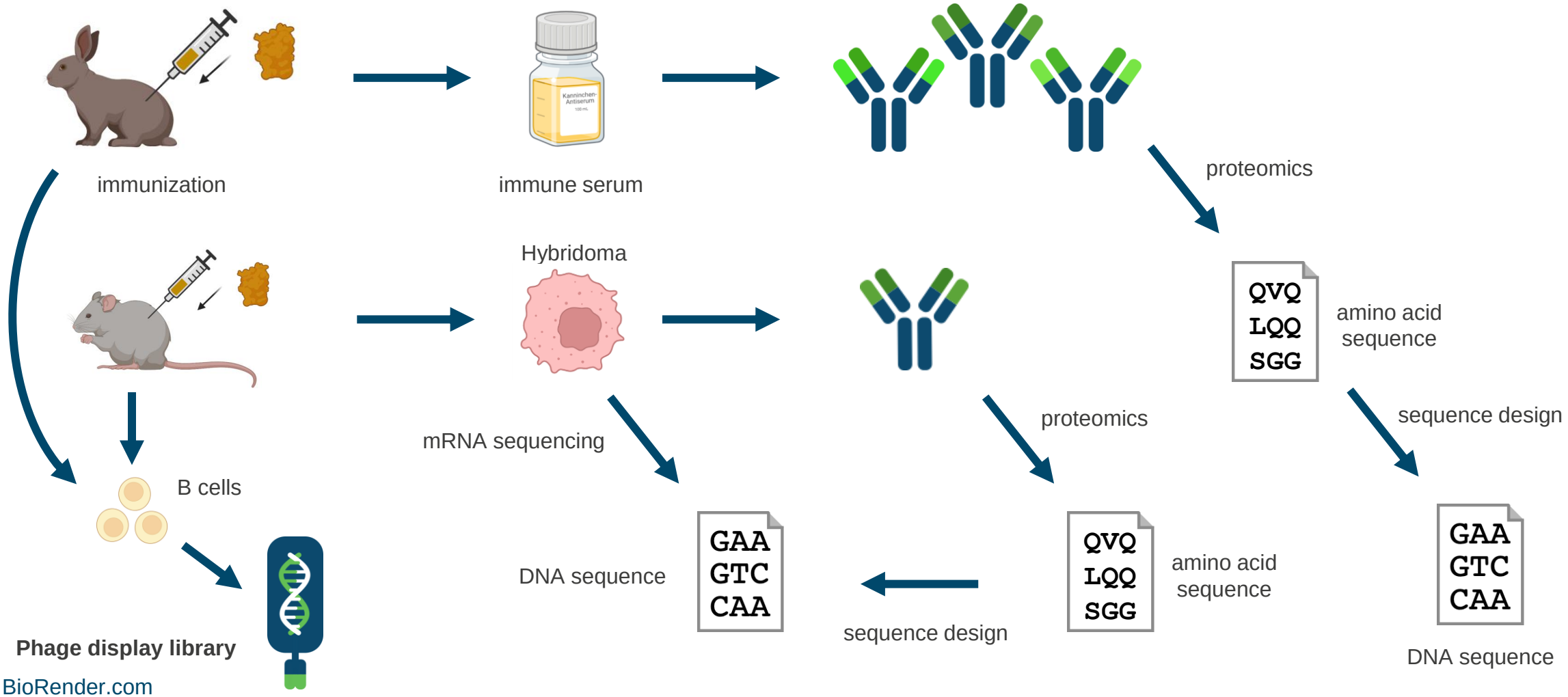




185 hybridomas sequenced
multicentric study (7 different labs in 5 countries)

Bradbury et al. (2018) mAbs 10, 539-546

“animal-freeing” → conversion to recombinant

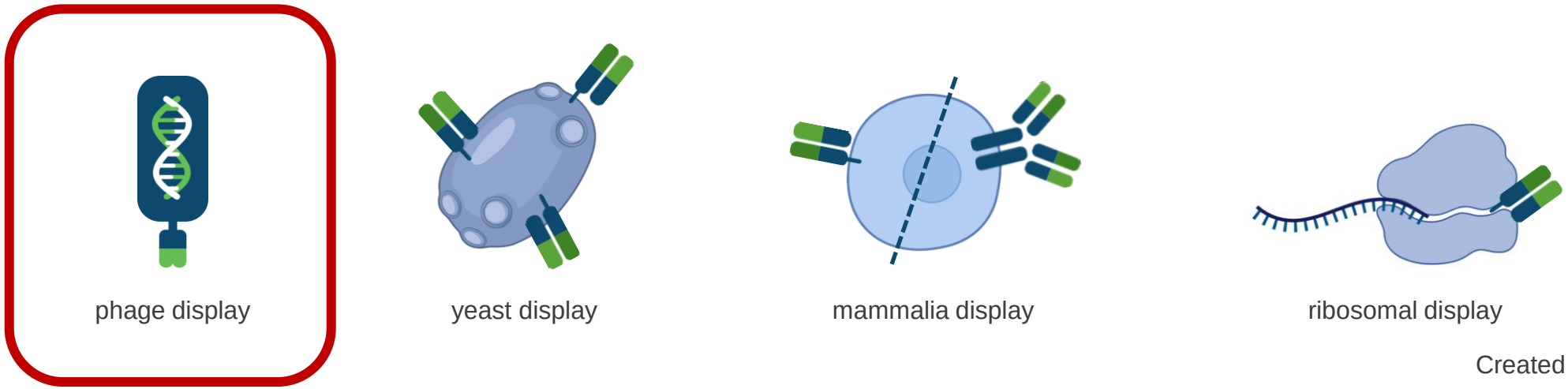


Created with BioRender.com

animal-free recombinant antibody technology

non-animal B cells

antibody-defining genes



phage display

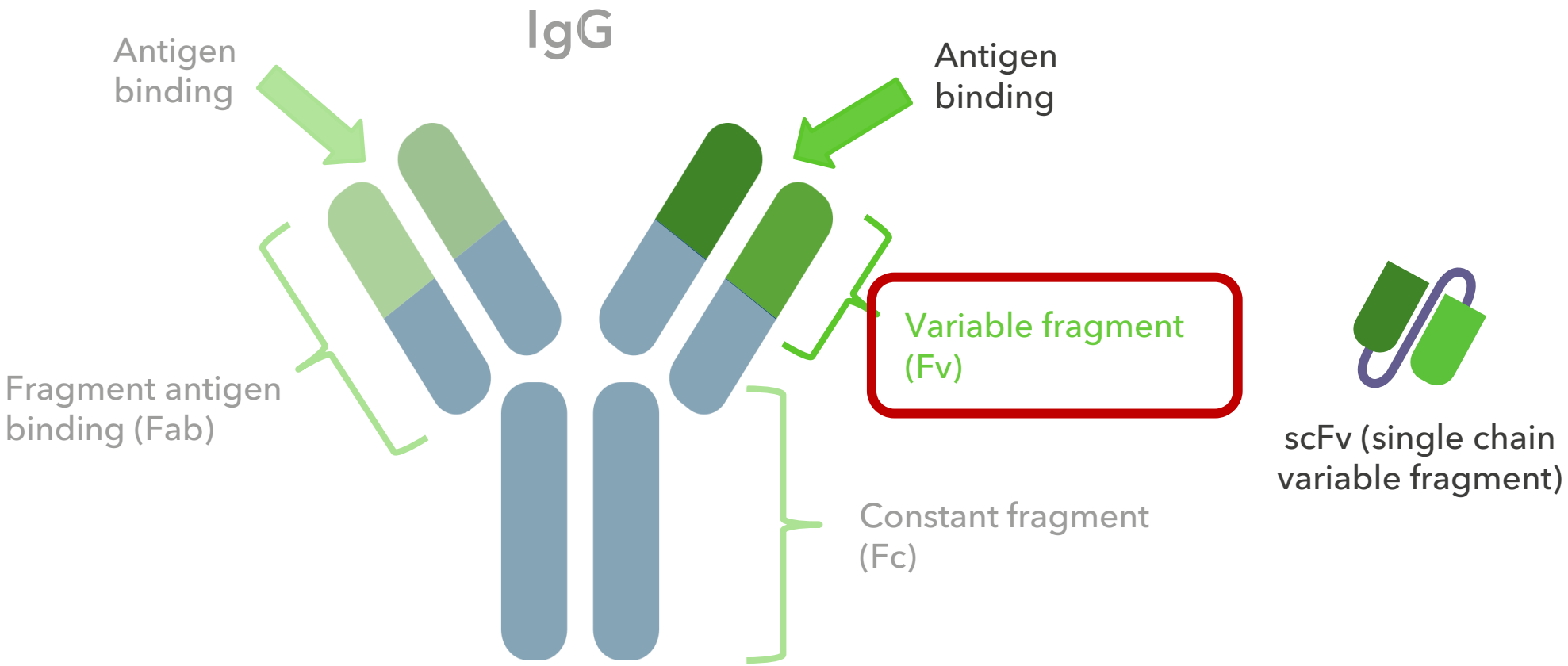
yeast display

mammalia display

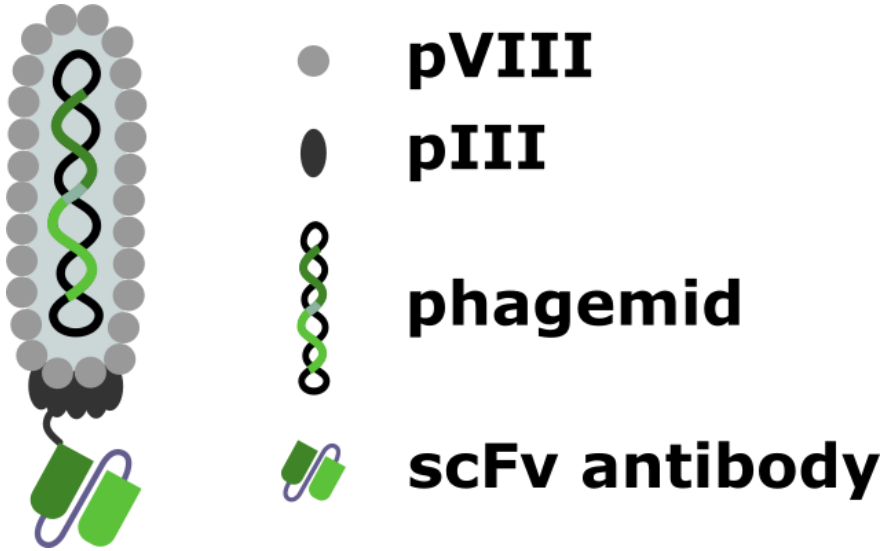
ribosomal display

Created with BioRender.com

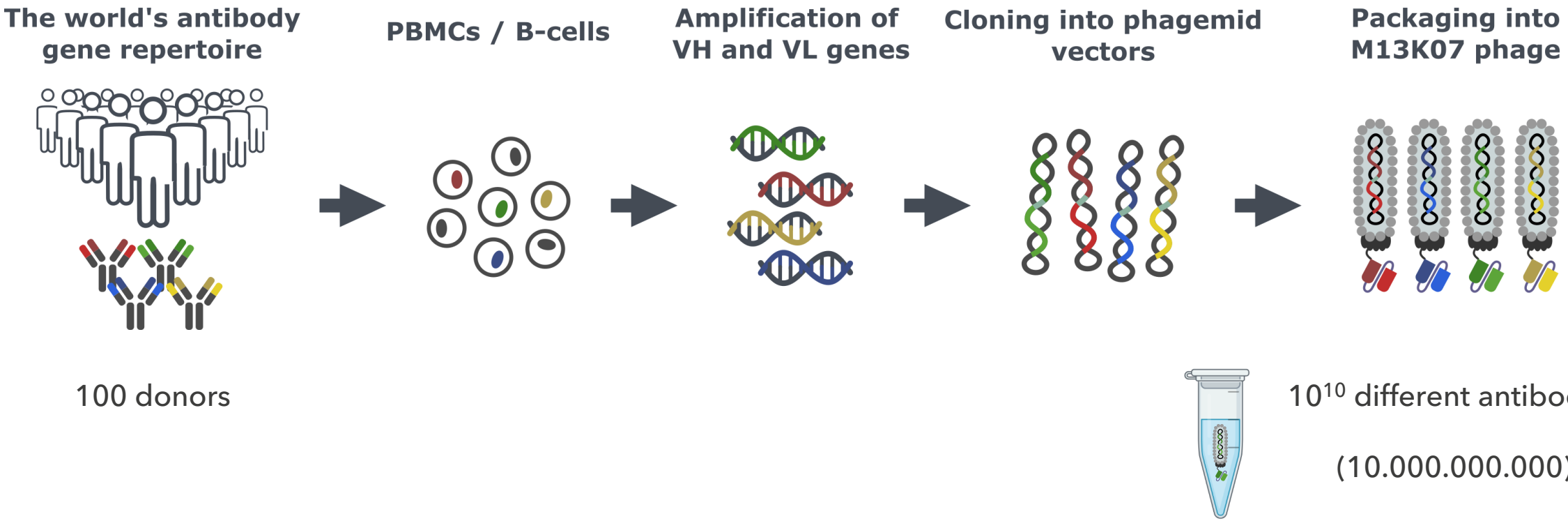
antibody phage display – why is it possible?



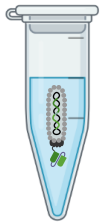
antibody phage display – M13 phage



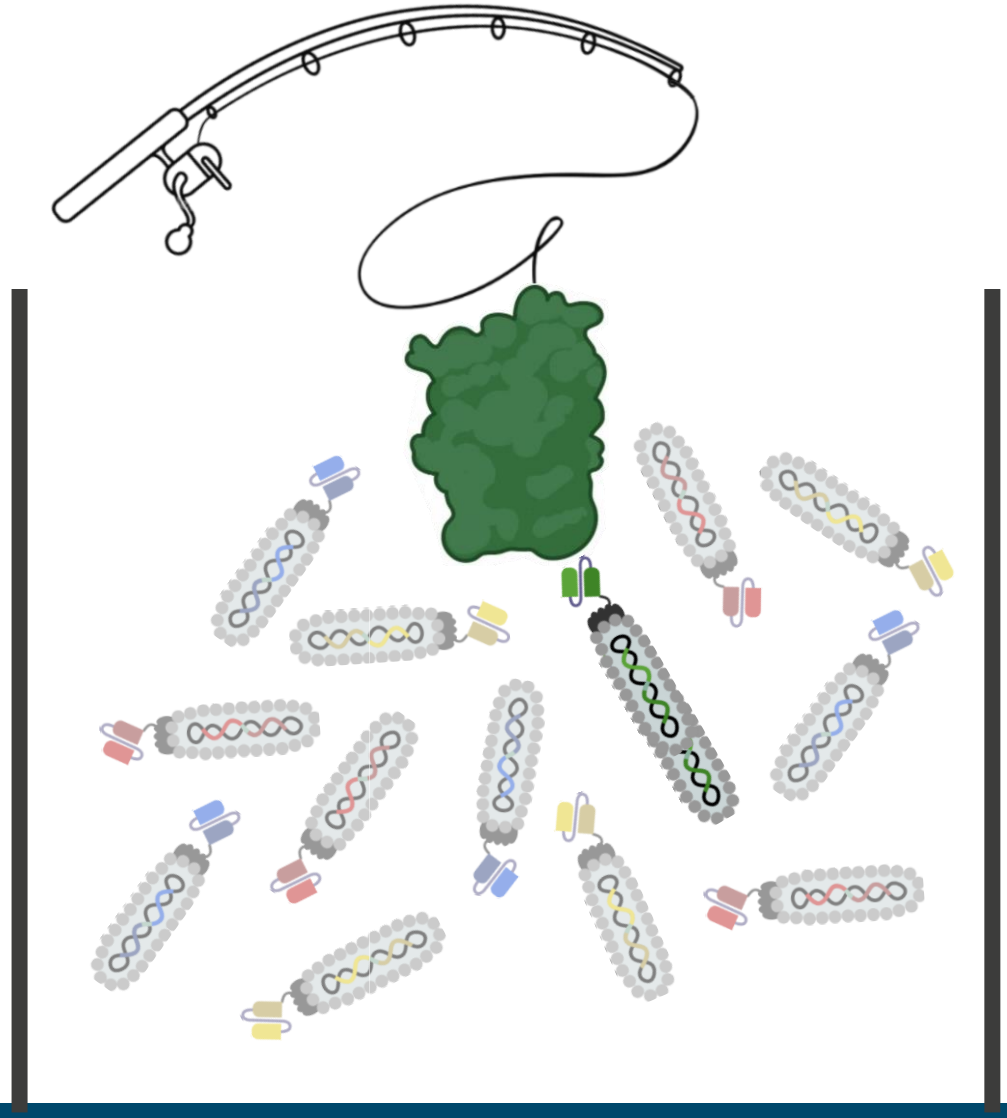
antibody phage display – library generation



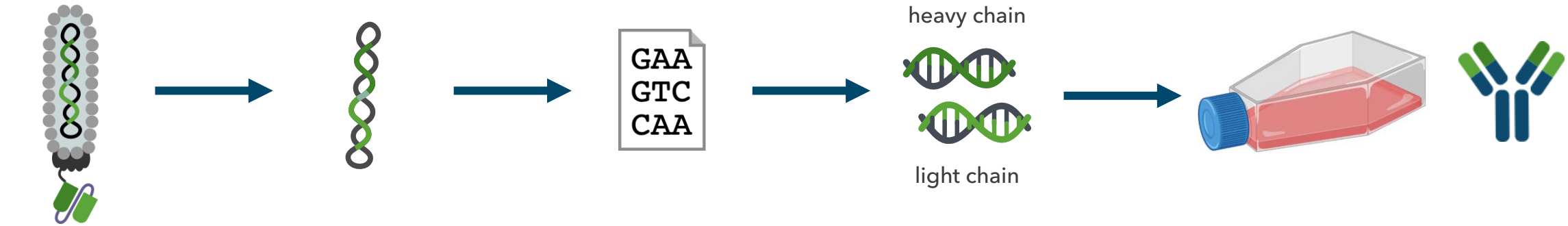
antibody phage display – antibody selection



> 10 Billion



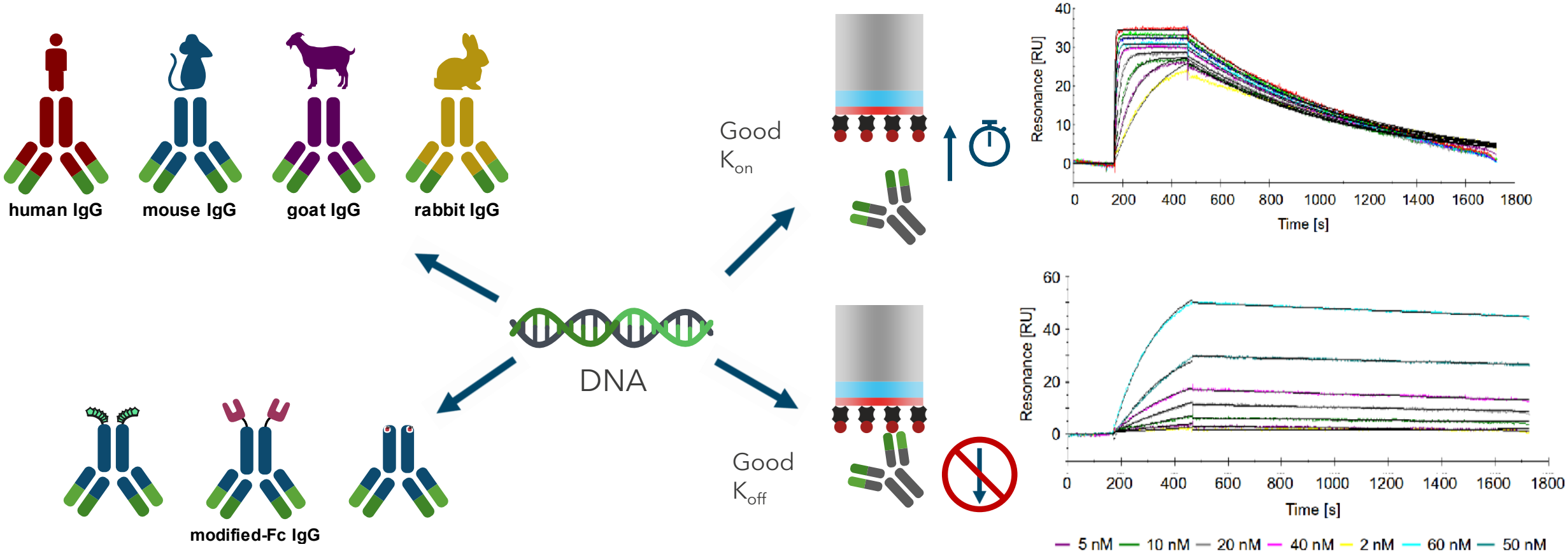
antibody phage display – antibody selection



scFv-phage → phagemid DNA → DNA sequencing → DNA cloning → cell culture production → full IgG

→ **“immortal” and easily scalable product**

antibody phage display – antibody engineering



NADA → blockbuster therapeutics

- **14** animal-free phage display-derived therapeutic antibodies are **approved** (Jul. 2022)
- **53** animal free phage display-derived therapeutic antibodies are **in clinical trials** (Aug. 2020)

(Atezolizumab, Avelumab, Belimumab, Necitumumab, Ramucirumab, Guselkumab, Lanadelumab, Emapalumab, Raxibacumab)

Shim H. Curr Pharm Des. 2016, 22:6538-59
Alfaleh et al., 2020, doi: 10.3389/fimmu.2020.01986

Fact:

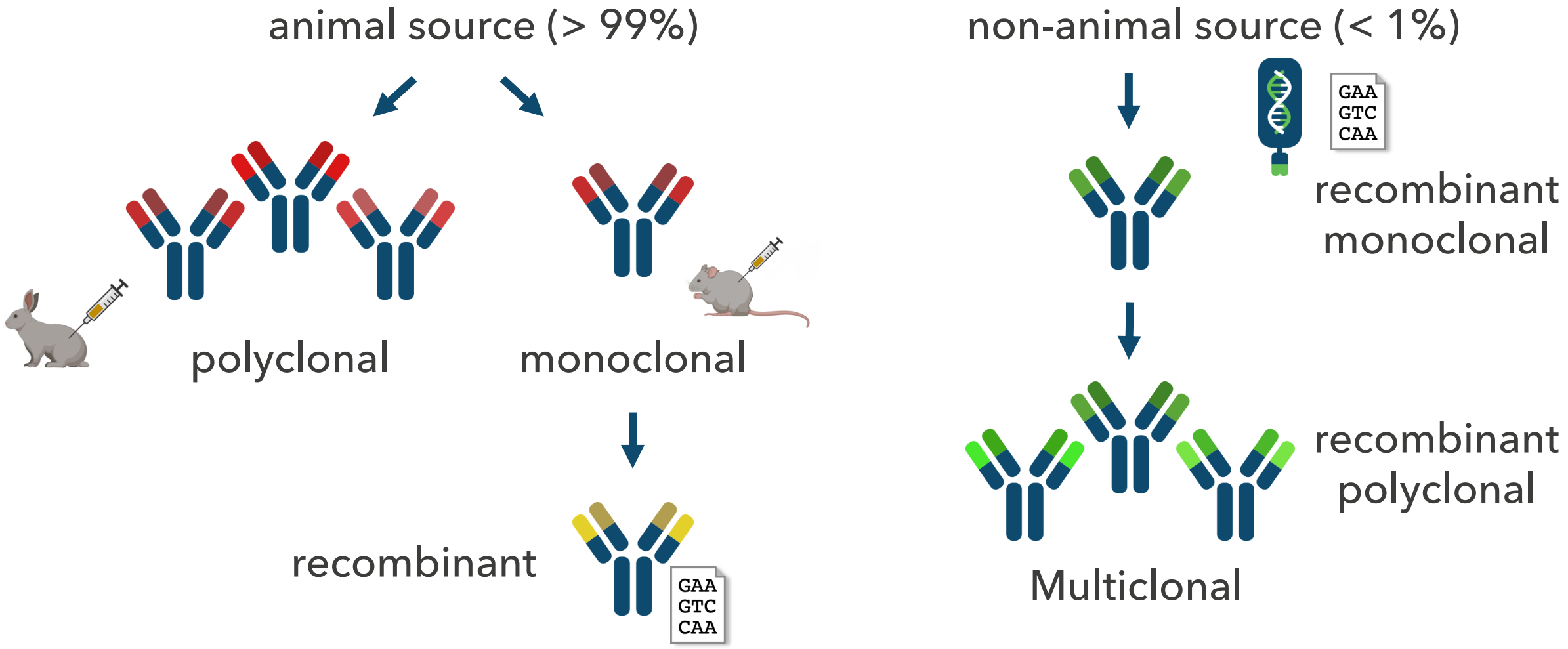
- Non-animal derived antibodies have the **largest market share** in the segment that requires the **highest** antibody **quality** (Therapy)

NADA → improved diagnostics

- NADA-based off-shelf products almost impossible to find

- @Abcalis:
  - since 2019: >20 animal-free antibody products generated
  - Focus on contract research work:
    - **12 successful** NADA projects
    - 11 NADA projects initialized and **ongoing**

Types of antibodies – recombinant ≠ animal-free



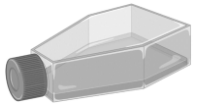
non-animal derived antibodies → **NADA**

Non-Animal Derived Antibodies Summary – pros and cons

Pro:

- sequence defined:
  → "immortal"
  → reproducible
  (data and products)

- scalable production



- fast generation
- antibodies can be improved in retrospect

- versatility!

Contra:

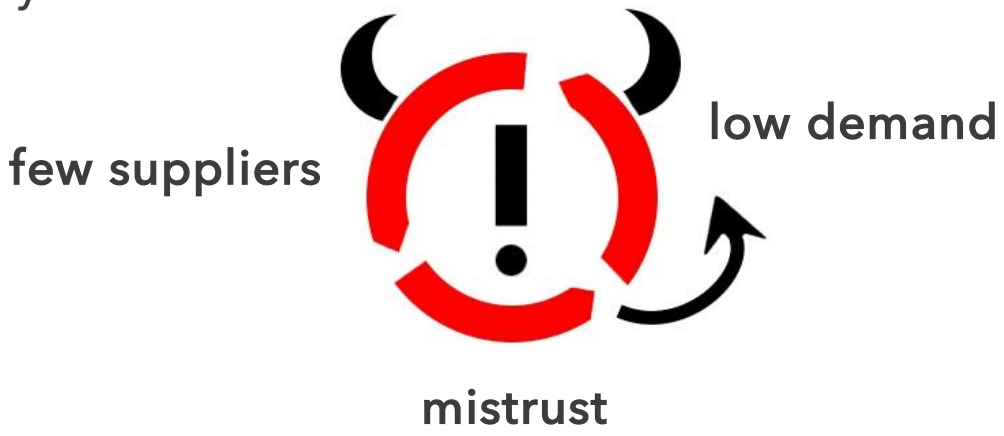
- higher initial cost for generation

- initial affinity lower from naïve sources
- new certification for products needed

- feels like repetition of work already done before

Why are animal-free alternatives not more widely used?

- no private funding
- 3R does not drive antibody research funding

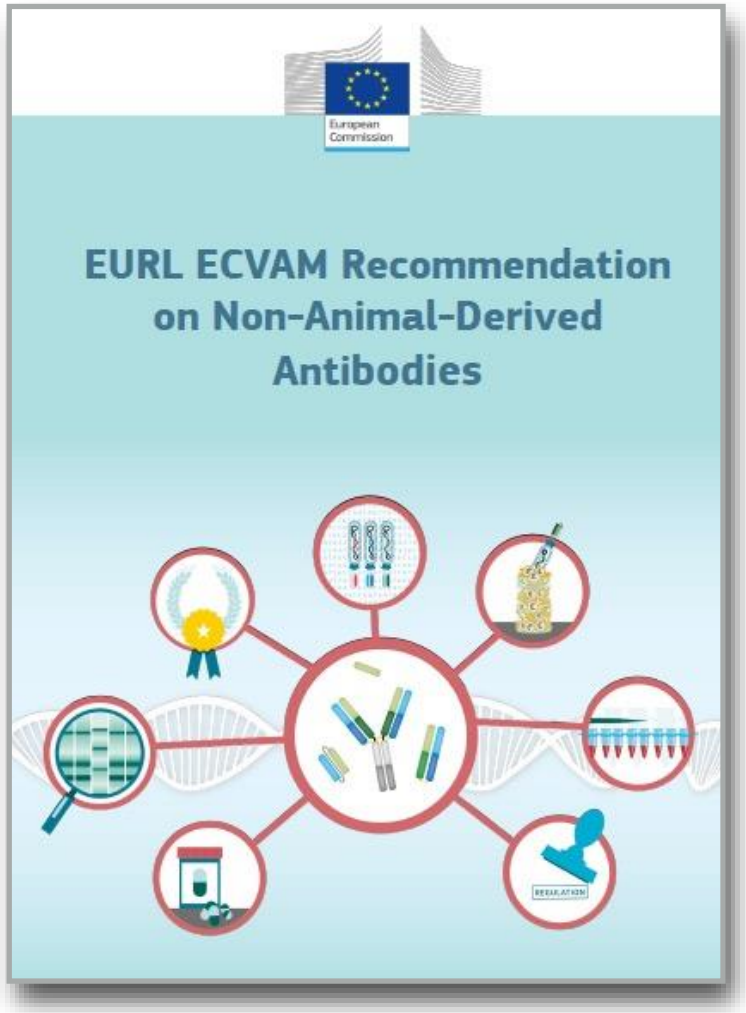


<u>unawareness:</u>

- high quality alternatives
- existing commercial sources
- many opportunities with animal-free recombinant technology

- conservatism (>40 years)
- old data (1990s – “low quality”)

New EU guidelines 2020



https://publications.jrc.ec.europa.eu/repository/handle/JRC120199

"EURL ECVAM recommends that animals should no longer be used for the development and production of antibodies for research, regulatory, diagnostic and therapeutic applications. In the EU, the provisions of Directive 2010/63/EU should be respected and EU countries should no longer authorise the development and production of antibodies through animal immunisation, where robust, legitimate scientific justification is lacking."

What can we do?

- **improve information** about advantages of recombinant Abs (quality, designer antibodies)
- **generate incentives** to use recombinant (= better quality) reagents
- **improve information** about NADA availability and sources etc.

Where to find

Database / Lists

PETA SCIENCE CONSORTIUM INTERNATIONAL e.V.

Advancing 21st Century Toxicology

https://www.thepsci.eu/antibody-availability/

Availability of Animal-Free Antibodies

Animal-free antibodies are available from the sources listed below. Most companies offer a selection of catalog antibodies and custom antibody development, and generate antibody fragments and full immunoglobulin format. Note that this list is not comprehensive and that a number of the suppliers listed sell animal-derived antibodies in addition to animal-free recombinant antibodies.

Abcalis offers animal-free recombinant monoclonal antibodies and multiclonal antibodies produced in animal-serum free media.

Abcam produces a selection of antibodies using phage display recombinant antibody technology.

Absolute Antibody sequences and produces antibodies developed via phage display.

Adimab offers therapeutic antibody discovery and an antibody discovery platform transfer service.

AdipoGen Life Sciences generates and characterises animal-free recombinant monoclonal antibodies (RecMAbs™).

AvantGen provides a complete antibody discovery service using human antibody libraries.

Bio-Rad uses its Human Combinatorial Antibody Libraries (HuCAL) library to offer animal-free recombinant monoclonal antibodies. Catalog HuCAL antibodies can be found here by searching the HuCAL isotype.

ANIMAL FREE RESEARCH UK

Animal Free Research UK
Animal Free Antibody Database

(coming soon)

What can we do?

- **improve information** about advantages of recombinant Abs (quality, designer antibodies)
- **generate incentives** to use recombinant (= better quality) reagents
- **improve information** about NADA availability and sources etc.
- provide **equal chances** to NADA (e.g.: by referring to the ECVAM report)
- **generate an incentives** to avoid animal use (e.g. in grants), e.g. by applying EU directive 2010/63 for research/diagnostic antibodies

Thank you very much for your attention!

Contact me:

✉esther@abcalis.com
/estherwenzel

https://abcalis.com