



Evaluation of Monoclonal Antibodies



Giulia Piccini, PhD

Senior Project Director

VisMederi

giulia.piccini@vismederi.com



How do monoclonal antibodies work?

Vaccines actively teach the body to recognize pathogens, through production of antibodies

Virus enters the body and replicate within epithelial cells

SARS-CoV-2

Activates
immune system

Monoclonal antibodies can be passively administered to patients

B cells produce antibodies

T helper cells are activated

Cytotoxic T cells (CTL) identify and destroy virus-infected cells

Help activate B cells

CTL
Infected cell

Antibodies bind to pathogen

Neutralize and block pathogen from entering cells

Tag pathogens for destruction

Immune cell

Benefits of mAbs:

- Can be a therapeutic treatment -> function rapidly
- Provide protection to exposed and not yet vaccinated (eg. *healthcare workers*)
- May be required for those that cannot maintain / develop an adequate immune response after vaccination (eg. *elderly / immunocompromised*)

Limitations of mAbs:

- Short-lived protection
- High specificity may rapidly lose efficacy
- More expensive than vaccines

Antibody-dependent cell cytotoxicity

Activation of complement

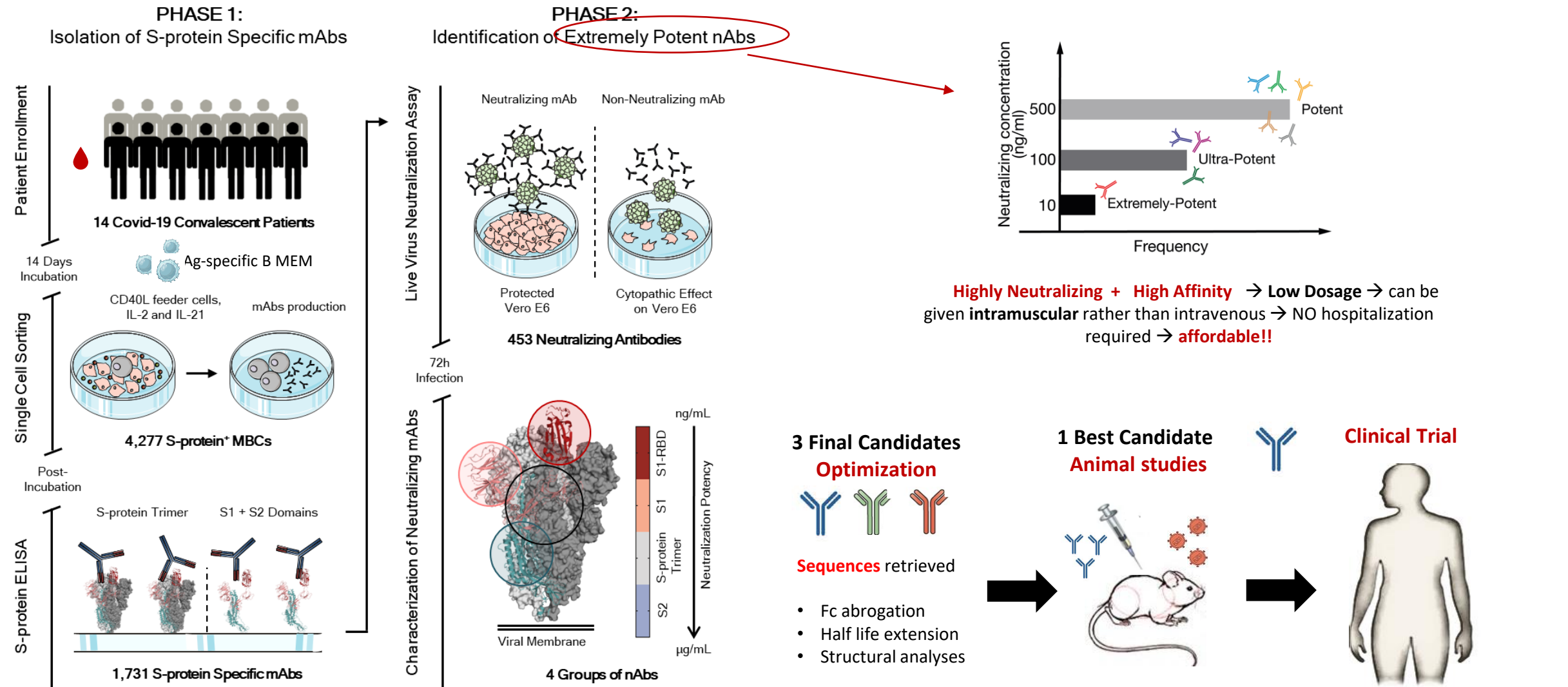
Opsonization

Generation of oxidants

Immunomodulation

Case study 1: How to identify and develop monoclonal antibodies

Identification of extremely potently neutralizing monoclonal antibodies from Italian Covid-19 convalescent patients



Andreato et al. [Extremely potent human monoclonal antibodies from COVID-19 convalescent patients](#). Cell. 2021. doi: 10.1016/j.cell.2021.02.035

→ Unfortunately mAb was not effective against Omicron

Characterization of monoclonal antibodies – Binding and Neutralization



ELISA Assay -> to determine if antibody **binds** the antigen (not functional)

Live Virus Neutralization Assay -> to determine if antibody block and neutralize virus (functional)

Virus: Live Virus

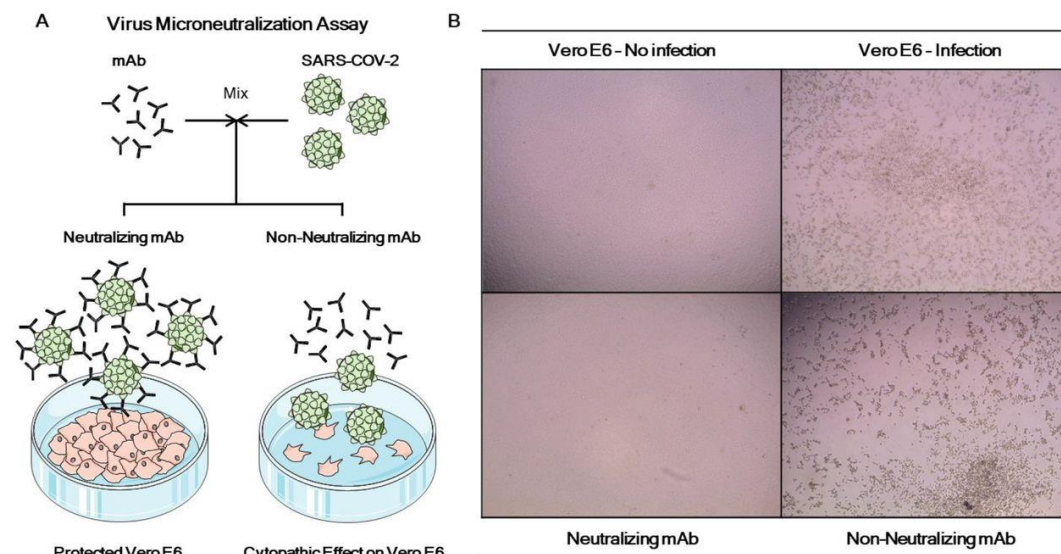
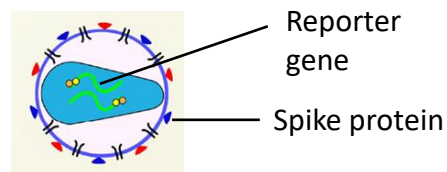
Readout: Cytopathic effect (MN-CPE) or Plaque reduction (PRNT)

Limits: **BSL3 required for some viruses** (such as SARS-CoV-2)

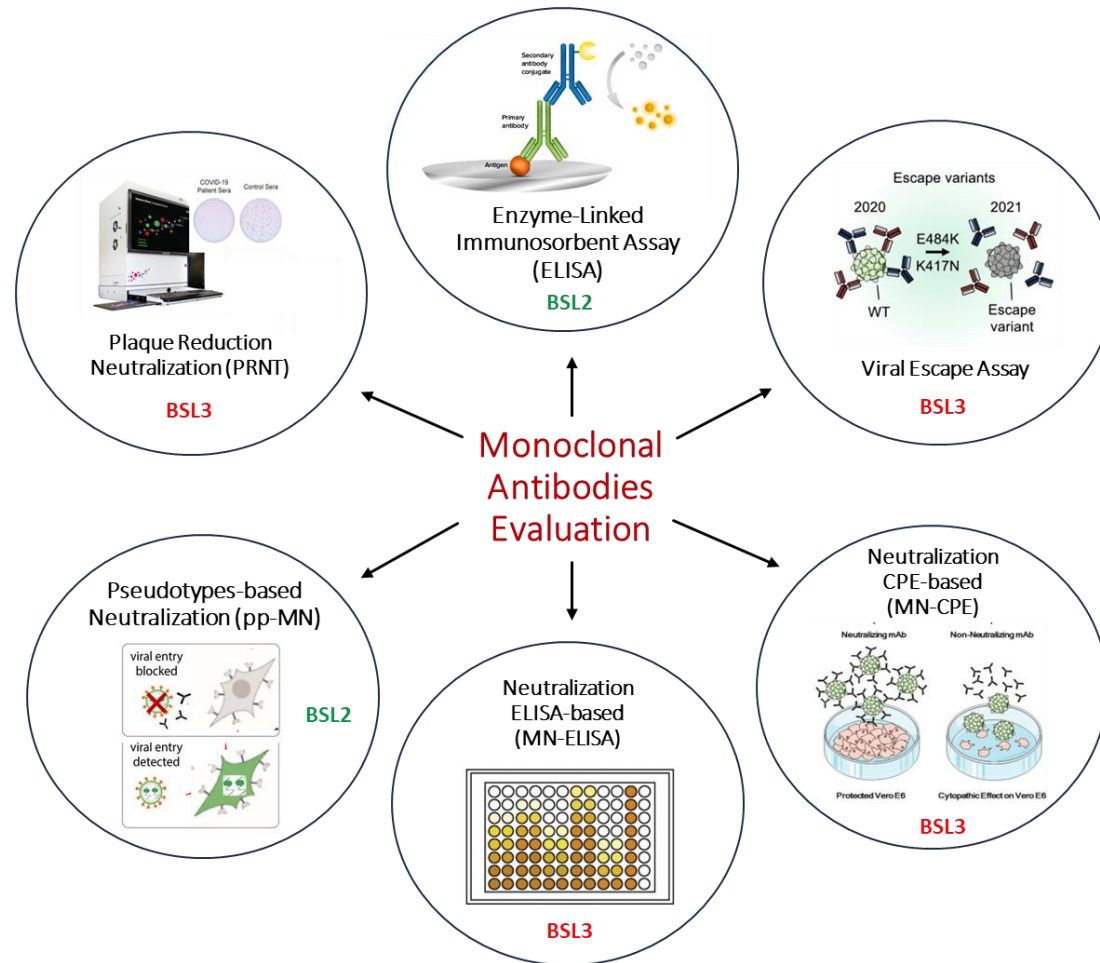
Pseudovirus Neutralization Assay -> to determine if antibody block cell entry (surrogate of functional)

Virus: VSV-based, LV-based expressing protein of interest and a reporter gene

Readout: Luminescence



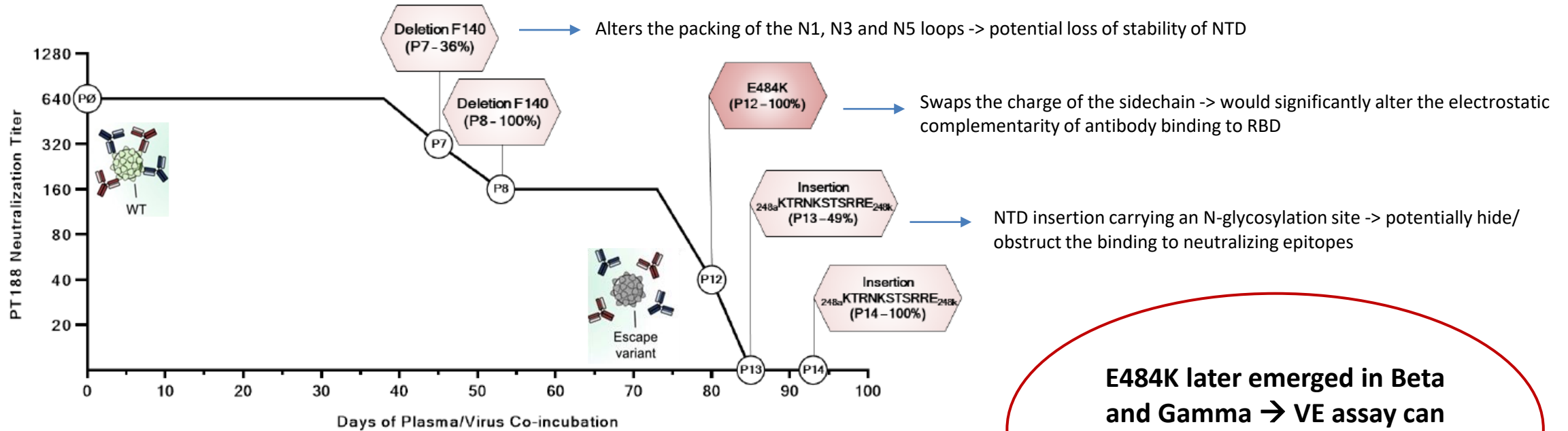
VisMederi Laboratory assays for monoclonal antibodies evaluation



- ✓ Methods **fully developed for SARS-CoV-2**
- ✓ Possibility to use **live virus** (functional, BSL3) or **pseudovirus / antigens** (not functional, BSL2)
- ✓ **Other assays** available on request
- ✓ Most methods are **validated**
- ✓ Possibility for **customization**
- ✓ **Possibility to develop the same/similar assays using other viruses (eg. Influenza, RSV...)**

Case study 2: How to predict mutations – Viral Escape Assay (Live)

SARS-CoV-2 escape in vitro from a highly neutralizing COVID-19 convalescent plasma



E484K later emerged in Beta and Gamma → VE assay can predict mutations in real setting!



...mAbs evaluation coming soon!



THANKS FOR YOUR ATTENTION