Rapid development of monoclonal antibody and protein reagents to guide and facilitate vaccine development

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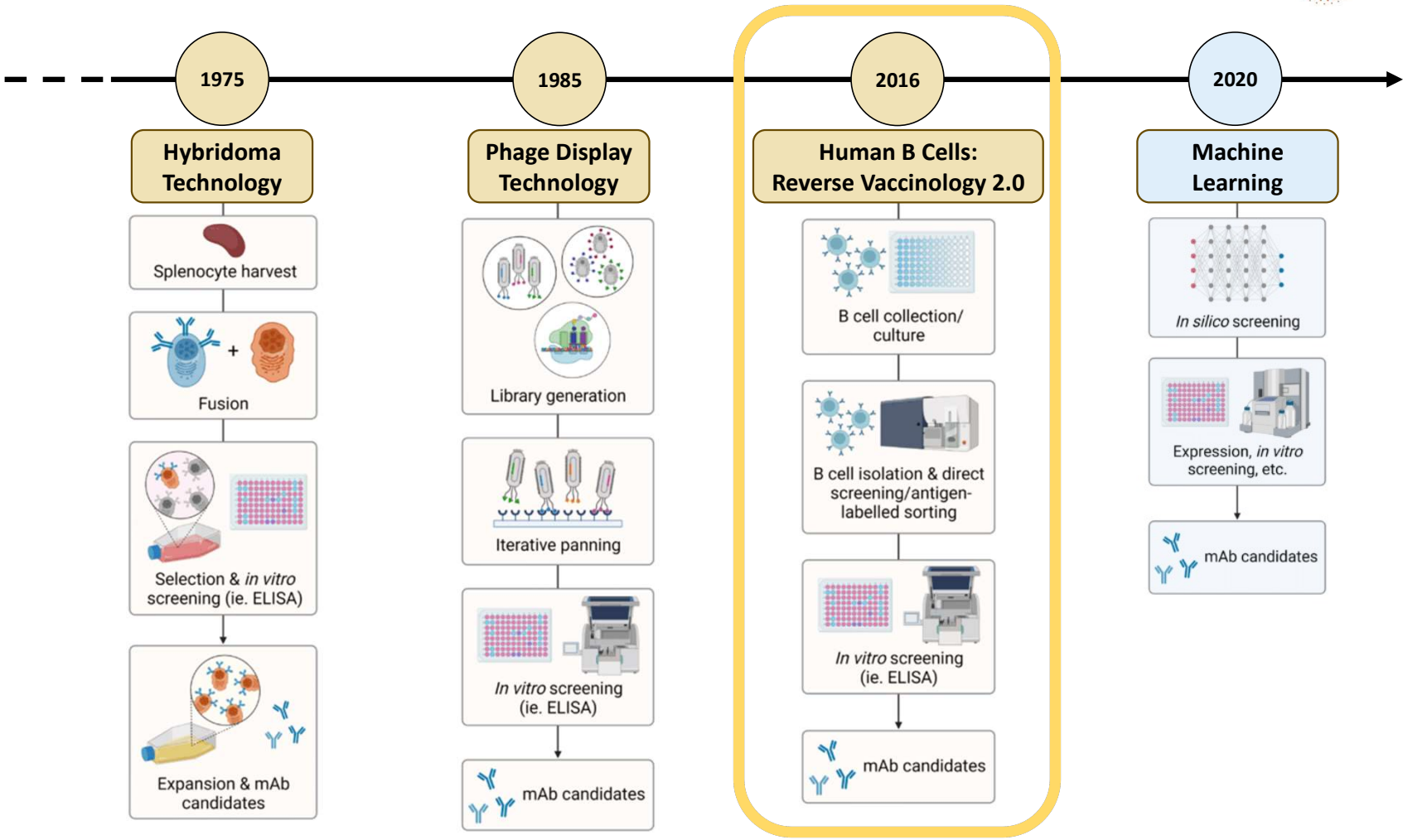
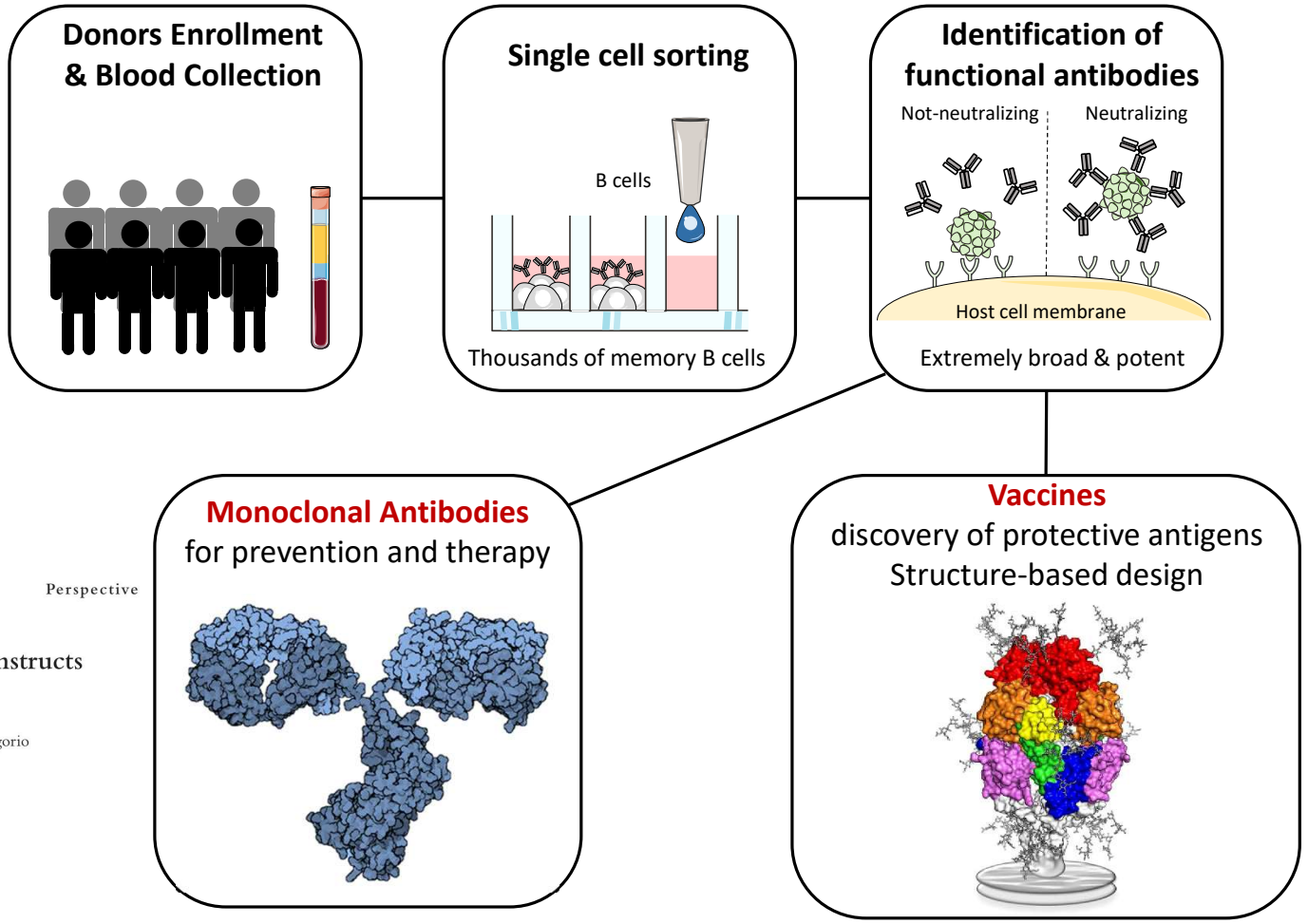
Monoclonal Antibody (mAb) Discovery Platforms



Modified from: https://www.rapidnovor.com/technologies-antibody-discovery-and-generation/ ; Troisi et al. Front. Microbiol., 14 December 2022

Reverse Vaccinology 2.0: monoclonal antibodies to fight infectious diseases



JEM Perspective

Reverse vaccinology 2.0: Human immunology instructs vaccine antigen design

Rino Rappuoli, Matthew J. Bottomley, Ugo D'Oro, Oretta Finco, and Ennio De Gregorio

GlaxoSmithKline Vaccines S.r.l., 53100 Siena, Italy

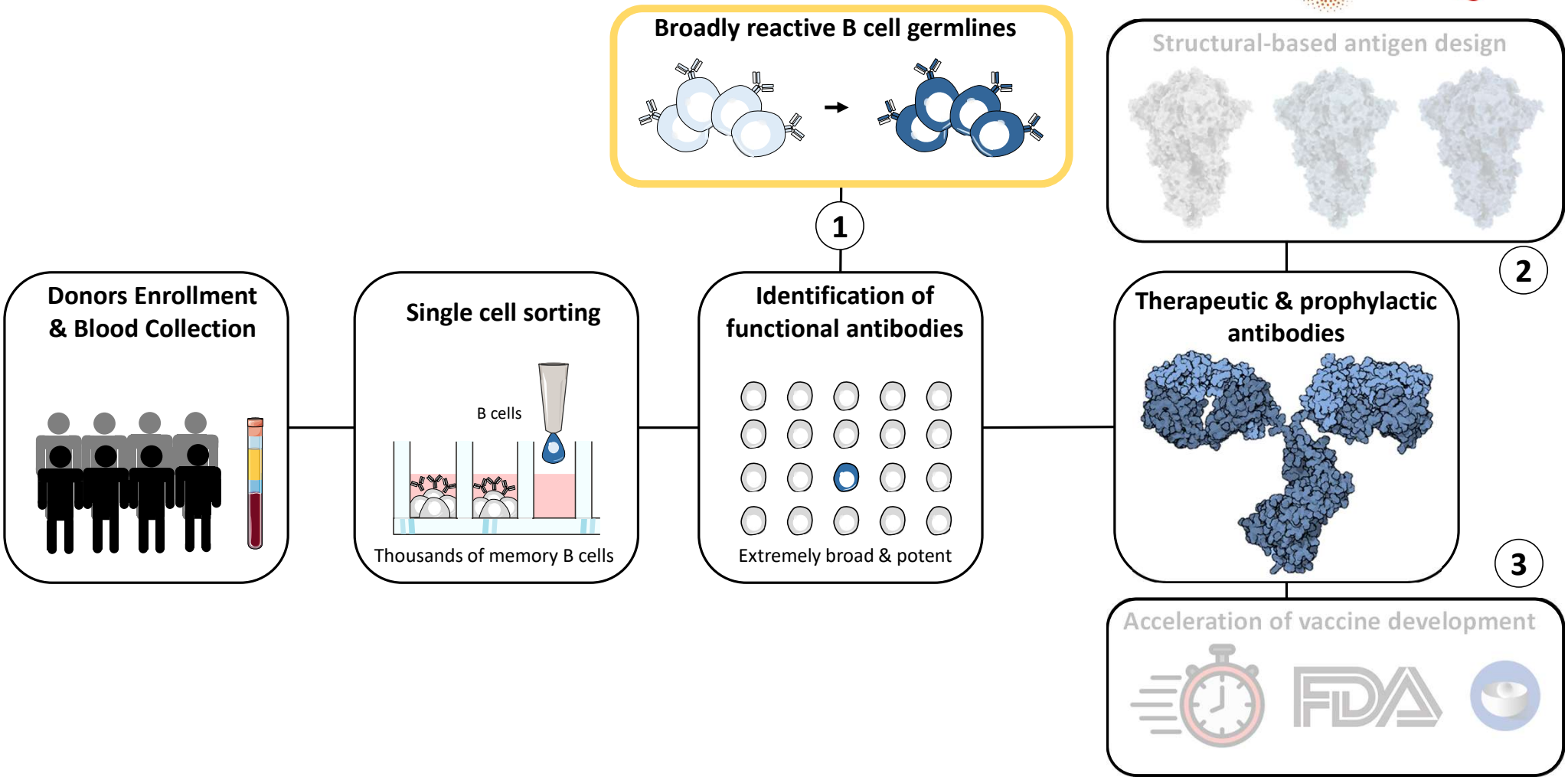
Modified from: Rappuoli R. et al. J Exp Med. 2016 Apr 4; 213(4): 469–481.; McLellan J. et al. Science. 2013 May 31;340(6136):1113-7

94 days from discovery to first human dose

- mAbs were the first molecules to be discovered and approved for emergency use authorization (Nov. 9, 2020) during the pandemic.

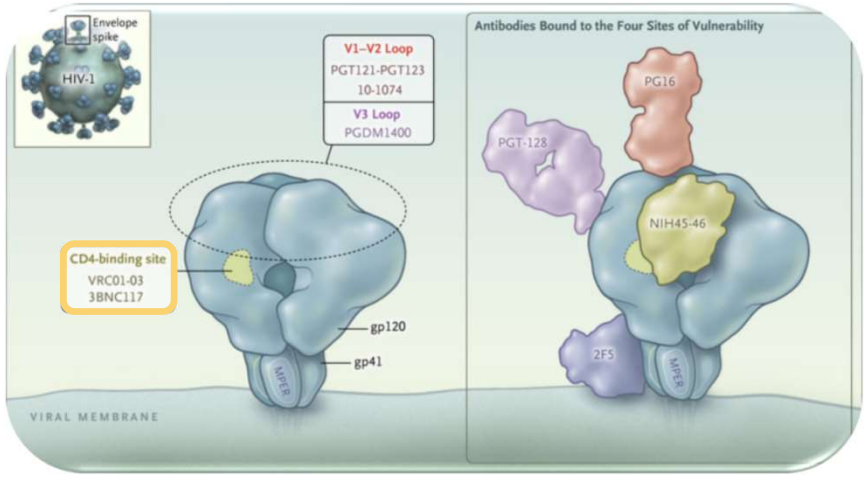
Modified from: Jones et al. Sci Transl Med. 2021 May 12;13(593):eabf1906.

How can mAbs accelerate vaccine development



The HIV case: Germline-targeting vaccinology

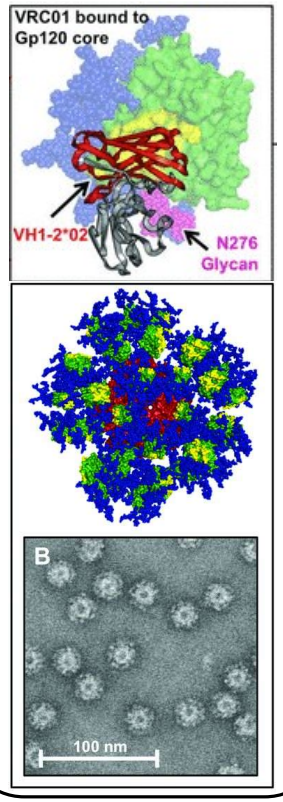
2010:
VRC01 broadly neutralizing antibodies (bnAbs)



VRC01 bnAbs are defined as:

- heavy chain (HC) V gene alleles VH1-2*02 or *04;
- any light chain (LC) complementarity determining region 3 (LCDR3) with a length of five amino acids.

2013:
Design of eOD-GT8 60mer

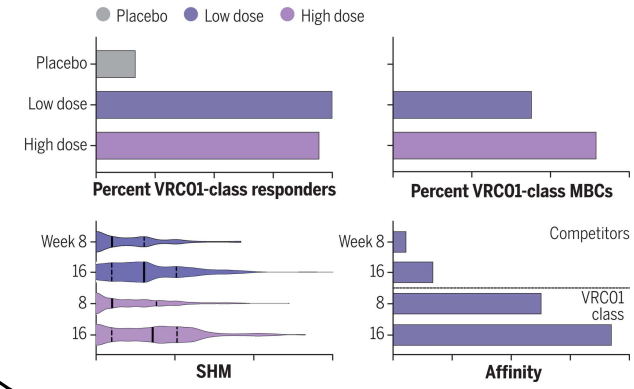


2018-2022:
Phase I trial for eOD-GT8 60mer

COMPLETED

A Phase I Trial to Evaluate the Safety and Immunogenicity of eOD-GT8 60mer Vaccine, Adjuvanted

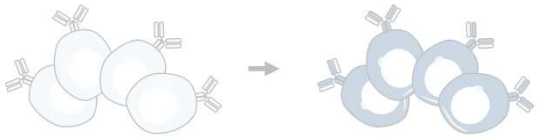
ClinicalTrials.gov ID NCT03547245
Sponsor International AIDS Vaccine Initiative
Information provided by International AIDS Vaccine Initiative (Responsible Party)
Last Update Posted 2022-05-12



Modified from: Caskey et al. N Engl J Med. 2016 Nov 24;375(21):2019-2021; Jardine et al. Science. 2013 May 10;340(6133):711-6.; Leggat et al. Science. 2022 Dec 2;378(6623):eadd6502.

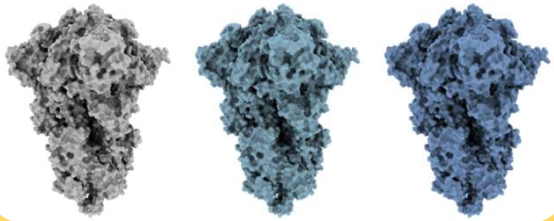
How can mAbs accelerate vaccine development

Broadly reactive B cell germlines



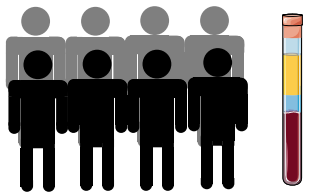
1

Structural-based antigen design

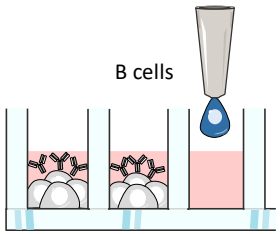


2

Donors Enrollment & Blood Collection

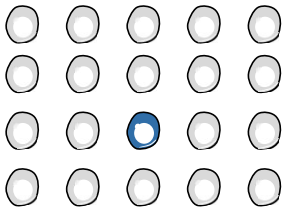


Single cell sorting



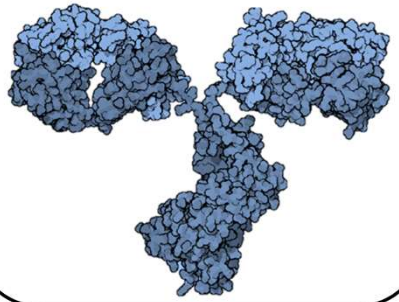
Thousands of memory B cells

Identification of functional antibodies



Extremely broad & potent

Therapeutic & prophylactic antibodies

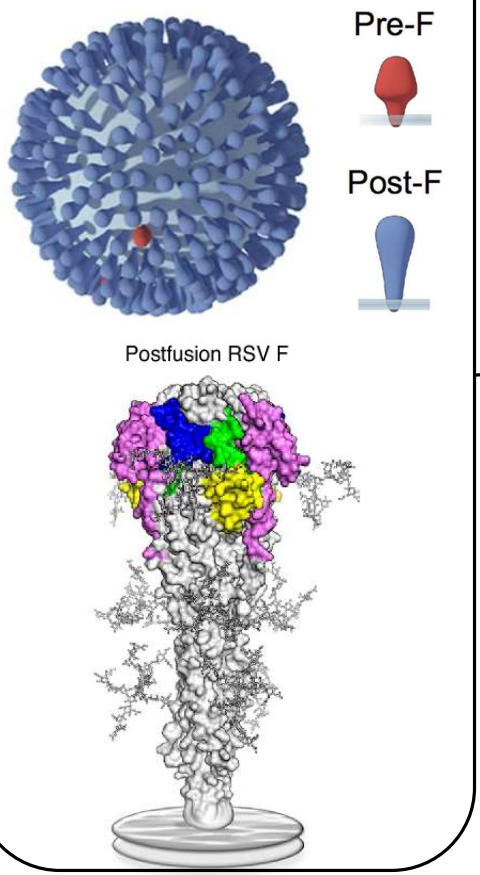


3

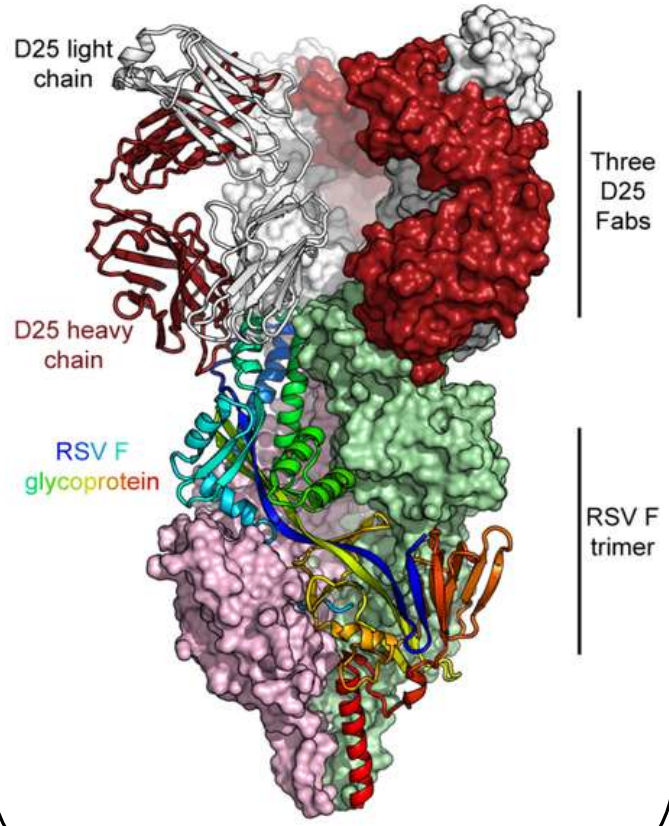
Acceleration of vaccine development

The RSV case: mAbs for structural-based antigen design

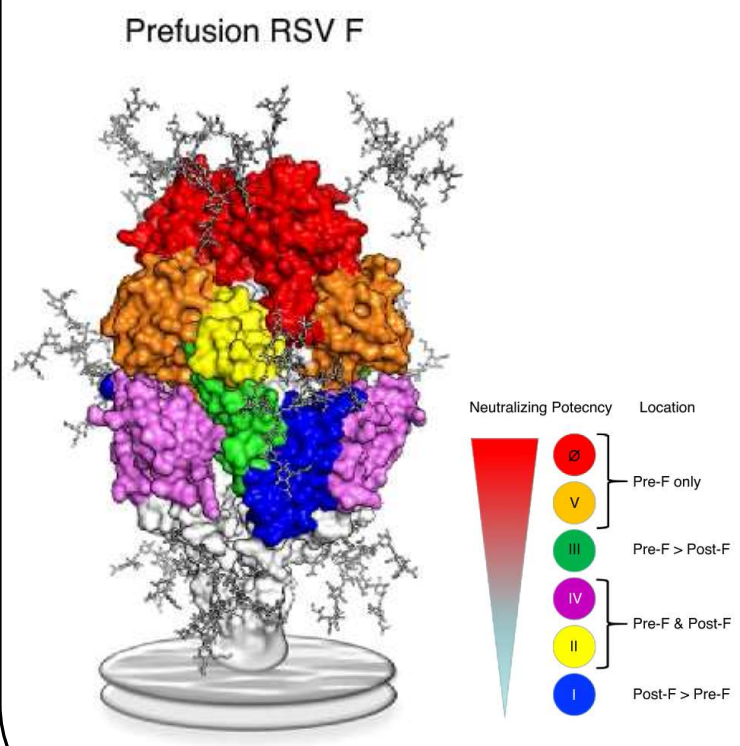
1960s:
Initial RSV vaccines



2013:
Antibody-guided antigen design



2017-2023:
FDA Approves first RSV vaccine



Modified from: McLellan J. et al. Science. 2013 May 31;340(6136):1113-7; Killikelly et al. Sci Rep 6, 34108 (2016).; Graham B. Curr Opin Virol. 2017 Apr:23:107-112.;

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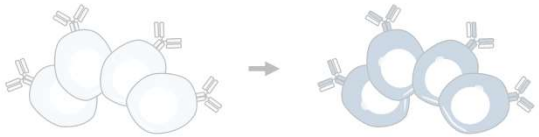
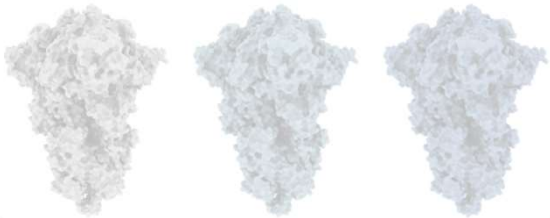


Structural-based antigen design



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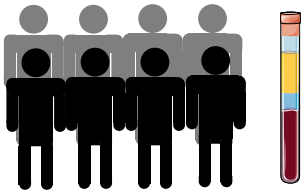

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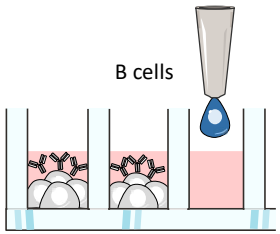

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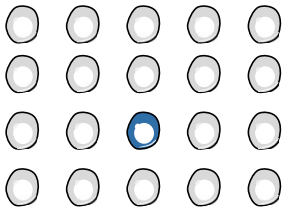

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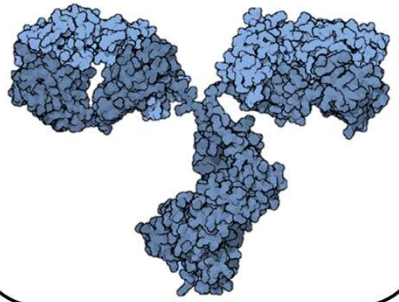
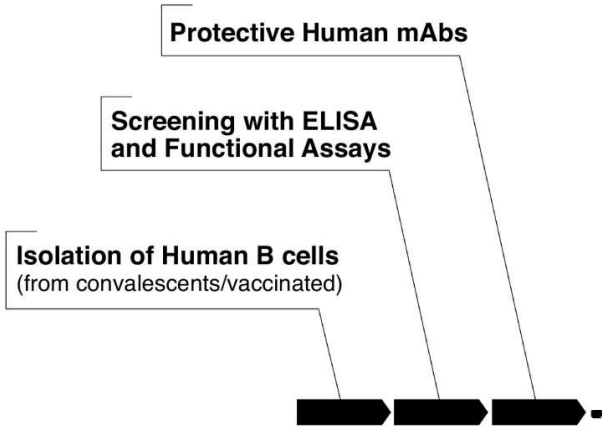


3

Acceleration of vaccine development

Human monoclonal antibodies for vaccine acceleration



Andreano E. et al. Curr Opin Immunol. 2019 Aug:59:130-134.

Current Opinion in Immunology

Conclusions

- Reverse vaccinology 2.0 accelerated the discovery of matured, broad and potent monoclonal antibodies.
- mAbs are the fastest molecules to be developed during emergencies.
- The rapid discovery of functional mAbs can be instrumental to accelerate vaccine development:
  - mAbs can be used to identify broadly reactive B cells and design germline-targeting immunogens;
  - mAbs can be used to stabilize antigens and define protective epitopes;
  - The scientific, regulatory and licensing knowledge acquired for mAbs can accelerate vaccine development.