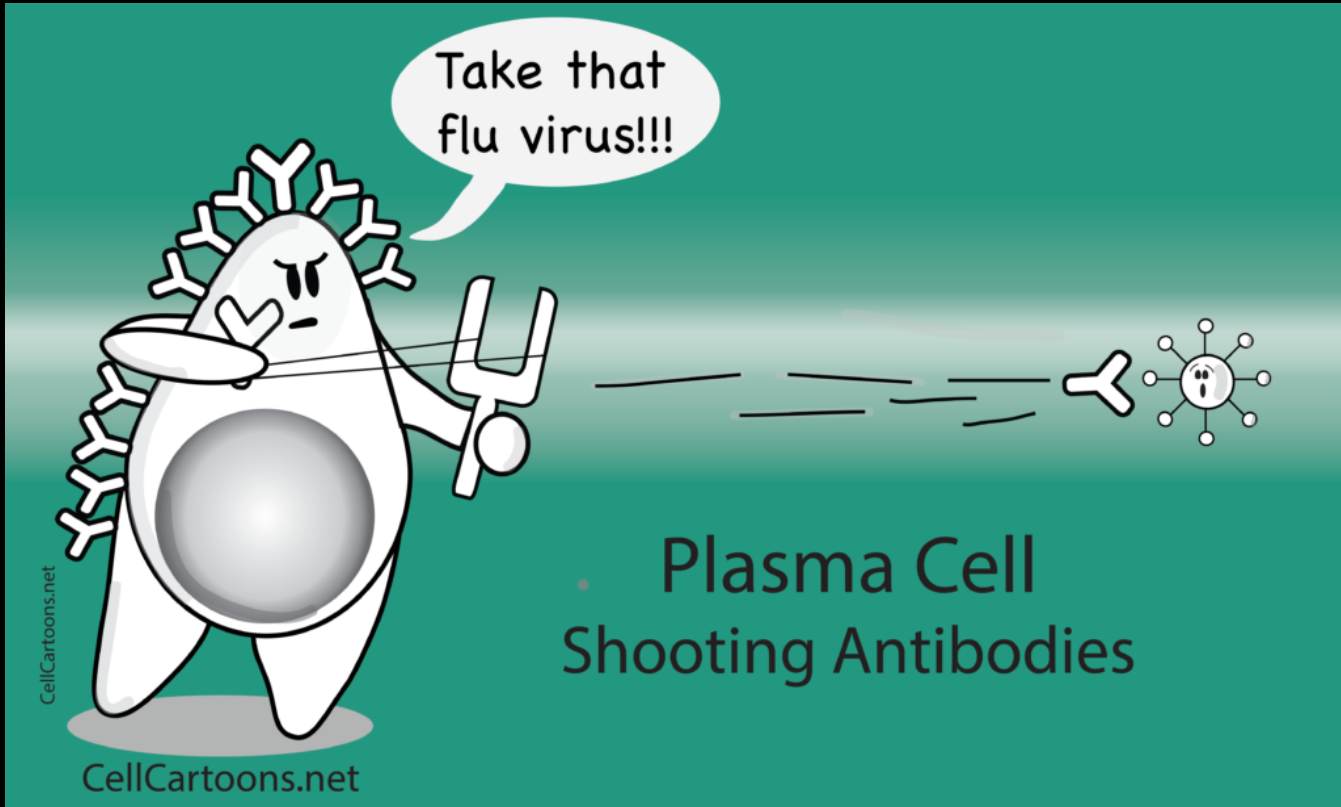


How do antibodies work?

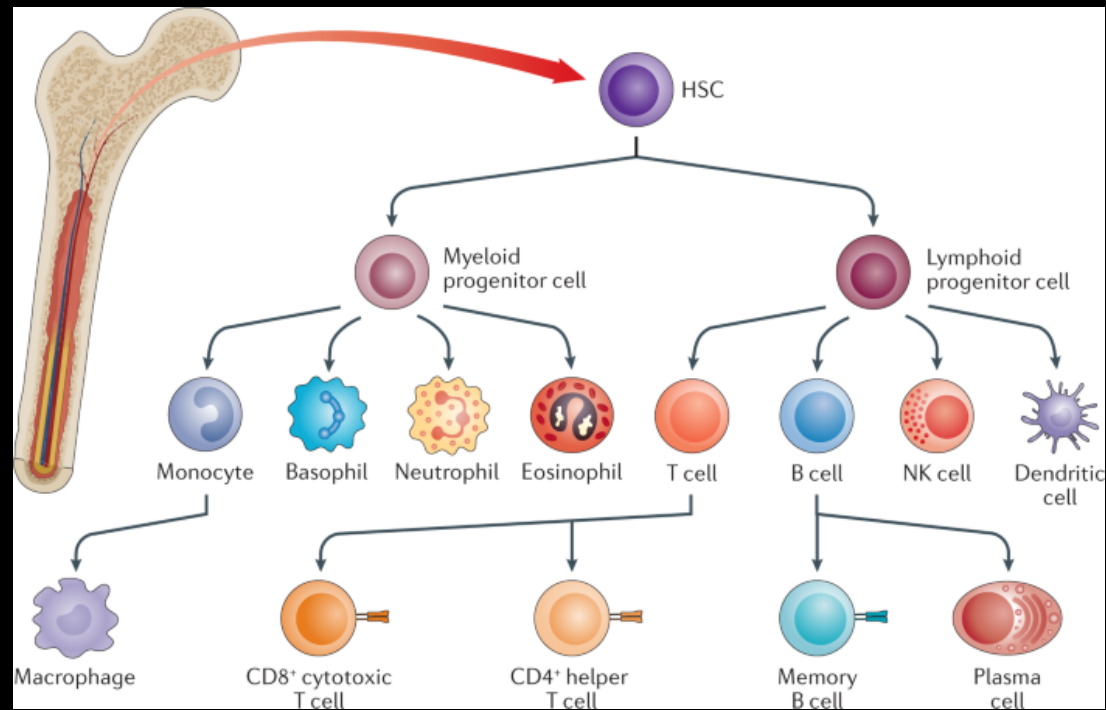
Galit Alter

Ragon Institute

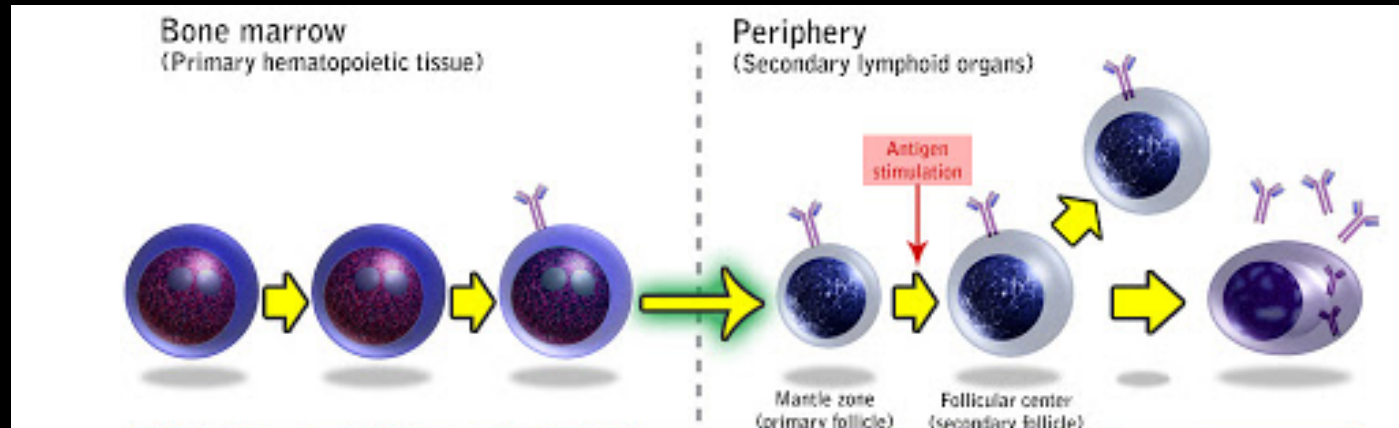


• Plasma Cell
Shooting Antibodies

Antibodies come from B cells

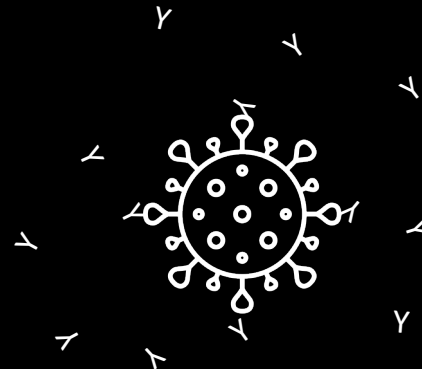
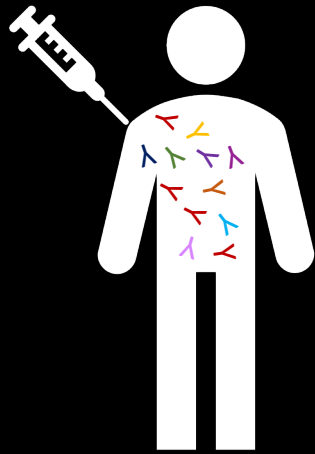


The maturation of the B cell

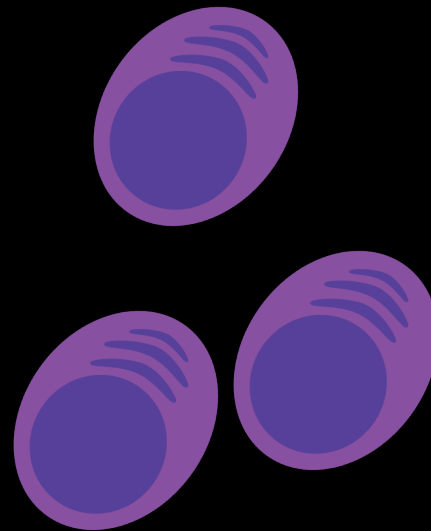
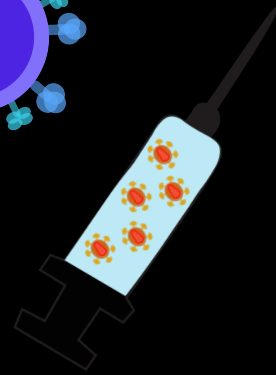
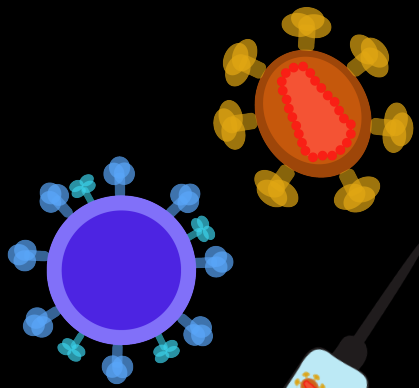


http://hematologyoutlines.com/atlas_topics/69.html

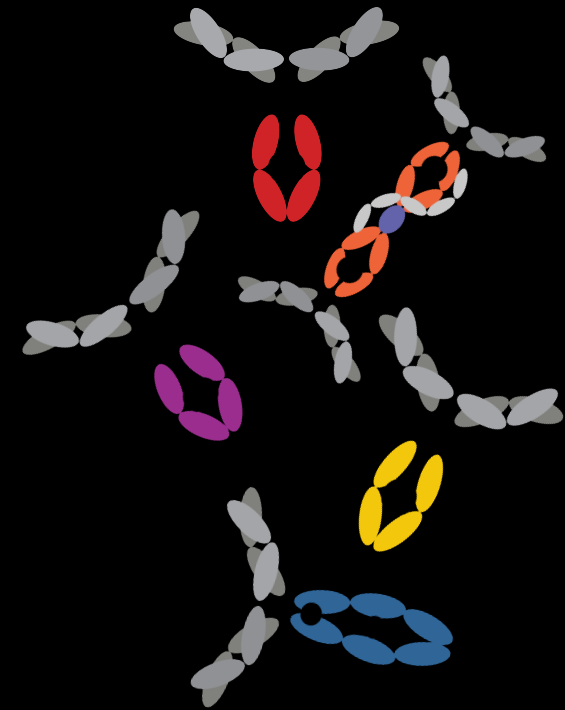
Vaccines and infection lead to the production of antibodies



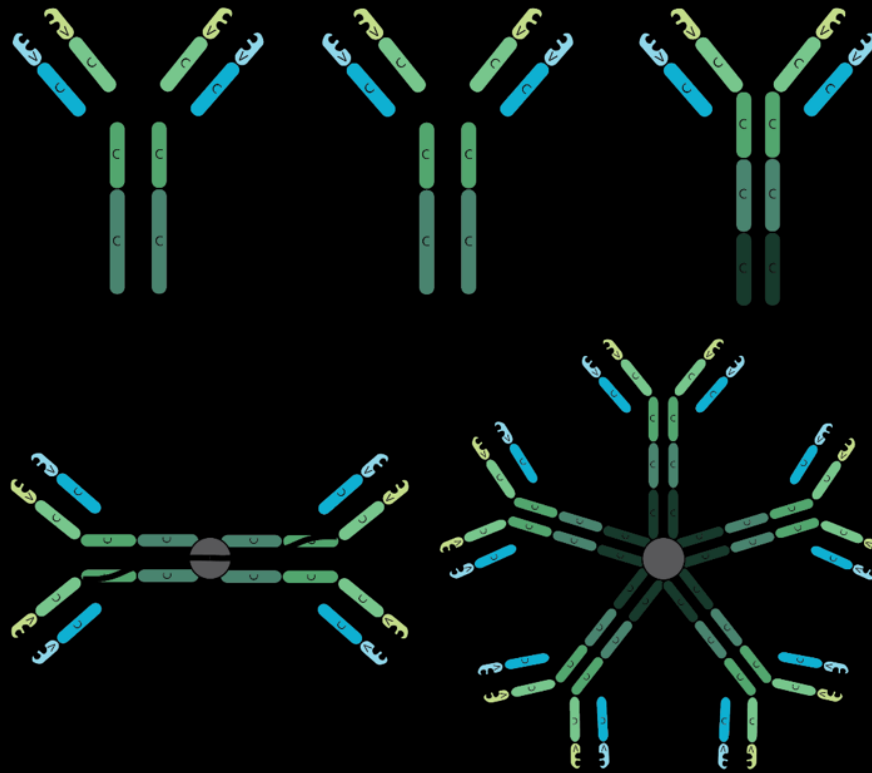
Antibodies are produced by antibody secreting cells and come in different structures and qualities



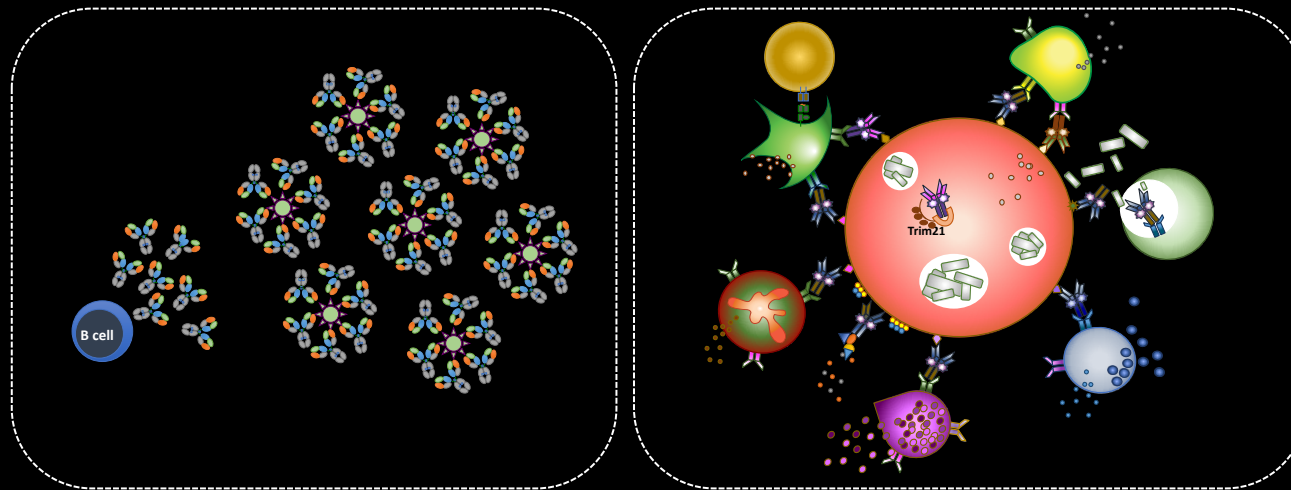
Antibody secreting cells



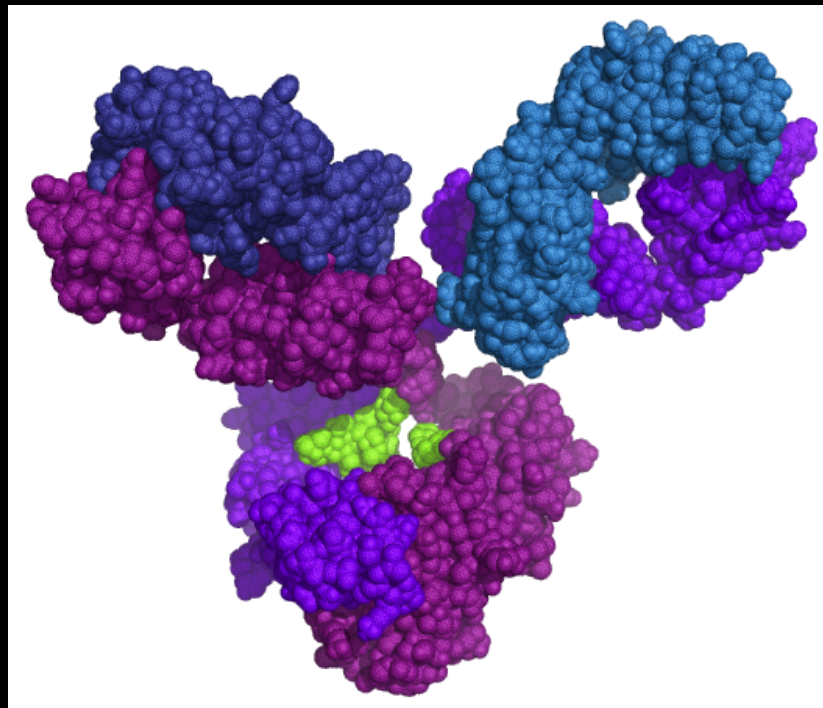
Different flavors of antibodies



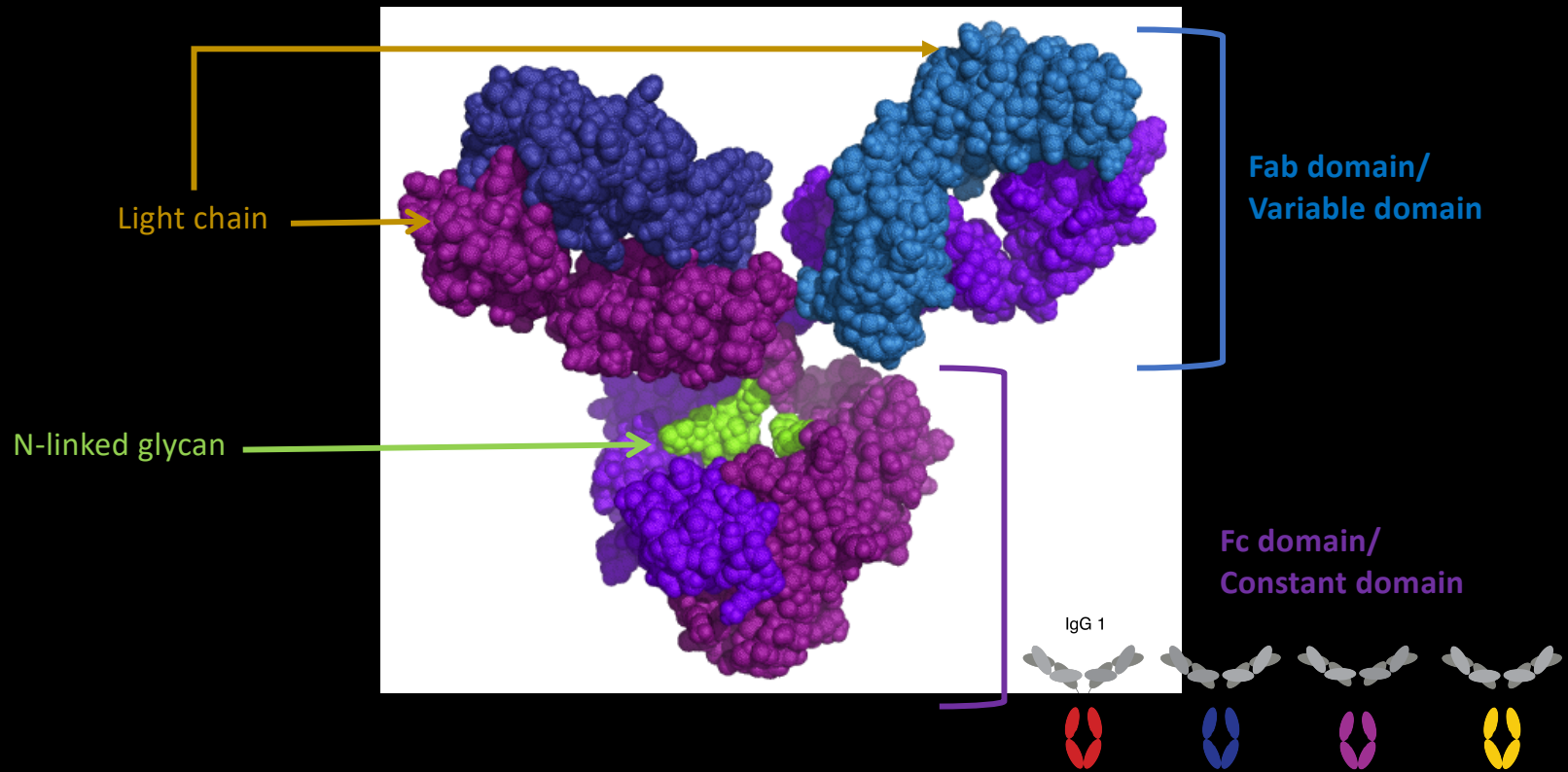
Antibodies can provide protection directly and indirectly



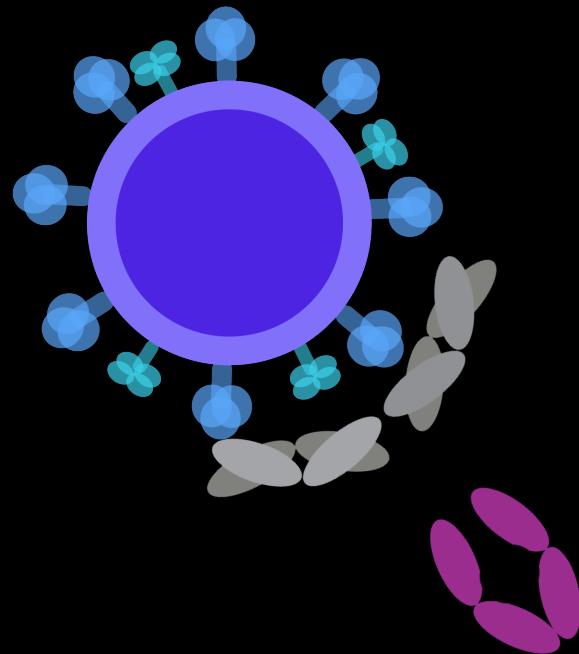
Antibody anatomy

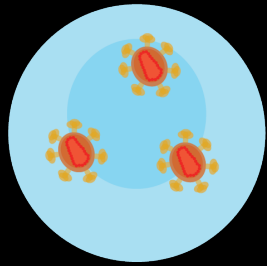


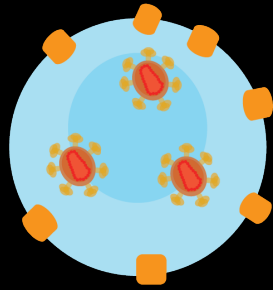
Antibody architecture

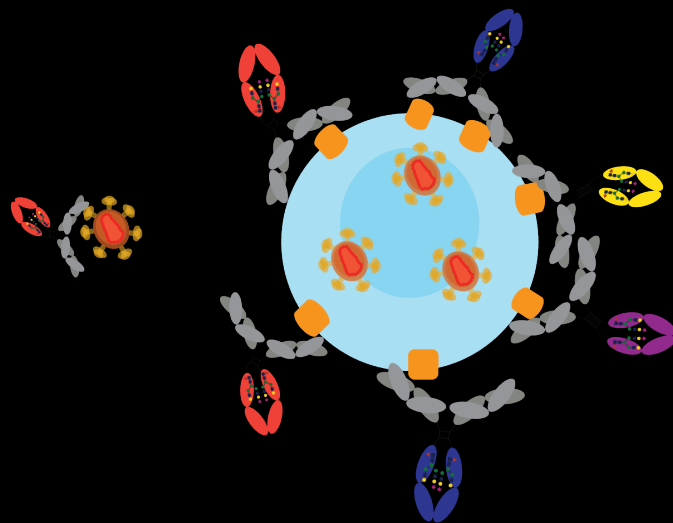


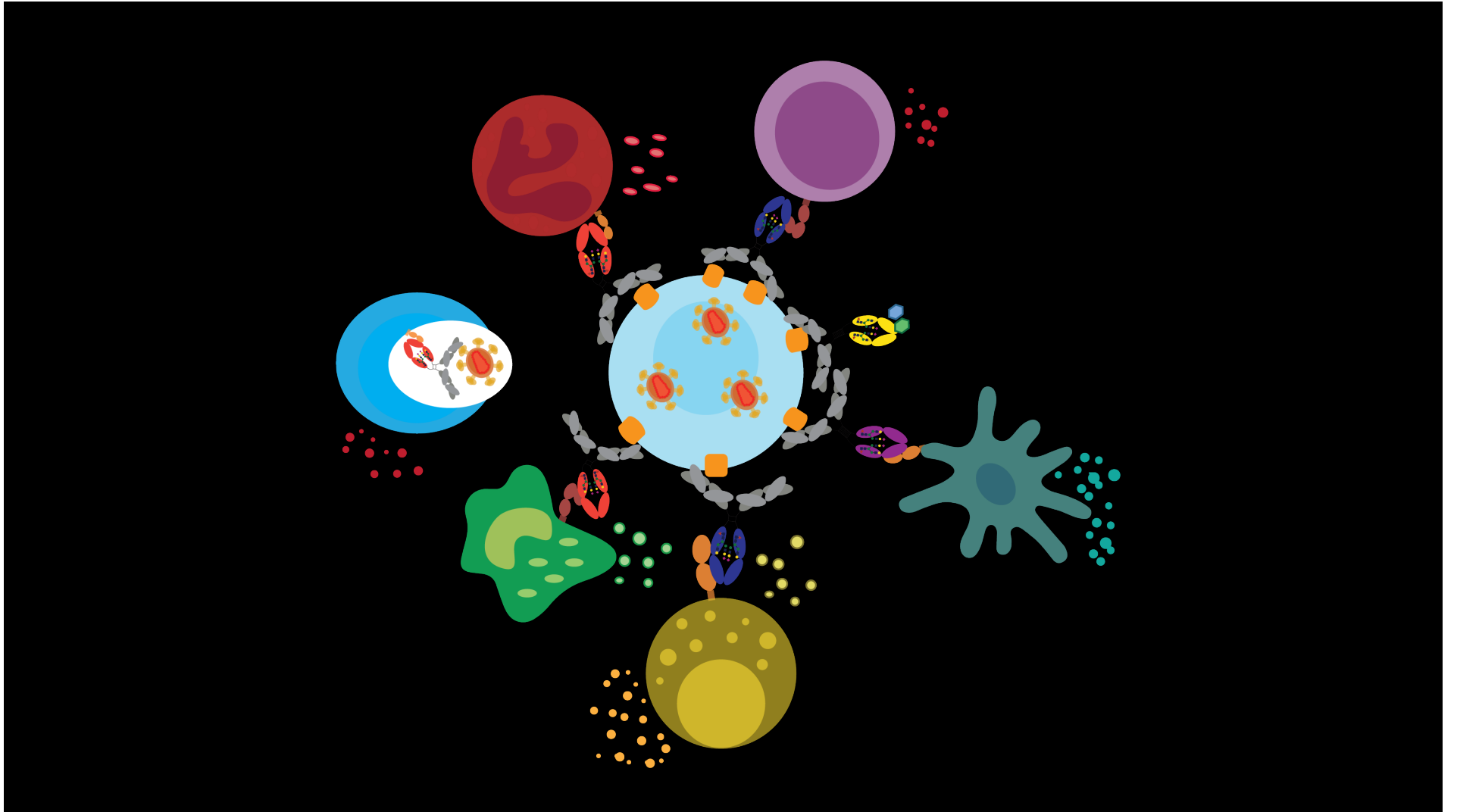
Antibodies bind and neutralize viruses



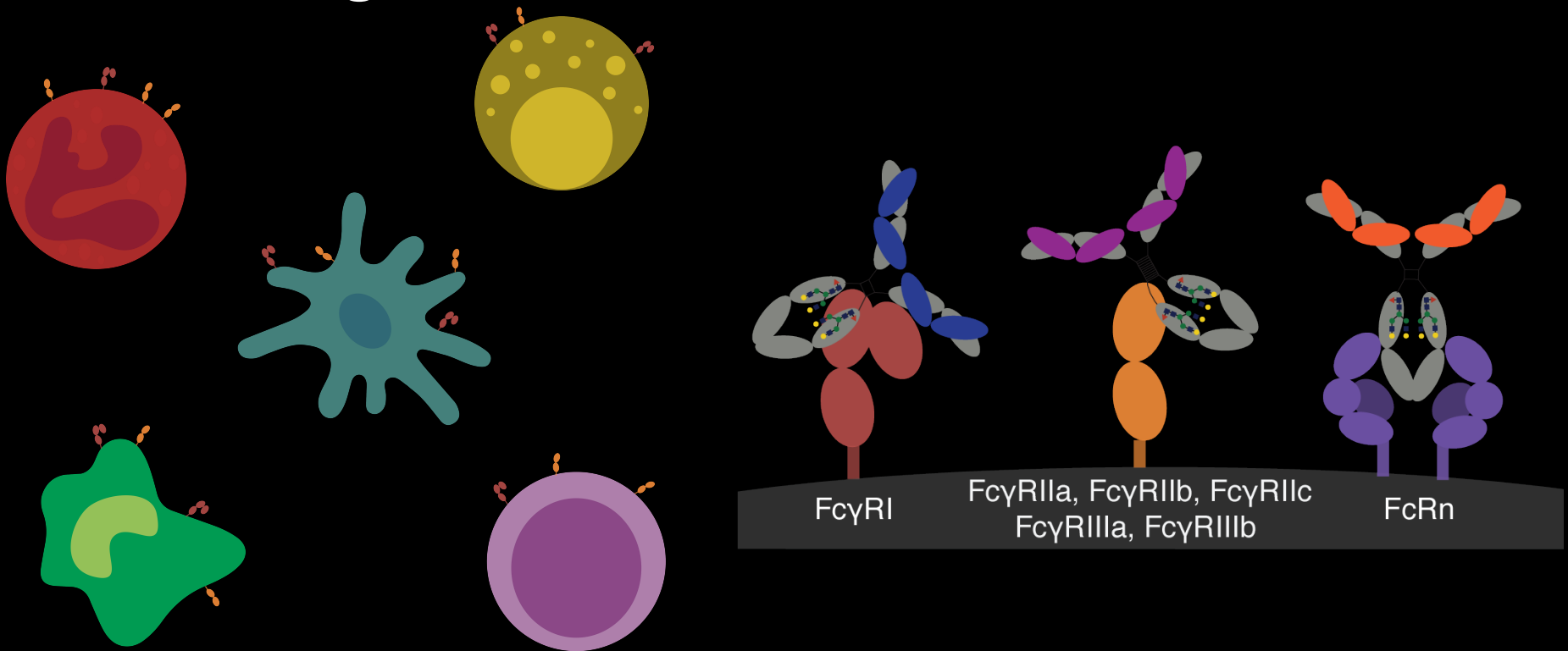








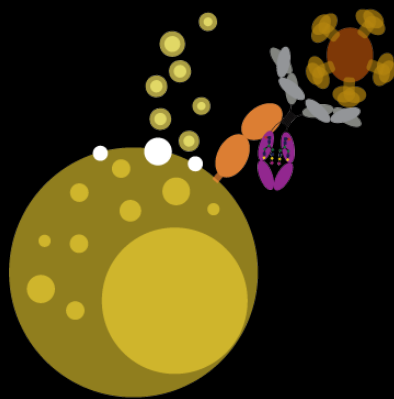
Antibodies recruit the innate immune system to direct killing



Antibodies recruit the innate immune system to direct killing



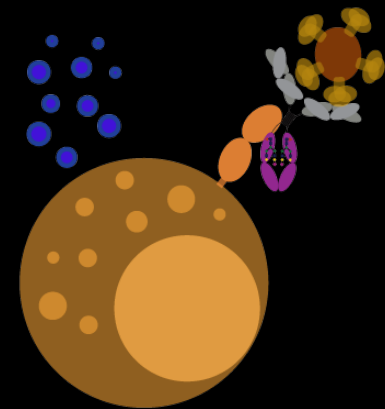
Phagocytosis



NK Degranulation

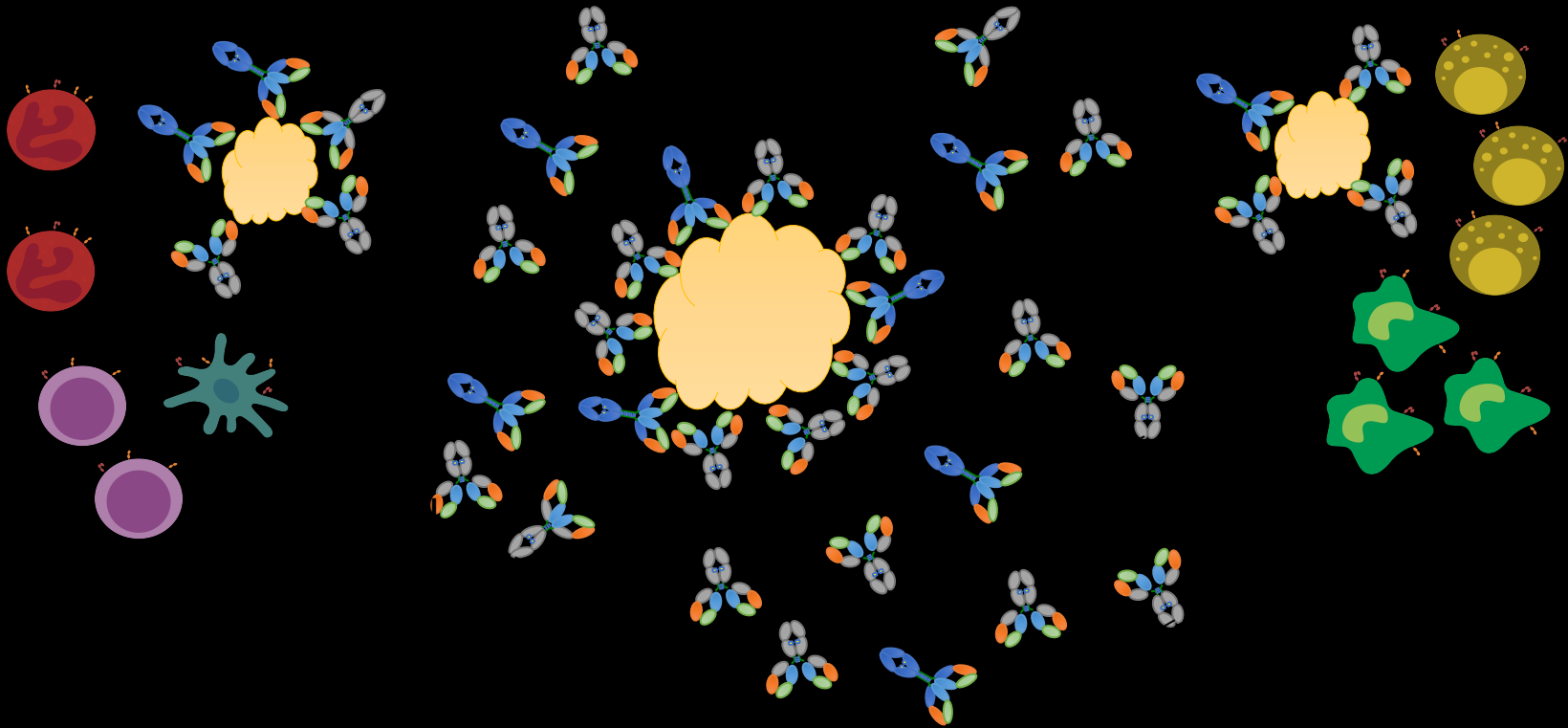


Complement activation

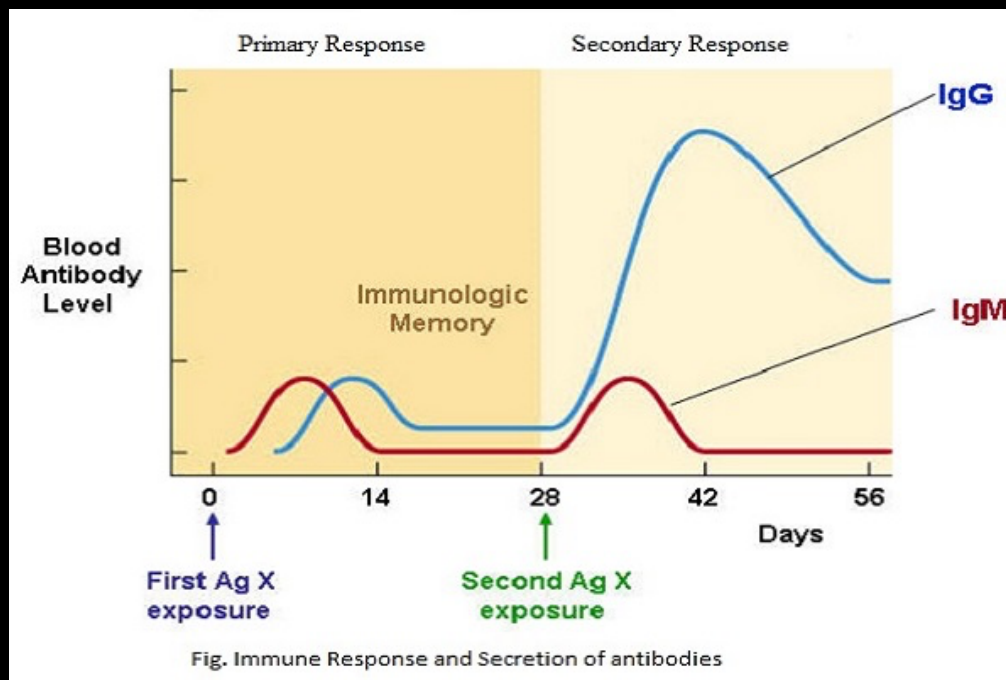


NK IFN γ and MIP1 β secretion

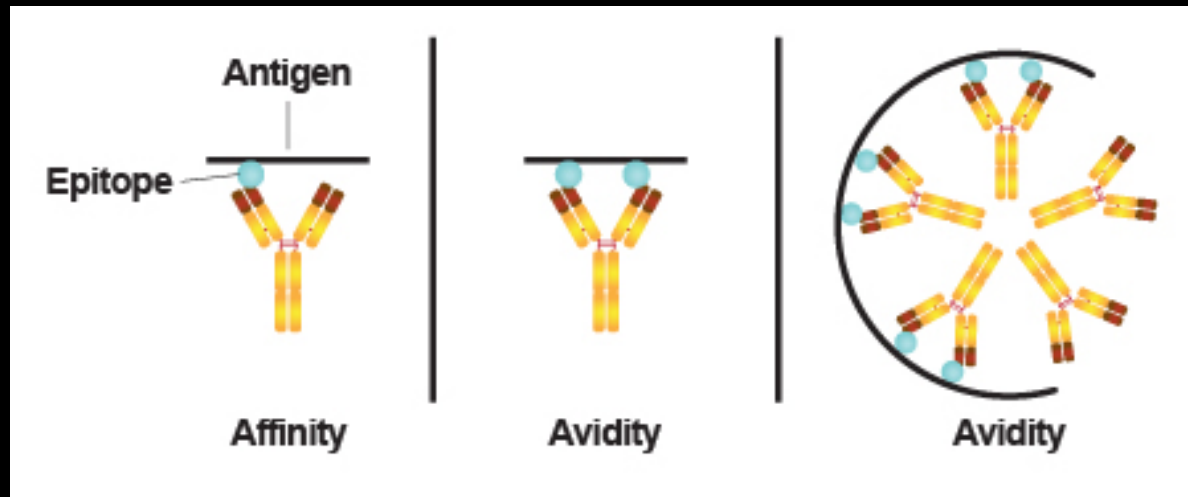
Antibodies act as swarms



Kinetics of the antibody response

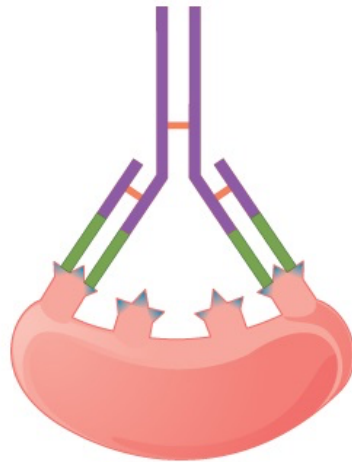


Advantage in numbers

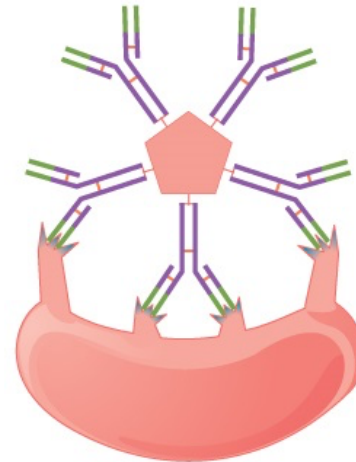


Avidity before affinity...

(a) Affinity versus avidity

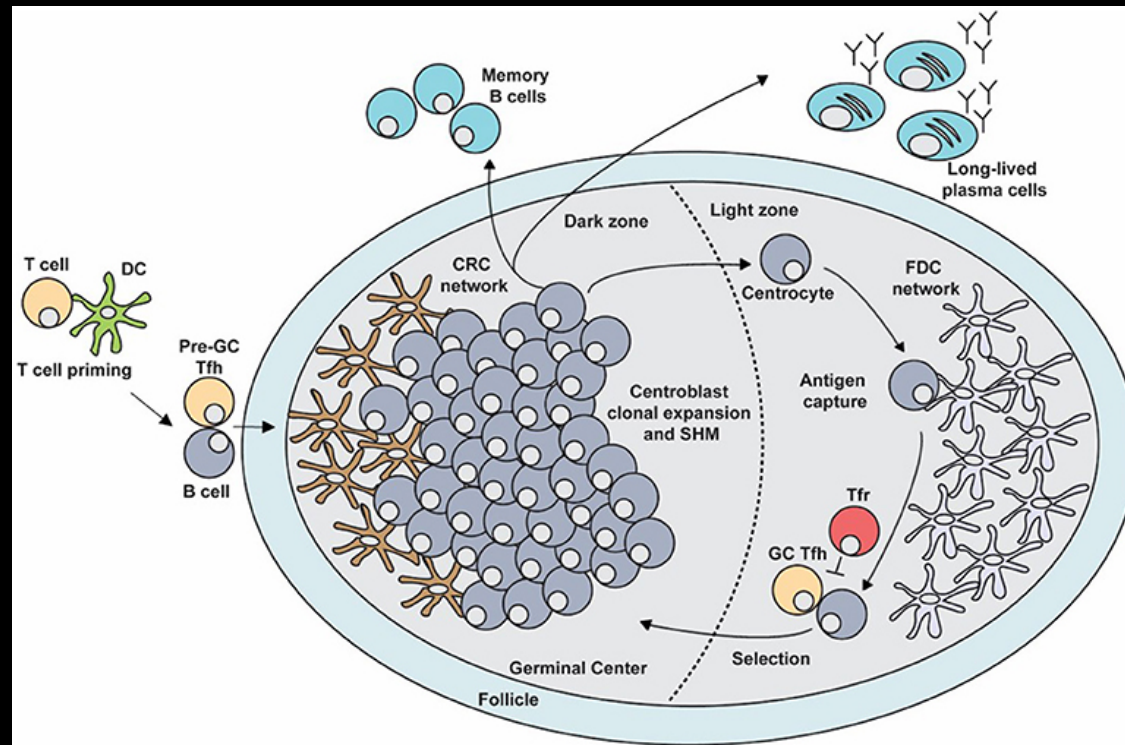


Affinity refers to the strength of a single antibody–antigen interaction. Each IgG antigen binding site typically has high affinity for its target.



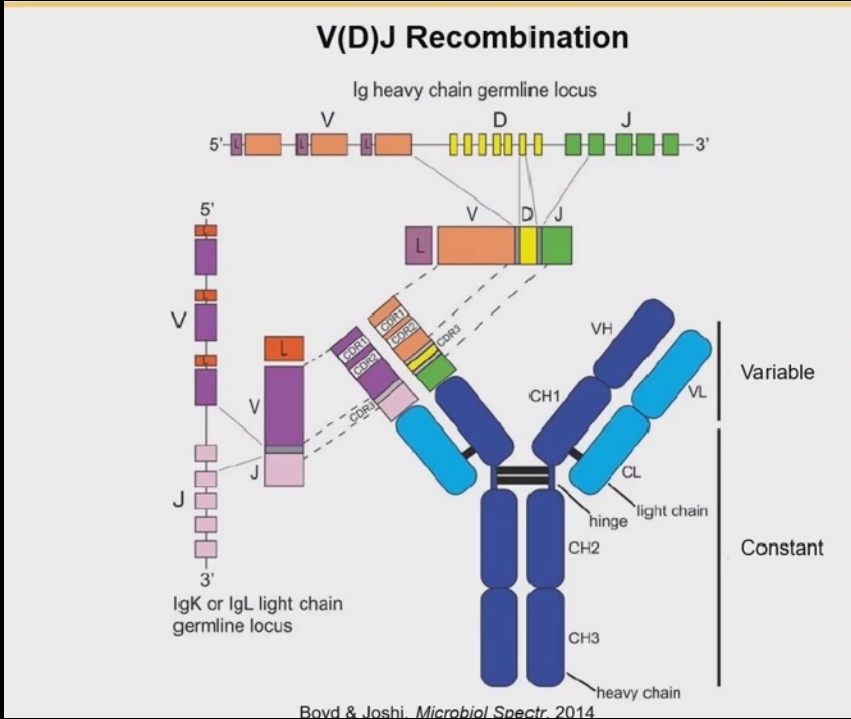
Avidity refers to the strength of all interactions combined. IgM typically has low affinity antigen binding sites, but there are ten of them, so avidity is high.

Somatic hypermutation and clonal selection

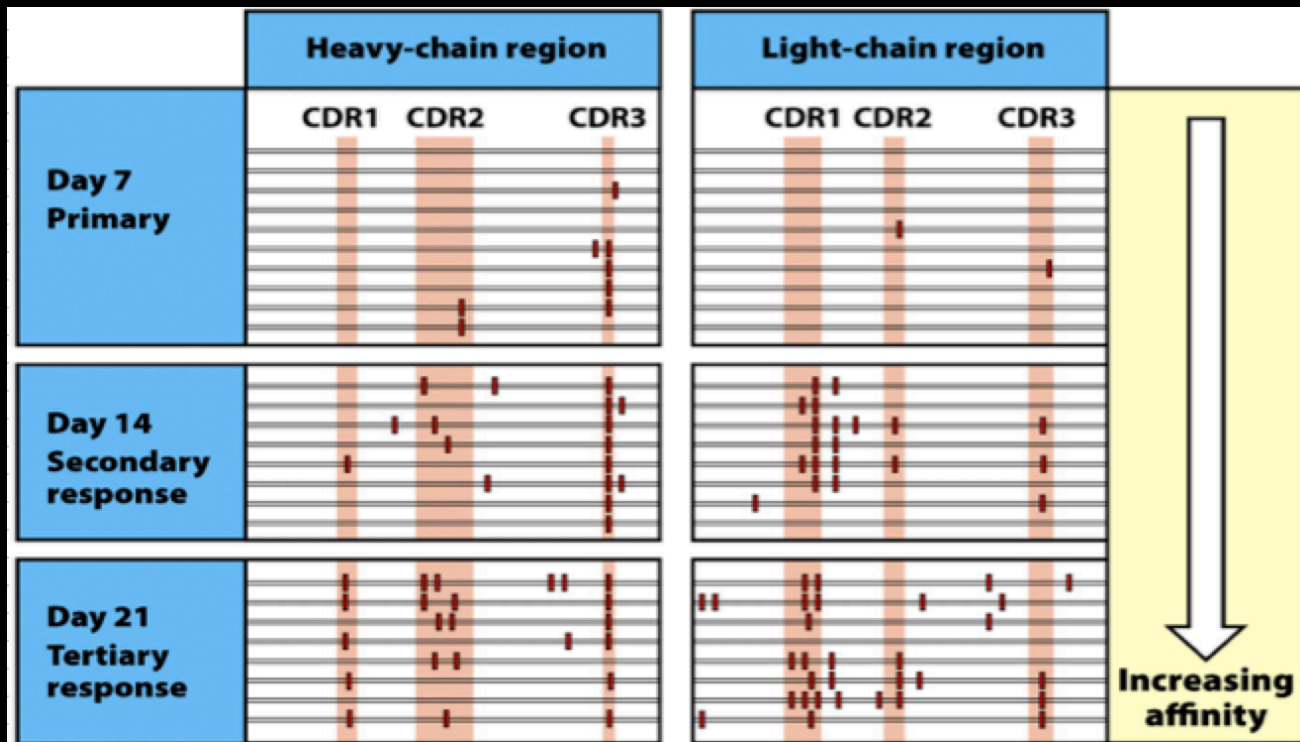


<https://www.frontiersin.org/articles/10.3389/fimmu.2018.02469/full>

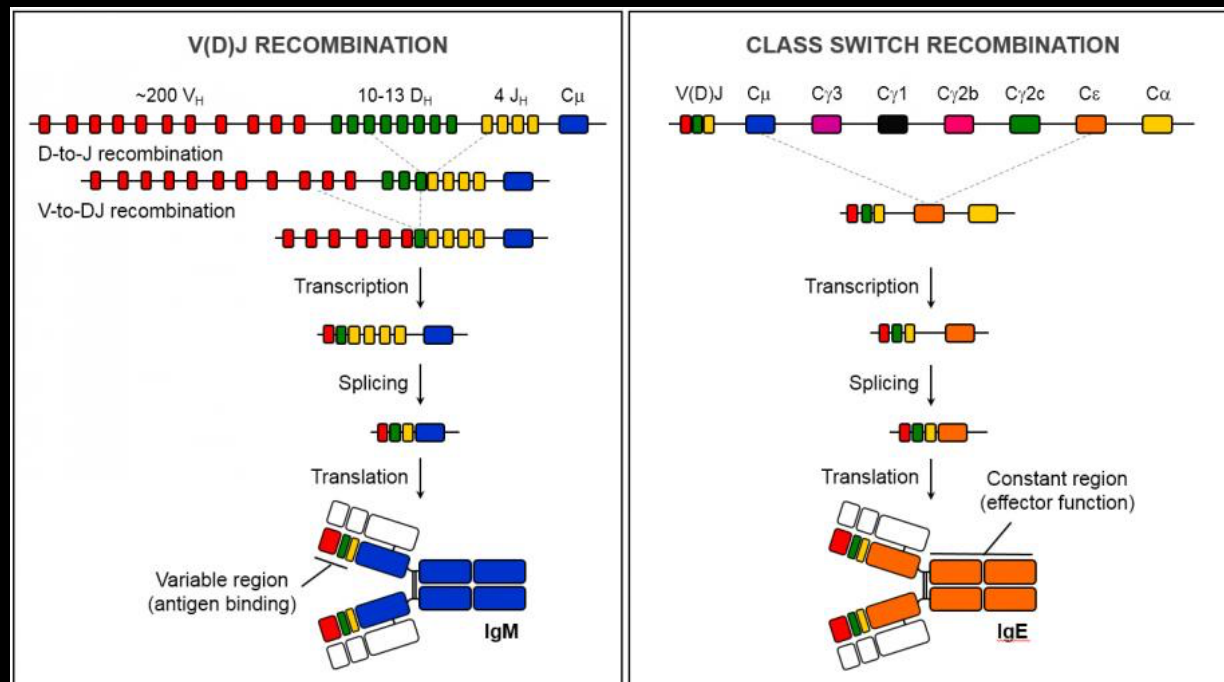
Generating diversity



Affinity maturation



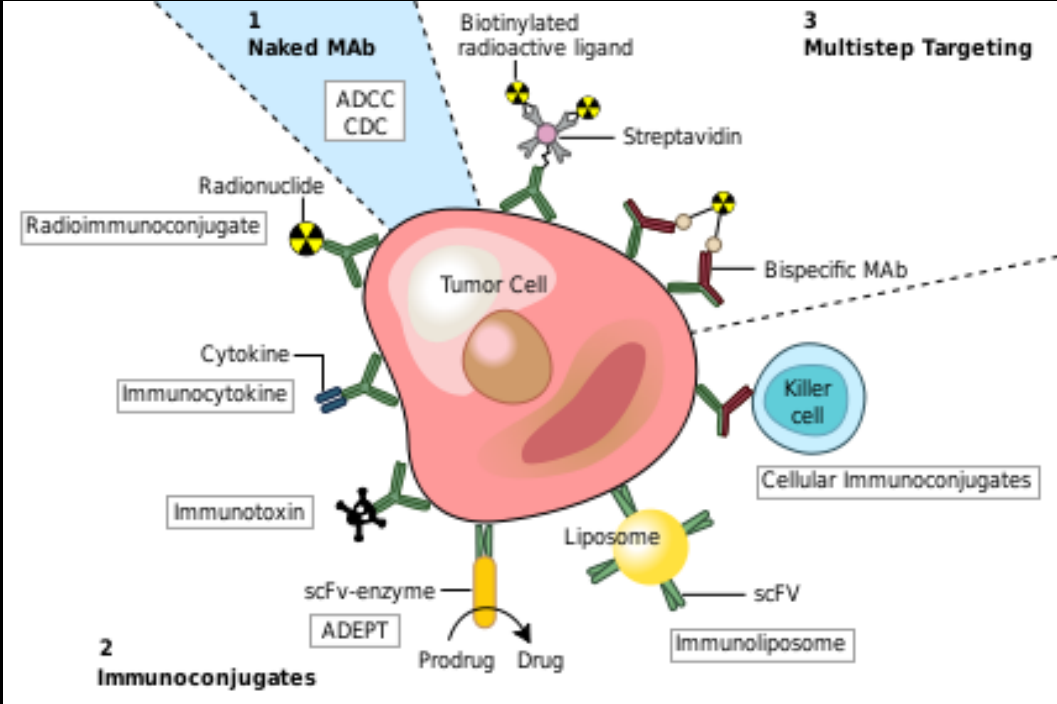
Making a B-cell receptor



Antibodies as drugs



Ways antibodies are used as drugs



https://en.wikipedia.org/wiki/Monoclonal_antibody

Antibody drug discovery process

The process of discovering and developing an antibody-based treatment

AstraZeneca 

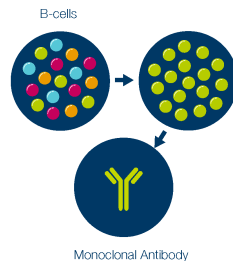
Sources for antibodies against the SARS-CoV-2 virus

- Patients who have recovered from COVID-19
- Humanised mice immunised with the SARS-CoV-2 spike protein
- Laboratory techniques such as phage display



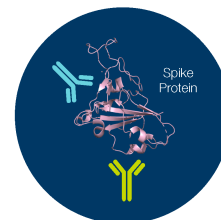
Harnessing multiple technology platforms

- Immune replica technology
- Hybridoma technology



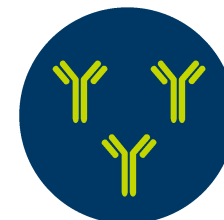
Screening to assess the characteristics of the potential monoclonal antibodies

- Binding
- Neutralisation
- Developability

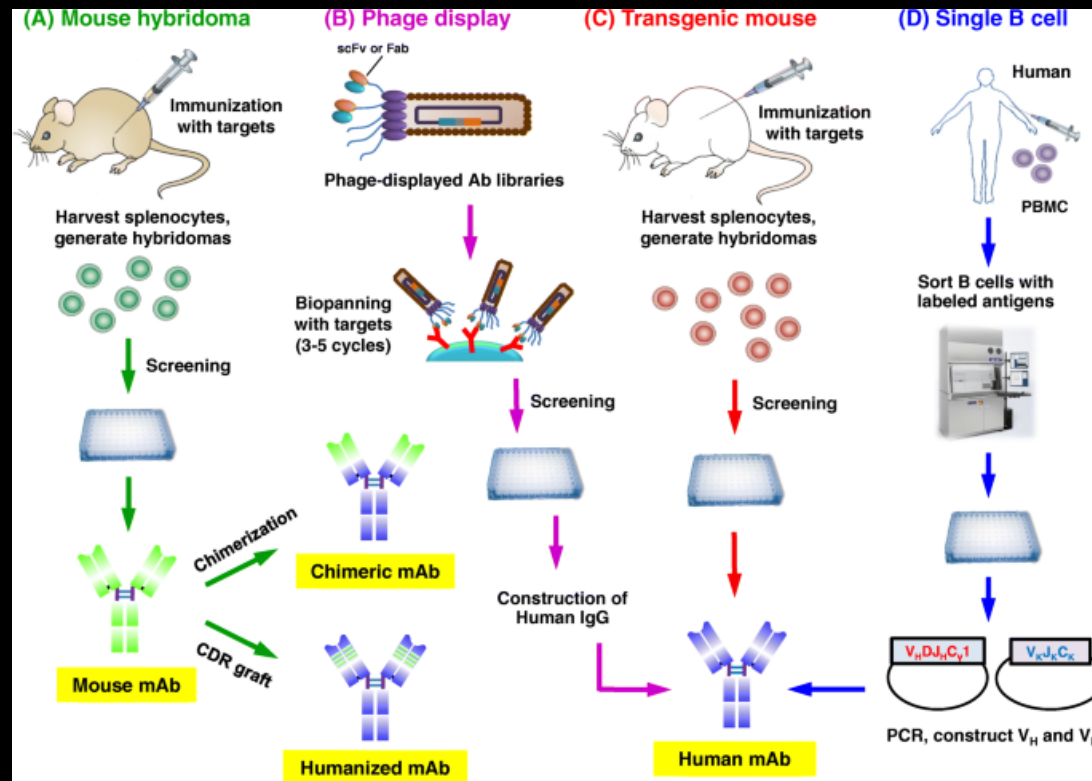


Testing, development, approval, manufacturing and distribution

- AstraZeneca is aiming for clinical evaluation in the next 3 to 5 months



Deeper view of discovery process...




<https://jbiomedsci.biomedcentral.com/articles/10.1186/s12929-019-0592-z>

The Lilly COVID antibody drug

Lilly announces proof of concept data for neutralizing antibody LY-CoV555 in the COVID-19 outpatient setting

September 16, 2020



- Primary endpoint of viral load change from baseline at day 11 was met for one of three doses; consistent effects of viral reduction seen at earlier time points  [Download PDF](#)
- Rate of hospitalizations and ER visits was 1.7 percent (5/302) for LY-CoV555 versus 6 percent (9/150) for placebo--a 72 percent risk reduction in this limited population

The Regeneron antibody drug

REGENERON

◀ Back

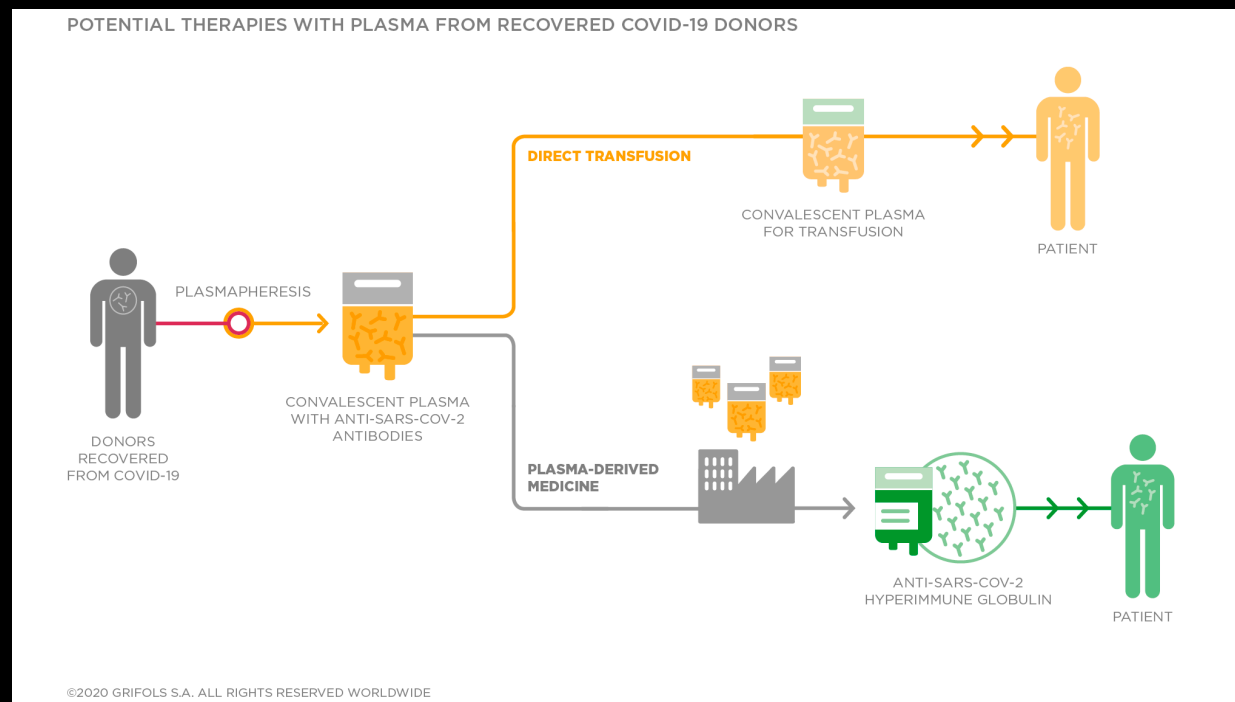


September 29, 2020 at 4:01 PM EDT

REGENERON'S REGN-COV2 ANTIBODY COCKTAIL REDUCED VIRAL LEVELS AND IMPROVED SYMPTOMS IN NON-HOSPITALIZED COVID-19 PATIENTS

called seronegative group. The monoclonal cocktail showed little effect on people who already had antibodies against the virus. But it appeared to help the seronegative patients, powerfully reducing the amount of virus found in nasopharyngeal swabs and alleviating symptoms more quickly. "These are provocative results," says Myron Cohen

An alternative to single antibody drugs



Serum transfer results

Clinical efficacy of convalescent plasma for treatment of COVID-19 infections: Results of a multicenter clinical study

[Hassan Abolghasemi](#),^a [Peyman Eshghi](#),^b [Abdol Majid Cheraghali](#),^{c,*} [Abbas Ali Imani Fooladi](#),^a [Farzaneh Bolouki Moghaddam](#),^d [Sina Imanizadeh](#),^d [Matin Moeini Maleki](#),^d [Mohammad Ranjkesh](#),^d [Mohammad Rezapour](#),^d [Ali Bahramifar](#),^e [Behzad Einollahi](#),^f [Mohammad Javad Hosseini](#),^g [Nematollah Joneidi Jafari](#),^h [Mohamad Nikpouraghdam](#),ⁱ [Nariman Sadri](#),^j [Mokhtar Tazik](#),^j [Shanaz Sali](#),^k [Shamsi Okati](#),^l [Elham Askari](#),^m [Payam Tabarsi](#),^m [Jafar Aslani](#),ⁿ [Ehsan Sharifipour](#),^o [Mohammad Hossein Jarahzadeh](#),^p [Nastaran Khodakarim](#),^q [Mahmood Salesi](#),ⁿ [Ramezan Jafari](#),ⁿ and [Samira Shahverdi](#)^f

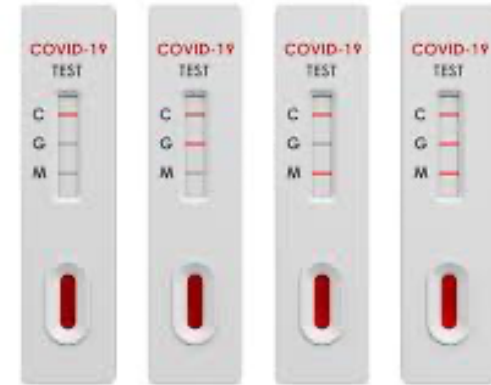
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This article has been [cited by](#) other articles in PMC.

Abstract

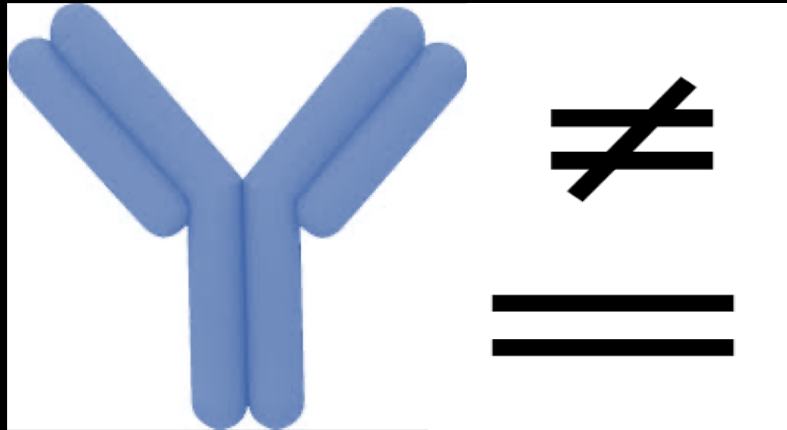
[Go to:](#) 

Since Dec. 2019 the new coronavirus (SARS-CoV-2) has infected millions and claimed life of several hundred thousand worldwide. However, so far no approved vaccine or drug therapy is available for treatment of virus infection. Convalescent plasma has been considered a potential modality for COVID-19 infection. One hundred eighty-nine COVID-19 positive patients including 115 patients in plasma therapy group and 74 patients in control group, registered in the hospitals with confirmed COVID-19 infection, entered this multi-center clinical study. Comparison of outcomes including all-cause mortality, total hospitalization days and patients' need for intubation between the two patient groups shows that total of 98 (98.2 %) of patients who received convalescent plasma were discharged from hospital which is substantially higher compared to 56 (78.7 %) patients in control group. Length of hospitalization days was significantly lower (9.54 days) in convalescent plasma group compared with that of control group (12.88 days). Only 8 patients (7%) in convalescent plasma group required intubation while that was 20 % in control group. This clinical study provides strong evidence to support the efficacy of convalescent plasma therapy in COVID-19 patients and recommends this treatment for management of these patients. Clinical efficacy, immediate availability and potential cost effectiveness could be considered as main advantages of convalescent plasma therapy.



What does a SARS-CoV-2 antibody test result mean?

What does a positive antibody test mean?

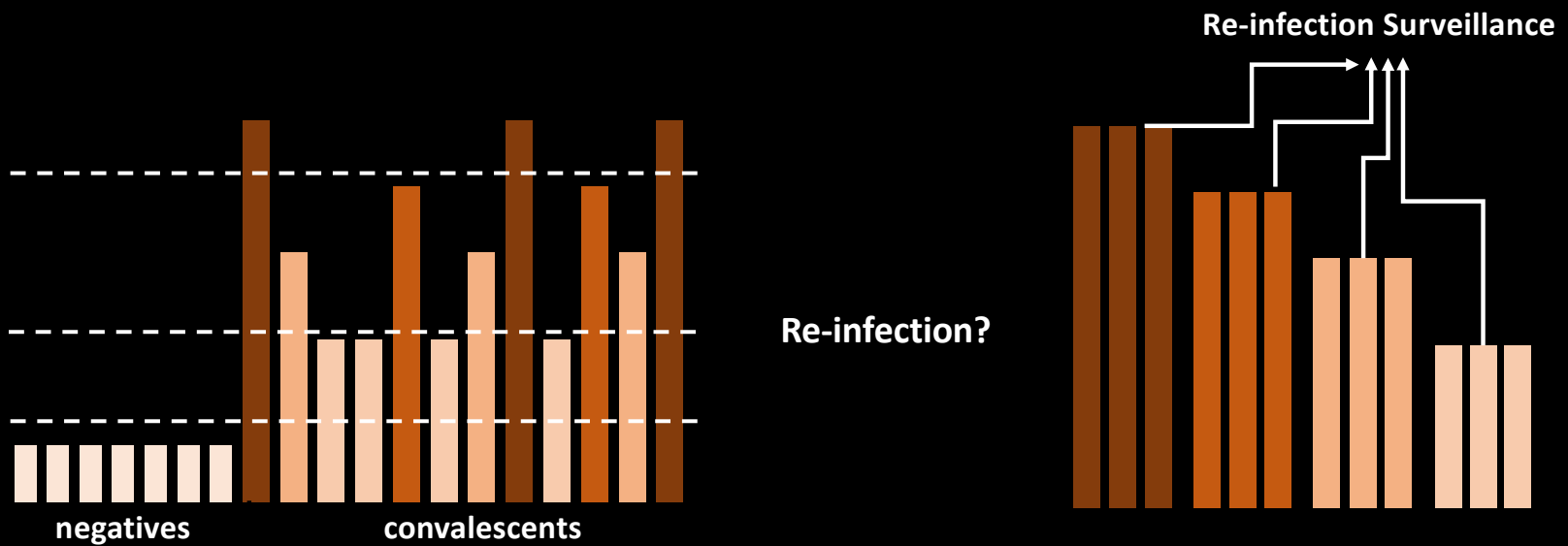


Immunity

Exposure

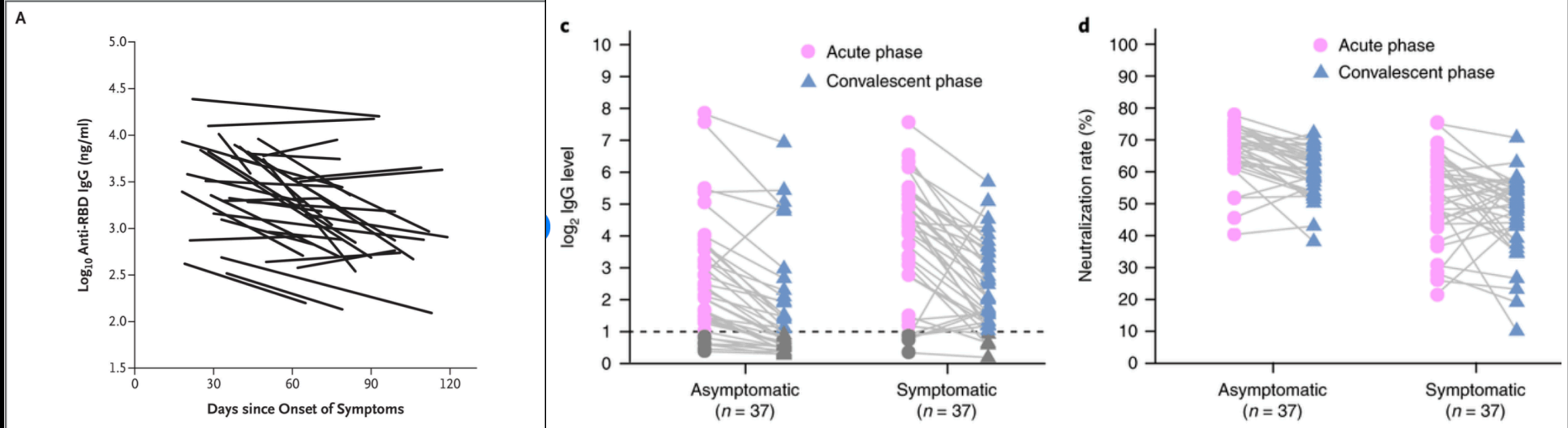
Sero-Epidemiological studies are needed to establish a threshold of immunity.

Defining a protective titer...



What level of antibodies = IMMUNITY?

Evidence of waning immunity???



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE
The New England Journal of Medicine
Controlled Trial of Bedaquiline
in Lipid Synthesis

ESC Congress 2020
The Digital Experience

PERSPECTIVE
Bridle and Orban —
Confronting the Full Spectrum
of SARS

POINTS OF VIEW
The Full Spectrum — An
American Approach to
Academic Medicine

A correction has been published: 1

CORRESPONDENCE

Rapid Decay of Anti-SARS-CoV-2 Antibodies in Persons with Mild Covid-19

Article | Publisher preview available

Clinical and immunological
assessment of asymptomatic
SARS-CoV-2 infections

nature research

August 2020 • Nature medicine 26(8)
DOI: 10.1038/s41591-020-0965-8

Stability of humoral immune responses over time

The NEW ENGLAND JOURNAL of MEDICINE

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nertinib in Resected EGFR-
ated Non-Small-Cell Lung
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PERSPECTIVE
Community Health Workers and
Covid-19 — Addressing Social
Determinants of Health...

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Survival with Olaparib in
Metastatic Castration-Resistant
Prostate Cancer

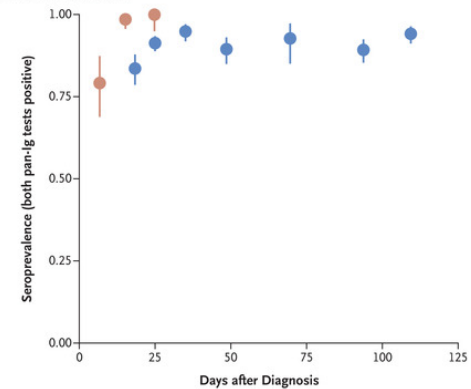


ORIGINAL ARTICLE

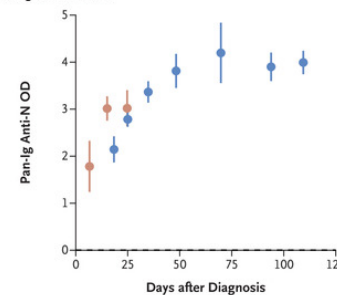
Humoral Immune Response to SARS-CoV-2 in Iceland

Daniel F. Gudbjartsson, Ph.D., Gudmundur L. Norddahl, Ph.D., Pall Melsted, Ph.D., Kristbjorg Gunnarsdottir, M.Sc., Hilma Holm, M.D., Elias Eythorsson, M.D., Ph.D., Asgeir O. Arnthorsson, M.Sc., Dadi Helgason, M.D., Ph.D., Kristbjorg Bjarnadottir, Ph.D., Ragnar F. Ingvarsson, M.D., Brynja Thorsteinsdottir, B.Sc., Steinunn Kristjansdottir, B.Sc., Kolbrun Birgisdottir, B.Sc., Anna M. Kristinsdottir, M.Sc., Martin I. Sigurdsson, M.D., Ph.D., Gudny A. Arnadottir, M.Sc., Erna V. Ivarsdottir, M.Sc., Margret Andresdottir, M.Sc., Frosti Jonsson, M.Sc., Arna B. Agustsdottir, M.Sc., Jonas Berglund, Ph.D., Berglind Eiriksottir, Run Fridriksdottir, M.Sc., Elisabet E. Gardarsdottir, Magnus Gottfredsson, M.D., Ph.D., Olafia S. Gretarsdottir, B.Sc., Steinunn Gudmundsdottir, M.Sc., Kjartan R. Gudmundsson, B.Sc., Thora R. Gunnarsdottir, B.Sc., Arnaldur Gylfason, M.Sc., Agnar Helgason, Ph.D., Brynjar O. Jonsson, M.Sc., Aslaug Jonasdottir, M.Sc., Hakon Jonsson, Ph.D., Thordur Kristjansson, M.D., Ph.D., Karl G. Kristinnsson, M.D., Ph.D., Droplaug N. Magnusdottir, M.Sc., Olafur T. Magnusson, Ph.D., Lovisa B. Olafsdottir, M.D., Solvi Rognvaldsson, B.Sc., Louise le Roux, M.Sc., Gudrun Sigmundsdottir, M.D., Asgeir Sigurdsson, B.Sc., Gardar Sveinbjornsson, M.Sc., Kristin E. Sveinsdottir, B.Sc., Maney Sveinsdottir, B.Sc., Emil A. Thorarensen, B.Sc., Bjarni Thorbjornsson, B.Sc., Marianna Thordardottir, Ph.D., Jona Saemundsdottir, B.Sc., S. Hjortur Kristjansson, M.D., Kamilla S. Josefsdottir, M.D., Gisli Masson, Ph.D., Gudmundur Georgsson, B.Sc., Mar Kristjansson, M.D., Alma Moller, M.D., Ph.D., Runolfur Palsson, M.D., Thorolfur Gudnason, M.D., Unnur Thorsteinsdottir, Ph.D., Ingileif Jonsdottir, Ph.D., Patrick Sulem, M.D., and Kari Stefansson, M.D., Ph.D.

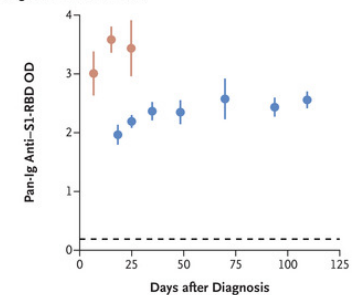
A Seroprevalence among SARS-CoV-2 Infected Persons



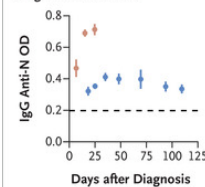
B Pan-Ig Anti-N Titers



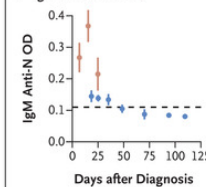
C Pan-Ig Anti-S1-RBD Titers



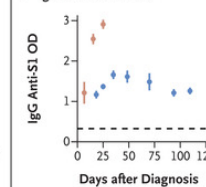
D IgG Anti-NN Titers



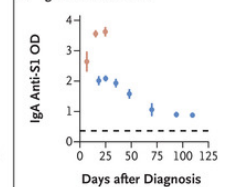
E IgM Anti-NN Titers



F IgG Anti-S1 Titers



G IgA Anti-S1 Titers



First case of SARS-CoV-2 re-infection

NEWS

HEALTH & MEDICINE

A man in Hong Kong is the first confirmed case of coronavirus reinfection

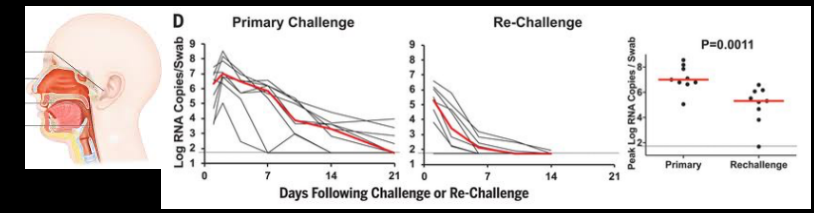
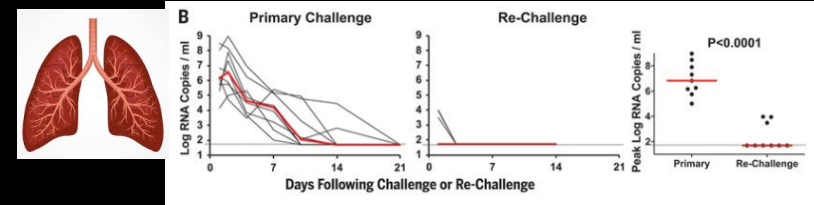
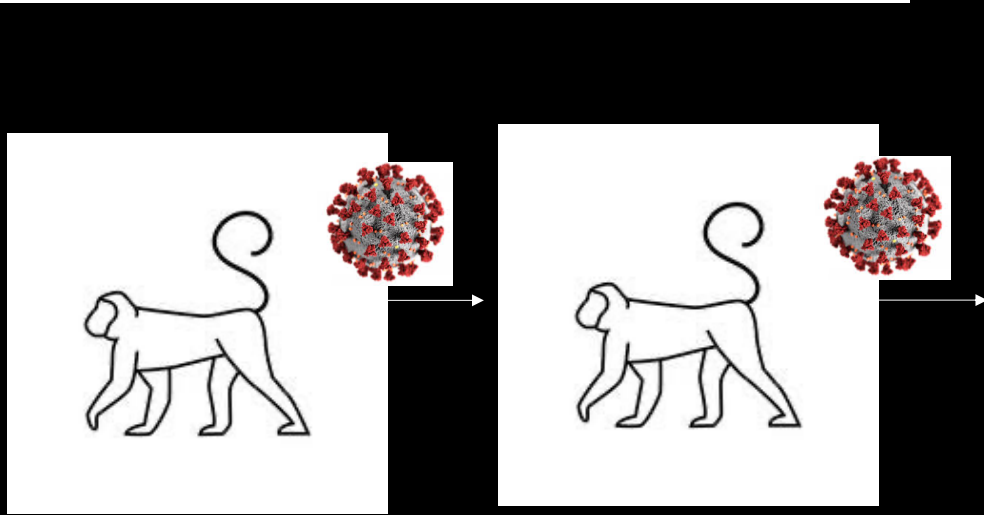
A 33-year-old got sick during his first round with the virus, but wasn't ill the second time

The first time the man was infected, he had a fever, cough, sore throat and headache for three days. He tested positive for the coronavirus on March 26 and was admitted to a hospital in Hong Kong three days later. At that point his symptoms had gone away. He was discharged on April 14 after he tested negative for the virus twice. But the man tested positive again more than four months later on August 15, when officials screened him upon returning to the Hong Kong airport from Spain. The second time, he never showed any indication of being sick — a sign that his immune system kicked in enough to protect him from the disease because he remained asymptomatic but not enough to prevent reinfection.

RESEARCH ARTICLE

SARS-CoV-2 infection protects against rechallenge in rhesus macaques

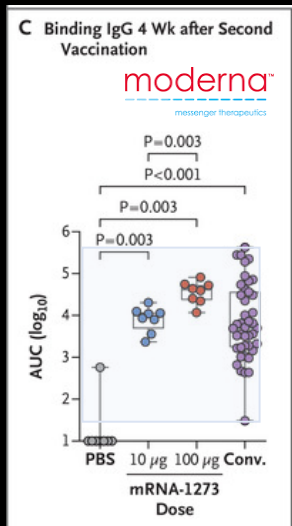
Abishek Chandrashekar^{1,*}, Jinyan Liu^{1,*}, Amanda J. Martinot^{1,2,*}, Katherine McMahan^{1,*}, Noe B. Mercado^{1,*}, Lauren Peter^{1,*}, Lisa H. Tostanoski^{1,*}, Jingyou Yu^{1,*}, Zoltan Maliga³, Michael Nekorchuk⁴, Kathleen Busman-Sahay⁴, Margaret Terry⁴, Linda M. Wrijji², Sarah Duca², David R. Martinez⁵, Caroline Atyeo^{3,6}, Stephanie Fischinger⁵, John S. Burke⁶, Matthew D. Slein⁶, Laurent Pessaint⁷, Alex Van Ry⁷, Jack Greenhouse⁷, Tammy Taylor⁷, Kelvin Blade⁷, Anthony Cook⁷, Brad Finneyfrock⁷, Renita Brown⁷, Elyse Teow⁷, Jason Velasco⁷, Roland Zahn⁸, Frank Wegmann⁸, Peter Abbink¹, Esther A. Bondzie¹, Gabriel Dagotto^{1,3}, Makda S. Gebre^{1,3}, Xuan He¹, Catherine Jacob-Dolan^{1,3}, Nicole Kordana¹, Zhenfeng Li¹, Michelle A. Lifton¹, Shant H. Mahrokhian¹, Lori F. Maxfield¹, Ramya Nityanandam¹, Joseph P. Nkolola¹, Aaron G. Schmidt^{6,9}, Andrew D. Miller¹⁰, Ralph S. Baric⁵, Galit Alter^{6,9}, Peter K. Sorger³, Jacob D. Estes⁴, Hanne Andersen⁷, Mark G. Lewis⁷, Dan H. Barouch^{1,6,9,†}



Does Coronavirus-specific immunity exist?



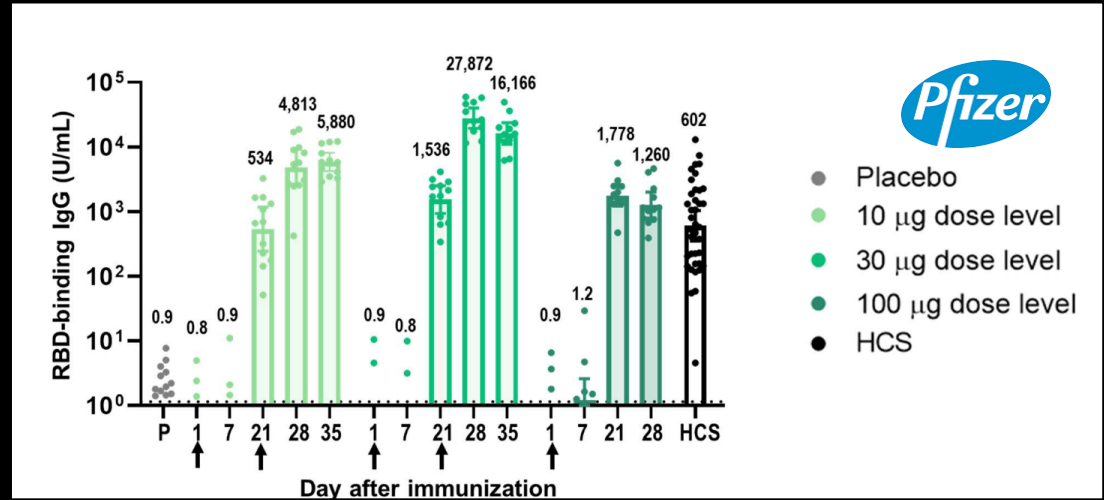
Vaccine Immunity is widely different than Natural Immunity



ORIGINAL ARTICLE

Evaluation of the mRNA-1273 Vaccine against SARS-CoV-2 in Nonhuman Primates

Kizzmekia S. Corbett, Ph.D., Barbara Flynn, M.S., Kathryn E. Foulds, Ph.D., Joseph R. Francica, Ph.D., Seyhan Boyoglu-Barnum, Ph.D., Anne P. Werner, B.S., Britta Flach, Ph.D., Sarah O'Connell, M.S., Kevin W. Bock, M.B., Mahnaz Minai, M.S., Bianca M. Nagata, M.S., Hanne Andersen, Ph.D., et al.



Positive Phase 1/2 Study Results of Pfizer COVID-19 mRNA Vaccine

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Thank you!