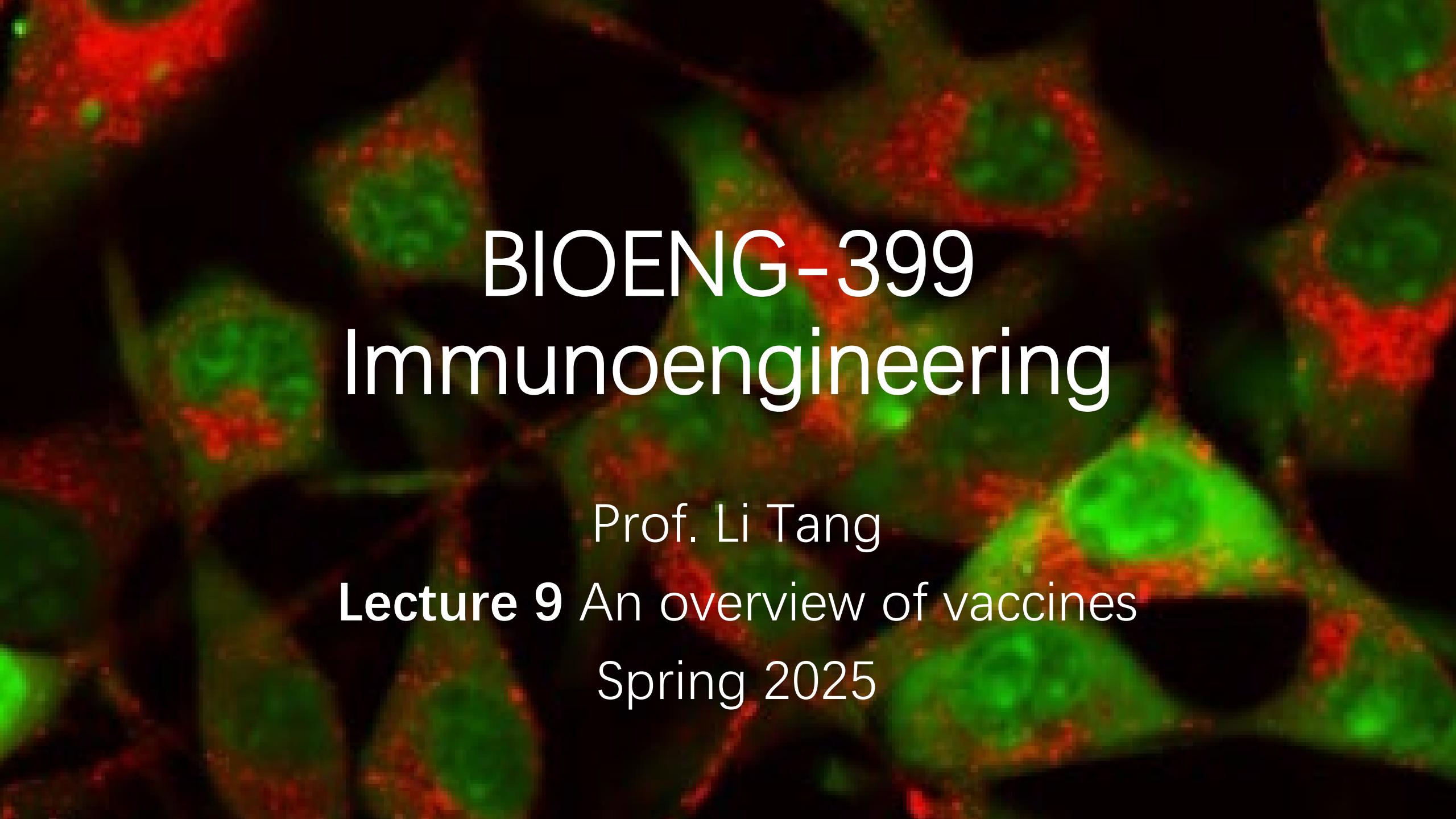


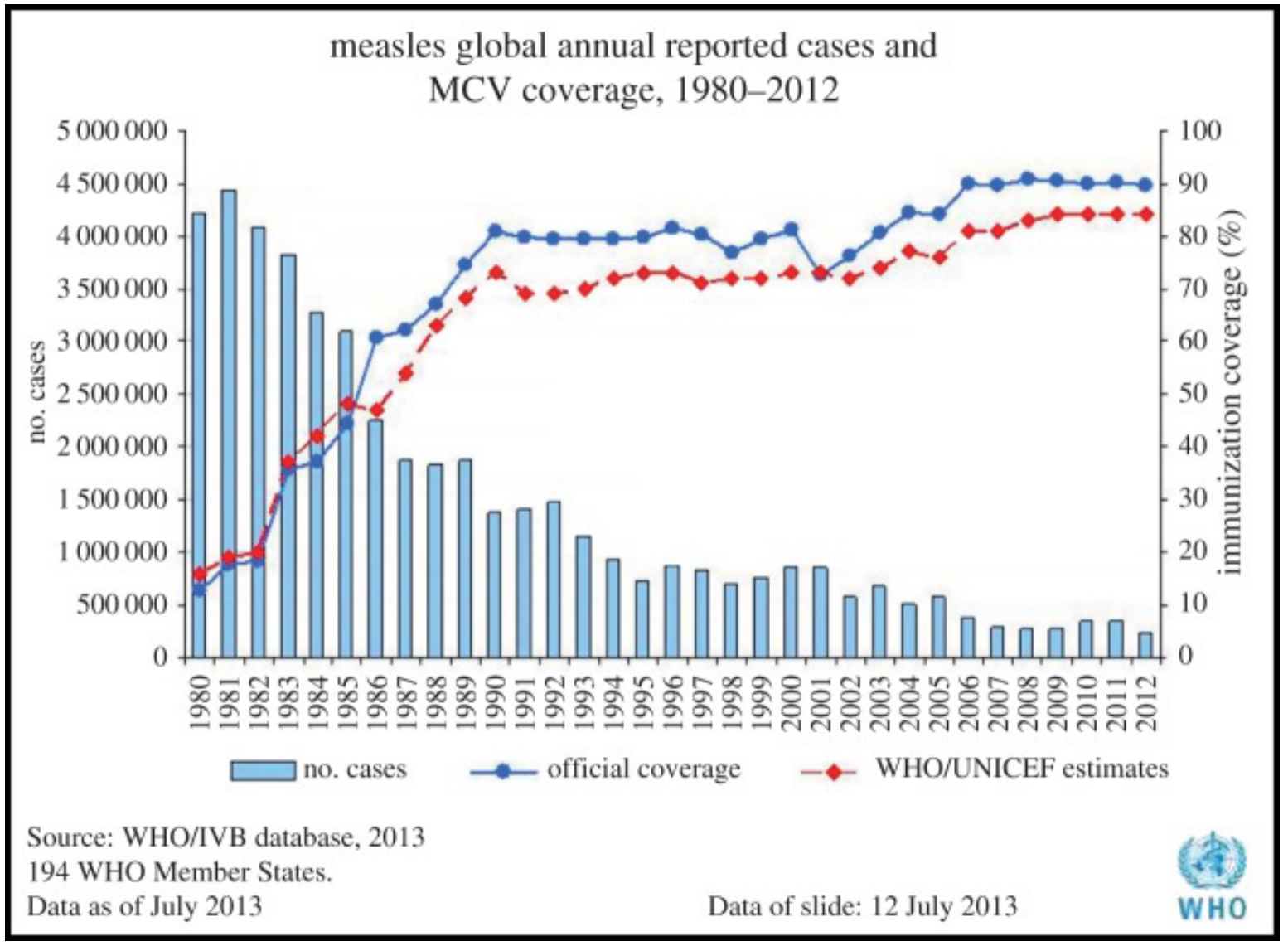
BIOENG-399 Immunoengineering

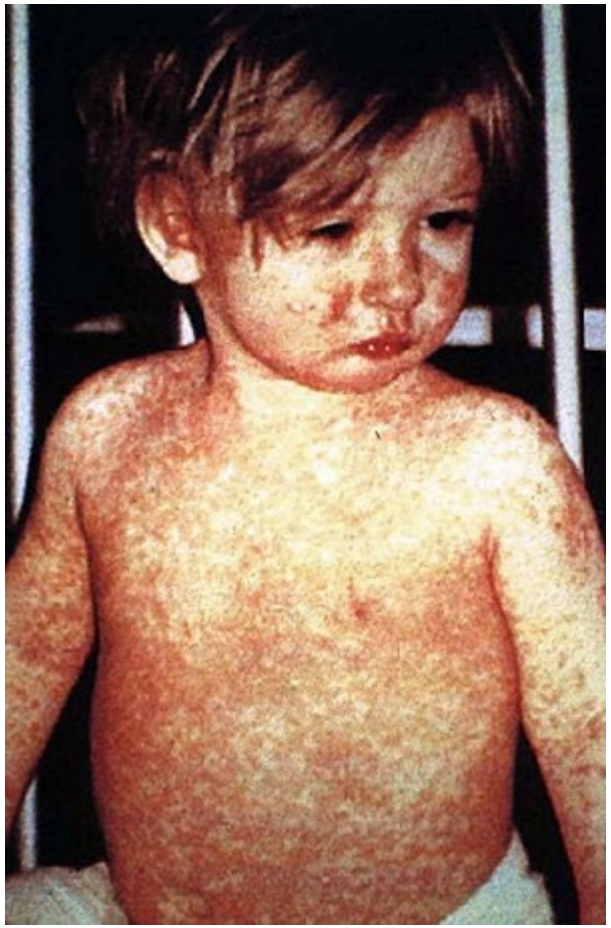
Prof. Li Tang

Lecture 9 An overview of vaccines

Spring 2025

Impact of vaccination on human health





Measles vaccine (MMR vaccine)

Philos Trans R Soc Lond B Biol Sci. 2014 Jun 19; 369(1645): 20130433.

Cases before and after vaccines

TABLE 1-1 Cases of selected infectious disease before and after the introduction of effective vaccines

Disease	ANNUAL CASES/YR Prevaccine	Postvaccine	CASES IN 2004 Reduction (%)
Smallpox	48,164	0	100
Diphtheria	175,885	0	100
Measles	503,282	37	99.99
Mumps	152,209	236	99.85
Pertussis (whooping cough)	147,271	18,957	87.13
Paralytic polio	16,316	0	100
Rubella (German measles)	47,745	12	99.97
Tetanus ("lockjaw")	1,314 (deaths)	26 (cases)	98.02
Invasive hemophilus influenzae	20,000	172	99.14

SOURCE: Adapted from W. A. Orenstein et al., 2005. *Health Affairs* 24:599.

Table 1-1
Kuby IMMUNOLOGY, Sixth Edition

In 1980, WHO officially announced the end of smallpox (Geneva).

There remain two highly-guarded stocks of the virus in laboratories in the USA and Russia. These are preserved for research purposes.

Smallpox: a curse or a gift?

Kangxi emperor (1654 to 1722)

The more history of immunology/vaccine

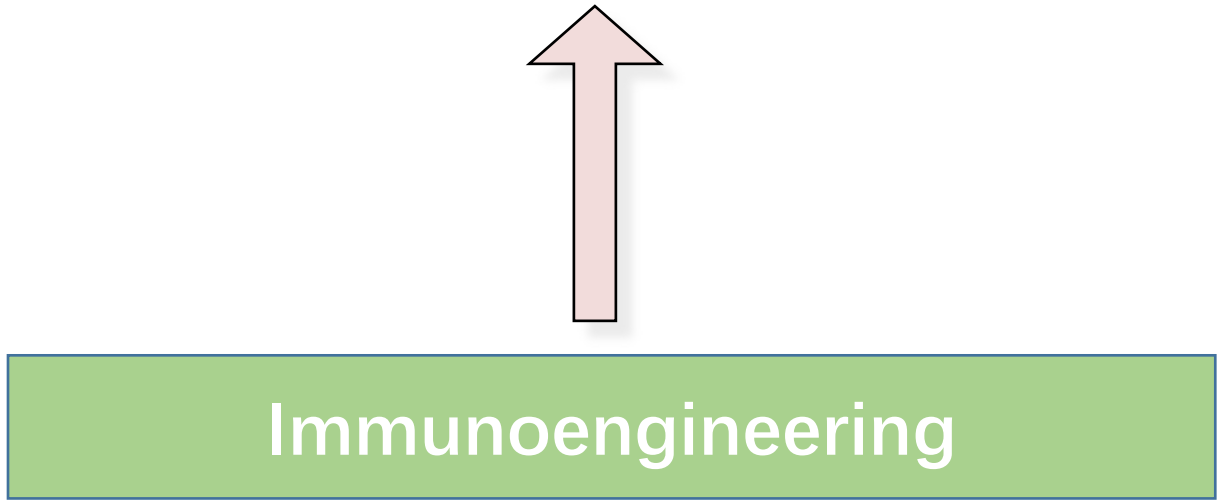
Edward Jenner (English physician) 1798. Observed that dairy maids are immune to smallpox. Role of cowpox?

In 1796 Jenner deliberately infected an eight year old boy with the pus from a cowpox sore. The boy became ill with cowpox but recovered. He was then infected with the normally deadly smallpox. As Jenner had predicted the earlier infection with the cowpox actually protected the boy who never caught smallpox. The practice of modern **vaccination** (L, *vacca*, cow) was born.

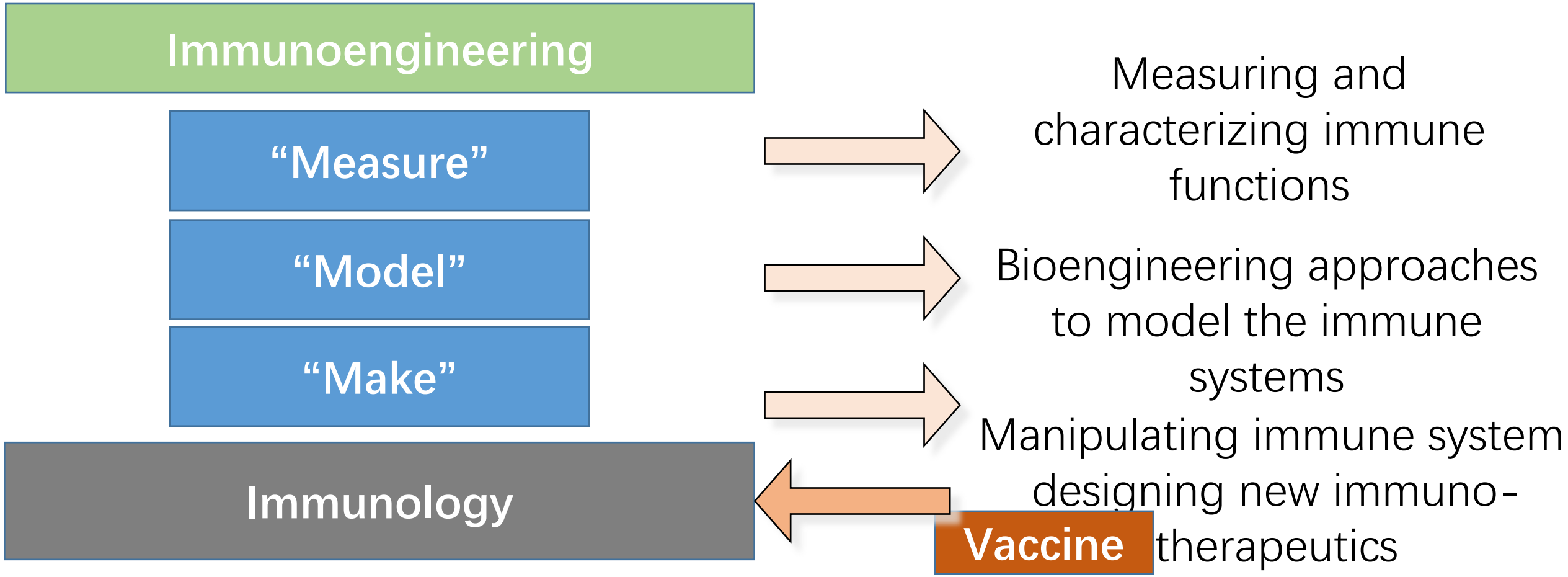
Louis Pasteur 1880s, extended these observations and introduced methods of ***artificially attenuating microorganisms*** by aging, heat, drying serial passage. Applied to anthrax, chicken cholera, rabies.

He defines **Vaccines** as: attenuated bacteria, killed bacteria, bacterial products such as toxins, even non-bacterial substances such as snake venoms. Non-harmful substances also give similar response.

Vaccination is an active immunization to elicit protective immunity and memory

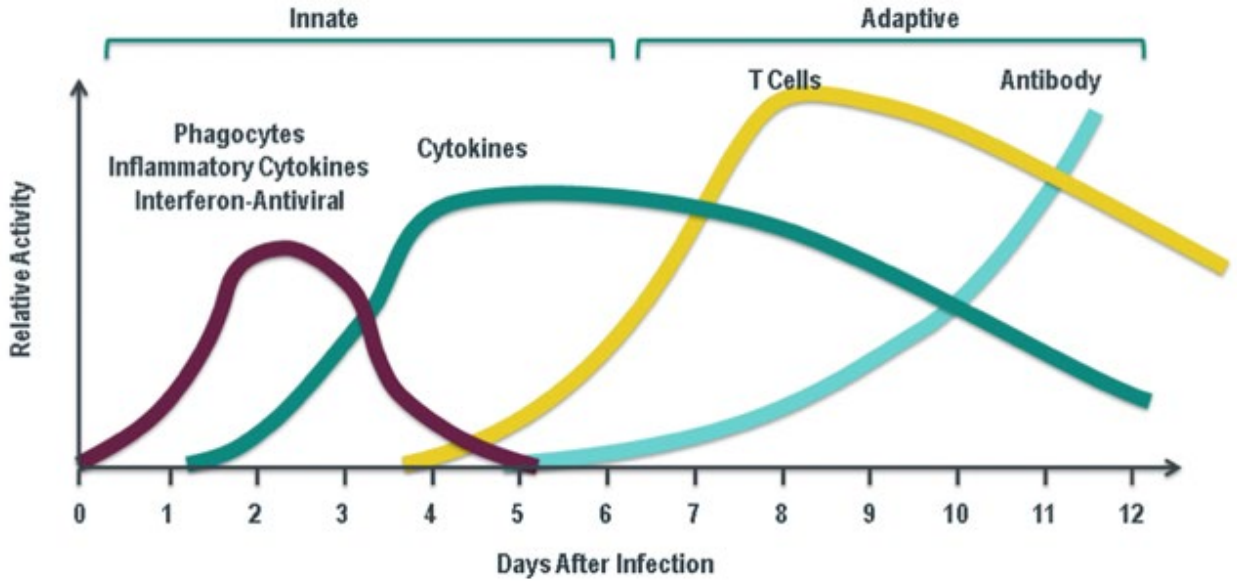


Vaccine: the first attempt of immunoengineering

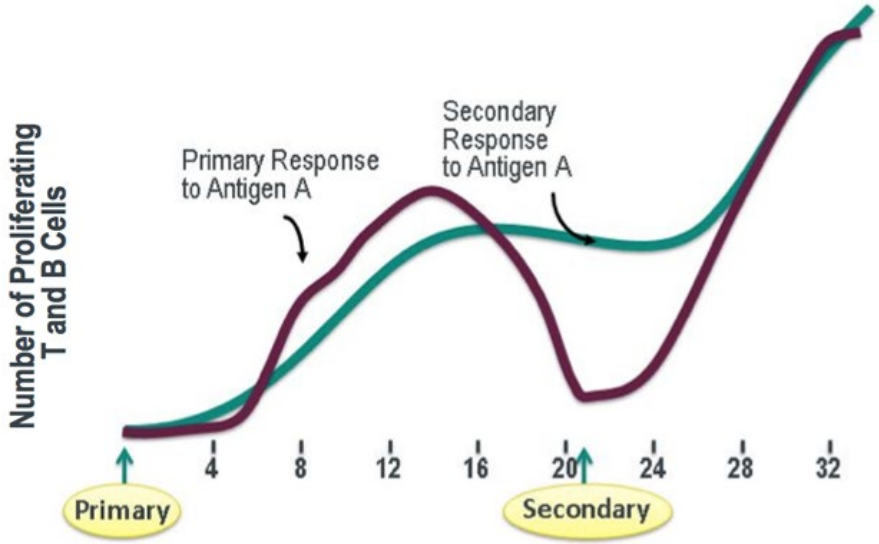


Modified from slides of Prof. Darrell Irvine (MIT)

Adaptive immunity



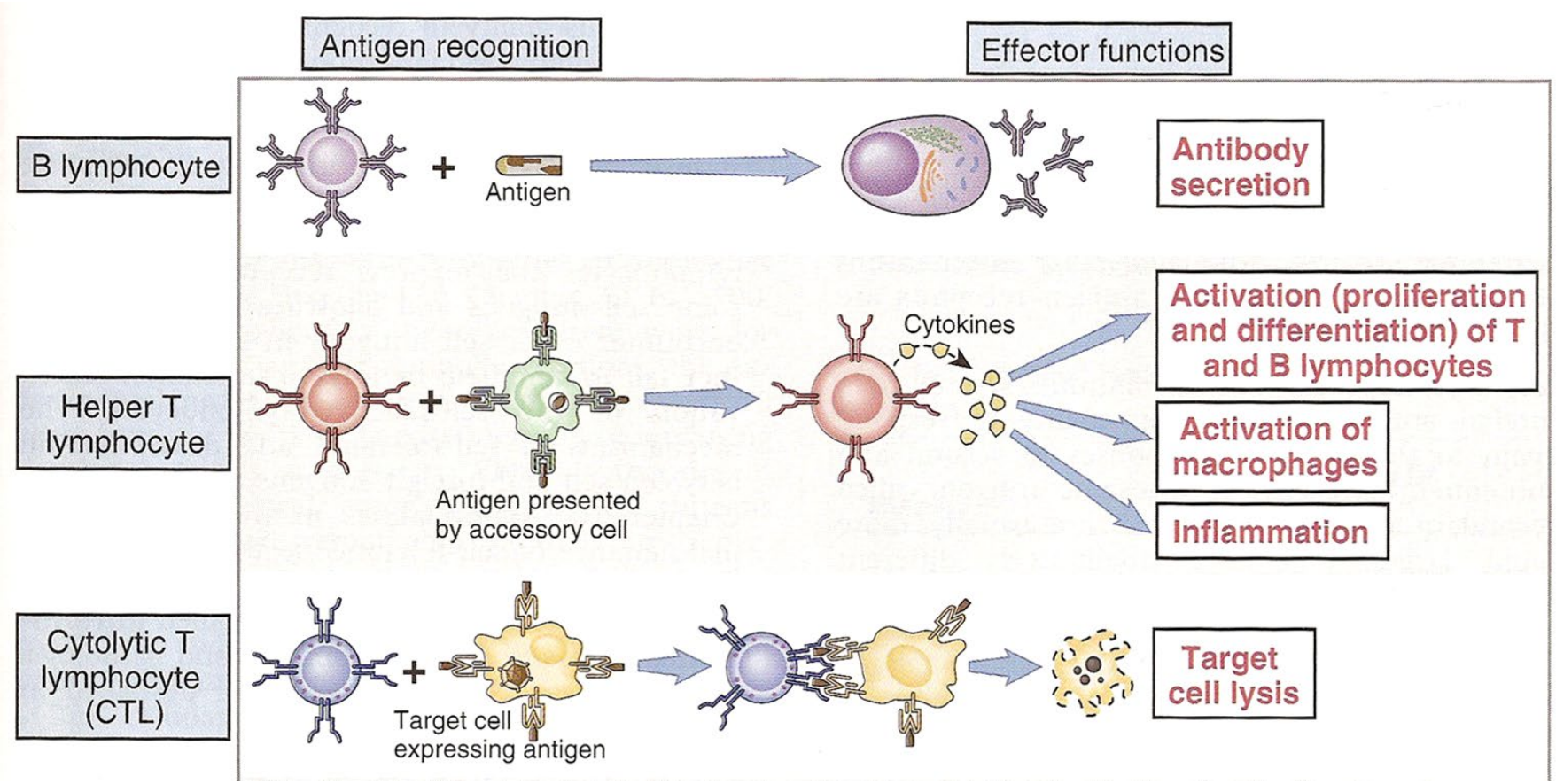
An **adaptive immune response** is generated when naive T cells contact mature, activated antigen-presenting cells in the peripheral lymphoid organs.



http://www.circumvent-g2.com/immunology.aspx

Infection or vaccination

Key cellular actors of adaptive immunity

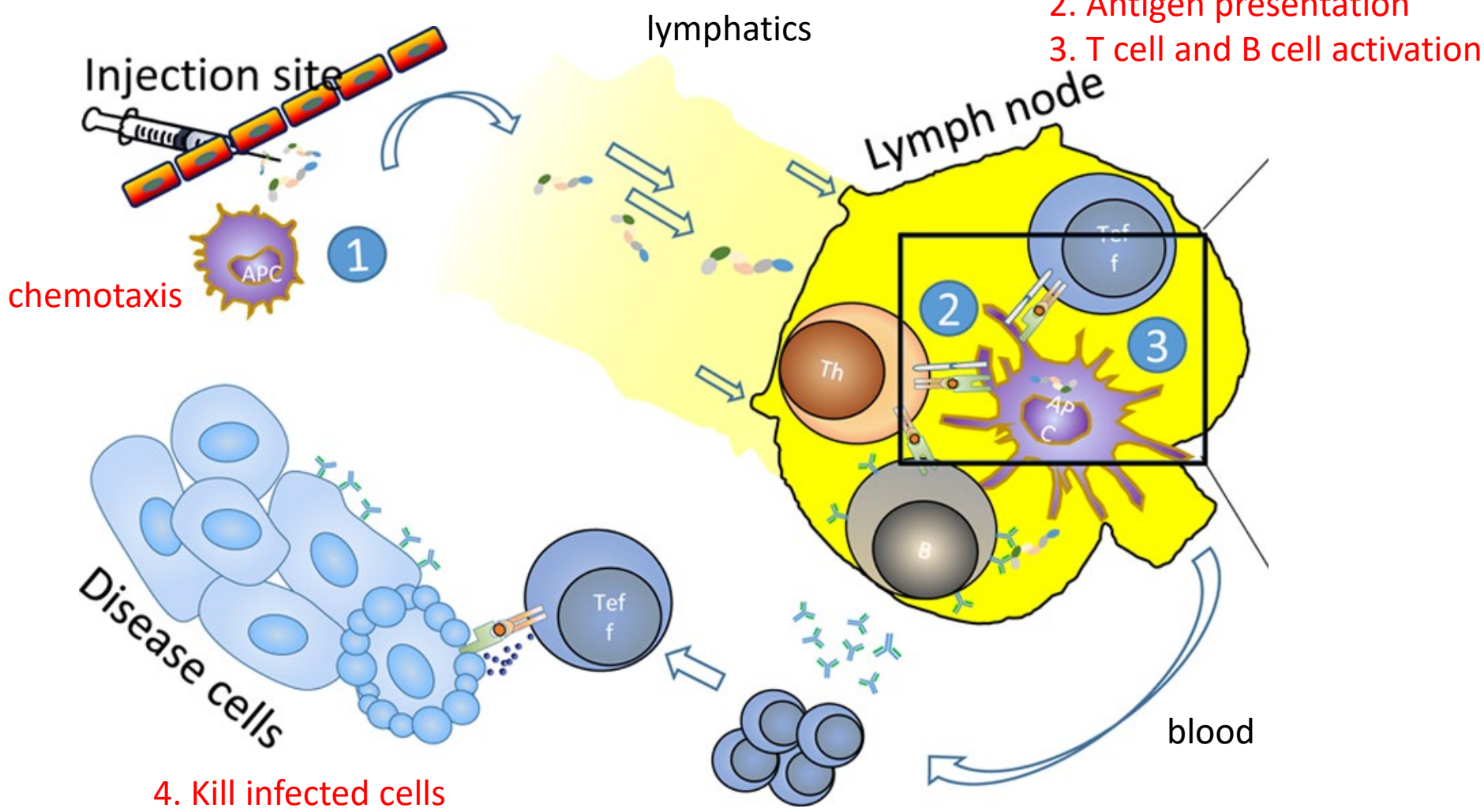


The adaptive immune response consists of two branches, a **cellular adaptive response**(effected by cytotoxic T cells) and a **humoral adaptive response** (effected by B cells).

Abbas, A. K.,et al. *Cellular and Molecular Immunology*

Basic physiology of the primary immune response (i)

1. Immunization or infection



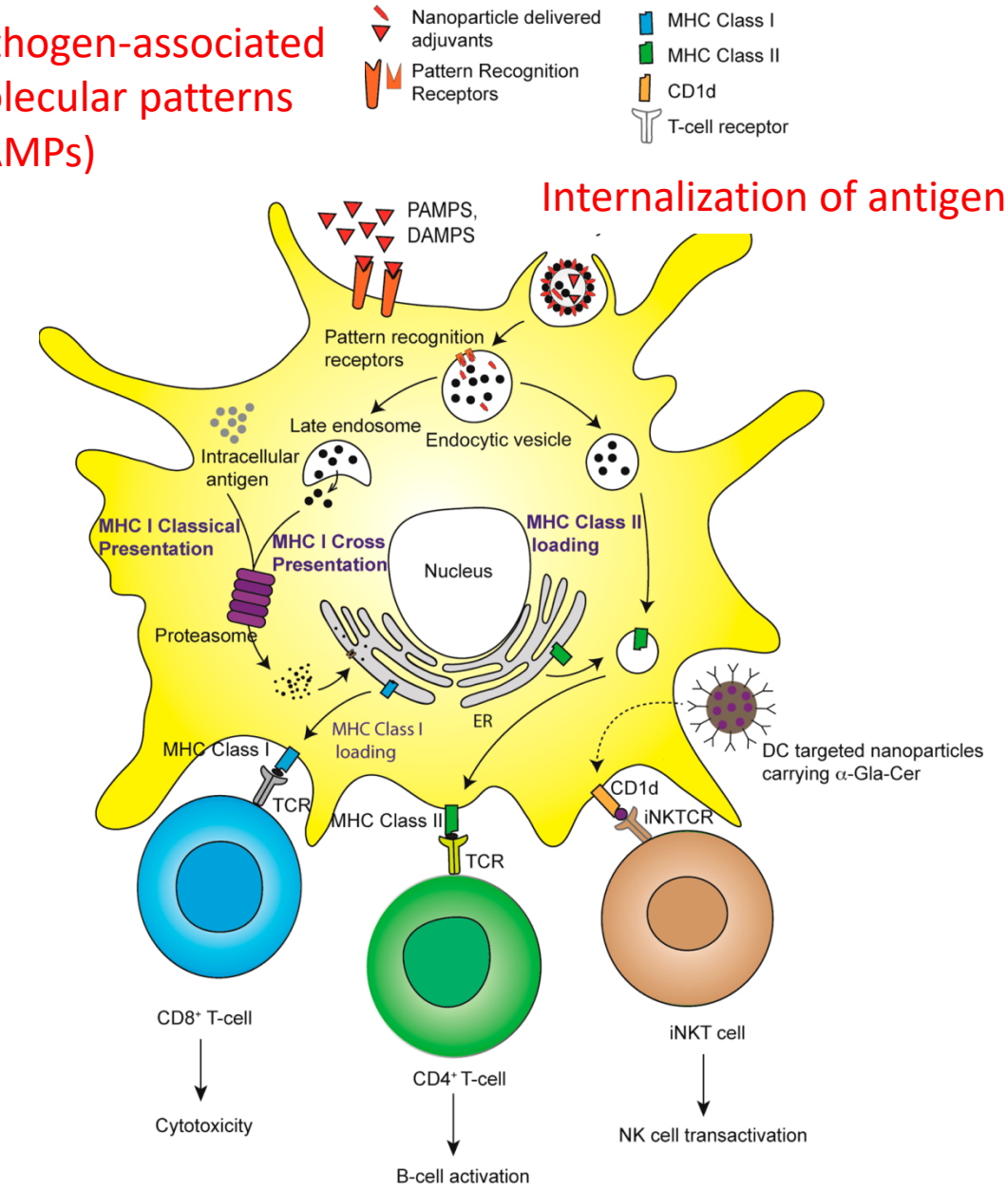
Bioconjug. Chem. **26**, 791-801 (2015)

Basic physiology of the primary immune response (ii)

Pathogen-associated molecular patterns (PAMPs)

Dendritic cells (DCs)

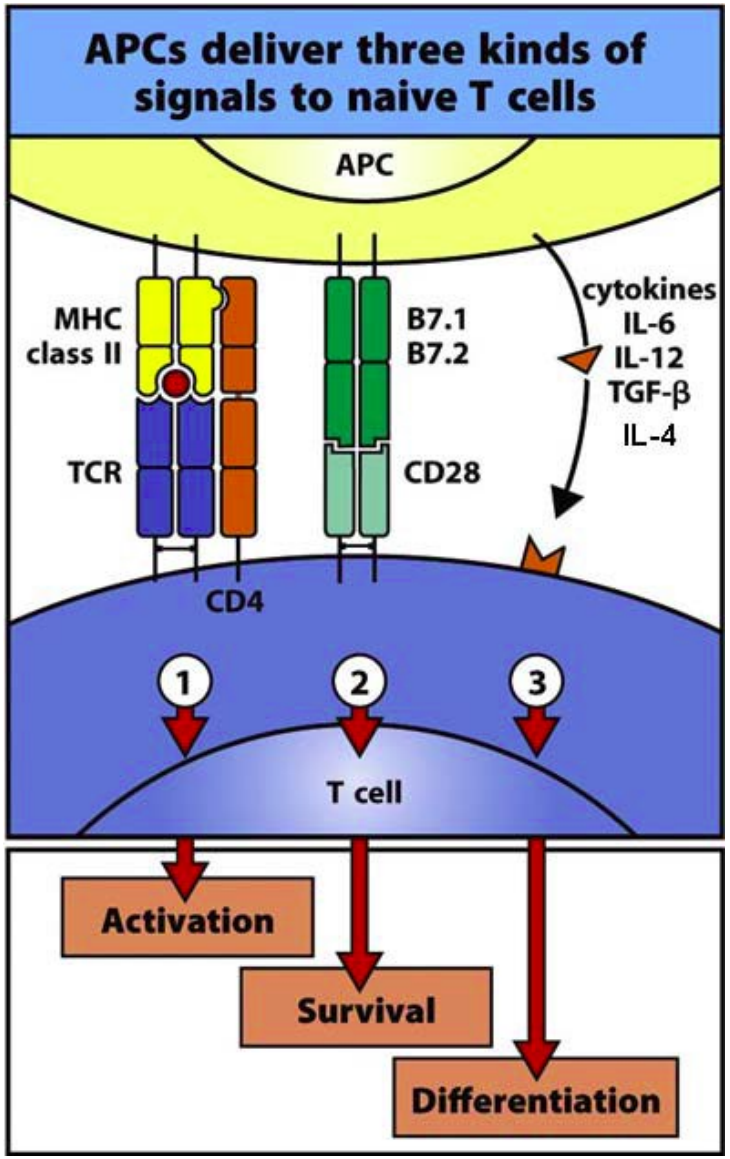
1) Chemotaxis
2) Antigen loading and activation
3) Trafficking to lymph nodes (LNs)
4) Activation of naïve T cells in LNs



Chem. Rev. **115**, 11109-11146 (2015).

Activation of naïve T cells by antigen-presenting cells

Signals required
1) Antigen
2) Costimulation
3) Secreted cytokines



Janeway, Immunobiology, 5th

B cell activation (i)

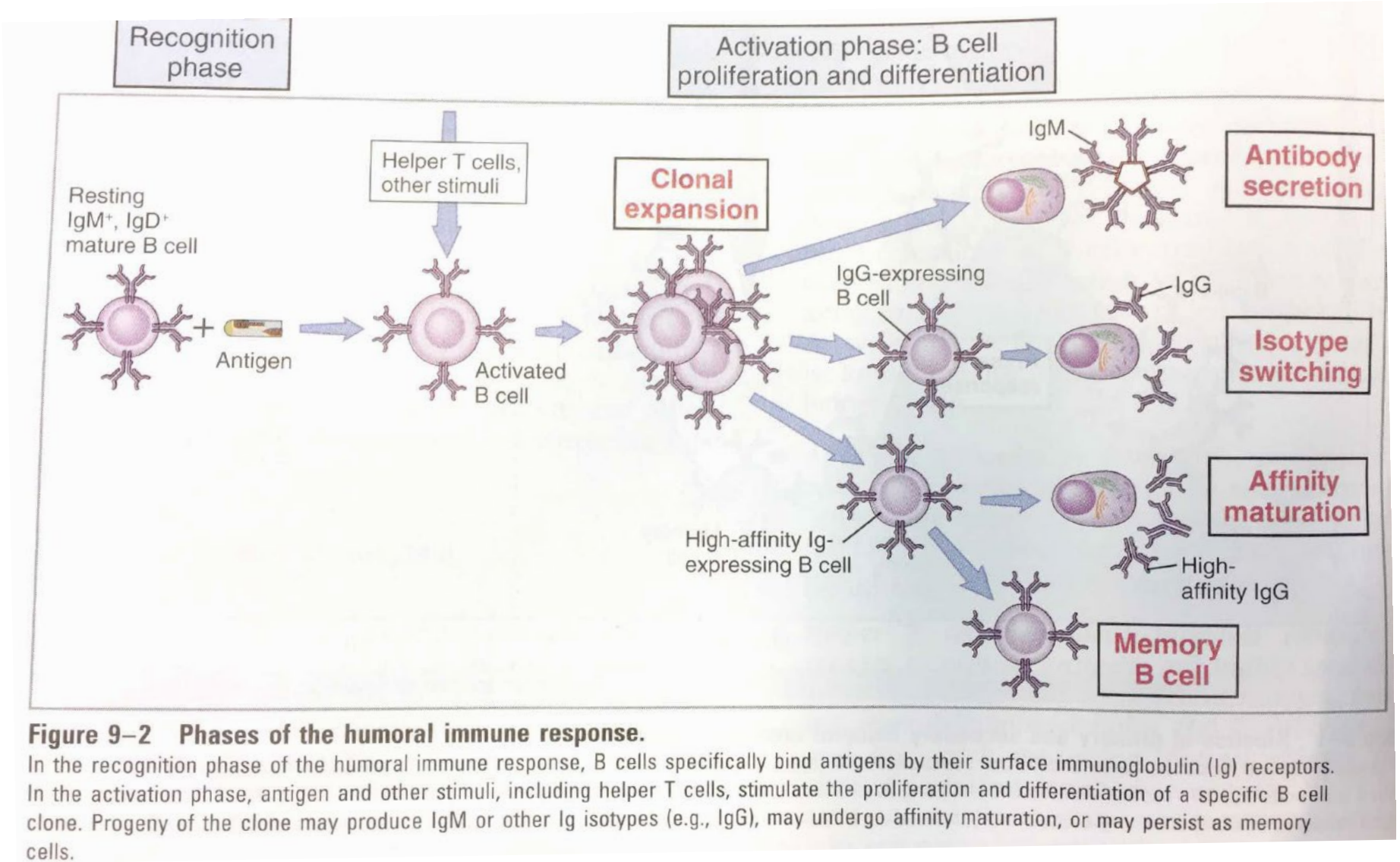
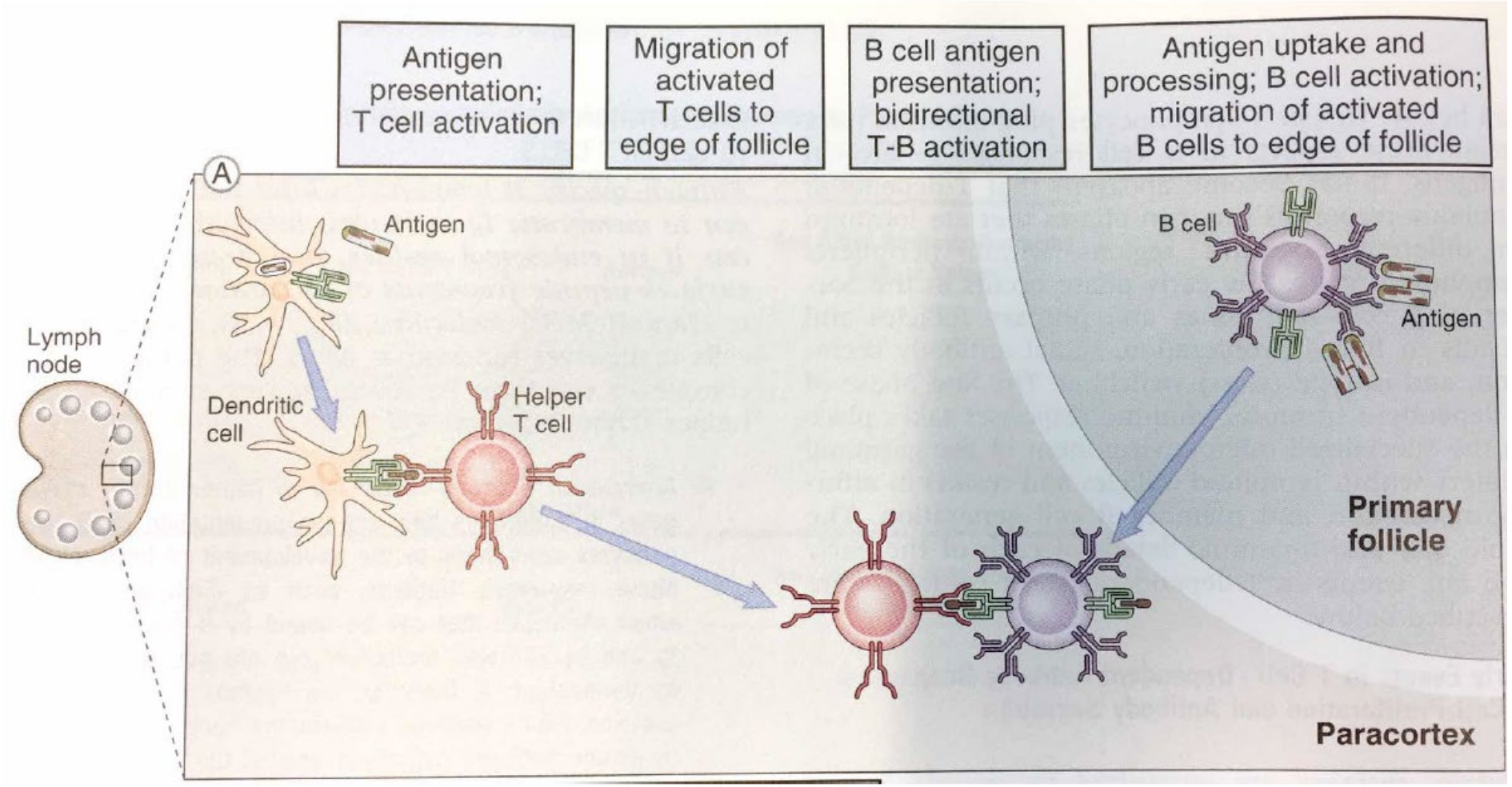


Figure 9–2 Phases of the humoral immune response.
In the recognition phase of the humoral immune response, B cells specifically bind antigens by their surface immunoglobulin (Ig) receptors. In the activation phase, antigen and other stimuli, including helper T cells, stimulate the proliferation and differentiation of a specific B cell clone. Progeny of the clone may produce IgM or other Ig isotypes (e.g., IgG), may undergo affinity maturation, or may persist as memory cells.

Abbas, A. K.,et al. *Cellular and Molecular Immunology*

B cell activation (ii)

B cell response to protein antigens



Abbas, A. K.,et al. *Cellular and Molecular Immunology*

B cell activation (iii)

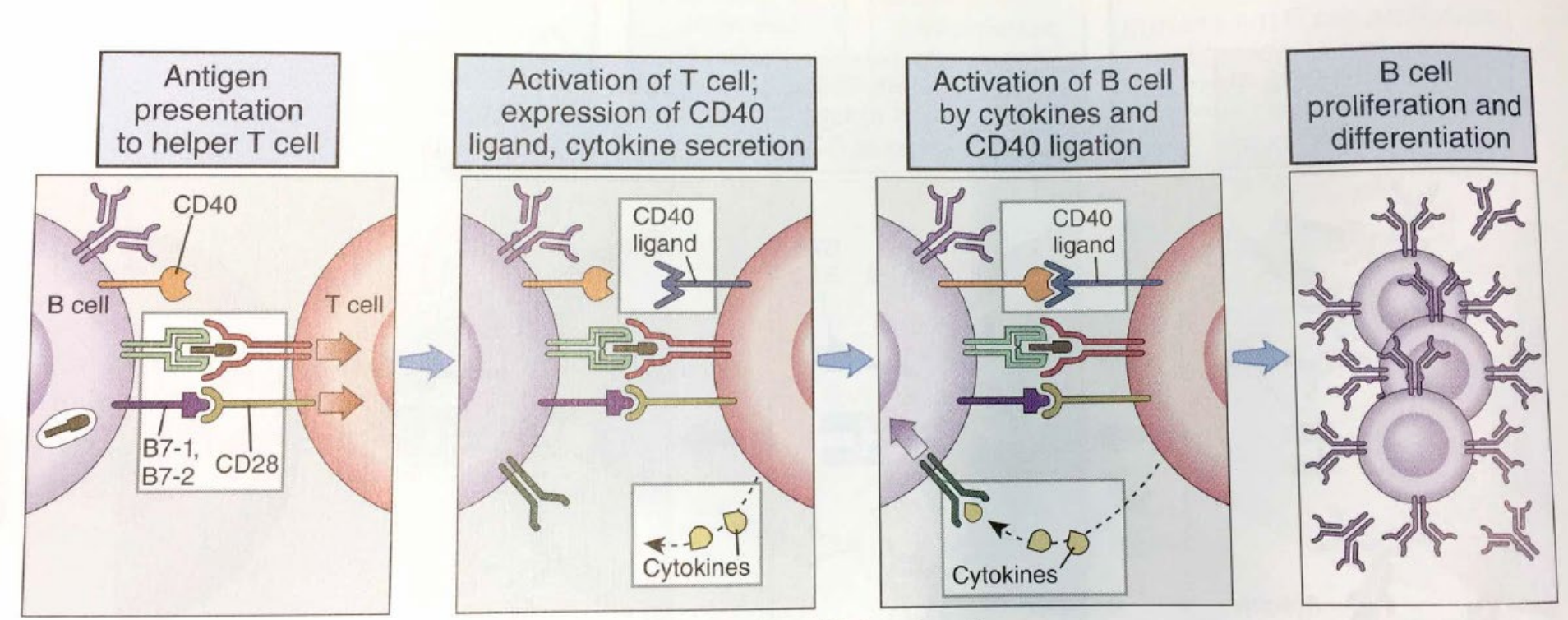


Figure 9–9 Bidirectional molecular interactions between B and T lymphocytes.
In this model for the role of multiple ligand-receptor pairs in T cell–dependent B cell activation, antigen is presented by B cells and induces the expression of costimulators B7-1 and B7-2. Helper T cells recognize the antigen (in the form of peptide-MHC complexes) and the costimulators and are stimulated to express CD40 ligand. CD40 ligand then binds to CD40 on the B cells and initiates B cell proliferation and differentiation. MHC, major histocompatibility complex.

Abbas, A. K.,et al. *Cellular and Molecular Immunology*

Examples of current approved vaccines

TABLE 1. THE STATUS OF VACCINES AGAINST SOME HUMAN PATHOGENS.

INFECTIOUS AGENT	VACCINE STATUS*	DISEASE	TYPES OF TRADITIONAL VACCINE	USE OR TARGET POPULATION
Bacteria				
Bacillus anthracis	Available	Anthrax	Inactivated	To limit biologic warfare
Bordetella pertussis	Available	Whooping cough	Inactivated, subunit	Children and adults
Borrelia burgdorferi	Available	Lyme disease	Subunit	Residents of areas of endemic disease in the United States
Clostridium tetani	Available	Tetanus	Toxoid	Children
Corynebacterium diphtheriae	Available	Diphtheria	Toxoid	Children
Coxiella burnetii	Available	Severe fever (Q fever)	Inactivated	Workers in slaughterhouses and meat-processing plants
Haemophilus influenzae	Available	Meningitis, epiglottitis, pneumonia type b	Conjugated	Children
Mycobacterium leprae	Phase 3 clinical trials	Leprosy	Inactivated	Residents of areas of endemic disease
M. tuberculosis	Available	Tuberculosis	Live attenuated	All persons
Neisseria meningitidis				
Serogroup B	Phase 3 clinical trials	Meningitis	Subunit, conjugated	Children
Serogroup C	Available	Meningitis	Conjugated	
Salmonella typhi	Available (Ty21a vaccine)	Typhoid fever	Live attenuated, polysaccharide	Residents of and travelers to areas of endemic disease, children
	Phase 3 clinical trials (Vi-rEPA vaccine)	Typhoid fever	Conjugated	
Staphylococcus aureus	Phase 3 clinical trials	Impetigo, toxic shock syndrome in women	Conjugated	Those at high risk, those with eczema, those with neutrophil dysfunction
Streptococcus pneumoniae	Available	Pneumonia, otitis media, meningitis	Conjugated	Elderly persons
Vibrio cholerae	Available	Cholera	Live attenuated, inactivated	Residents of and travelers to areas of endemic disease
Viruses				
Adenovirus	Available	Respiratory disease	Live attenuated	Military personnel
Hepatitis A	Available	Liver disease, cancer	Live attenuated, inactivated	Residents of and travelers to areas of endemic disease
Hepatitis B	Available	Liver disease, cancer	Subunit	All persons
Influenzavirus				
A	Available	Respiratory disease	Live attenuated, inactivated, subunit	Children (live attenuated vaccine only), elderly persons
B	Phase 3 clinical trials			
Japanese encephalitis virus	Available	Brain infection	Inactivated	Residents of and travelers to areas of endemic disease
Measles virus	Available	Respiratory tract infection, SSPE†	Live attenuated	Children and adolescents
Mumps virus	Available	Mumps, meningitis, orchitis	Live attenuated	Children and adolescents
Poliovirus	Available	Poliomyelitis, paralysis	Live attenuated, inactivated	Children
Rabies virus	Available	Rabies	Inactivated	Exposed persons, residents of areas of endemic disease
Rubella virus	Available	German measles, fetal malformations	Live attenuated	Children
Vaccinia virus	Available	Smallpox	Live attenuated	Laboratory workers
Varicella–zoster virus	Available	Chickenpox	Live attenuated	Children
Yellow fever virus	Available	Jaundice, kidney and liver failure	Live attenuated	Residents of areas of endemic disease, particularly children
Parasites				
Leishmania	Phase 3 clinical trials	Kala-azar, tropical sores	Live attenuated, inactivated	Residents of countries where disease is endemic
Fungus				
Coccidioides immitis	Phase 3 clinical trials	Lung infection	Inactivated	Residents of countries where disease is endemic

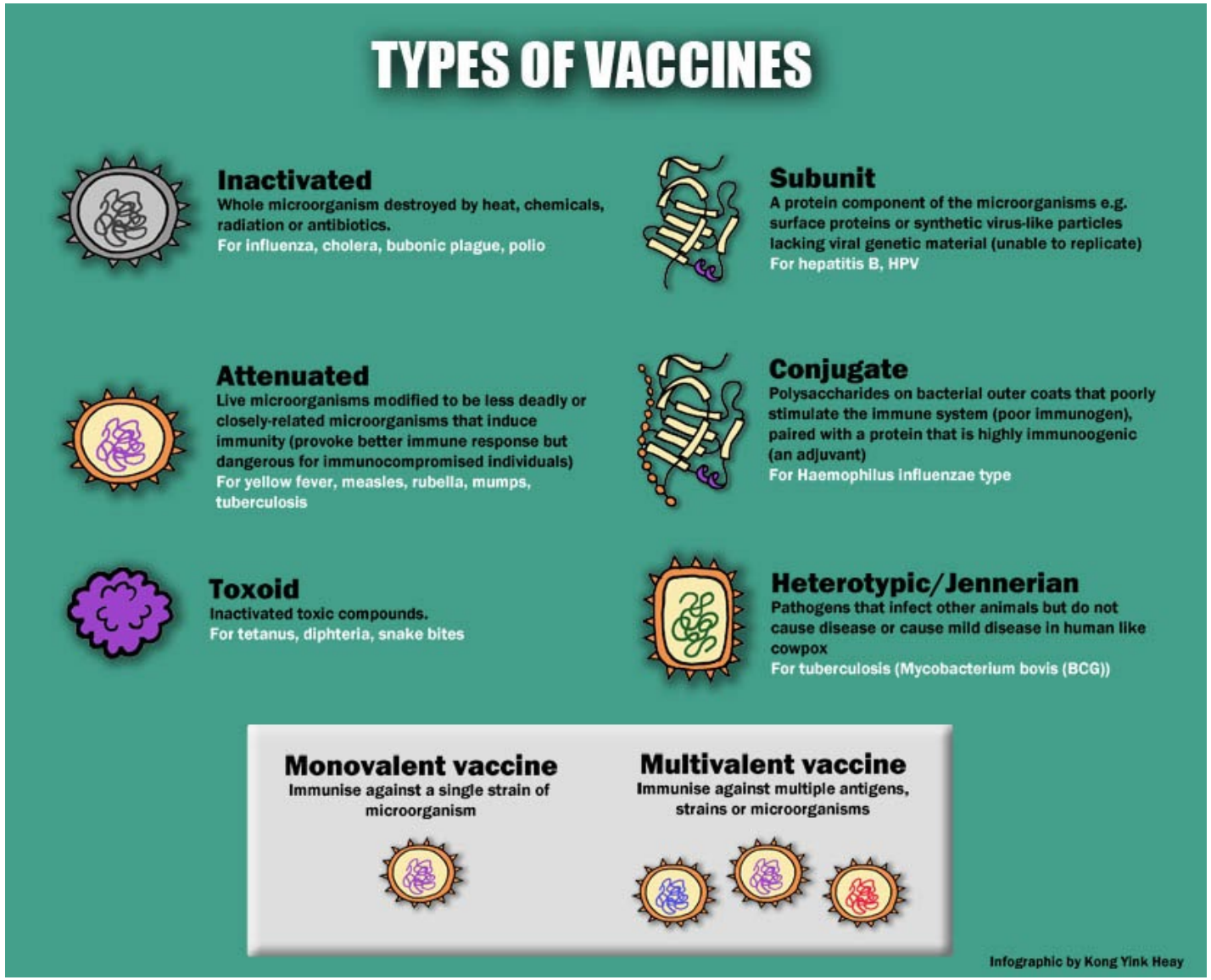
*Vaccines that have been evaluated in phase 3 clinical trials should be available in 5 to 10 years.

†SSPE denotes subacute sclerosing panencephalitis.

The New England journal of medicine **345**, 1042-1053 (2001).

Types of vaccines

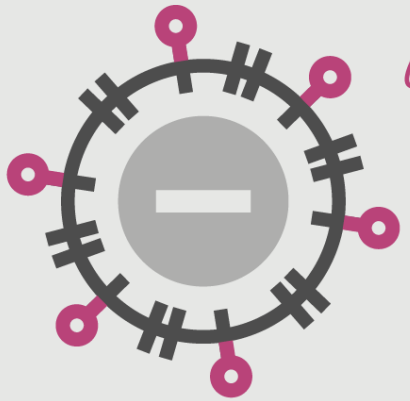
Vaccines are dead or inactivated organisms or purified products derived from them.



Types of SARS-CoV-2 vaccines for COVID-19

Inactivated vaccines

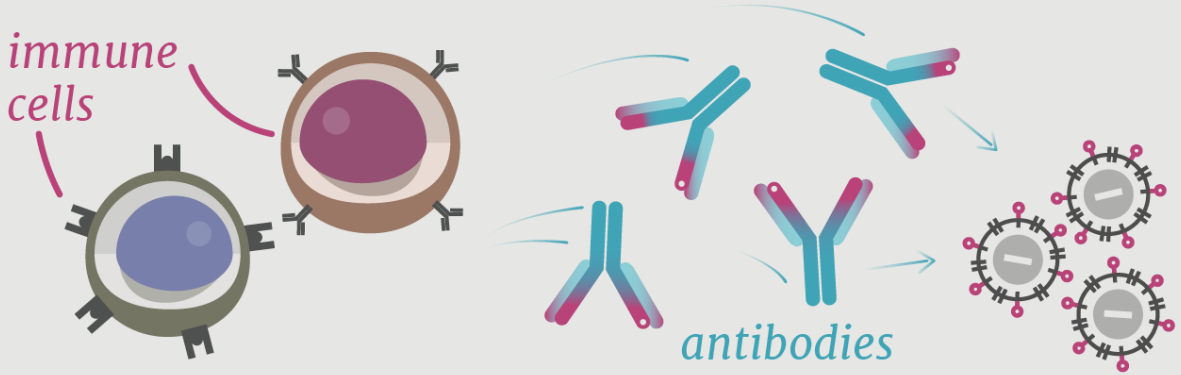
British Society for immunology
www.immunology.org



Contain **killed SARS-CoV-2 virus**.

The killed virus is recognised by the immune system to trigger a response without causing illness.

This response builds immune memory, so your body can fight off SARS-CoV-2 in future.



Considerations

May need to be administered with an adjuvant to boost immune response.

Examples in human use for other disease

Influenza vaccine

Approved elsewhere in the world for COVID-19

Sinovac, Sinopharm, Bharat Biotech

In clinical trials for COVID-19

Shifa-Pharmed, Chinese Academy of Medical Sciences

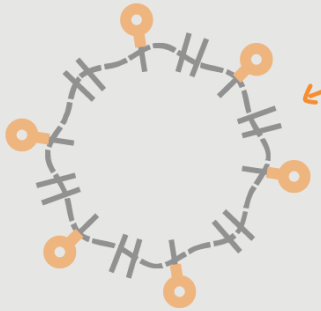
British Society for Immunology

https://www.immunology.org/coronavirus/connect-coronavirus-public-engagement-resources/types-vaccines-for-covid-19

Types of SARS-CoV-2 vaccines for COVID-19

Attenuated vaccines

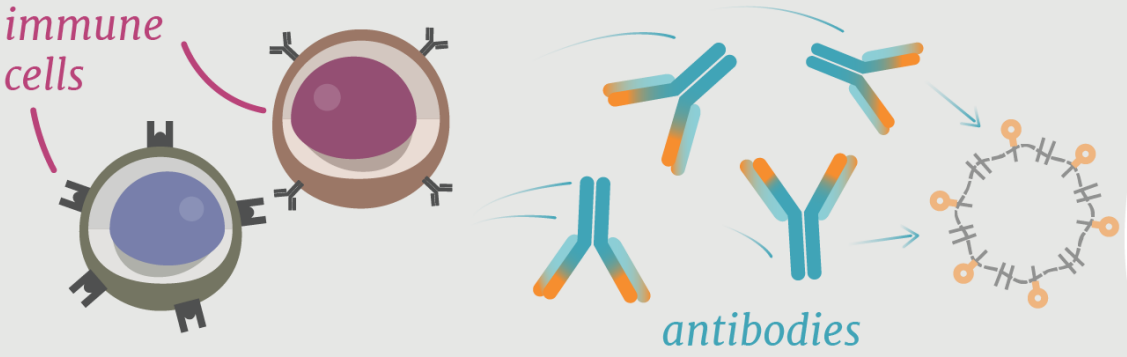
British Society for immunology
www.immunology.org



Contain **weakened SARS-CoV-2 virus**.

The weakened virus is recognised by the immune system to trigger a response without causing illness.

This response builds immune memory, so your body can fight off SARS-CoV-2 in future.



Considerations

A well-known approach which requires time and extensive testing.

The immune response resembles the natural infection.

Examples in human use for other disease

Oral Polio vaccine

In clinical trials for COVID-19

Codagenix

https://codagenix.com/vaccine-programs/covid-19/

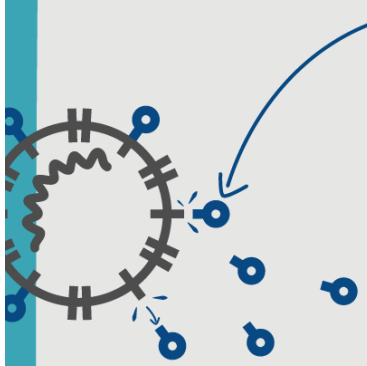
Live vaccines use a weakened (or attenuated) form of the germ that causes a disease. Because these vaccines are so similar to the natural infection that they help prevent, they create a strong and long-lasting immune response.

Viruses may be attenuated using the principles of evolution via serial passage of the virus through a foreign host species. Bacteria is typically attenuated by passage, similar to the method used in viruses.

Types of SARS-CoV-2 vaccines for COVID-19

Protein vaccines

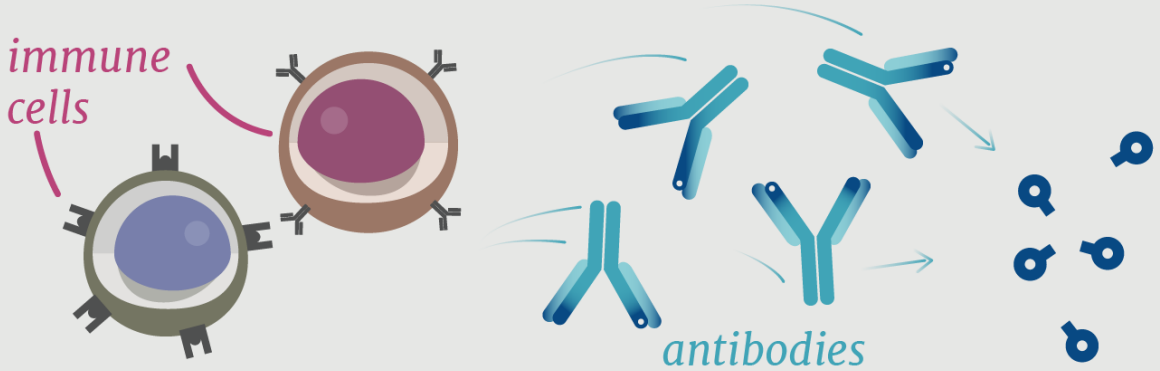
British Society for immunology
www.immunology.org



Contain **proteins** from the SARS-CoV-2 virus, which are recognised by the immune system to trigger a response.

Can be whole proteins, protein fragments, or many protein molecules packed into nanoparticles.

This response builds immune memory, so your body can fight off SARS-CoV-2 in future.



Considerations

Have good previous safety records.

Usually administered with an adjuvant to boost immune response.

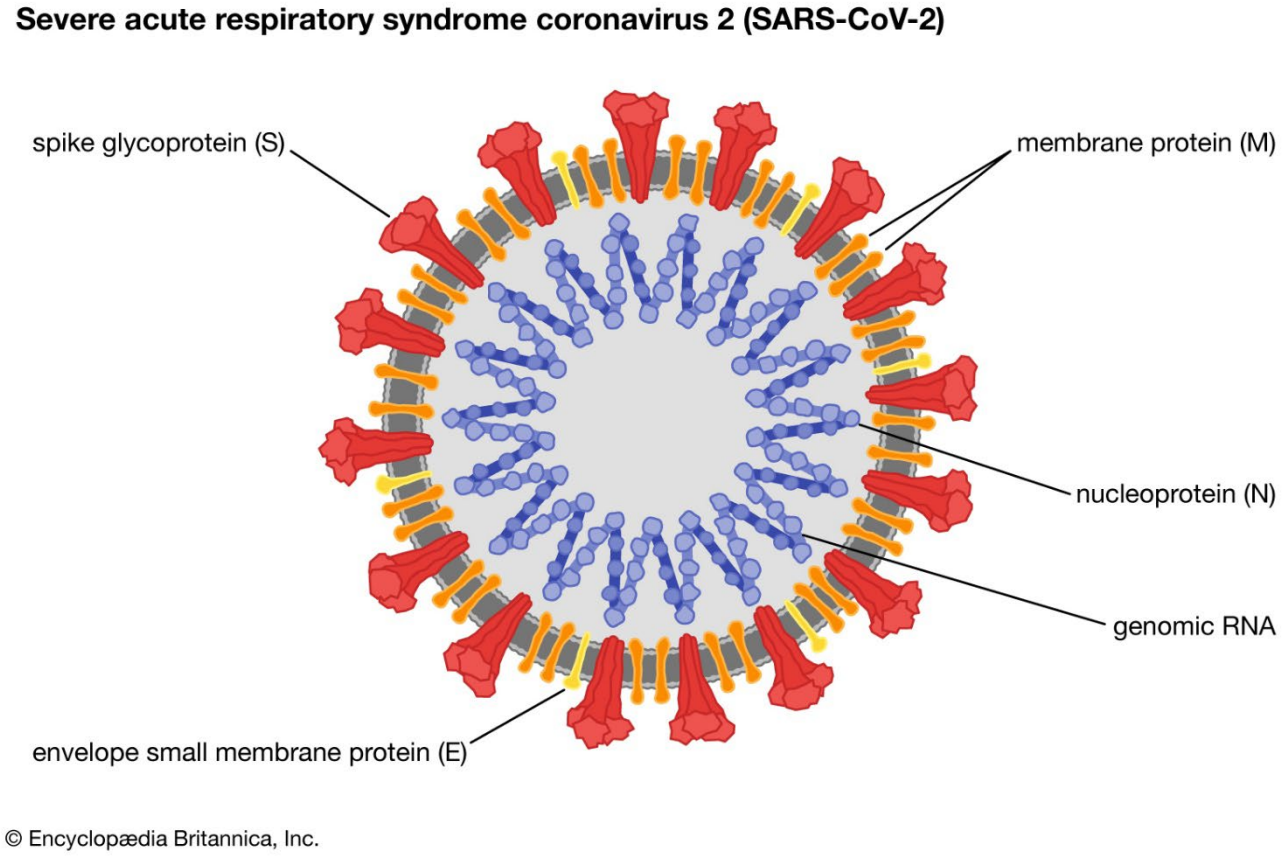
Examples in human use for other diseases

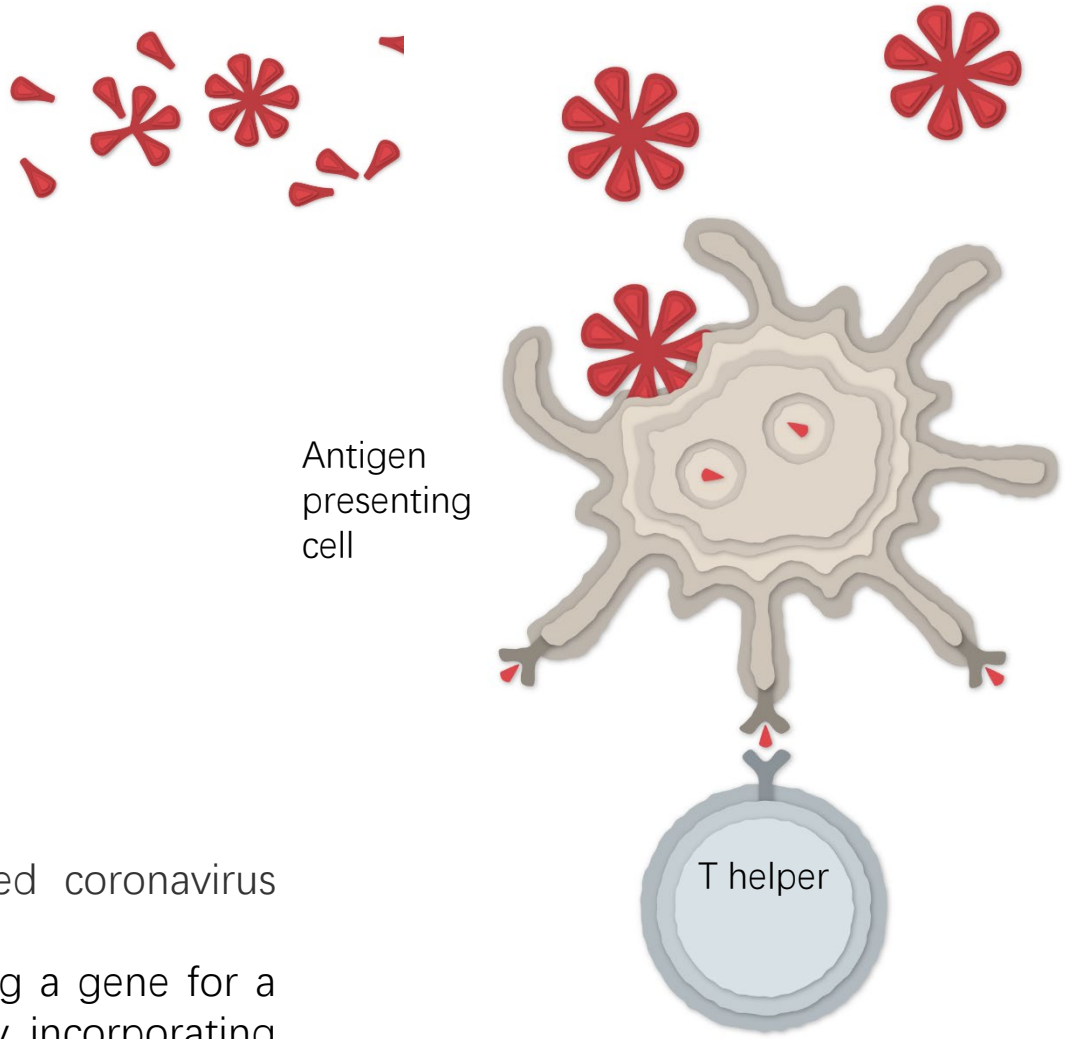
Hepatitis B vaccine

In clinical trials for COVID-19

Novavax, Sanofi/GSK

subunit vaccine: presents one or more antigens to the immune system without introducing pathogen particles, whole or otherwise.



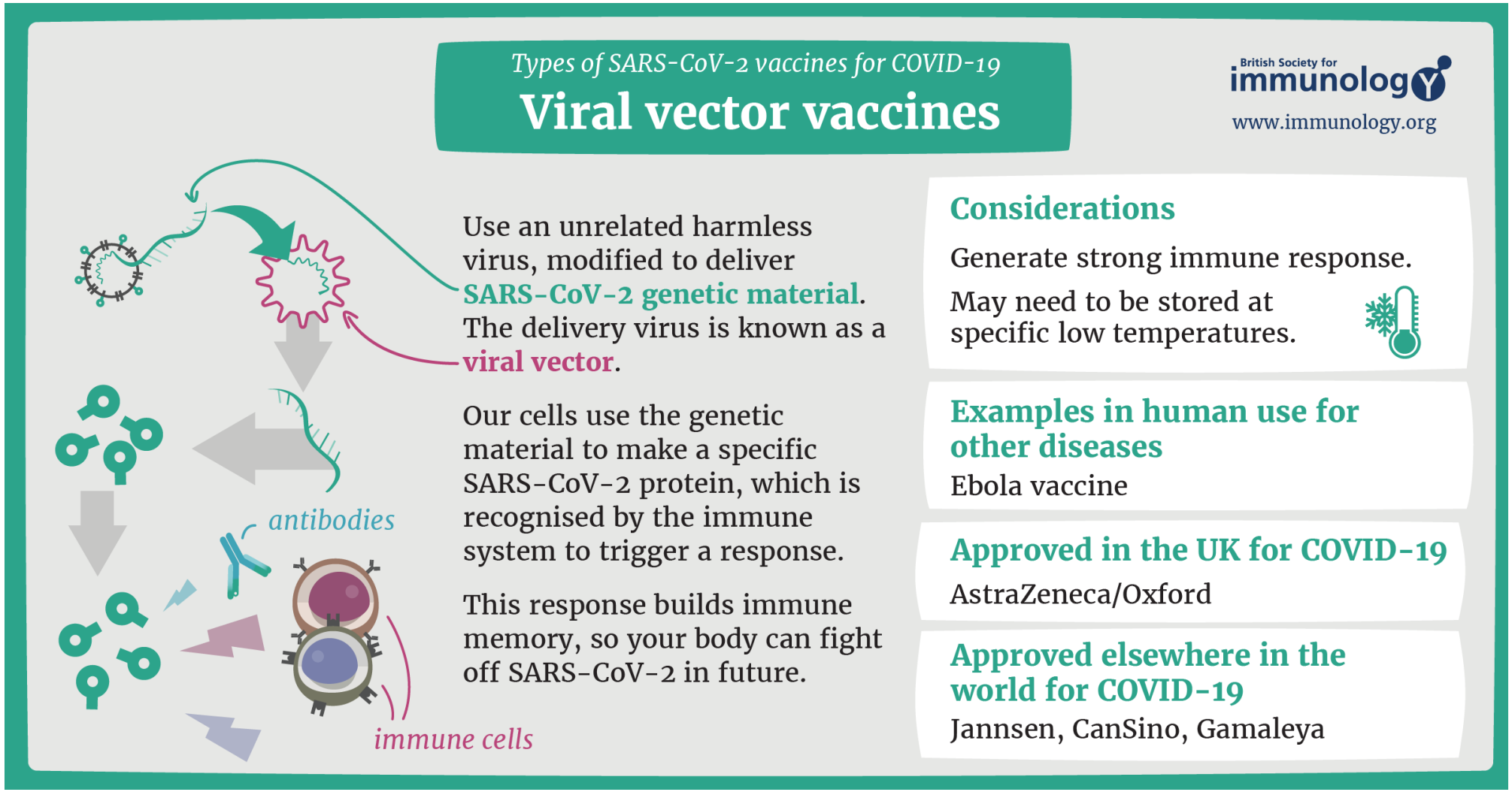


The Maryland-based company Novavax has developed a protein-based coronavirus vaccine called **NVX-CoV2373.**

The vaccine is produced by creating an engineered baculovirus containing a gene for a modified SARS-CoV-2 spike protein. The spike protein was modified by incorporating two proline amino acids in order to stabilize the pre-fusion form of the protein; this same 2P modification is being used in several other COVID-19 vaccines.[11] The baculovirus then infects a culture of Sf9 moth cells, which create the spike protein and display it on their cell membranes. The spike proteins are then harvested and assembled onto a synthetic lipid nanoparticle about 50 nanometers across, each displaying up to 14 spike proteins.[5][6][10]

The formulation includes a saponin-based adjuvant.

https://www.nytimes.com/interactive/2020/health/novavax-covid-19-vaccine.html



This type of vaccine uses an unrelated harmless virus (the viral vector) to deliver SARS-CoV-2 genetic material. When administered, our cells use the genetic material to produce a specific viral protein, which is recognised by our immune system and triggers a response.

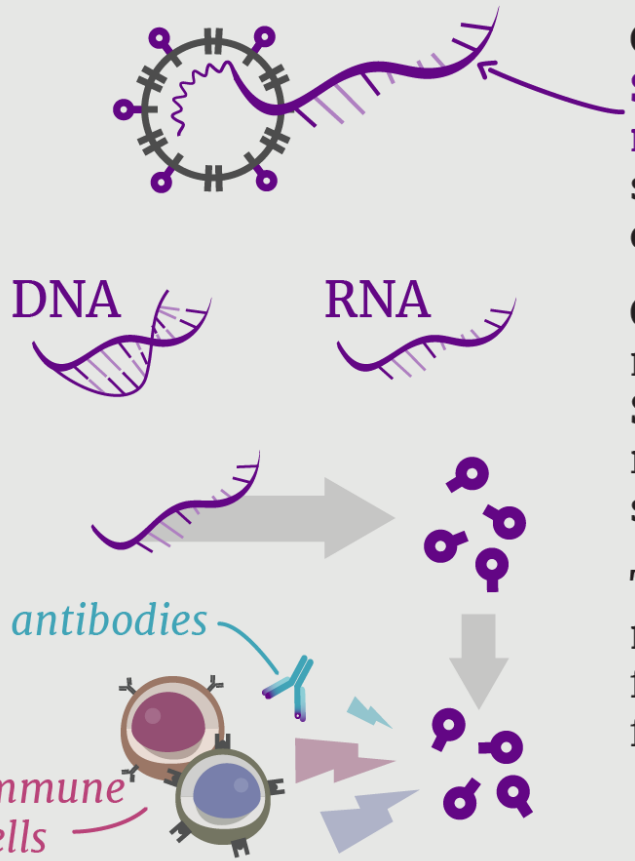
Example:

Sputnik V (Russian: Спутник V) is a viral vector vaccine for COVID-19: based on two human adenoviruses – a common cold virus – containing the gene that encodes the full-length spike protein (S) of SARS-CoV-2

Types of SARS-CoV-2 vaccines for COVID-19

Genetic vaccines
(nucleic acid vaccines)

British Society for immunology
www.immunology.org



Contain a segment of **SARS-CoV-2 virus genetic material** that codes for a specific protein. Can be DNA or RNA.

Our cells use the genetic material to make the SARS-CoV-2 protein, which is recognised by the immune system to trigger a response.

This response builds immune memory, so your body can fight off SARS-CoV-2 in future.

Considerations

Low cost and fast to develop.

May need to be stored at specific low temperatures.

Approved in the UK for COVID-19

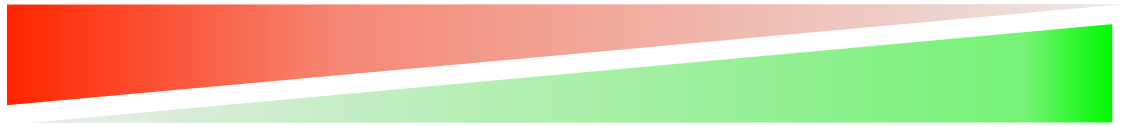
Pfizer/BioNTech & Moderna

In clinical trials for COVID-19

CureVac, Inovio Pharmaceuticals

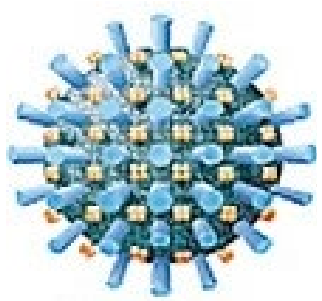
Two classes of successful, licensed vaccines:

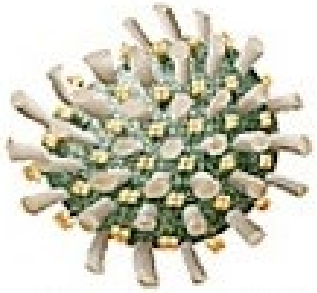
increasing immunogenicity (strength/durability of immune response)



increasing safety

whole microbe





subunit

Type of vaccine:	Live-attenuated	inactivated	subunit
Examples:	Oral Polio, yellow fever, smallpox	Influenza, polio, typhoid	Pneumoccocal, hepatitis B, HPV

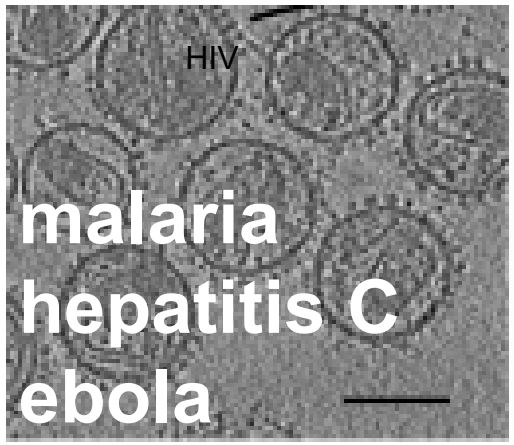
live-attenuated unsafe for highly mutable pathogens, inactivated approach is ineffective for many microbes

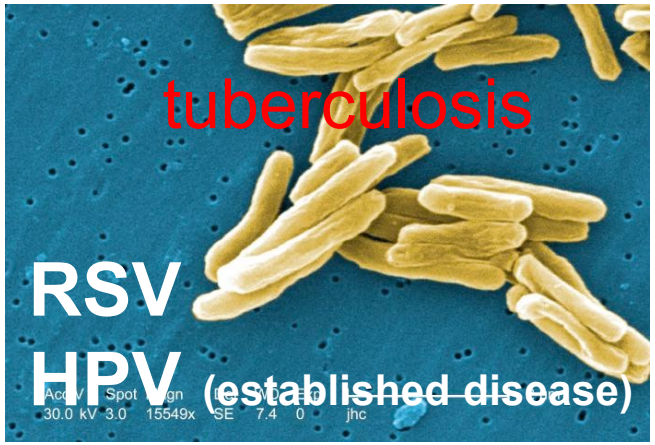
Issues of potency, durability of response, no CD8 T-cell responses

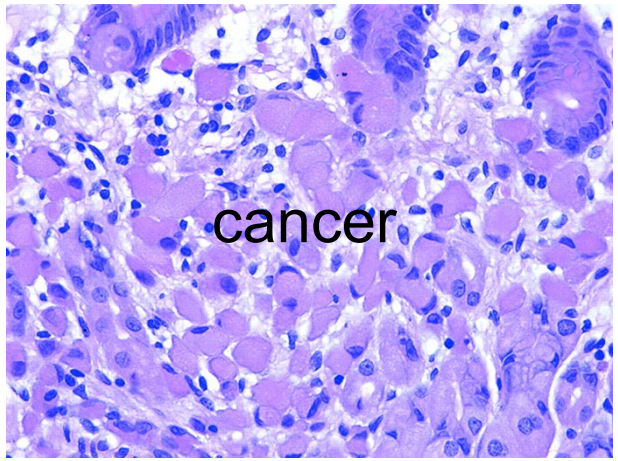
images: www.ifpma.org

Vaccines – triumphs and challenges

However, many diseases remain unsolved challenges for vaccination:







J Med Genet 2010;**47**:433-435

Many shared challenges:

- characteristically, native response is not protective
- highly mutable target antigens
- Need for cytotoxic T-cell responses
- complex effects of immunodominance

...

HIV virions: Zanetti et al. (2006).PLoS pathogens, 2(8), e83

poliomyelitus data: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4905a1.htm

Tuberculosis bacteria
Photo: Janice Haney Carr,Public Health Information Library