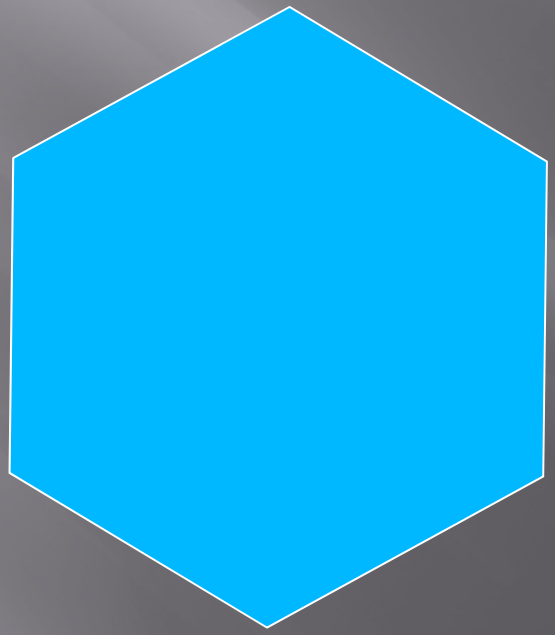
THE BATTLE AGAINST VIRUSES

THE IMMUNE RESPONSE AND VACCINES



J. A. Sands, 5 November 2010, Lehigh University

Introduction

Animals have evolved a multifaceted defense system that helps protect against the ravages of infectious diseases.

The combination of the innate and adaptive immune responses in humans is what allows you to recover from an infection and sometimes (but not always) acquire immunity to re-infection with the same agent.

Specific antiviral drugs and vaccines can help this process, and sometimes even prevent a clinically significant primary infection.

In this lecture, we will take a very quick look at the human immune response, available vaccines against viruses, and the prospects for new viral vaccines as we move into the second decade of the century.

Immune system cells arise from stem cells in the bone marrow.

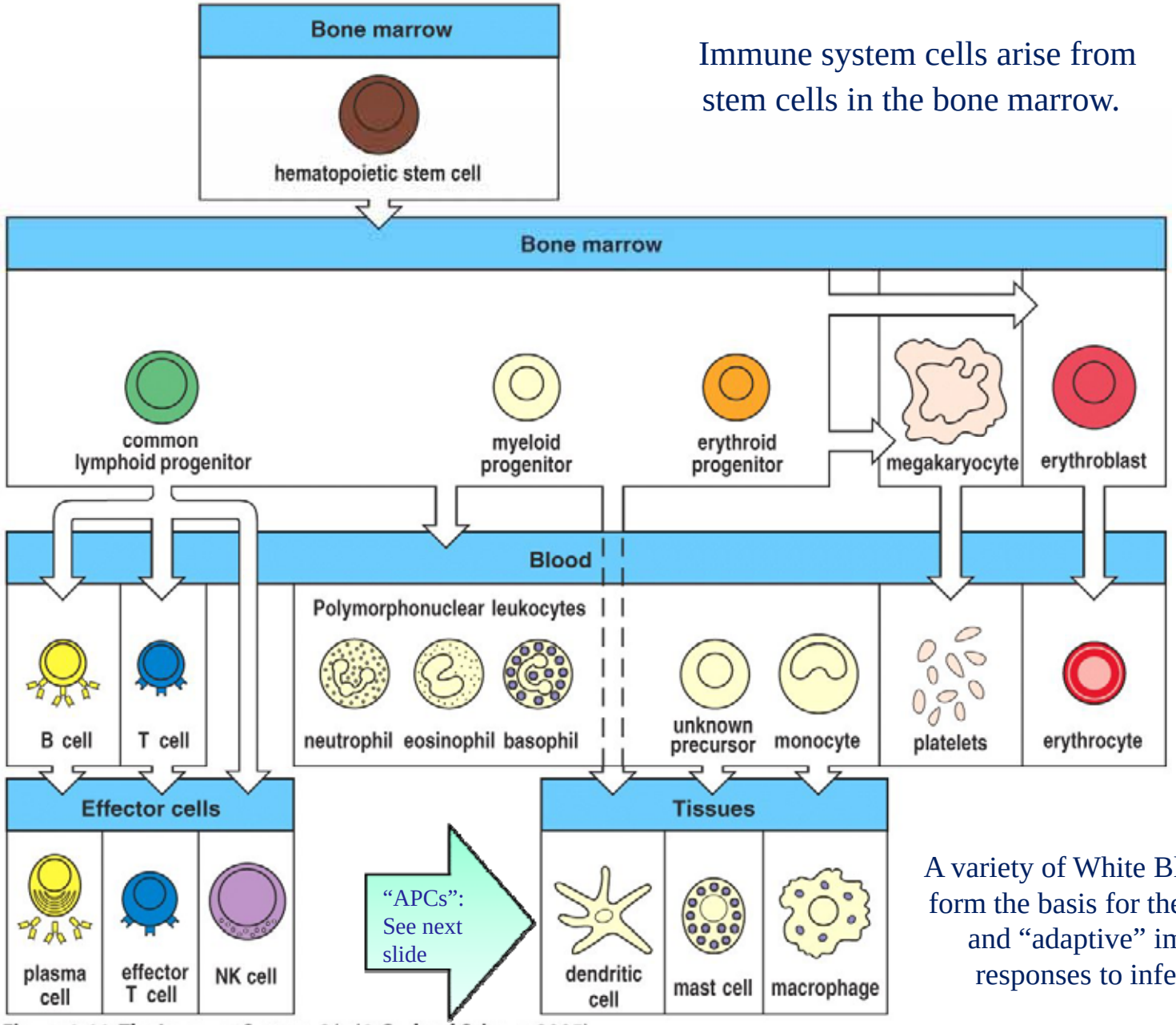
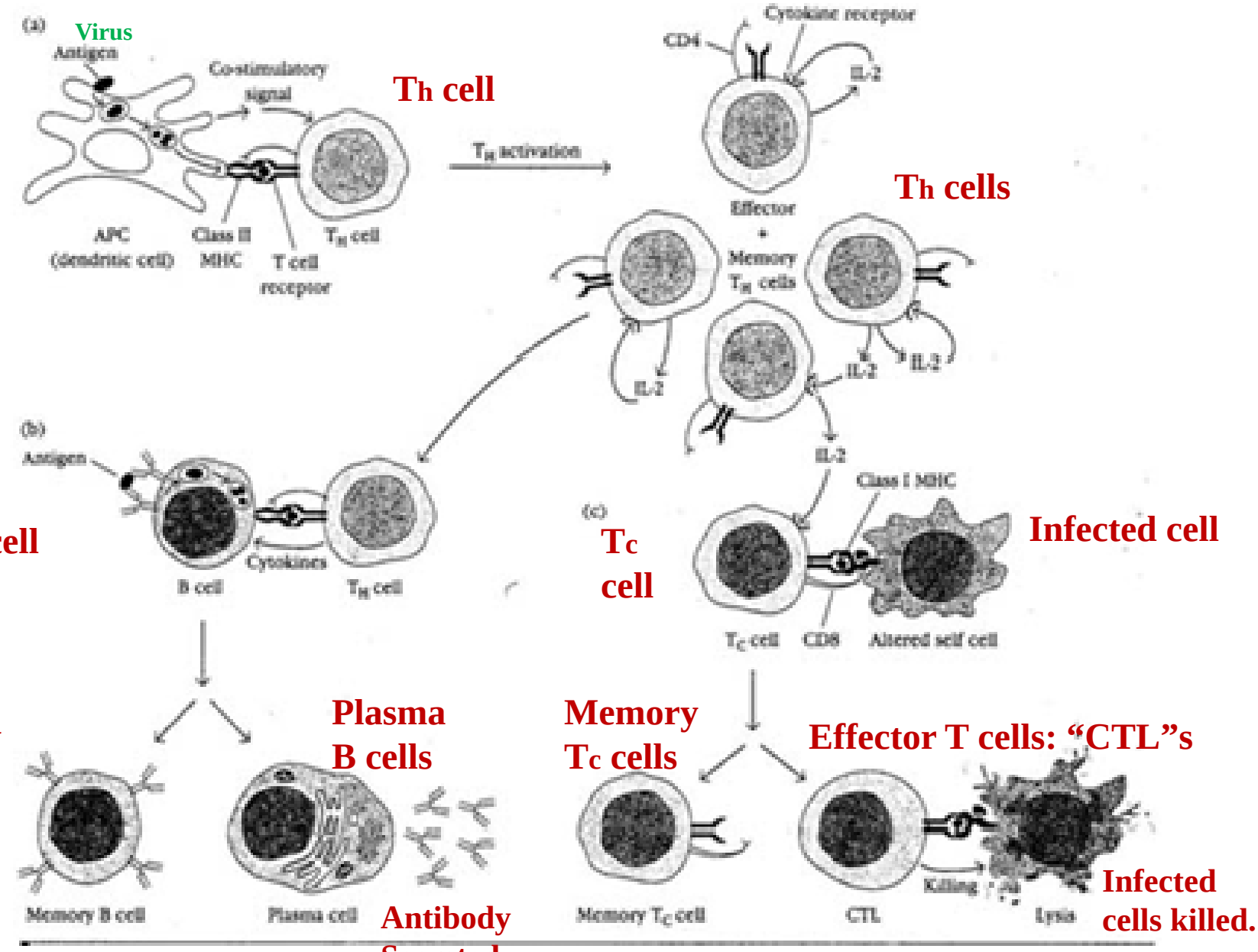


Figure 1-11 The Immune System, 2/e (© Garland Science 2005)

A variety of White Blood Cells form the basis for the "innate" and "adaptive" immune responses to infection.

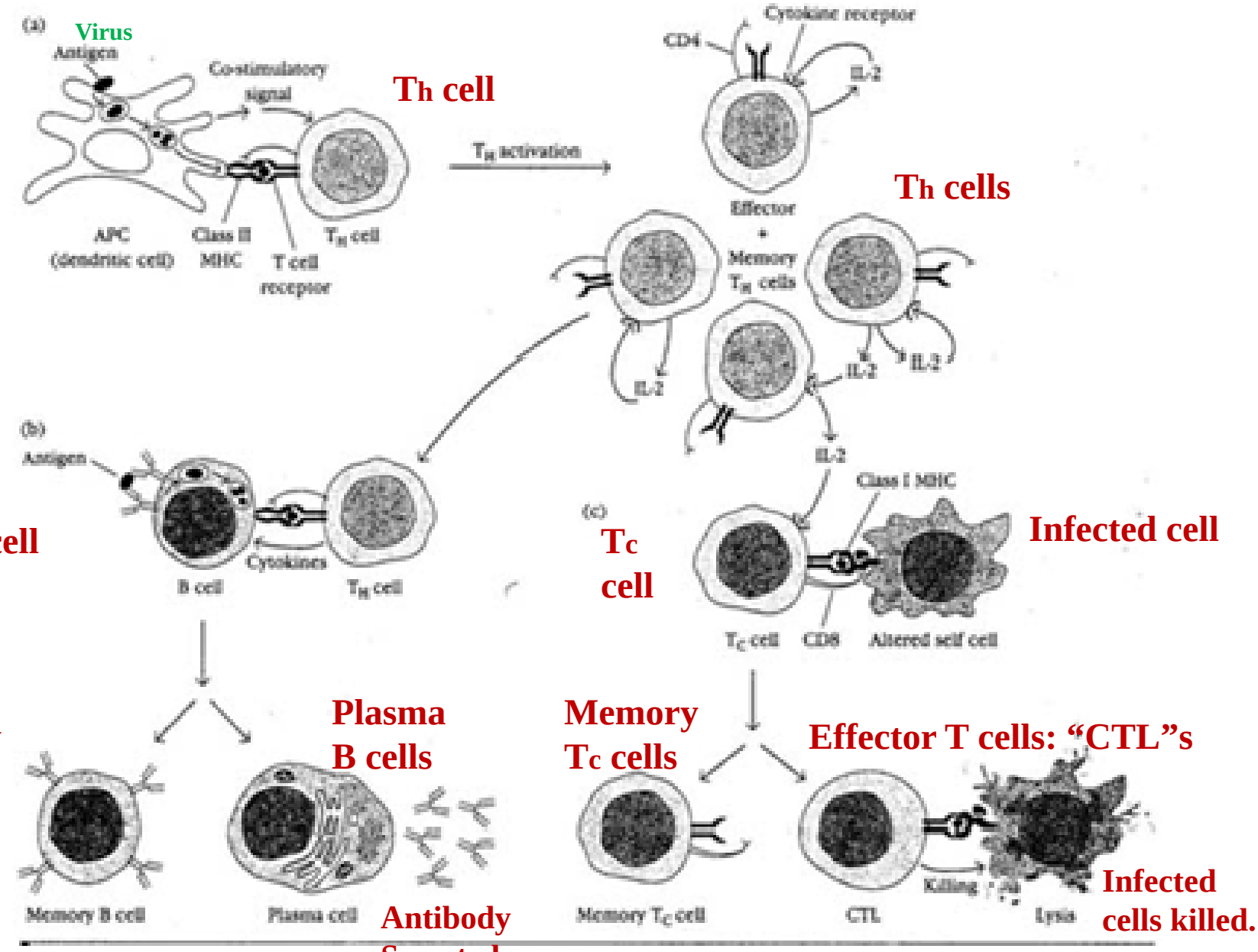
Diagrammatic Overview of Adaptive Immune Response to Virus Infection



Summary of the Adaptive Immune Response to Viruses

1. Virus particles enter body via infection or vaccine inoculation (attenuated live virus, inactivated virus particles, or virus-like particles).
2. Virus particles are processed by "Antigen Presenting Cells" (APCs) to display virus-specific molecules on cell surface.
3. Specific T_h cells (which can bind to these virus-specific molecules) get activated and proliferate.
4. Humoral Response: The T_h cells stimulate the proliferation of similarly specific B cells, which secrete antibody that binds to (and inactivates) extracellular virus particles.
5. Cell-Mediated Response: The T_h cells stimulate the proliferation of similarly specific T_c cells, which bind to (and kill) infected cells.
6. Some of the B and T_c cell populations become Memory cells which provide long-lived immunity to re-infection with this virus.

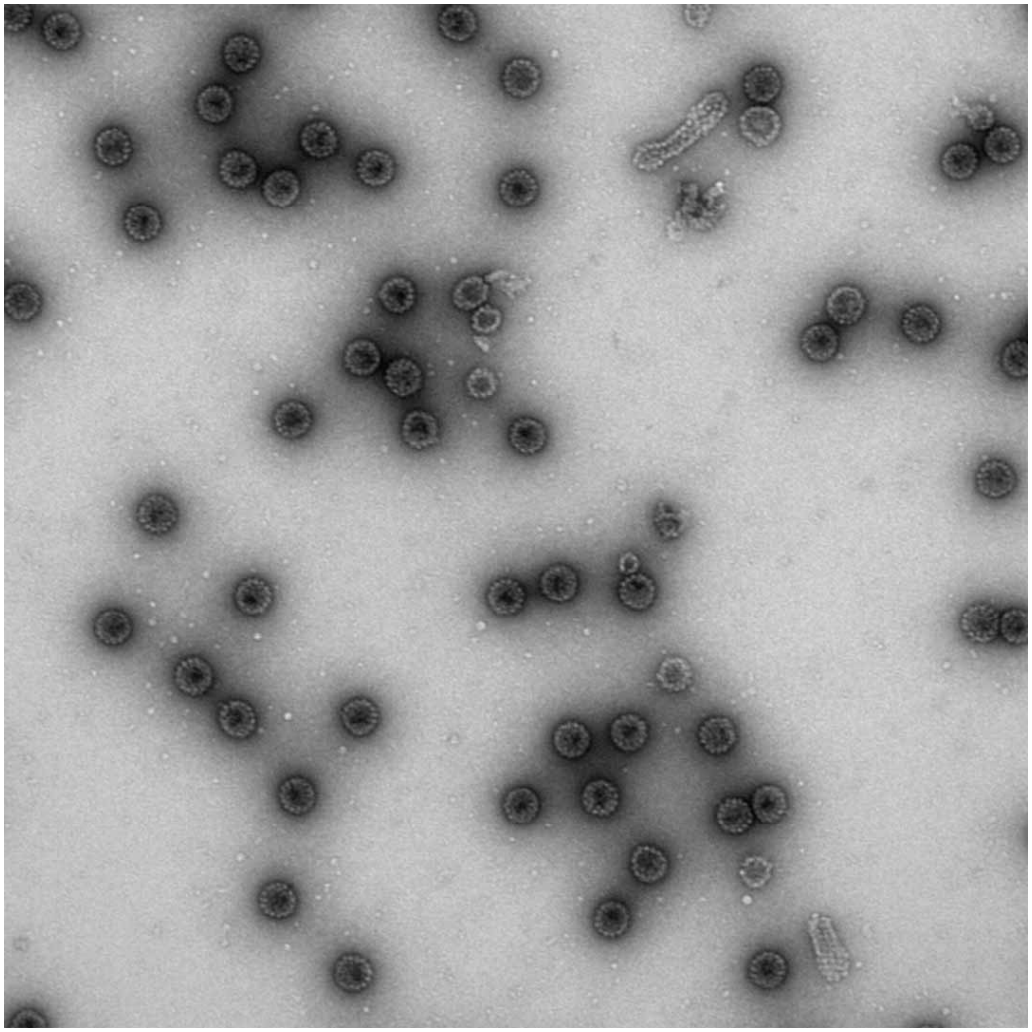
Diagrammatic Overview of Adaptive Immune Response to Virus Infection



Human Viral Vaccines

Smallpox	Live Vaccinia virus (Global elimination of smallpox in 1970's.)
Yellow fever	Live attenuated strain (of yellow fever virus)
Measles	Live attenuated strain
Mumps	Live attenuated strain
Rubella	Live attenuated strain
Polio	Inactivated virions (*Salk*) or Live attenuated strain (*Sabin*)
Influenza	Inactivated virions or Live attenuated strain
Rabies	Inactivated virions (for post-exposure use in humans)
Hepatitis B	Viral envelope glycoprotein
Varicella-zoster	Live attenuated strain
Hepatitis A	Inactivated virions
Rotavirus	Live strains (attenuated & human-bovine reassortment)
HPV	“Virus-like particles”

An early 21’st century vaccine: HPV VLPs



Lowy, D. R. et al. J. Clin. Invest. 2006;116:1167-1173

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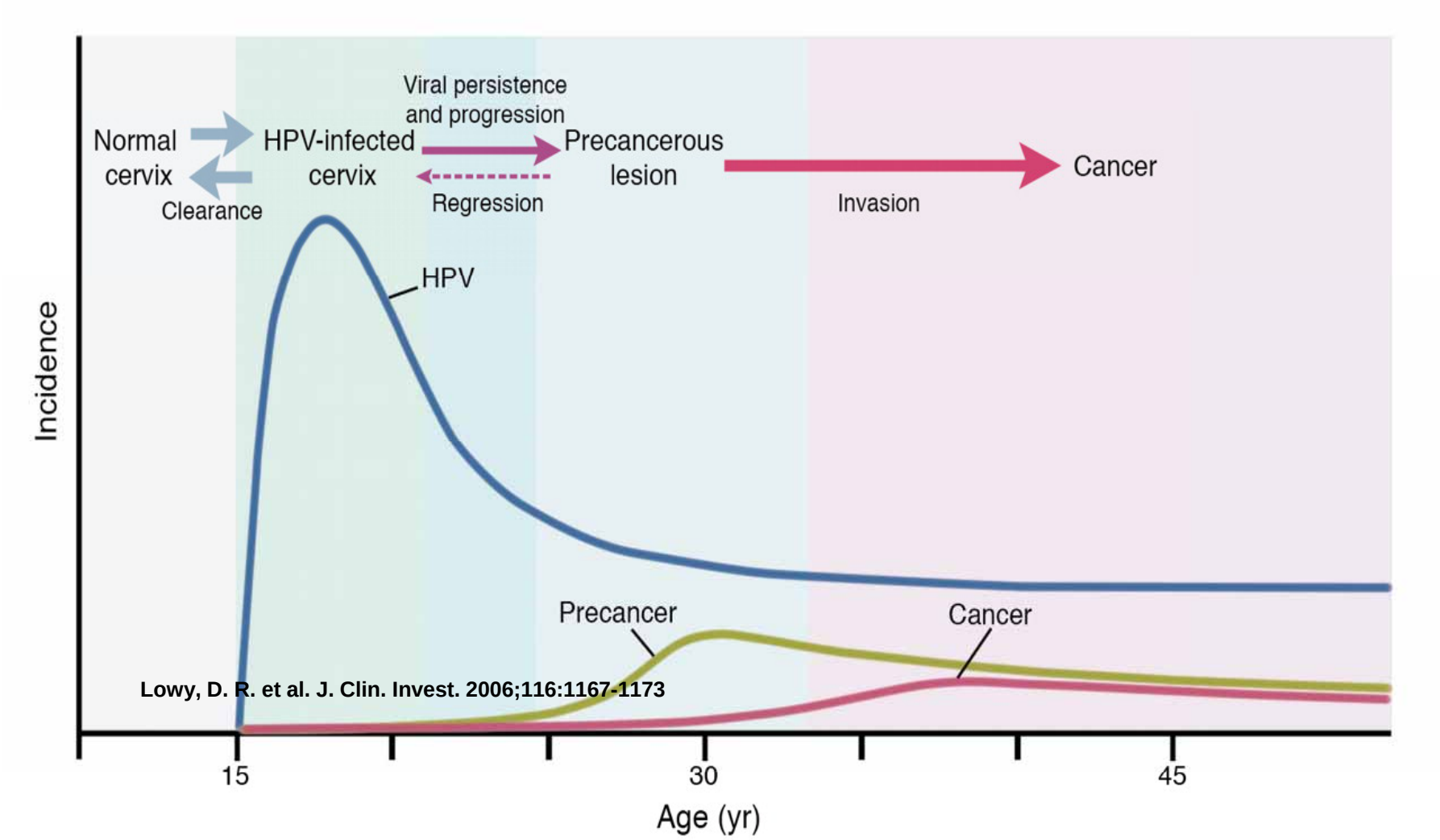
Relationship among incidences of cervical HPV infection, precancer, and cancer



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Where are we now in research on vaccine design for Influenza and HIV?

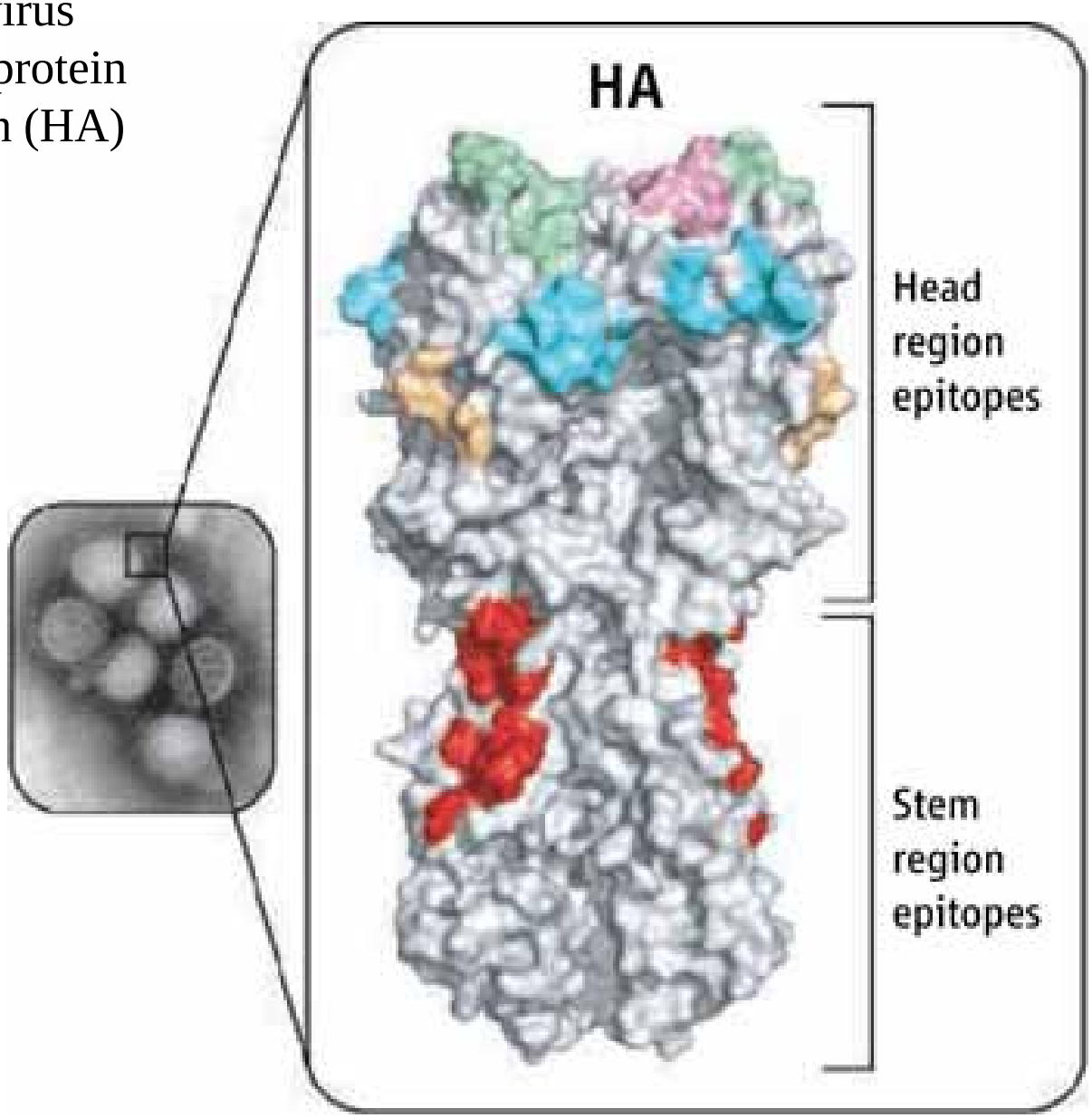
Recent major studies published in ***Science*** (August 2010):

Wei et al.: *"Induction of Broadly Neutralizing H1N1 Influenza Antibodies by Vaccination"*

Zhou et al.: *"Structural Basis for Broad and Potent Neutralization of HIV-1 by Antibody VRC01"*

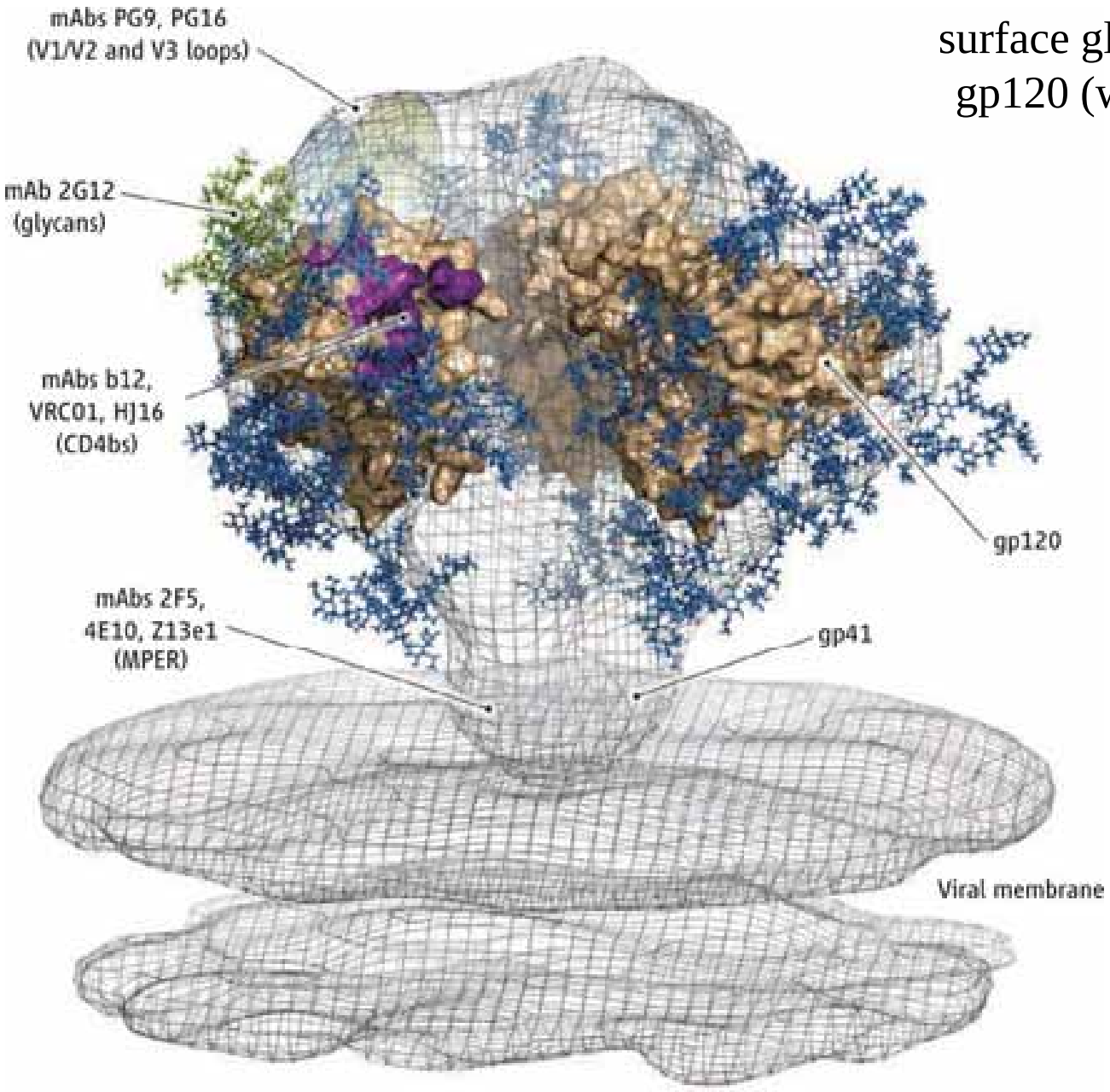
Wu et al.: *"Rational Design of Envelope Identifies Broadly Neutralizing Human Monoclonal Antibodies to HIV-1"*

Influenza virus surface glycoprotein hemagglutinin (HA)



From Doms Perspective "*Prime, Boost, and Broaden*"; ***Science 329***: 1021, 27 August 2010.

HIV
surface glycoprotein
gp120 (with gp41)



From Burton and Weiss Perspective “A Boost for HIV Vaccine Design”; Science 329, 770 , 13 August 2010.

Where might we be about 10 years or so from now?

Available vaccines that induce a strong
“broadly neutralizing” immune response
against diverse, multiple strains of
Influenza and HIV.