"Advances in Genetic Engineering: The Nuts, The Bolts, Frankenstein Monsters?, and Ethics"

Science Circle
February 25th 2018

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New Advances in Genetic Engineering

Background

DNA, Bacterial Immunology

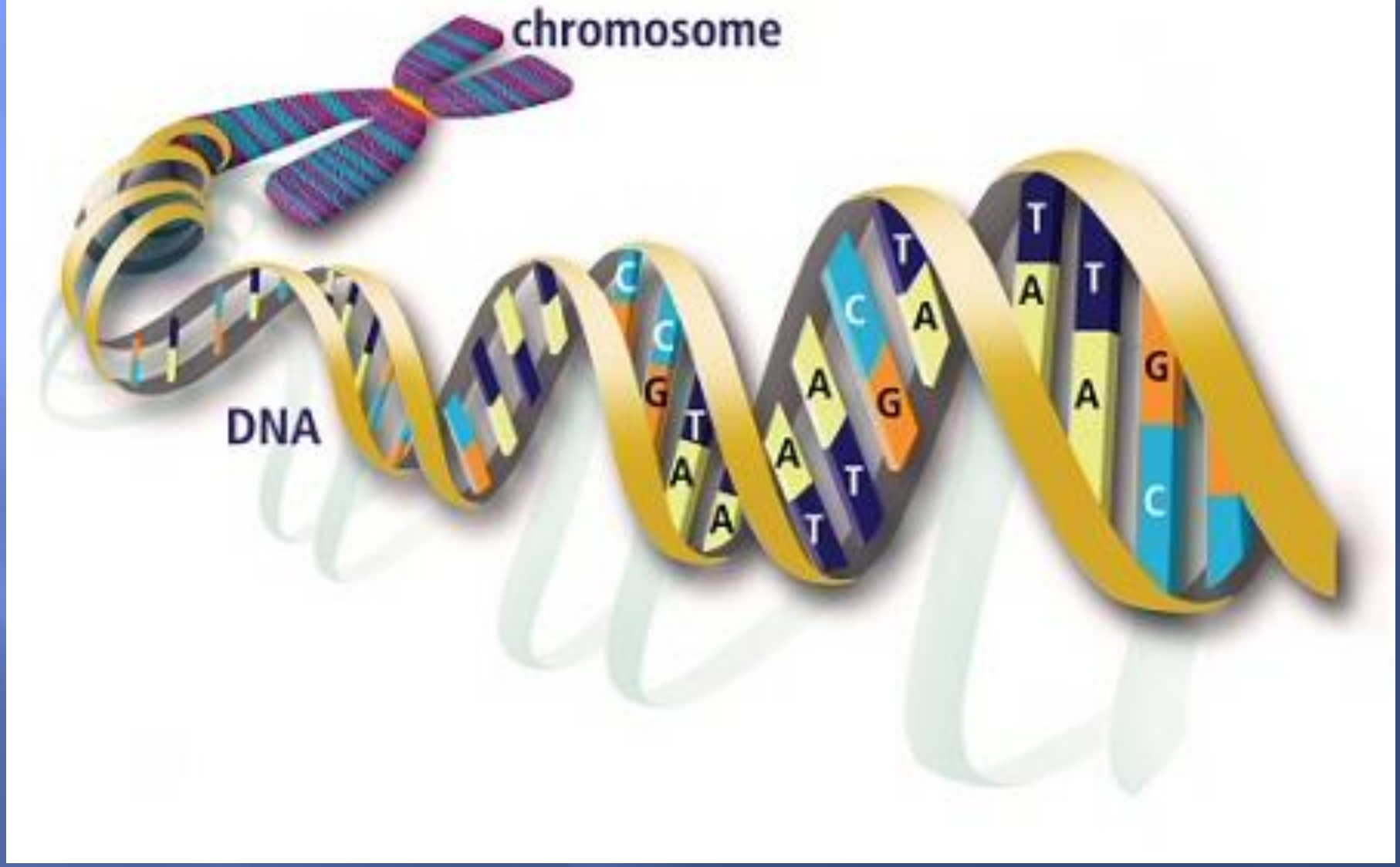
CRISPER/Cas9 Applications

Disease, Agriculture, Pest Management

Future Possibilities and Ethics

Moral Dilemmas of Human Enhancement

DNA Structure



DNA Structure

Hybridization

Hybridization: from a chemistry perspective, a stretch of DNA can find and bind to its complementary sequence

"seek and find and bind"

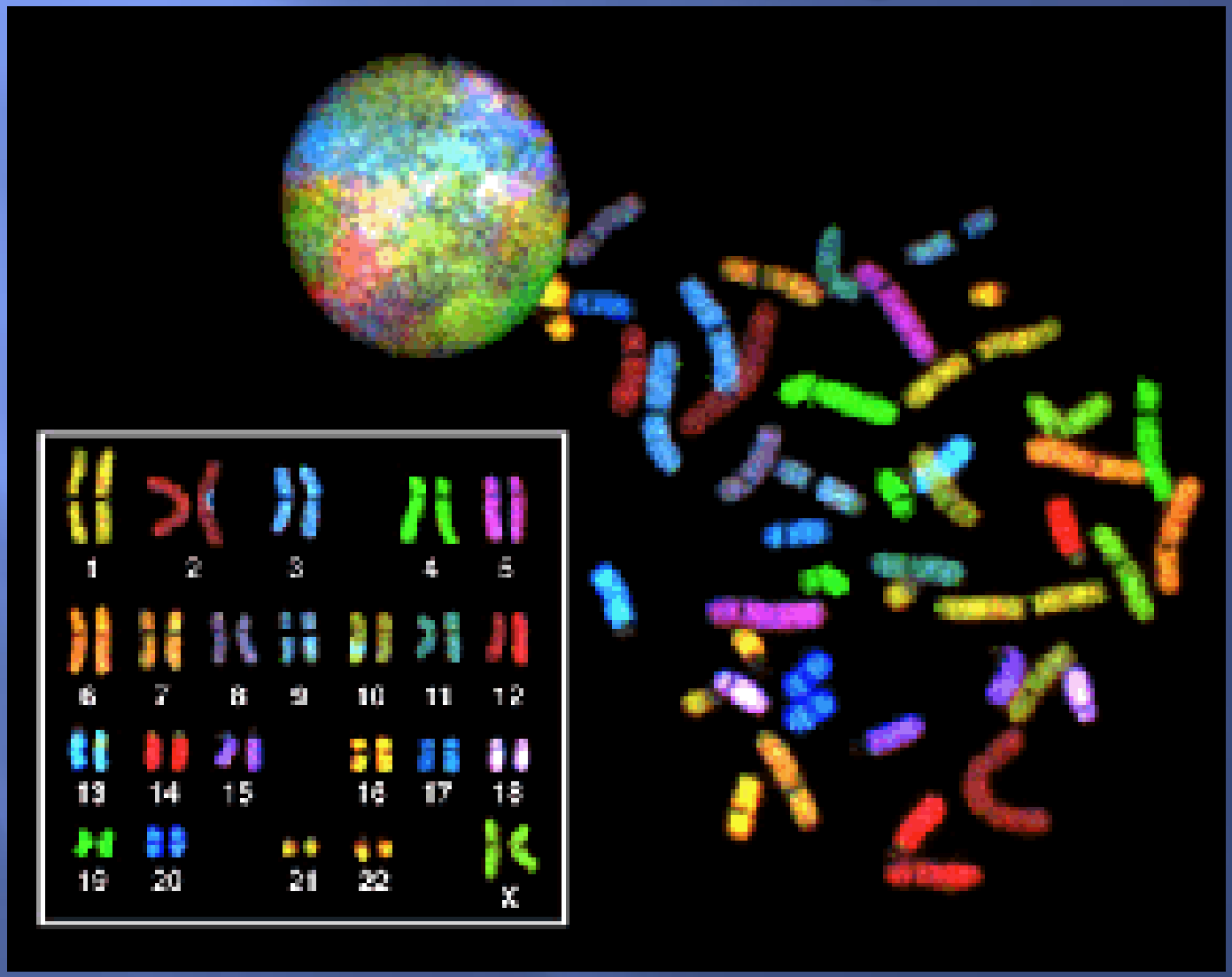
DNA Structure

Hybridization—It doesn't have to be a perfect match

"off-target"

DNA Technologies

Chromosome Painting



DNA Technologies

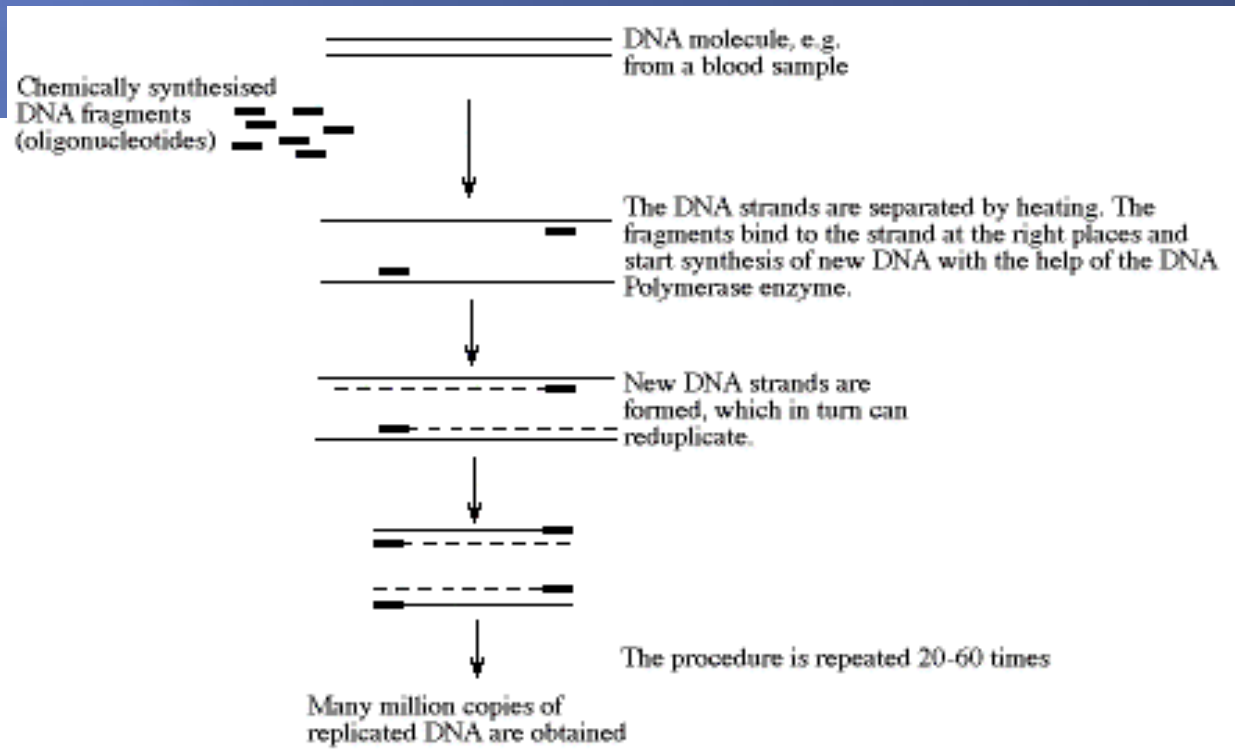
PCR

The Nobel Prize in Chemistry 1993

Kary B. Mullis
Prize share: 1/2

Michael Smith
Prize share: 1/2

The Nobel Prize in Chemistry 1993 was awarded *"for contributions to the developments of methods within DNA-based chemistry"* jointly with one half to Kary B. Mullis *"for his invention of the polymerase chain reaction (PCR) method"* and with one half to Michael Smith *"for his fundamental contributions to the establishment of oligonucleotide-based, site-directed mutagenesis and its development for protein studies"*.



Forensics
Paternity
Evolutionary Biology
Anthropology

DNA Technologies

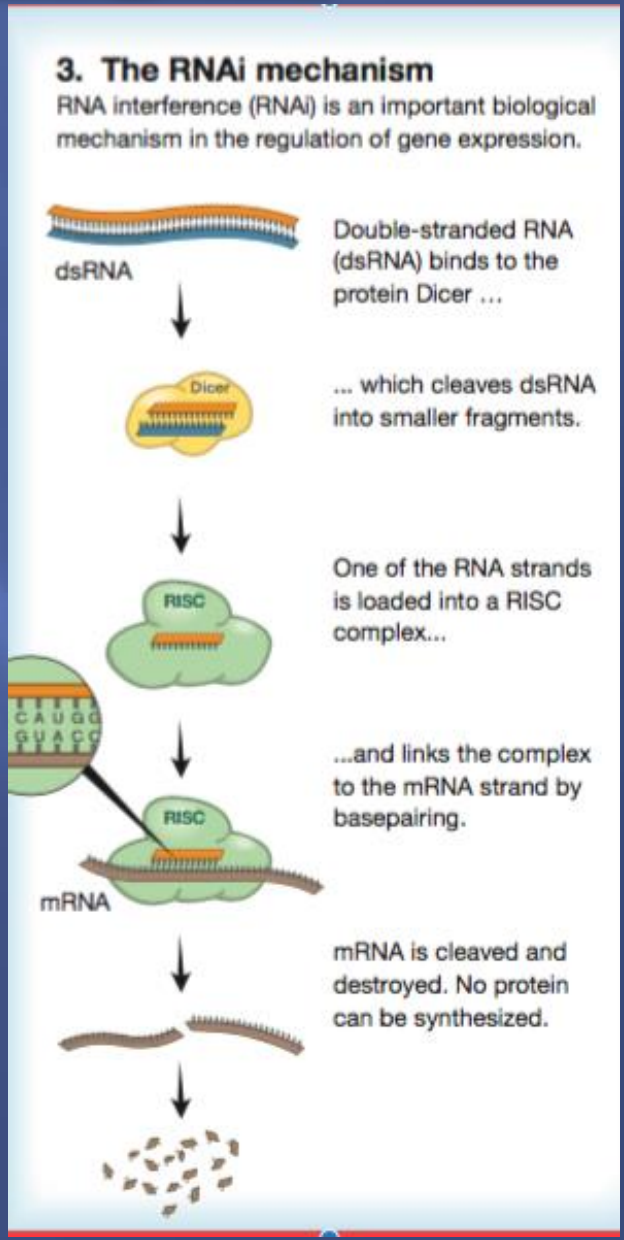
RNAi

The Nobel Prize in Physiology or Medicine 2006

Photo: L. Cicero
Andrew Z. Fire
Prize share: 1/2

Photo: J. Mottern
Craig C. Mello
Prize share: 1/2

The Nobel Prize in Physiology or Medicine 2006 was awarded jointly to Andrew Z. Fire and Craig C. Mello *"for their discovery of RNA interference - gene silencing by double-stranded RNA"*



Gene Silencing

DNA Technologies

Detection,
Amplification
Gene Silencing

But not Precise Manipulation at any sequence…
until CRISPR/Cas9

Human Immune System

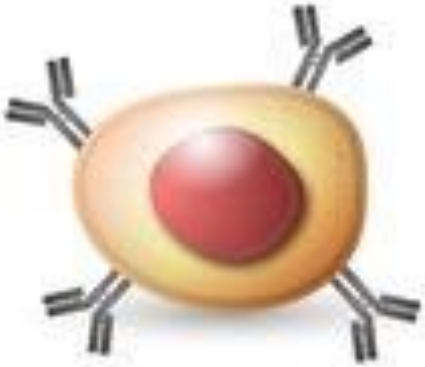
Neutrophil

Eosinophil

Basophil

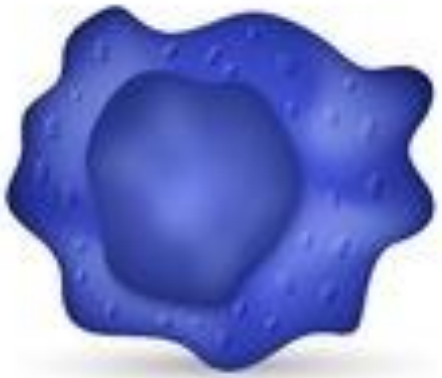
Monocyte

T Cell



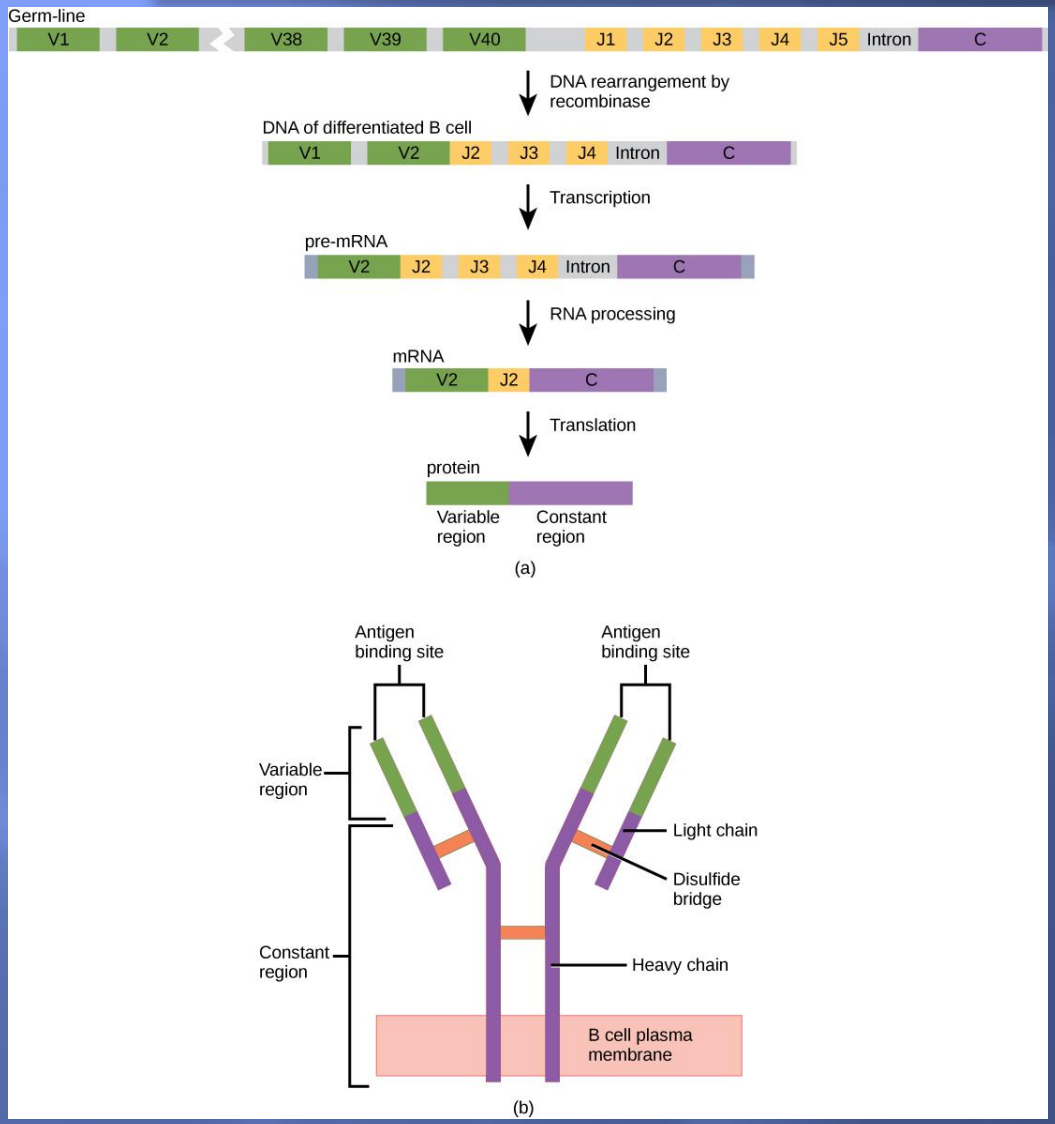
B Cell

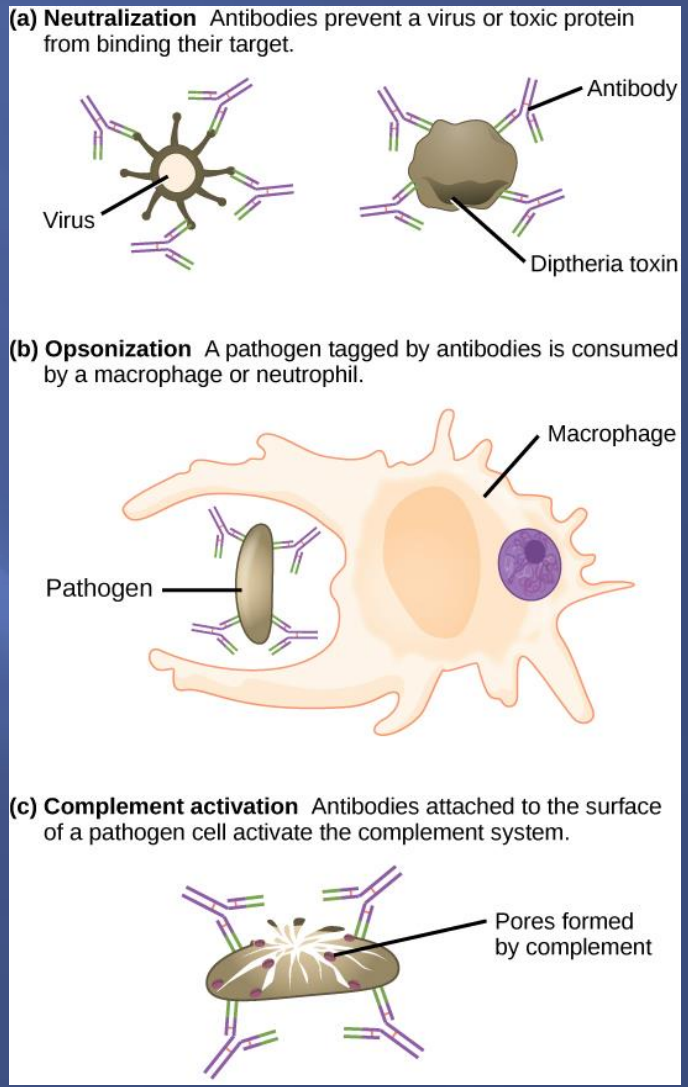
Natural killer



Macrophage

Mammalian Immune System

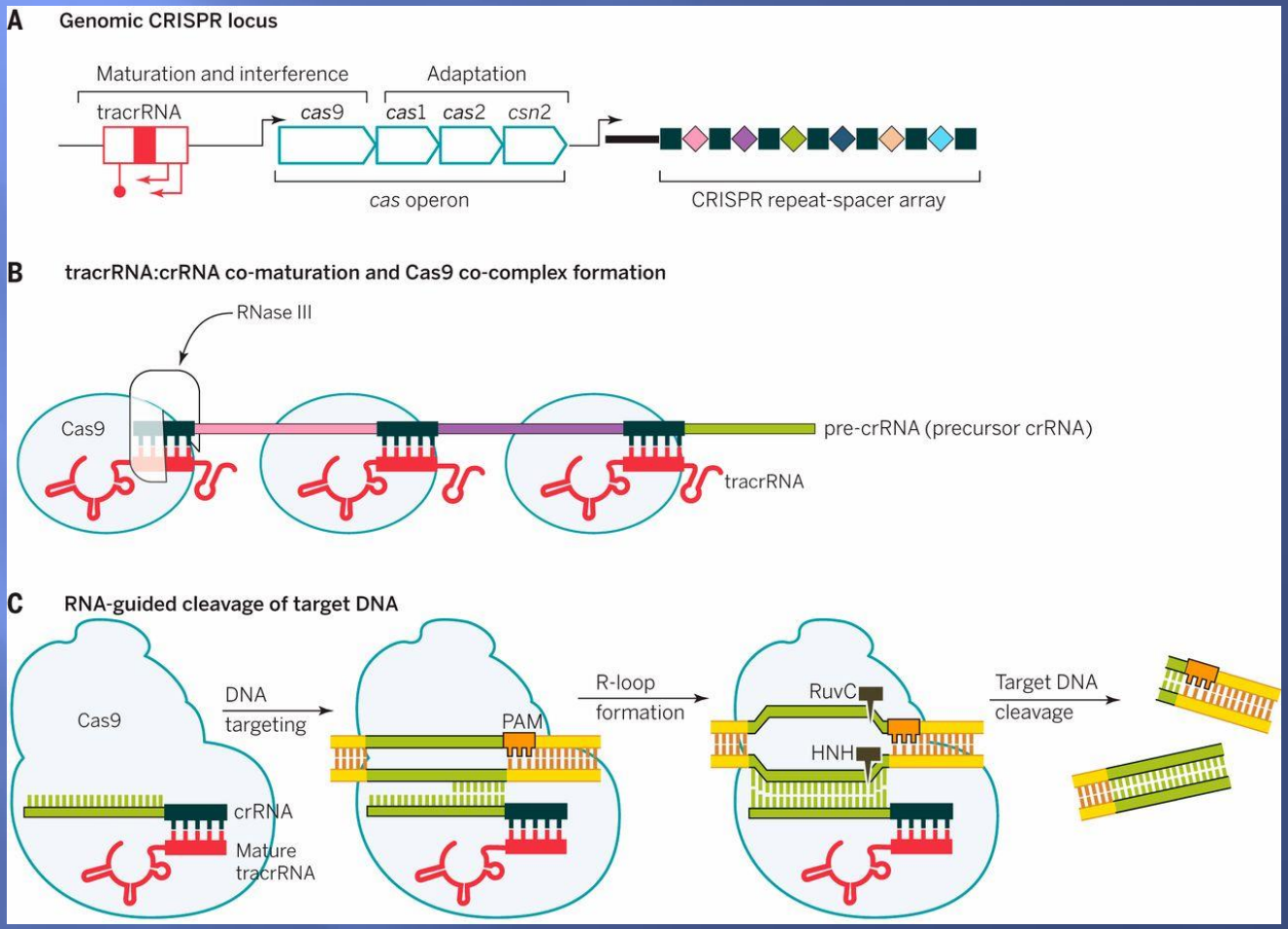




OpenStax, Biology. OpenStax CNX. Dec 19, 2017 http://cnx.org/contents/185cbf87-c72e-48f5-b51e-f14f21b5eabd@10.120.

Bacterial Immune System

Fig. 2 Biology of the type II-A CRISPR-Cas system.The type II-A system from *S. pyogenes* is shown as an example.

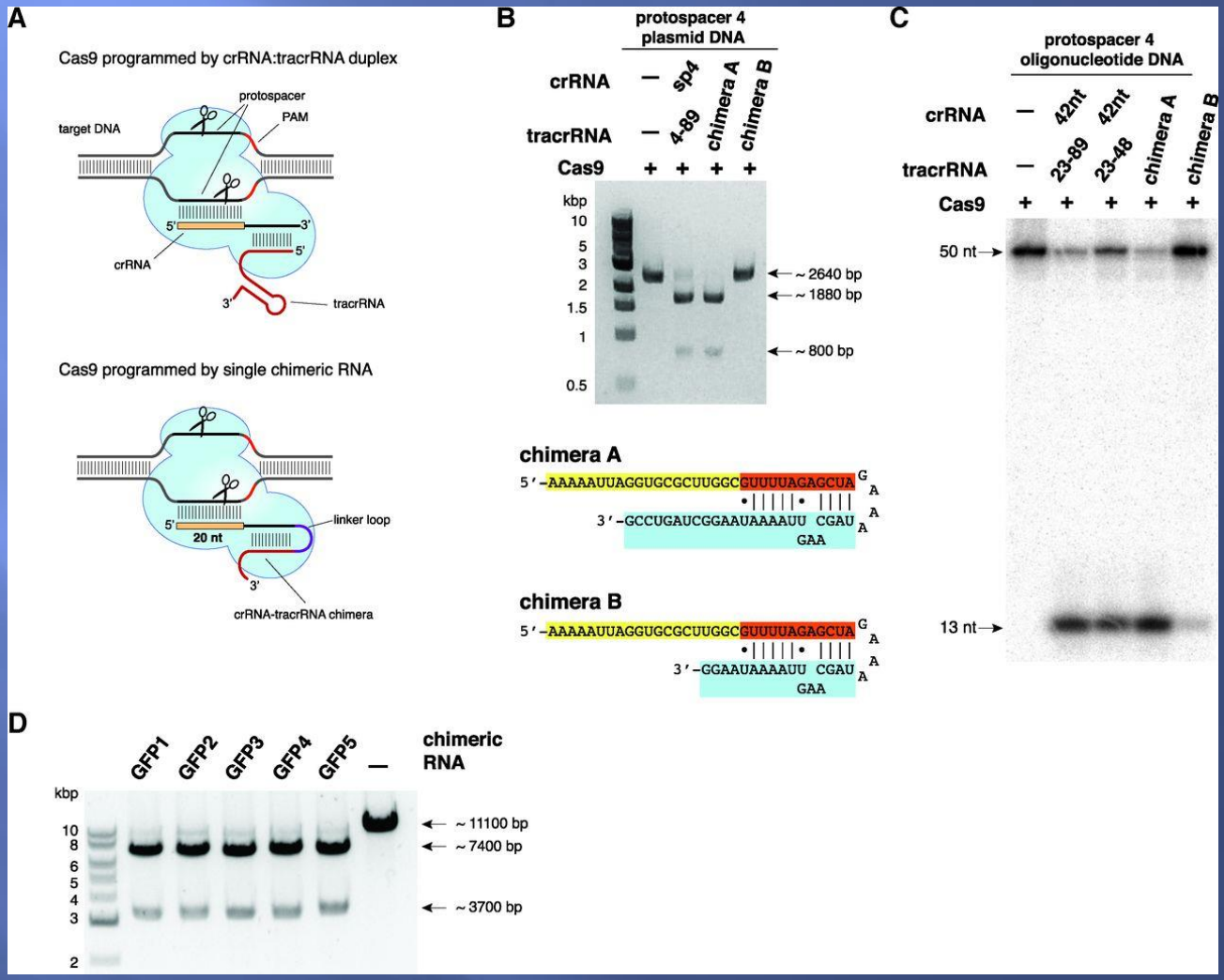


Jennifer A. Doudna, and Emmanuelle Charpentier Science 2014;346:1258096

Published by AAAS

CRISPR/Cas9 System

Fig. 5 Cas9 can be programmed using a single engineered RNA molecule combining tracrRNA and crRNA features.

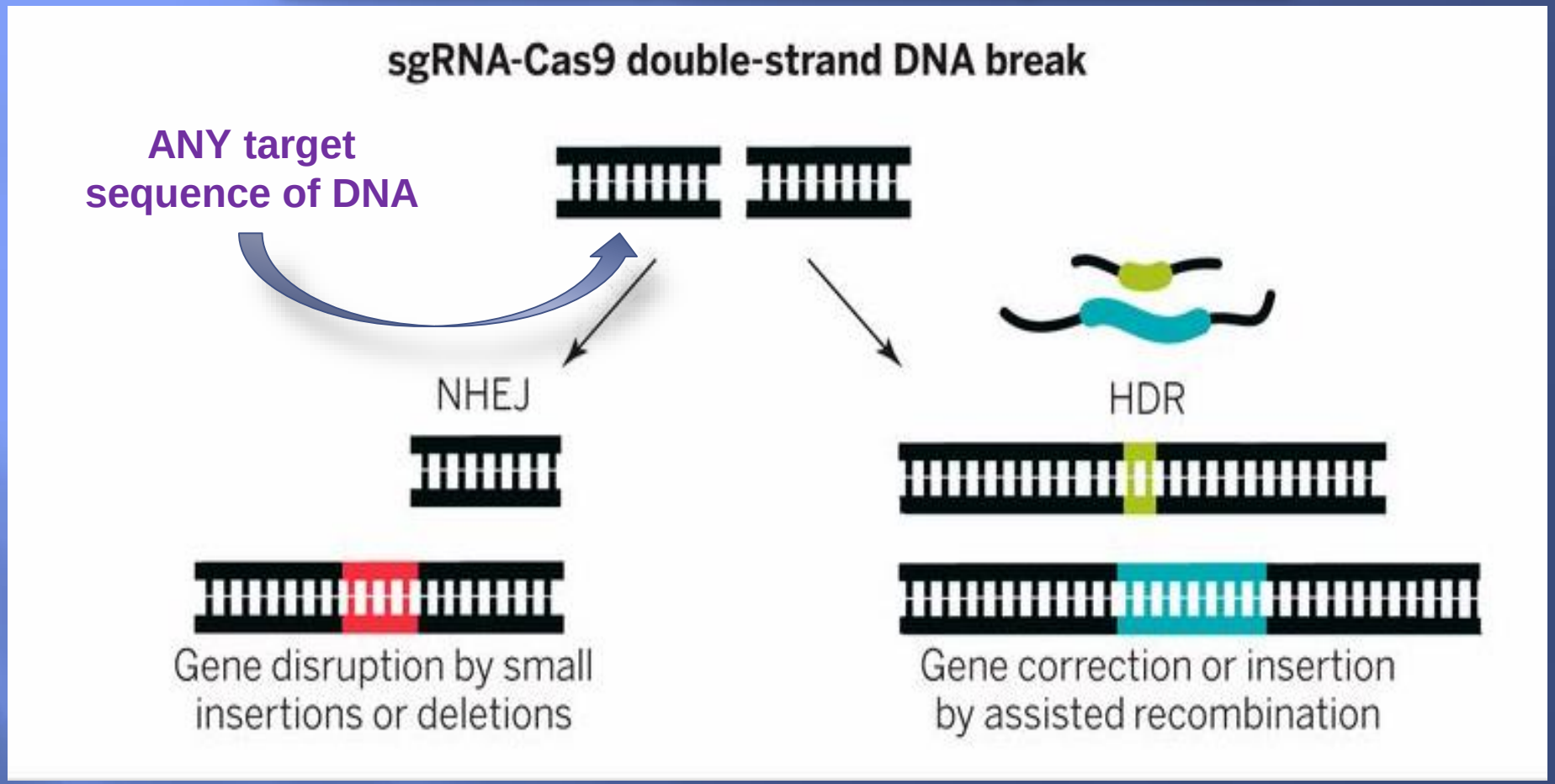


Martin Jinek et al. Science 2012;337:816-821

Science

AAAS

CRISPR/Cas9 System



Jennifer A. Doudna, and Emmanuelle Charpentier Science 2014;346:1258096

Science
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Genome Editing Examples

AIDS

Cancer

Drought Resistance

Genome Editing Examples

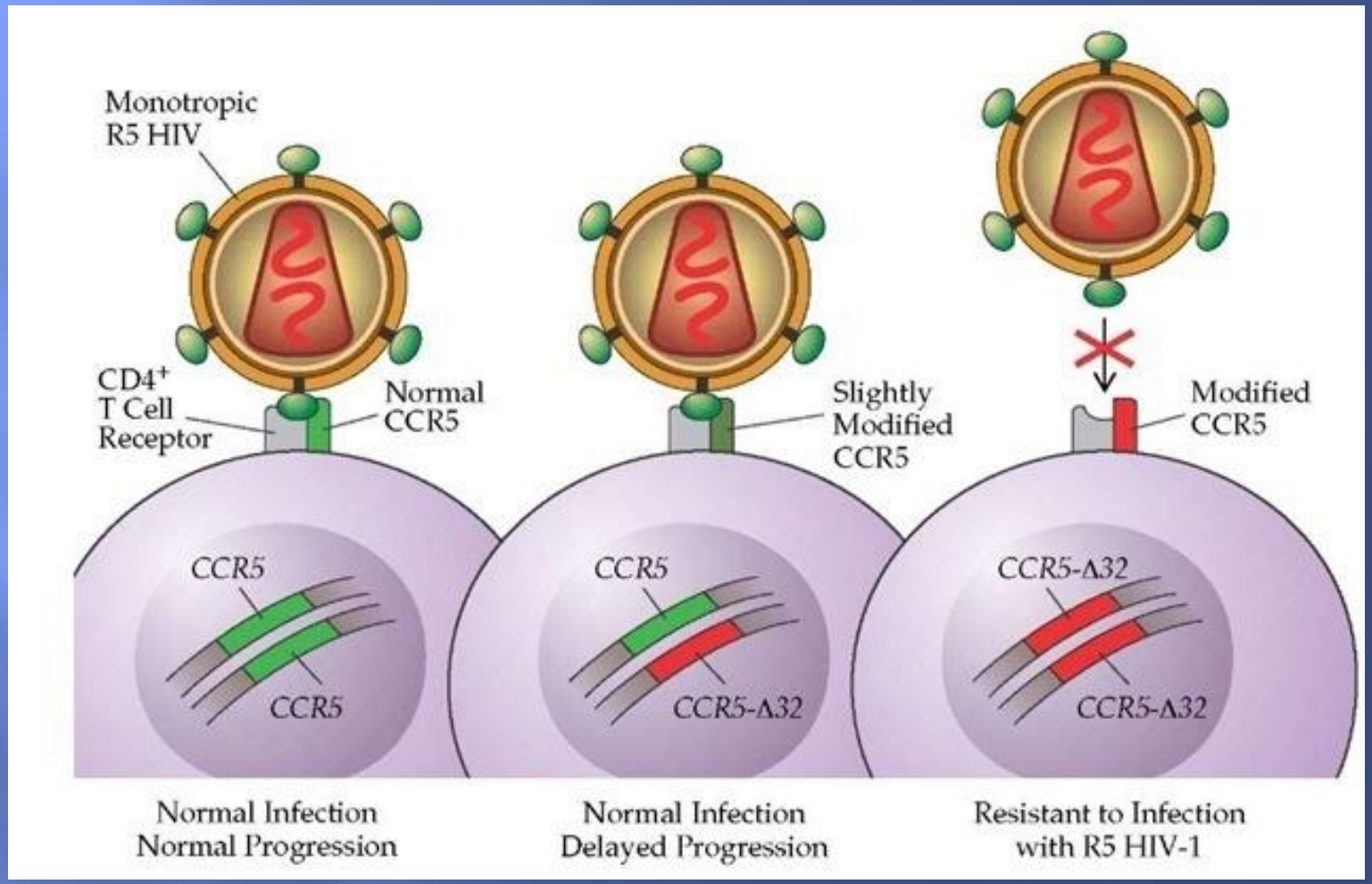
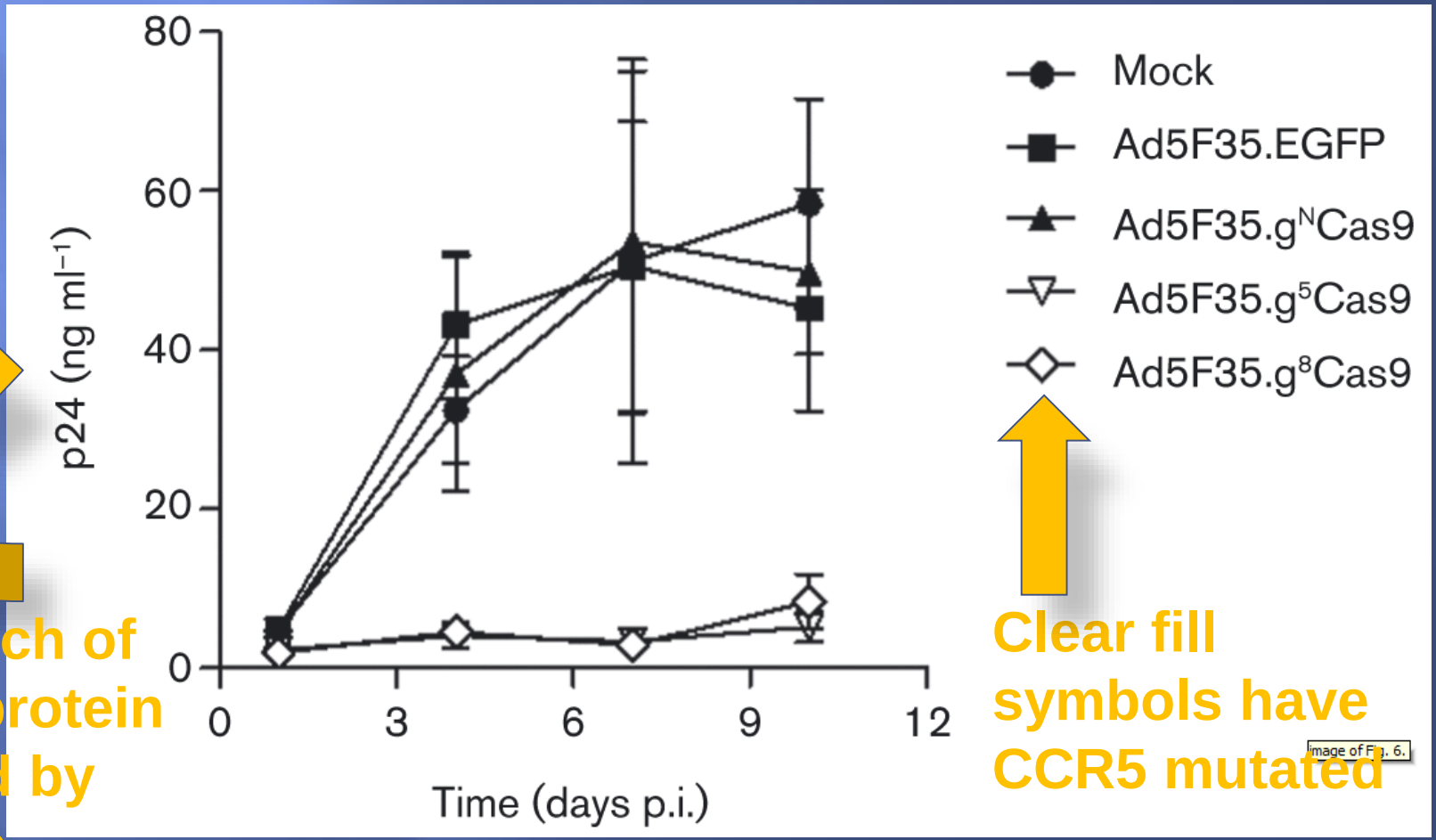


Figure 6 This diagram shows the relationship of genetic diversity of the CCR5 coreceptor to progression of and susceptibility to HIV infection.
http://what-when-how.com/acp-medicine/hiv-and-aids-part-2/

Genome Editing Examples

Inhibition of HIV-1 infection of primary CD4+ T-cells by gene editing of CCR5 using adenovirus-delivered CRISPR/Cas9
J. Gen. Virol., August 2015 96: 2381-2393



How much of an HIV protein secreted by the cells

Clear fill symbols have CCR5 mutated

Genome Editing Examples

The CRISPR/Cas9 system inactivates latent HIV-1 proviral DNA
Retrovirology 2015, 12:22

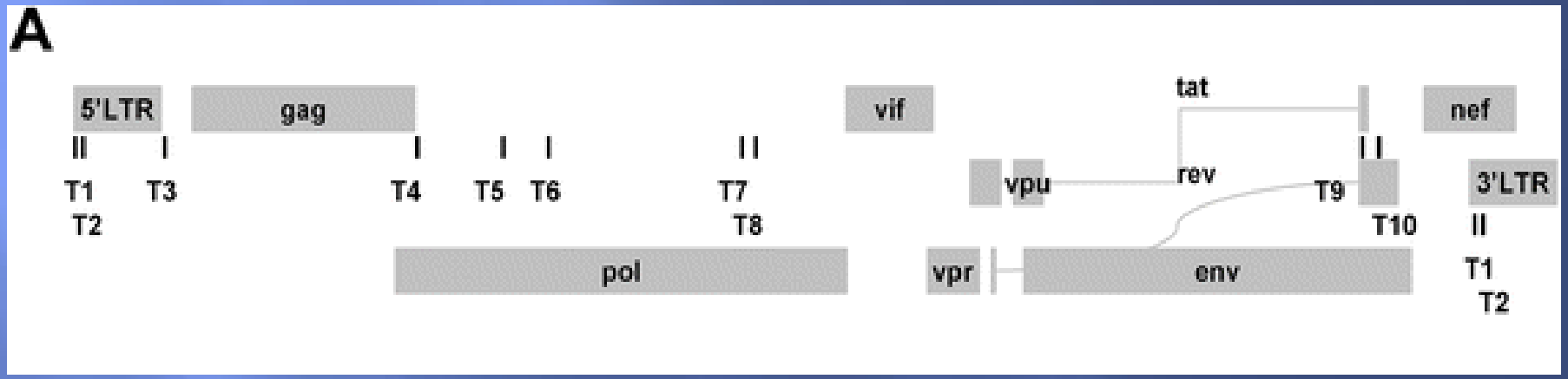
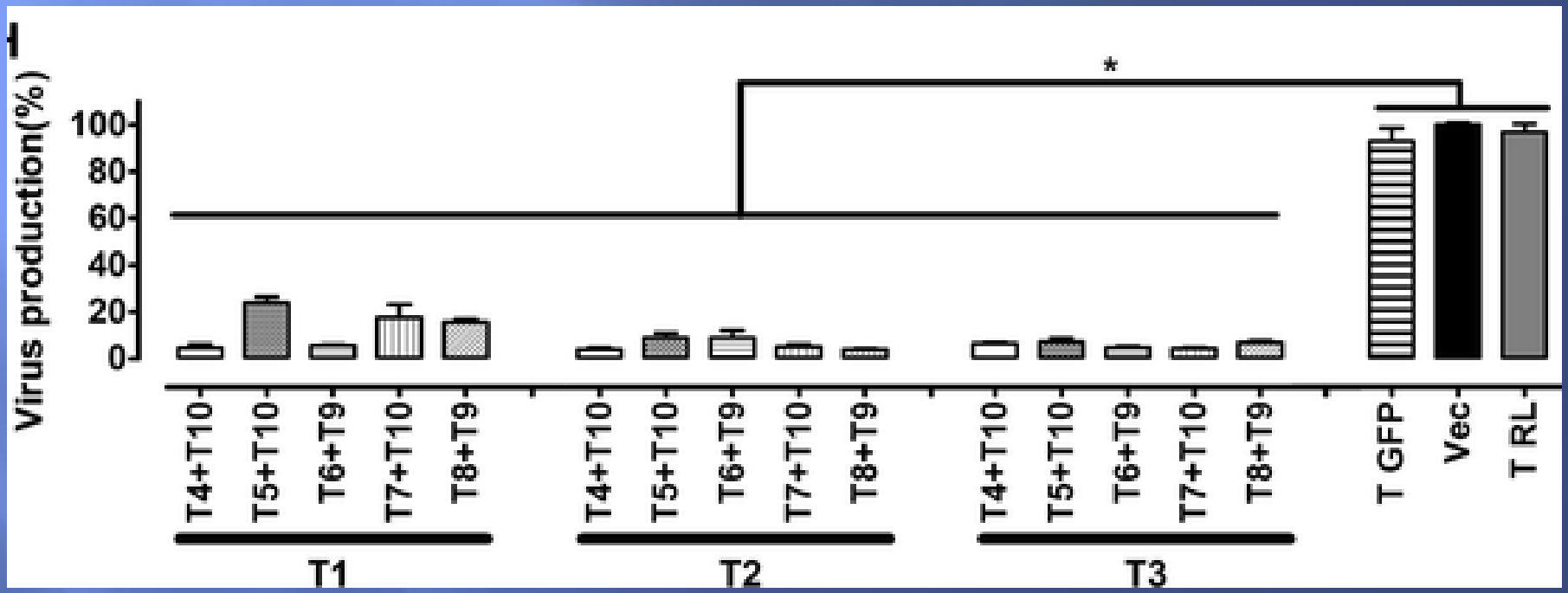


Figure 1
Illustration of the ten HIV-1 guide RNAs tested in this study. (A) Locations of the 10 guide RNAs (T1 to T10) in HIV-1 genome.

Genome Editing Examples

The CRISPR/Cas9 system inactivates latent HIV-1 proviral DNA
Retrovirology 2015, 12:22

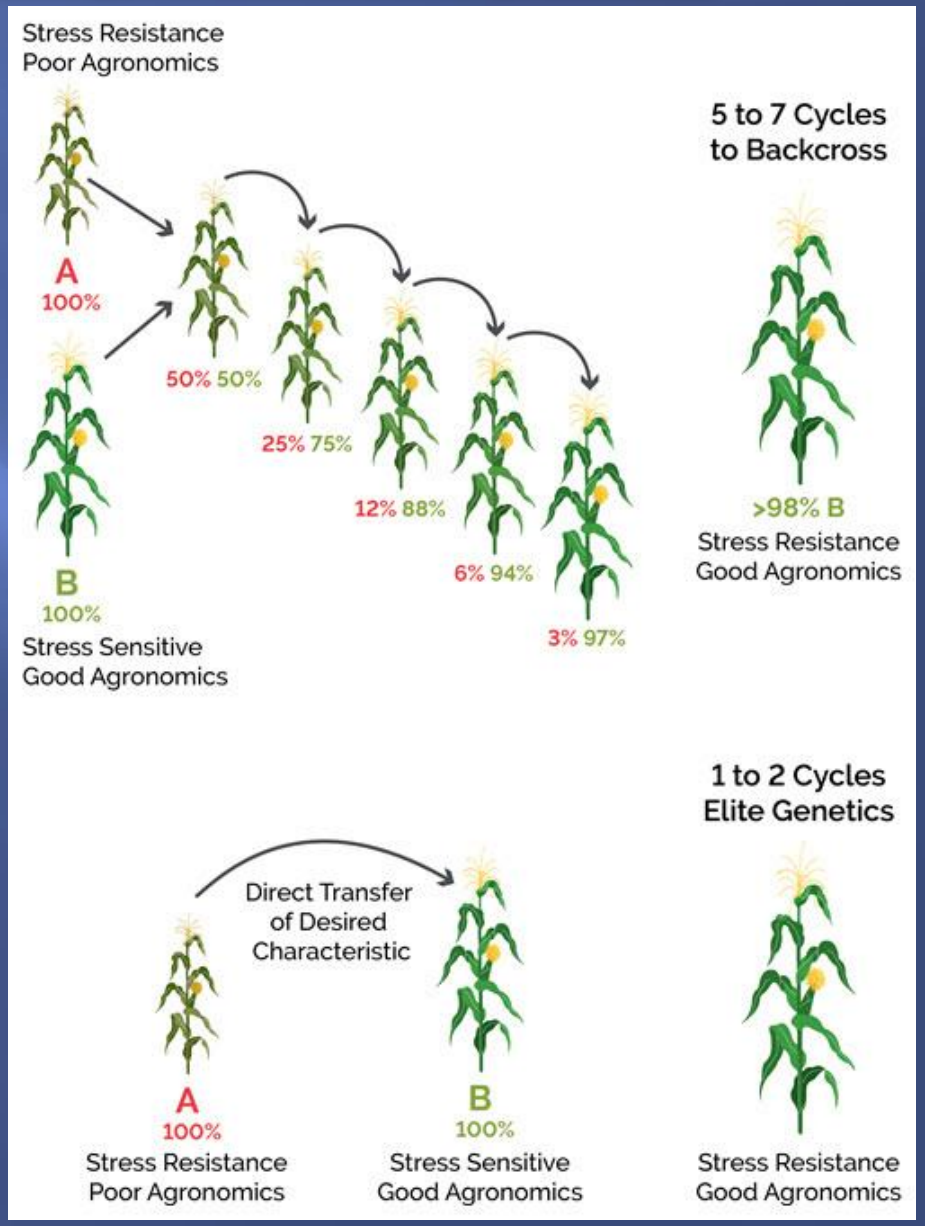


Genome Editing Examples

CRISPR-Cas Advanced Plant Breeding https://www.pioneer.com/home/site/us/agronomy/library/crispr-cas/

ARGOS8 variants generated by CRISPR-Cas9 improve maize grain yield under field drought stress conditions

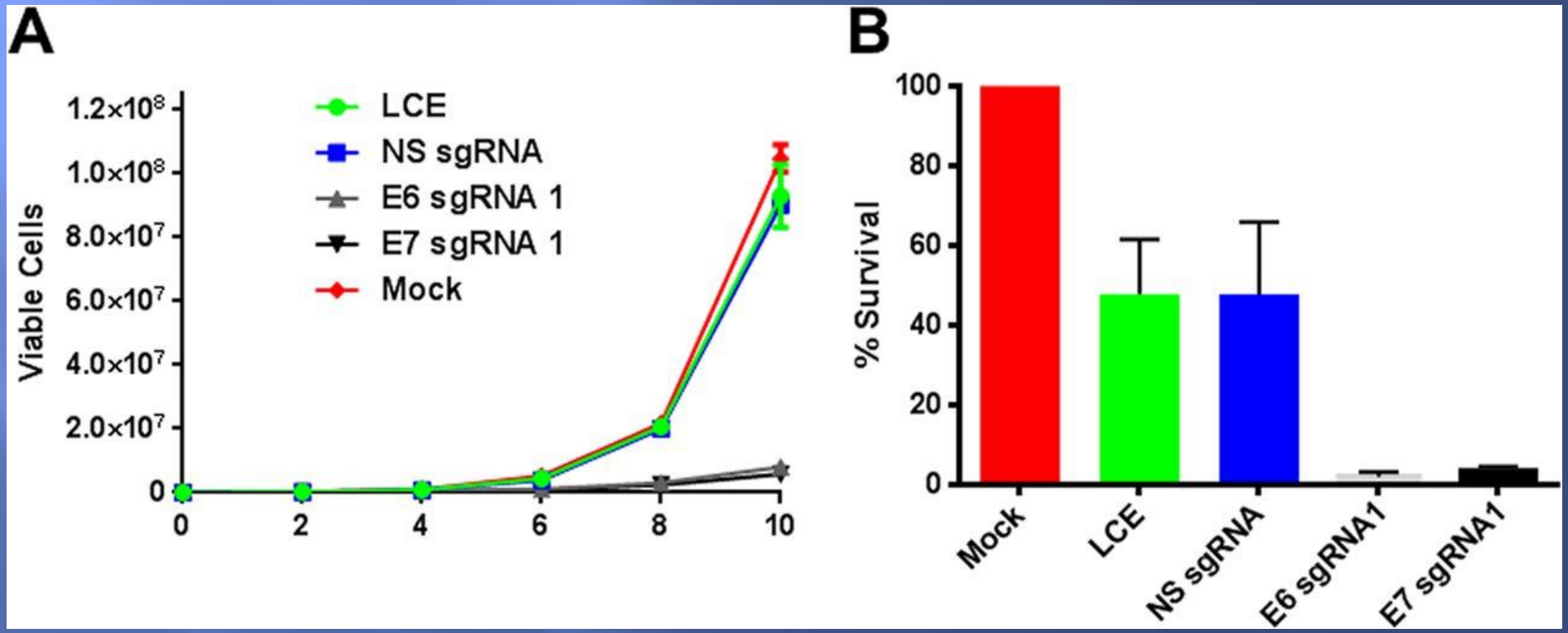
Plant Biotechnology Journal (2016), pp. 1–10



Genome Editing Examples

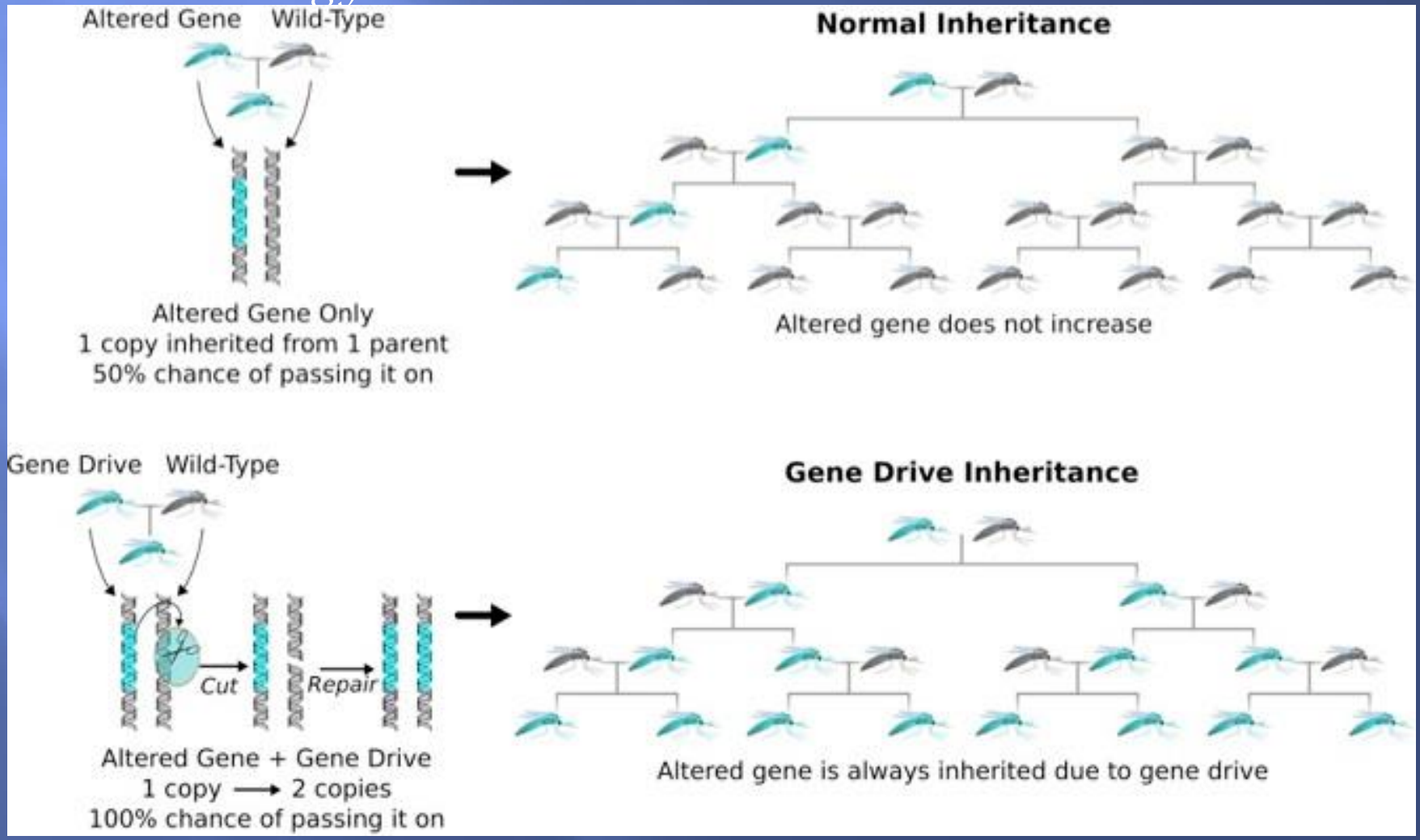
Inactivation of the Human Papillomavirus E6 or E7 Gene in Cervical Carcinoma Cells by Using a Bacterial CRISPR/Cas RNA-Guided Endonuclease

J. Virol. October 2014 vol. 88no. 20 11965-11972



Genome Editing Examples

A CRISPR-Cas9 gene drive system targeting female reproduction in the malaria mosquito vector *Anopheles gambiae*
Nature Biotechnology: 7 December 2015



Future Directions

Human germline or somatic tissue editing

-Can we control “off-target” effect?

-don’t want to cure cancer and make new ones at the same time

Future Directions

Human Germline editing

-are we content with just treating diseases after they manifest?

-is it not a moral obligation to avoid trauma and suffering before it begins?

Future Directions

Human Germline editing

-Do we understand the implications in all situations of all genetic “defects?”

Cystic Fibrosis and Sickle Cell Anemia have selective advantages when heterozygous

Future Directions