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Viral genetics

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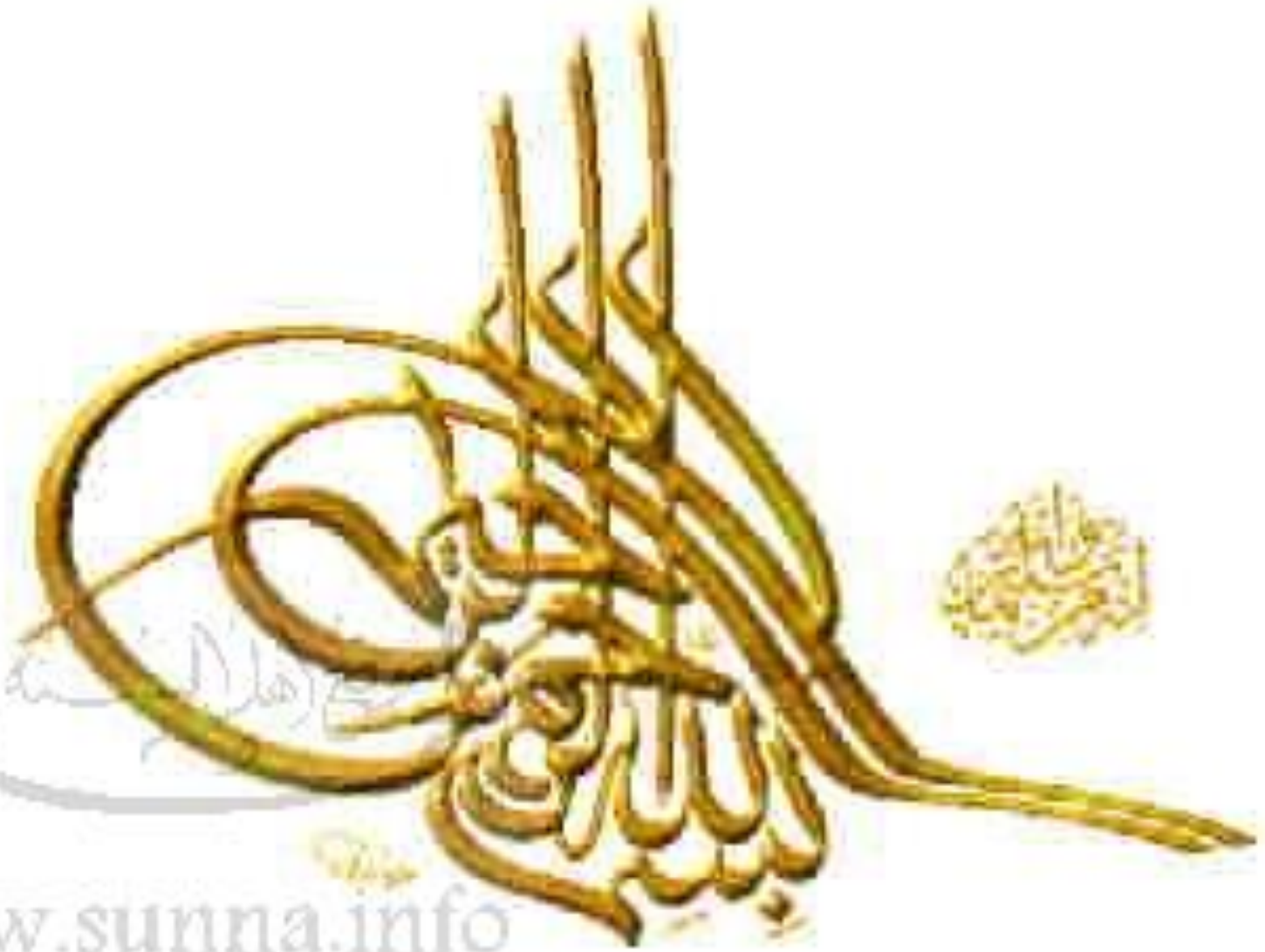


Genetics of Animal Viruses

- ***Genetic analysis*** is *a powerful approach toward understanding the structure and function* ***of the viral genome***, its ***gene products***, and ***their roles*** in infection and disease.

- Variation in viral properties is of ***great importance for human medicine***:
  - ✓ Viruses that **have stable antigens** on their surfaces (poliovirus, measles virus) can be controlled by vaccination,
  - ✓ Other viruses that exist as **many antigenic types** (rhinoviruses),
  - ✓ **Or change frequently** (influenza virus A) are difficult to control by vaccination.

- Viral genetics analysis may help to develop more **effective vaccines** and ***antiviral therapy***.

Genetics of Animal Viruses

- The following terms are basic to a discussion of genetics:

- The **genome** is the sum of the genes of an organism.

- **Genotype** refers to the genetic constitution of an organism.
- ***Phenotype*** refers to the observable properties of an organism, which are produced by the genotype in cooperation with ***the environment*** and other factors such as ***epigenetic factors***

- ***Wild-type virus*** denotes the original virus from which mutants are derived and with which the mutants are compared.

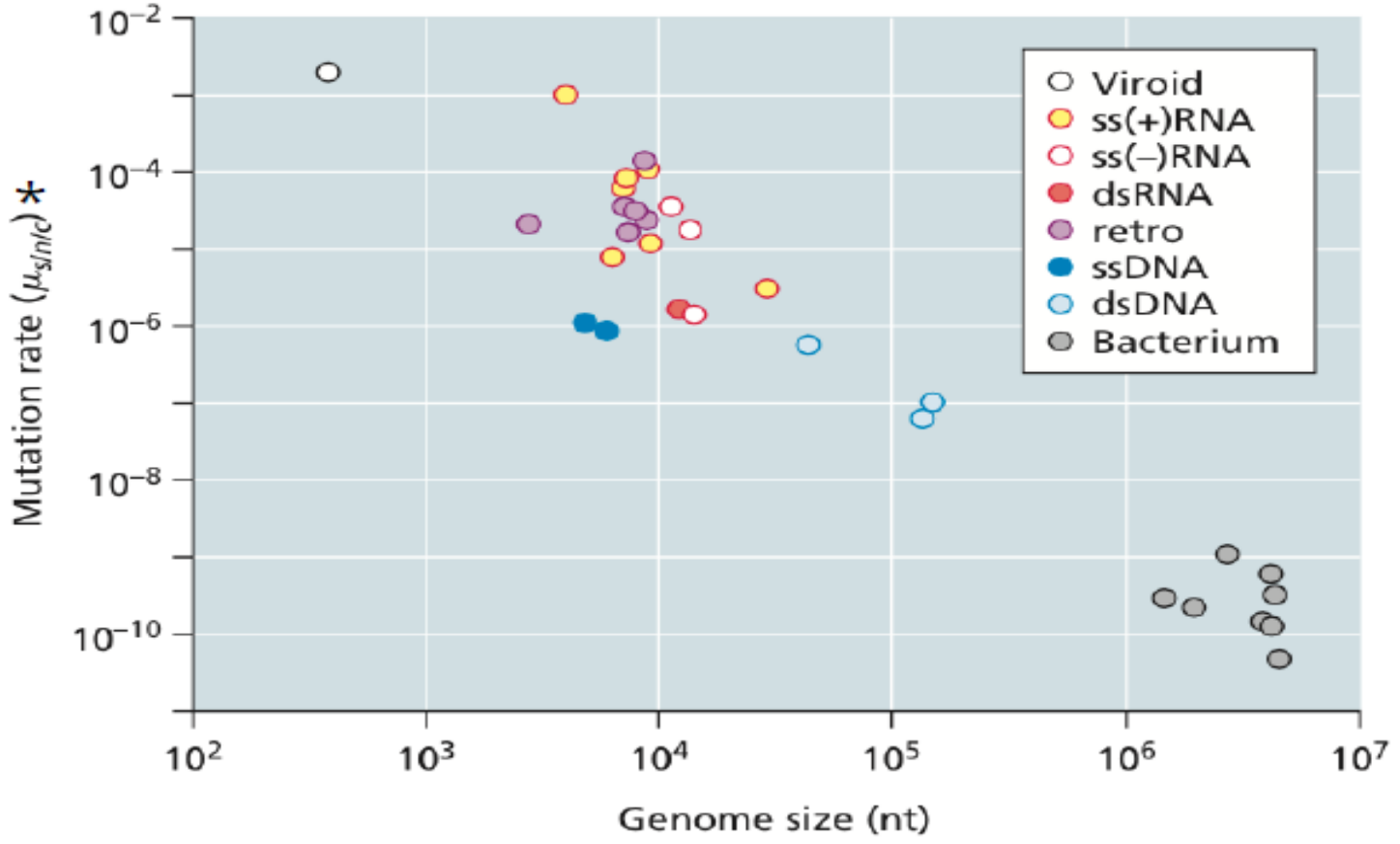
- A **mutation** is a heritable change in the genotype.

- **Defective Viruses** A defective virus is one that lacks one or more functional genes required for viral replication.

Viral genetics

- The study of viral genetics falls into two general areas:
- (1) mutations and their effect on replication and pathogenesis
- (2) the interaction of two genetically dis-
- tinct viruses that infect the same cell.

Genome size and mutation Rate



Types of Virus Mutants

- Some markers commonly used FOR DETECTION OF MUTATIONS include :

  plaque morphology, antibody escape or resistance to neutralizing antisera, loss of a virus protein, drug resistance, host range, and inability to grow at low or high temperatures

  (Conditional-lethal mutants) .
- Defective Viruses

Types of Virus Mutants

- Mutations that inactivate essential genes are termed **lethal mutations. These mutants are difficult to isolate** because the virus cannot replicate.
- A **deletion mutant** results from loss or selective removal of a portion of the genome and the function it encodes.
- Other mutations may produce **plaque mutants**, which differ from the **wild type** in the size or appearance of the infected cells;
- **host range mutants, which differ in the tissue type or species of target** cell that can be infected;
- **attenuated mutants, which** are variants that cause less serious disease in animals or humans.
- **Conditional mutants, such as temperature-sensitive (ts) or cold-sensitive mutants,**
- have a mutation in a gene for an essential protein that allows virus production only at certain temperatures. Whereas ts mutants generally grow well or relatively better at 30° C to 35° C, the encoded protein is inactive at elevated temperatures of 38° C to 40° C, preventing virus production.
- Live virus vaccines are often conditional or host range mutants and attenuated for human disease.

INTERACTIONS

- When two genetically distinct viruses infect a cell, different phenomena can ensue.
  (1) Recombination
  (2) Genetic Reactivation
  - Multiplicity reactivation
  - Marker rescue
  (3) Re assortment
  (4) Phenotypic mixing
  (5) Complementation
  (6) Interference

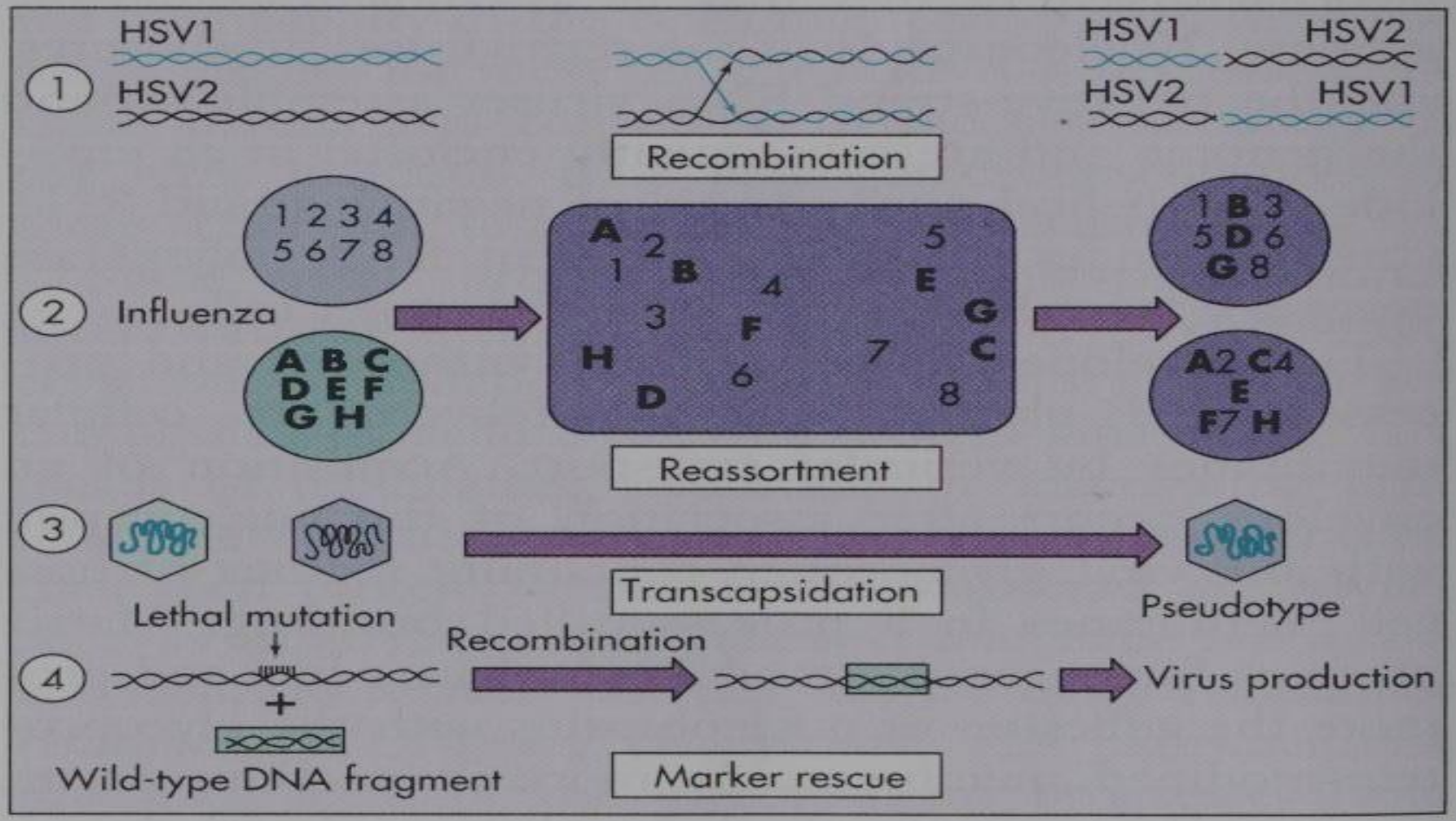


FIGURE 6–15. Genetic exchange between viral particles can give rise to new viral types, as illustrated. Representative viruses include the following: 1, intertypic recombination of herpes simplex virus type 1 *(HSV1)* and type 2 *(HSV2)*; 2, reassortment of two strains of influenza virus; 3, rescue of a papovavirus defective in assembly by a complementary defective virus (transcapsidation); and 4, marker rescue of a lethal or conditional mutation.

Genetics of Animal Viruses

- ***Interactions*** Among Viruses:

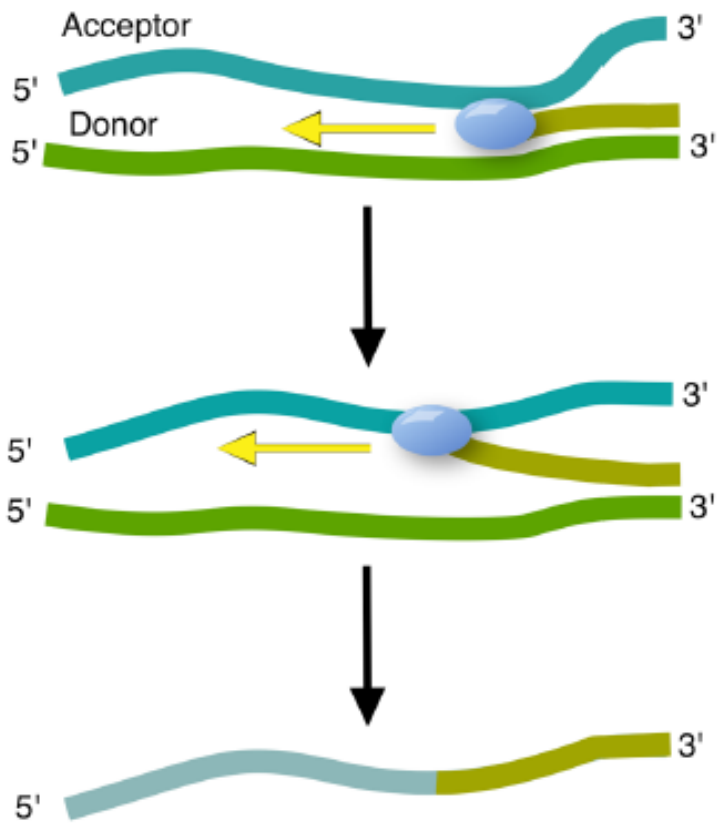
When two or more virus particles infect the same host cell, they may interact in a variety of ways. They must be sufficiently closely related, usually within ***the same viral family***, for most types of interactions to occur:

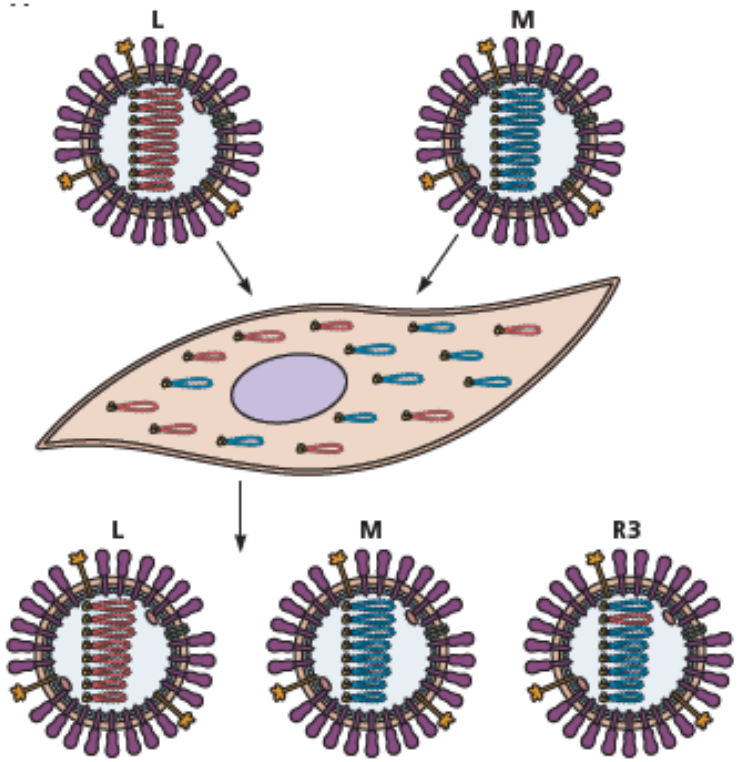
- ***Genetic interaction*** results in some progeny that are heritably (genetically) *different from either parent.*
- \

A) ***Recombination****:* Recombination results in the production of progeny virus (**recombinant**) that carries traits not found together in either parent.

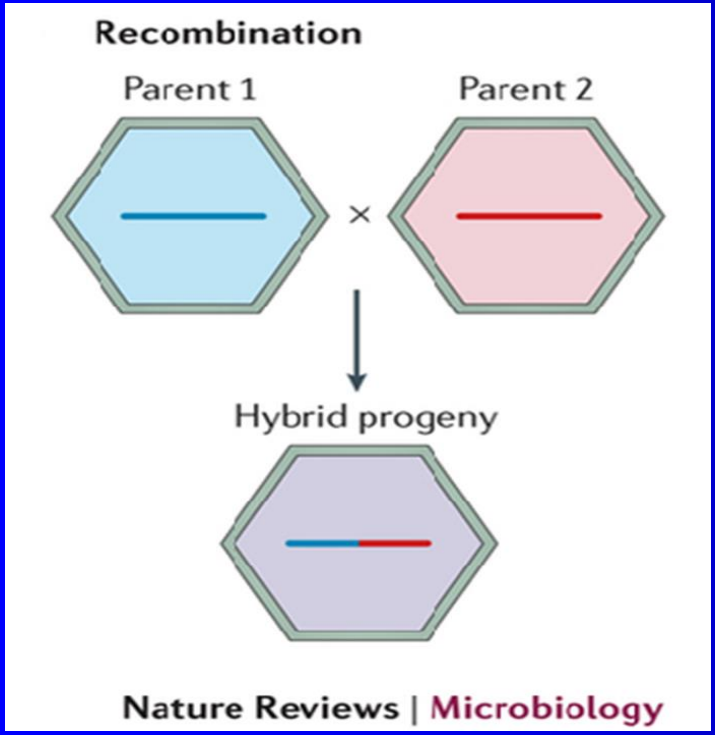
B) **Reassortment**: In the case of viruses with ***segmented genomes***, eg, influenza virus, the formation of recombinants is due to reassortment.

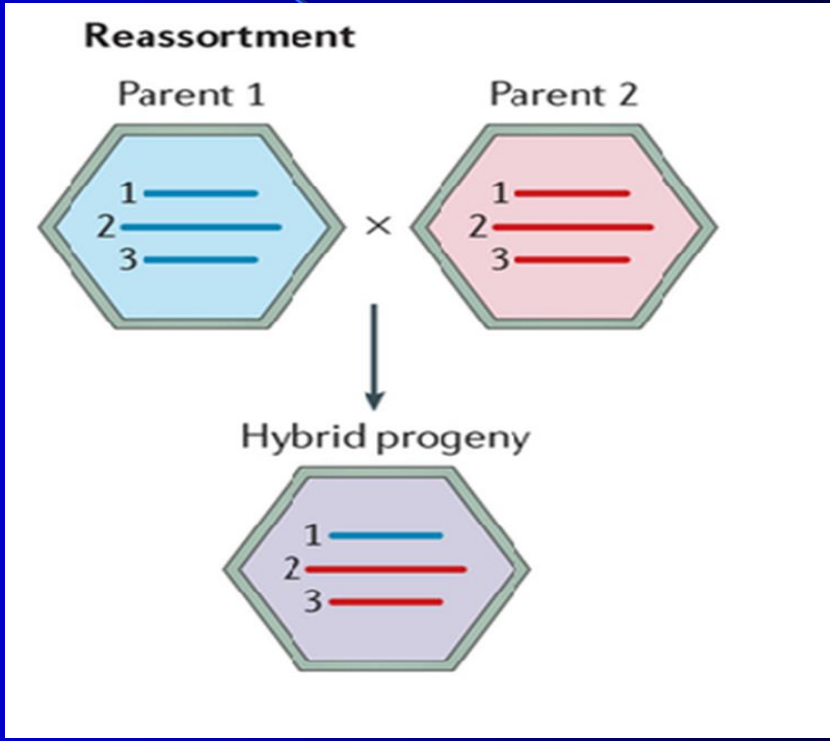
Variation further generated by recombination and reassortment



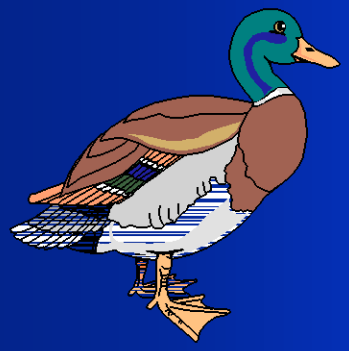


Principles of Virology, ASM Press


Recombination
Parent 1
Parent 2
Hybrid progeny
Nature Reviews | Microbiology


Reassortment
Parent 1
Parent 2
1
2
3
Hybrid progeny

Mechanism of antigenic shift

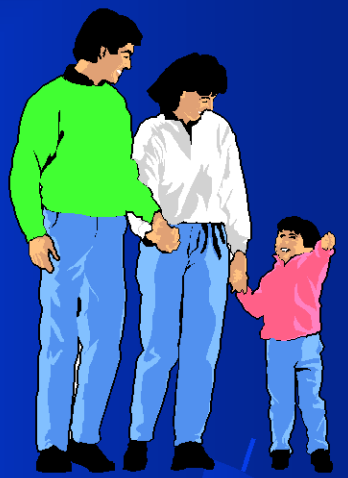


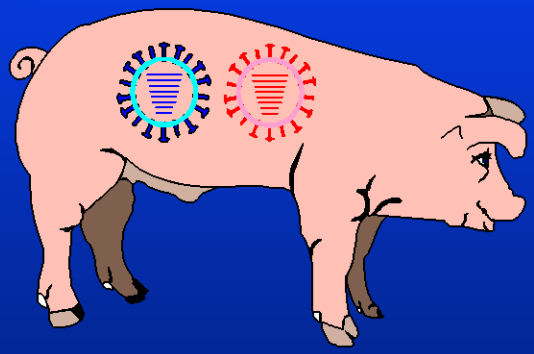
15 HAs
9 NAs

Non-human virus

DIRECT

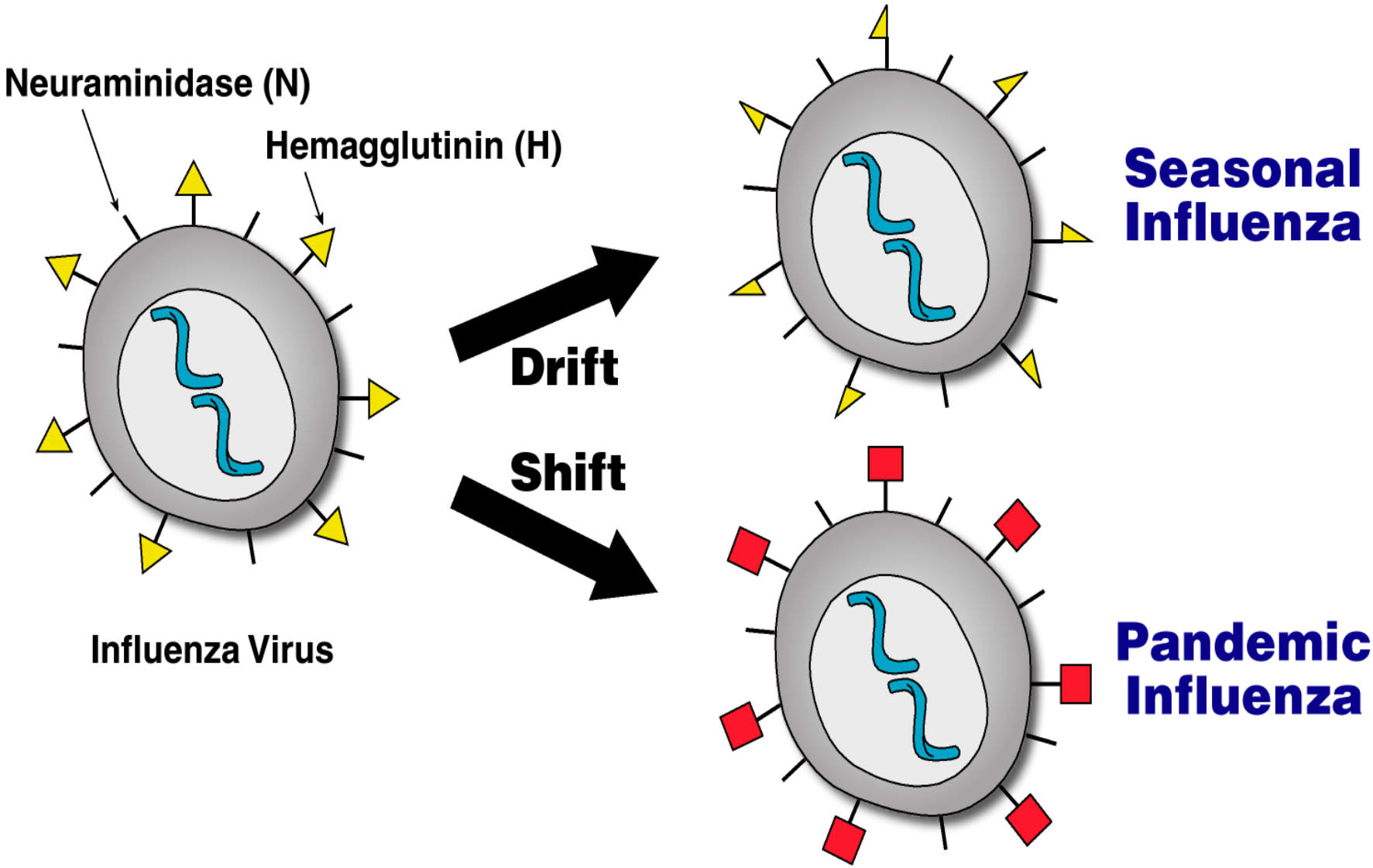
Human virus

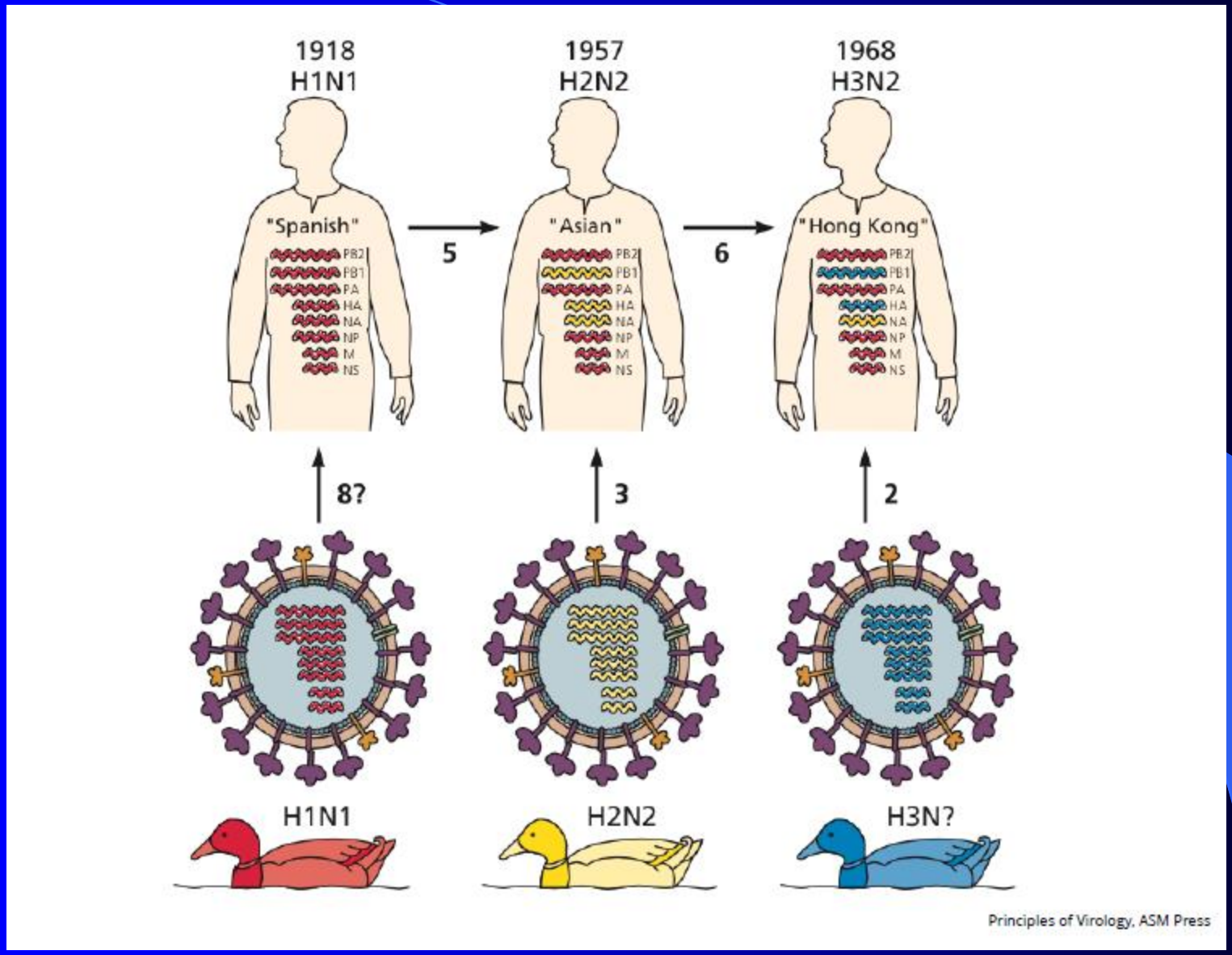




Reassortant virus

Influenza: Antigenic Drift and Shift




1918
H1N1
"Spanish"
PB2
PB1
PA
HA
NA
NP
M
NS
5
1957
H2N2
"Asian"
6
1968
H3N2
"Hong Kong"
8?
3
2
H1N1
H2N2
H3N?
Principles of Virology, ASM Press

Genetics of Animal Viruses

- C. **Complementation**: This refers to the interaction of viral gene products in cells infected with two viruses, ***one or both*** of which ***may be defective***.
  - It results in the replication of one or both under conditions in which replication would not ordinarily occur. **The basis for complementation is that one virus provides a gene product in which the second is defective**, allowing the second **virus to grow**.

- D. **Phenotypic Mixing**: This occurs when **the genome of one virus becomes randomly incorporated within capsid proteins** specified by a different virus or a capsid consisting of components of both viruses.

  - If the genome is encased in a ***completely heterologous protein coat***, this extreme example of phenotypic mixing may be called "***phenotypic masking***" or "**transcapsidation**."

Genetics of Animal Viruses

E) ***Interference:*** Infection of either cell cultures or whole animals with two viruses often leads to an inhibition of multiplication of one of the viruses, an effect **called interference**.

- **Several *mechanisms*** have been elucidated as causes of interference:

(1) One virus may inhibit the ability of the second to adsorb to the cell, either **by blocking its receptors** (retroviruses, enteroviruses) or by **destroying its receptors** (orthomyxoviruses).

(2) One virus may **compet**e with the second for components of the replication apparatus (eg, polymerase, translation initiation factor).

(3) The first virus may cause the infected cell to produce an inhibitor (**interferon**) that prevents replication of the second virus.

By exchange of genetic information