

Viral Voyages

Structural Biologist Mavis Agbandje-McKenna:

Understanding Viruses

FINDINGS

National Institutes of Health
National Institute of General Medical Sciences

Mavis Agbandje-McKenna Closes in on Viruses

Structural biologist Agbandje-McKenna wants to solve the mysteries of how viruses hop from one host to another.



Viruses

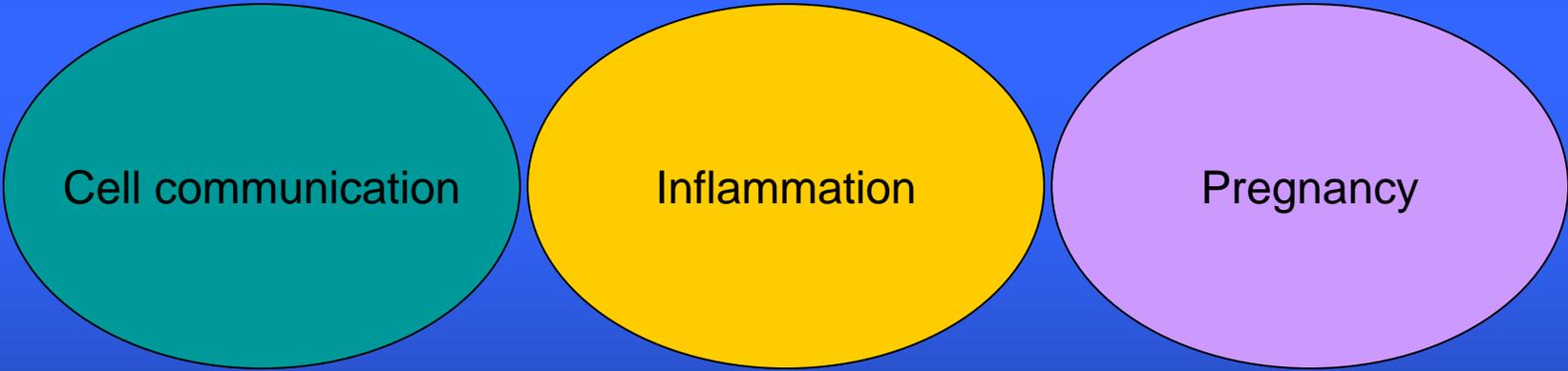
- Range from harmless to deadly
- Can change from harmless to deadly
- Need carbohydrates to enter cells

Question:

What is another name for carbohydrates?

Answer: Glycans

Carbohydrates: essential for many biological processes



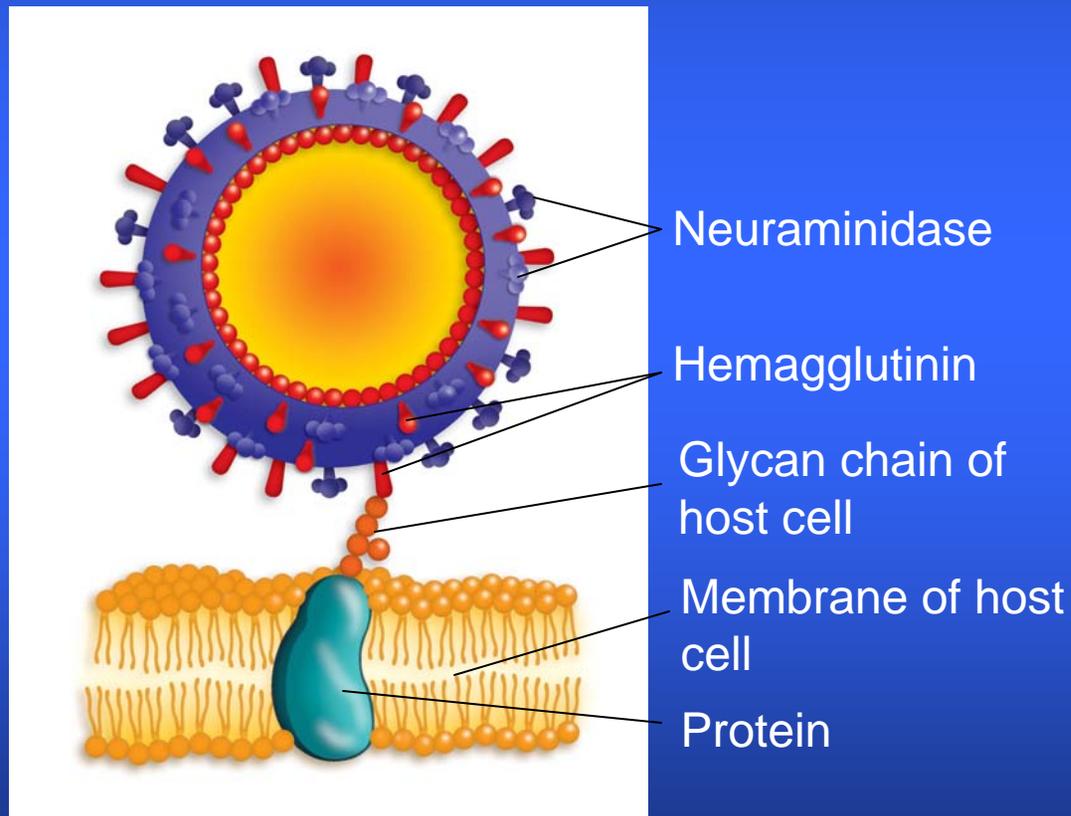
Cell communication

Inflammation

Pregnancy

Gripping Glycans

Influenza A virus infects a host cell

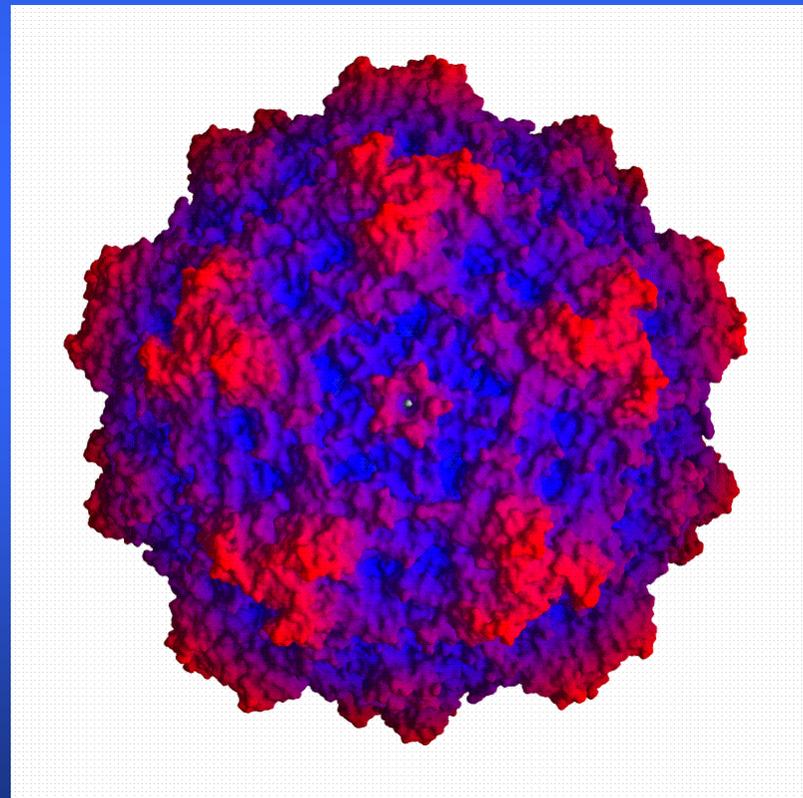


- Most cells have carbohydrates (glycans) on their outer surfaces
- Influenza A virus infects cells by attaching to glycans on host cells

Visualizing Viruses

- Outer layer (capsid protein) of MVM resembles 20-sided soccer ball
- MVM capsid protein contains cavity it uses to recognize and bind specific glycans

3-dimensional crystal structure showing surface of usually mild strain of minute virus of mice (MVMp)



Unraveling Viral Mysteries Step-By-Step

Make an observation

Formulate a research question

Review known facts

Formulate hypothesis

Investigate

Draw conclusions from discoveries

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Solving Viral Mystery #1

Observation: MVMP-infected mice are suddenly dying.

Research question: What made MVMP become deadly?

Known facts: Both strains of MVM are molecularly similar but have alterations in 14 of 587 amino acids that make up the virus' protective capsid protein shell.

Hypothesis: Genetic change created mutant capsid protein.

Investigation: Decode genetic sequence of deadly MVMP and compare with normal MVMP genetic sequence.

Discoveries: 3 mutations, each causing a unique change in 1 amino acid in the capsid protein.

Solving Viral Mystery #2

Observation: Mutated MVMp has 1 amino acid that differs from normal MVMp.

Research question: What makes the mutation deadly?

Known facts: MVM capsid protein contains a cavity it uses to recognize and bind specific glycans so that the virus can enter and infect cells.

Hypothesis: Change is located in critical region of capsid shell.

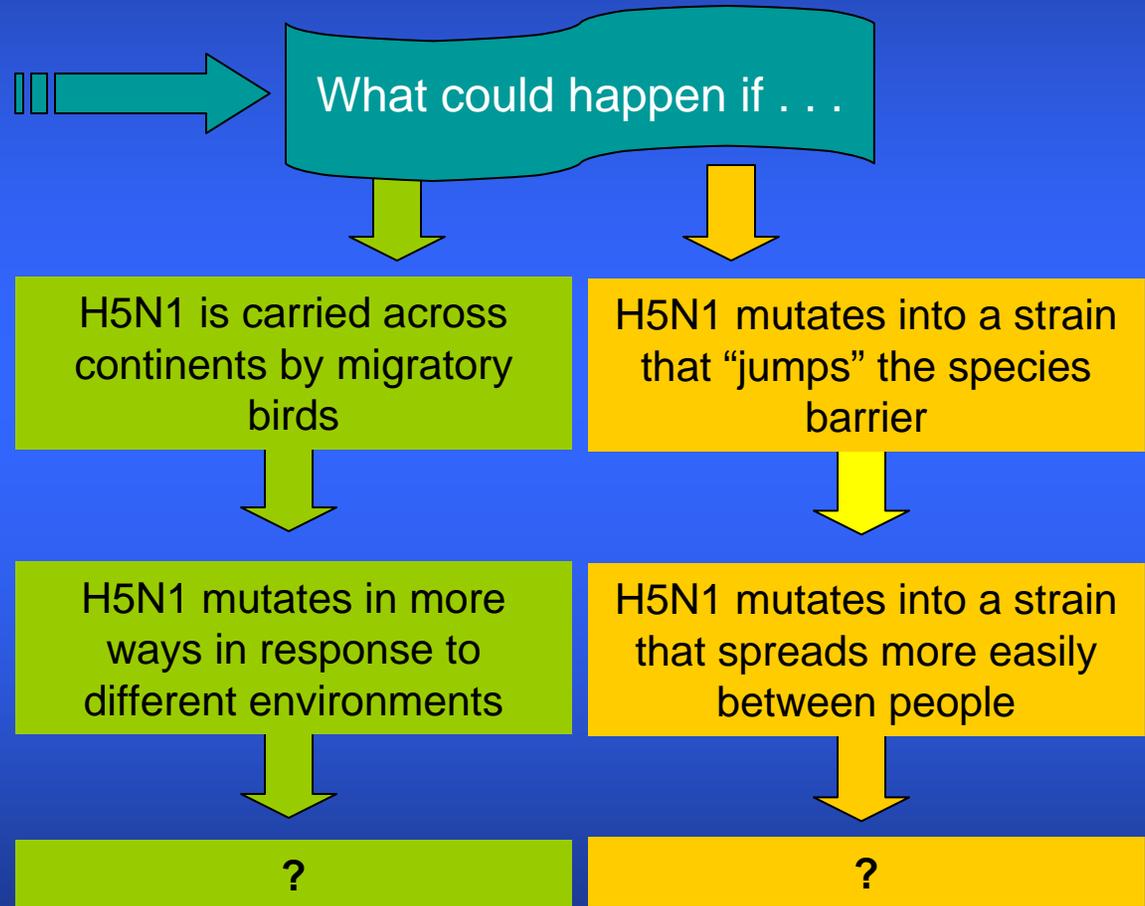
Investigation: Develop 3-D structure of MVM to identify locations of 3 mutant amino acids.

Discoveries: At least 2 changed amino acids sit inside the capsid shell cavity.

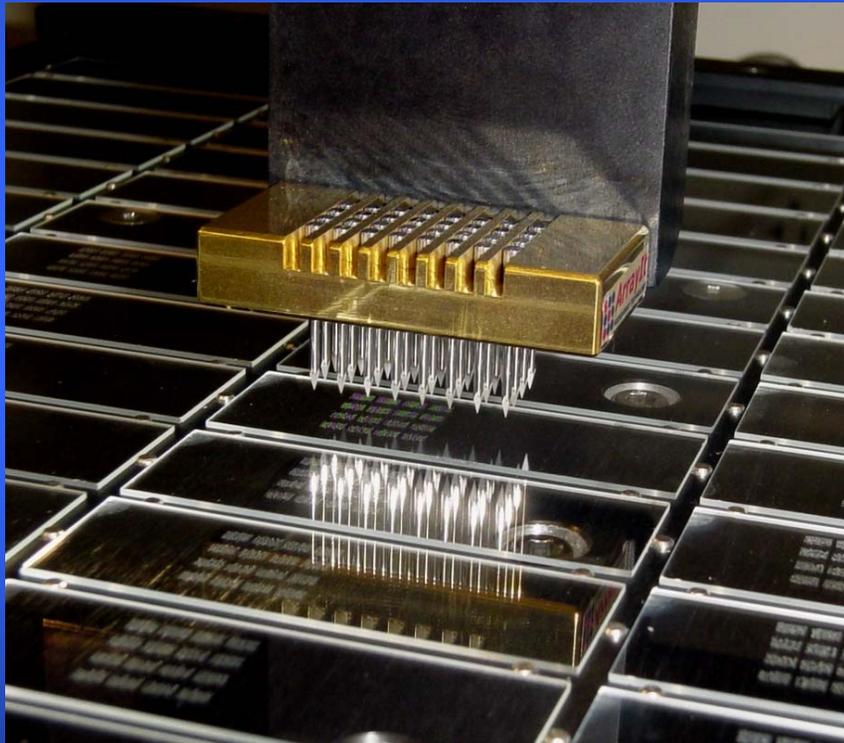
Poultry, People, and a Possible Pandemic

H5N1

- Largest and most lethal epidemic on record
- Migratory birds
 - Spread virus
 - Infect domestic birds
- Lethal strain of bird flu
 - Constantly changing genetically
 - Humans who handle infected birds can get virus



Glycobiology and Pandemics



What is glycobiology?

What is the name of the technique shown in the picture?

How might glycobiology help prevent a pandemic flu?

Research Applications

In what ways might Agbandje-McKenna's research about how viruses infect cells be applied to help patients with cancer?