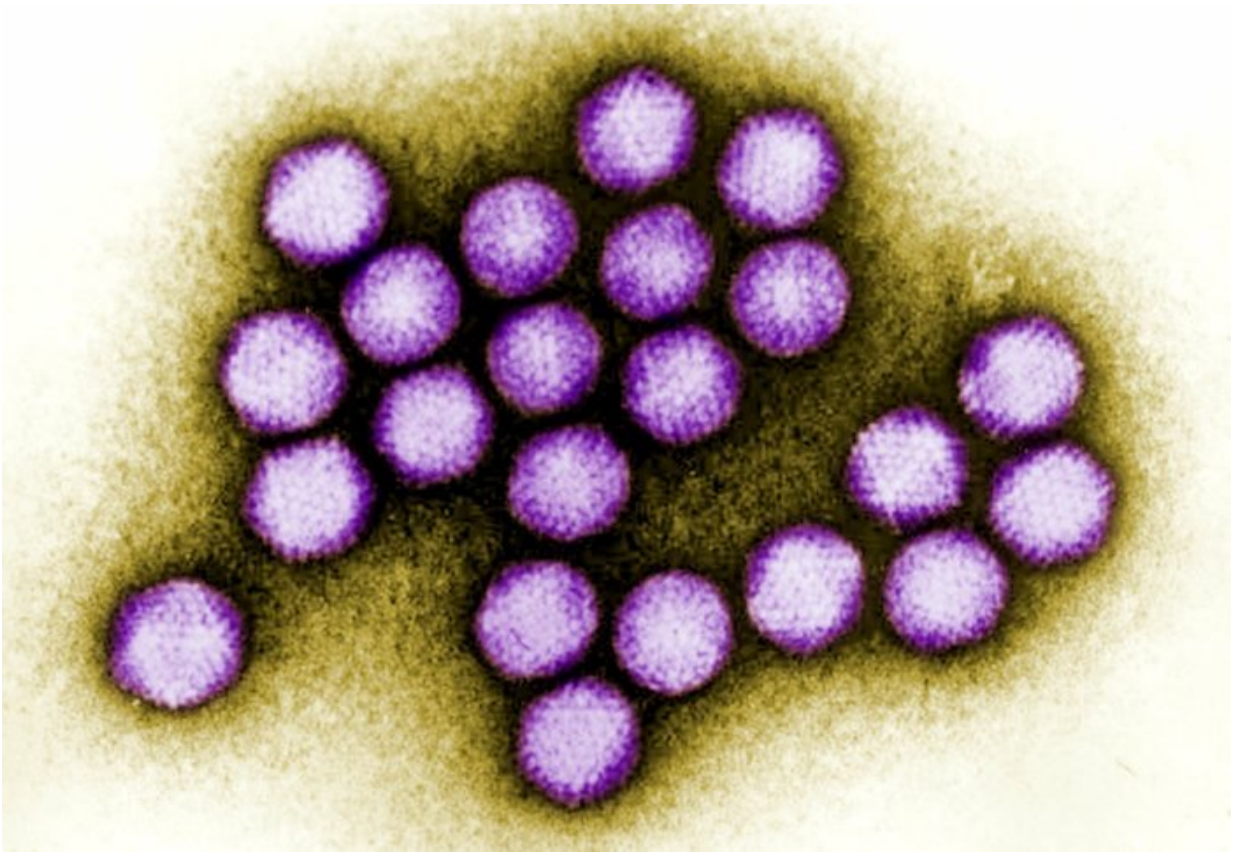
Virus's 'taste' for unusual sugar could lead to new cancer treatments

April 10 2018, by Ryan O'hare



Human adenoviruses (pictured) could hold the key to new therapies for aggressive cancers. Credit: Imperial College London

The way in which a rare virus attacks cells could hold the key to new therapies for aggressive brain and lung cancers, according to new

research.

Human adenoviruses (HAdVs) are common microorganisms which can cause eye infections as well as respiratory and gastrointestinal infections in humans and animals.

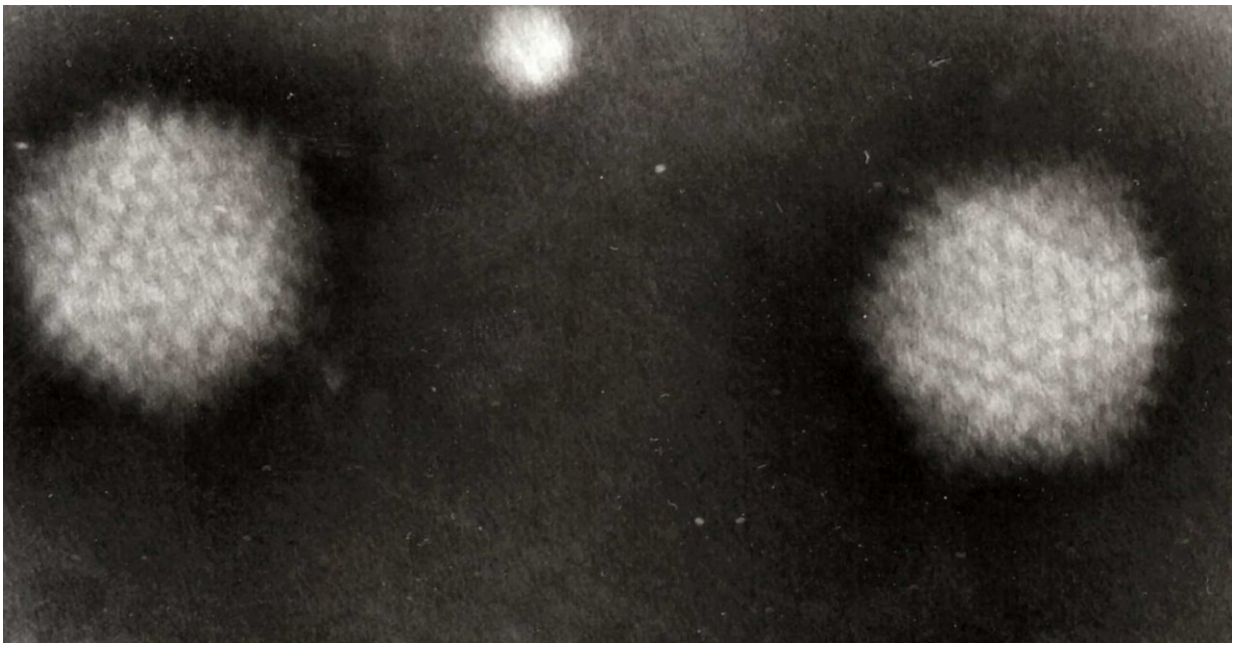
Now, an international team including Imperial College London, together with research groups in Sweden, Germany, and Hungary, has discovered a new mechanism used by a rare type of the virus (HAdV-52) to attack cells.

In a paper, published in the journal *Proceedings of the National Academy of Sciences*, the group explains that the HAdV-52 virus binds to a specific type of sugar on the surface of cells, called polysialic acid, which is more prevalent on cells of brain and lung cancers.

According to the researchers, the discovery opens up new opportunities for the development of virus-based cancer therapies, which could potentially use this adenovirus to target and kill cancerous cells.

Attacking host cells

Adenoviruses use a fibre protein on their surface to attach to cells, in order to gain entry and hijack the host cell's machinery so they can replicate.



Researchers have uncovered how a rare type of the virus (HAdV-52) attack host cells. Pictured is the adenovirus under an electron microscope. Credit: Wikicommons/Graham Colm

It was known that the viruses use this protein to tether themselves to the surface of the host cell, but HAdV-52 also has a second, shorter fibre protein, whose function was unclear.

But in the latest study, researchers discovered that this shorter fibre binds specifically to polysialic acid.

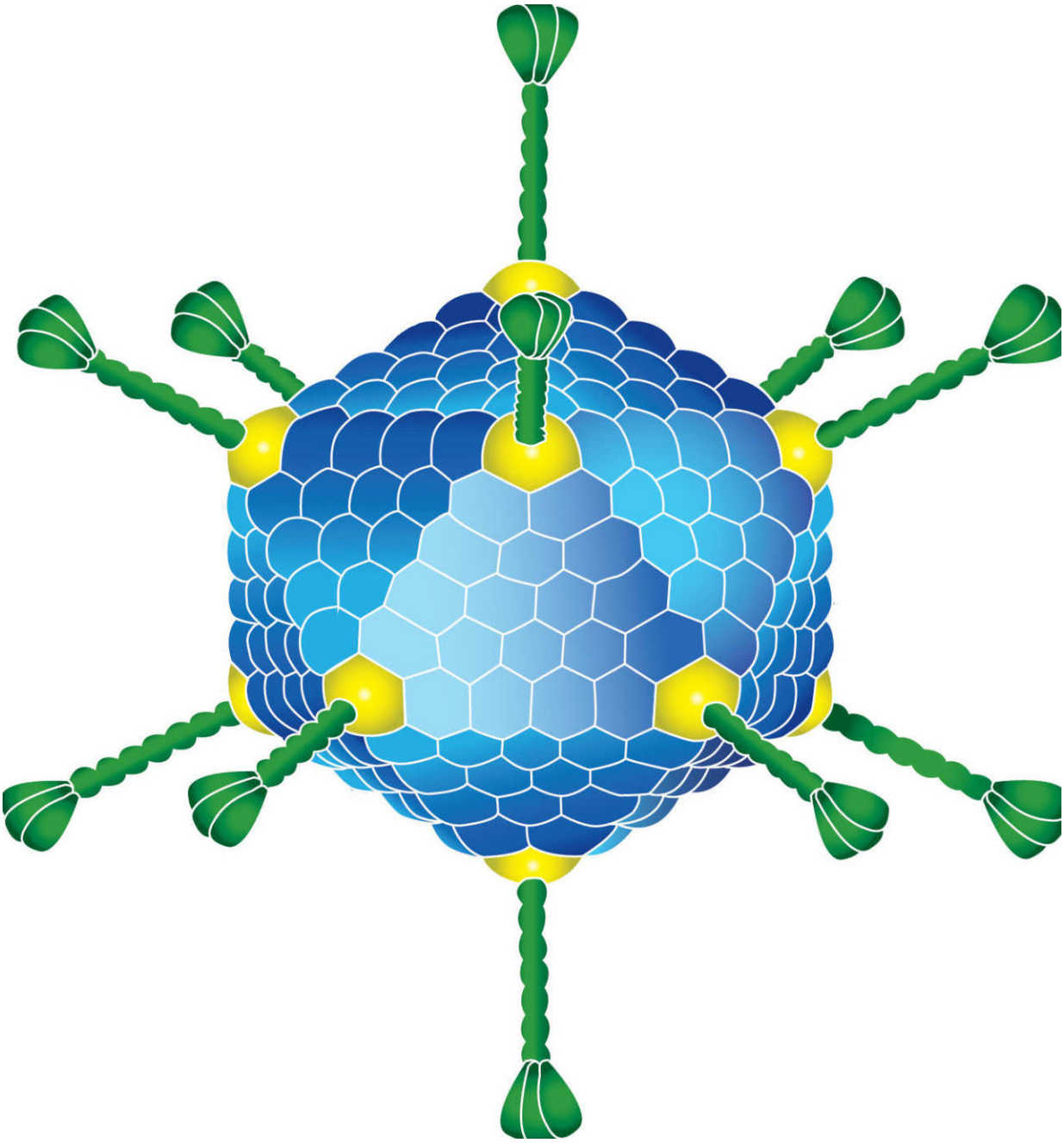
Polysialic acid is a carbohydrate typically found in the developing brain, however, previous studies have shown that the sugar is also present in a number of cancer tissue samples.

In these studies it was also frequently associated with tumours that are highly aggressive and fail to respond to traditional treatments, resulting

in poor prognosis for the patient.

The team suggest that while viral-based cancer treatments may be a number of years away, HAdV-52 could potentially be used to target cancerous cells which overexpress the sugar, hunting them down to infect and kill them.

Dr Annasara Lenman, from Umeå University and first author of the study said: "We knew earlier that the short fiber binds to sialic acid, but we did not how the underlying carbohydrate chain was constructed."



Human adenoviruses (HAdVs) can cause infections of the eye, respiratory tract and gastrointestinal tract. Credit: Niklas Anberg

"To our knowledge, this is the first time that polysialic acid has been

reported to function as a cellular receptor for a human viral pathogen," said Dr Yan Liu, the Project Leader of the Carbohydrate Microarray Facility in the Glycosciences Laboratory at Imperial.

"This finding is a good example of how our carbohydrate microarray system enables discoveries of receptors on cells that viruses bind to at the initial stages of infection."

Professor Ten Feizi, Director of the Glycosciences Laboratory at Imperial, said: "Perhaps the most important known function of polysialic acid is its involvement in the development of the brain. However, not much is known about how polysialic acid interacts with its environment in the brain."

Professor Feizi added: "Our research makes it pertinent to investigate whether polysialic acid plays a part in brain development by interacting with specific molecules in the brain."

"Using viruses to target key markers on the surface of cells could be one avenue to tackle cancers which do not respond to traditional treatments.

"While these treatments may be a number of years from the clinic, in future they could offer hope to patients with aggressive cancers which currently have very poor prognoses."

More information: Annasara Lenman el al., "Polysialic acid is a cellular receptor for human adenovirus 52," *PNAS* (2018). www.pnas.org/cgi/doi/10.1073/pnas.1716900115

Provided by Imperial College London