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Combatting viruses: Code breakers turn code writers

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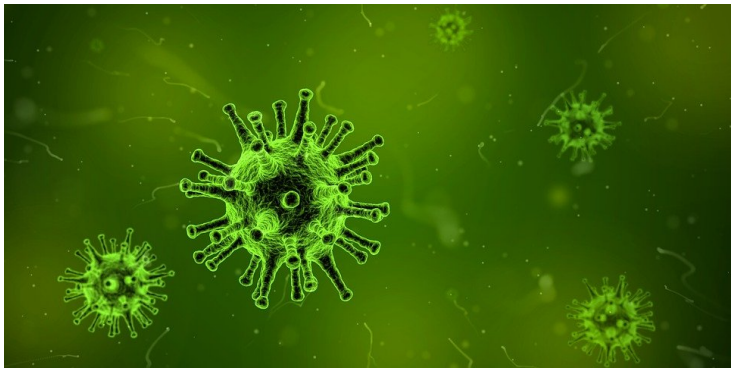
Viruses' ability to decode and repurpose the self-assembly instructions within viral genomes is so efficient thatthey can write artificial instructions for assembly that are even better than those found in nature.



Researchers who successfully cracked a code that governs infections by a major group of viruses have gone a step further, creating their own artificial code, reports University of York.

Previously, scientists at the Universities of York and Leeds discovered that many simple viruses use a hidden code within their genetic instructions for the production of viral proteins that gets decoded during viral assembly.

Now the same researchers have moved beyond simply reading the hidden assembly instructions to writing their own messages to regulate viral assembly. Their ability to decode and repurpose the self-assembly instructions within viral genomes is so efficient that they can write artificial instructions for assembly that are even better than those found in nature.

Since the artificial messages are written in the form of RNA molecules that, unlike viral genomes, no longer encode messages for creating viral proteins, these are completely harmless to the human body.

This new understanding of viral self-assembly codes could prove hugely important in a range of clinical applications, such as cancer therapy and immunisation.

Trojan horse

Professor Reidun Twarock, a Mathematical Biologist with the University of York's Departments of Mathematics, Biology, and the York Centre for Complex Systems Analysis, said: "If you were to compare our research to household DIY, it's like taking a set of instructions for building a shelf, learning what makes the assembly so efficient, then using the instructions to build a different shelf using better-quality wood.

"In the future, our research should allow the introduction into the body of something that looks like a virus from the outside, but contains a different cargo inside the shell of coat proteins. It would be completely harmless as everything that makes it infectious has been stripped away, leaving only the message of the assembly code that makes formation of the protein shell efficient.

"The idea is to enable efficient formation of coat protein shells that 'trick' the immune system, triggering a response, which

would mean it was primed to act immediately if it were to encounter a real infection. Or, in a different application of the same technology, to transport other cargoes into a cell for therapeutic purposes, like a Trojan horse."

The research, which also involved the Rutherford Appleton Laboratory and the University of Oxford, is presented in the journal *Proceedings of the National Academy of Sciences (PNAS).*

Applications

Professor Peter Stockley, a Biological Chemist from the Astbury Centre for Structural Molecular Biology at the University of Leeds, said: "Our research means it is now possible to create virus-like particles highly efficiently, that encompass the artificial assembly manual and potentially also other cargoes, but that are unable to replicate.

"Such particles have a wide range of potential applications, including in the production of synthetic vaccines and systems to deliver genes to specific cells."

Professor Stockley added: "During the Second World War the need to decode the German military codes known as Enigma drove the development of electronic computing, which in turn led to the digital world of today. In the same way, this new understanding of viral self-assembly codes is likely to trigger multiple applications of the technology, just as digital computers proved to be useful for more than simple code-breaking."

The research was funded by the Biotechnology and Biological Sciences Research Council (BBSRC), a Royal Society Leverhulme Trust Senior Research Fellowship and a Joint Wellcome Trust Investigator Award to Professors Stockley and Twarock.