Researchers use viral particles to trap intact mammalian protein complexes

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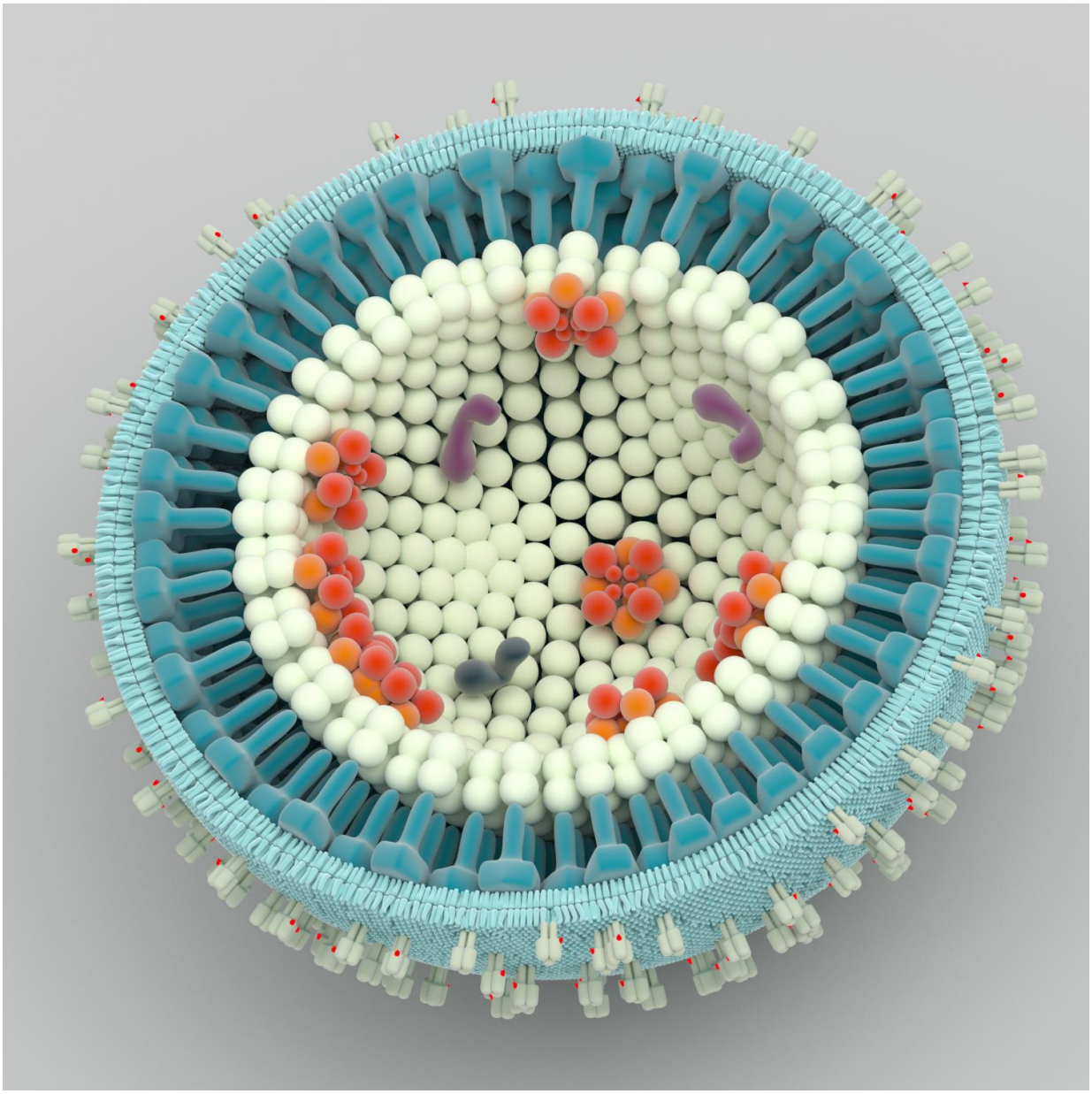

Virotrap. Credit: ©Sven Eyckerman(VIB-UGent)

Belgian scientists from VIB and UGent developed Virotrap, a viral particle sorting approach for purifying protein complexes under native conditions. This method catches a bait protein together with its associated protein partners in virus-like particles that are budded from human cells. Like this, cell lysis is not needed and protein complexes are preserved during purification. The development and application of this pioneering technique are described in a paper published this week in *Nature Communications*.

With his feet in both a proteomics lab and an interactomics lab, VIB/UGent professor Sven Eyckerman is well aware of the shortcomings of conventional approaches to analyze protein complexes. The lysis conditions required in mass spectrometry–based strategies to break open cell membranes often affect protein-protein interactions. "The first step in a classical study on protein complexes essentially turns the highly organized cellular structure into a big messy soup", Eyckerman explains.

Inspired by virus biology, Eyckerman came up with a creative solution. "We used the natural process of HIV particle formation to our benefit by hacking a completely safe form of the virus to abduct intact protein machines from the cell." It is well known that the HIV virus captures a number of host proteins during its particle formation. By fusing a bait protein to the HIV-1 GAG protein, interaction partners become trapped within virus-like particles that bud from mammalian cells. Standard proteomic approaches are used next to reveal the content of these particles. Fittingly, the team named the method 'Virotrap'.

The Virotrap approach is exceptional as protein networks can be

characterized under natural conditions. By trapping protein complexes in the protective environment of a virus-like shell, the intact complexes are preserved during the purification process. The researchers showed the method was suitable for detection of known binary interactions as well as mass spectrometry-based identification of novel protein partners.

Virotrap is a textbook example of bringing research teams with complementary expertise together. Cross-pollination with the labs of Jan Tavernier (VIB/UGent) and Kris Gevaert (VIB/UGent) enabled the development of this platform.

Jan Tavernier: "Virotrap represents a new concept in co-complex analysis wherein complex stability is physically guaranteed by a protective, physical structure. It is complementary to the arsenal of existing interactomics methods, but also holds potential for other fields, like drug target characterization. We also developed a small molecule-variant of Virotrap that could successfully trap protein partners for small molecule baits."

Kris Gevaert: "Virotrap can also impact our understanding of disease pathways. We were actually surprised to see that this virus-based system could be used to study antiviral pathways, like Toll-like receptor signaling. Understanding these protein machines in their natural environment is essential if we want to modulate their activity in pathology."

More information: Sven Eyckerman et al. Trapping mammalian protein complexes in viral particles, *Nature Communications* (2016). DOI: 10.1038/ncomms11416

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