Chilling the courier: How cryo-EM can be used to improve therapeutic nano-delivery systems

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Cryo-electron microscopy (cryo-EM) has emerged as a promising structural biology technique that complements X-ray crystallography and nuclear magnetic resonance. Recent advances in imaging have dramatically improved the resolution of cryo-EM structures, helping us to better understand how multi-protein complexes are assembled. Virus-like nano-particles (VNPs), cages consisting of viral protein shells, are emerging as versatile tools in nano-technology, as their composition and morphology can be controlled to deliver therapeutic payloads to specific targets.

Here, we combine both of these cutting-edge developments and highlight the importance of structural analysis of VNPs to validate their molecular organisation and to aid their design and further modication. We present a 9.1 Å resolution cryo-EM structure of the Bluetongue virus core-like particle (BTV-CLP) assembled by transiently expressing the capsid proteins VP3 and VP7 in plant leaves, and a 5.2 Å resolution structure of the modified core-like particle containing 120 green fluorescent protein (GFP) molecules fused to the N-termini of VP3 (GFP-BTV) (Fig. 1). The structure of BTV-CLP, which has been proposed as a nano-delivery particle, reveals a significant difference in assembly to the infection-derived viral particle [1]. Regardless, encapsidation of GFP at the N-terminus of VP3 does not alter the structure of the CLP, suggesting that incorporation of therapeutic peptides at the VP3 N-terminus might be a useful tool in targeted cargo delivery.

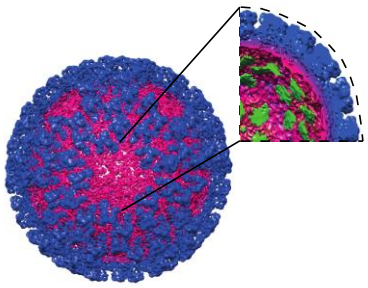

Fig. 1: cryo-EM 3D map of GFP-BTV refined at 5.2 Å resolution. Green densities inside the capsid are thought to be the GFPs.

References

Brillault L., Jutras P. V., Dashti N., Thuenemann E. C., Morgan G., Lomonosoff G. P., Landsberg M. J., Sainsbury F., (2017) *Engineering Recombinant Virus-like Nanoparticles from Plants for Cellular Delivery*, ACS Nano, 11:3476-3484.