Structural insight into capsid assembly and viral infection of piscine betanodavirus

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Betanodaviruses belong to the family *Nodaviridae* and cause the mortality of numerous larval-stage fish species with viral nervous necrosis. *Nodaviridae* is a family of positive-sense single-stranded RNA viruses with a non-enveloped *T*=3 capsid. The structure of a *T*=3 Grouper nervous necrosis virus-like particle (GNNV-LP) of a diameter ~30 nm is determined by the *ab initio* method with non-crystallographic symmetry averaging at 3.6 Å resolution [1]. Each capsid protein (CP) shows three major domains: (i) the N-terminal arm, an inter-subunit extension at the inner surface; (ii) the shell domain (S-domain), a jelly-roll structure; and (iii) the protrusion domain (P-domain) formed by three-fold trimeric protrusions. In addition, we have determined structures of the T=1 subviral particles (SVPs) of (i) the delta-P-domain mutant (residues 35−217) at 3.1 Å resolution; and (ii) the N-ARM deletion mutant (residues 35−338) at 7 Å resolution; and (iii) the structure of the individual P-domain (residues 214−338) at 1.2 Å resolution [2]. The P-domain reveals a novel DxD motif asymmetrically coordinating two Ca^{2+} ions, and seems to play a prominent role in the calcium-mediated trimerization of the GNNV CPs during the initial capsid assembly process. The flexible N-ARM (N-terminal arginine-rich motif) appears to serve as a molecular switch for *T*=1 or *T*=3 assembly. Finally, we find that polyethylene glycol, which is incorporated into the P-domain during the crystallization process, enhances GNNV infection. Several hypervariable regions on the P-domain coincide with the protrusion surface associated with the functionalities of the receptor binding and host-cell specificity. The present structural studies together with the biological assays enhance our understanding of the role of the P-domain of GNNV in the capsid assembly and viral infection by betanodaviruses.

References

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