VIROLOGY

Structural insights into calicivirus function

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URLs

Online Links:
Entrez Genome: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=genome
Norwalk Virus
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=genome&cmd=Retrieve&dopt=Overview&list_uids=13999

A recent report by Prasad and colleagues describes the first high-resolution X-ray structure of a native calicivirus.

Our understanding of human caliciviruses, which include noroviruses (such as the Norwalk virus), is limited by a lack of *in vitro* culture systems and *in vivo* disease models. By contrast, there is much immunological information on the vesiviruses, a calicivirus genus that mainly infects animals. Therefore, the authors studied the San Miguel sea lion virus (SMSV), a prototypical vesivirus. The X-ray structure of SMSV was similar to the previously determined structure of a recombinant calicivirus in terms of capsid architecture and domain organization of the major capsid protein VP1. But these structures differed in several ways, including the presence of additional points of flexibility between the domains of VP1 in SMSV. Such altered flexibility affects the orientation of the domains, and the authors postulate that this might allow increased antigenic diversity, by enabling the structure to change within the context of the same domain organization.

Previous studies have suggested that the hypervariable P2 subdomain of VP1 might have a role in antigenicity and in interactions with host-cell receptors. The authors found that neutralizing epitopes of other vesiviruses mapped to several highly exposed loops within the conserved polypeptide fold of P2. They suggest that these loops are the immunodominant regions of caliciviruses and that these viruses could achieve antigenic diversity by incorporating amino-acid changes into these loops. In addition, the regions that these epitopes map are flanked by conserved regions, which map to the VP1 dimer interface and therefore might be involved in the structural integrity of the capsid. Conservation of these regions occurs in caliciviruses that infect similar hosts, so this could be a mechanism for conferring host specificity and might be associated with the recognition of specific host-cell receptors.

These findings show how the modular organization of the major capsid protein enables both antigenic diversity and host specificity of caliciviruses. Furthermore, the mapping of the regions that might contain neutralizing epitopes has implications for vaccine development against various human caliciviruses.

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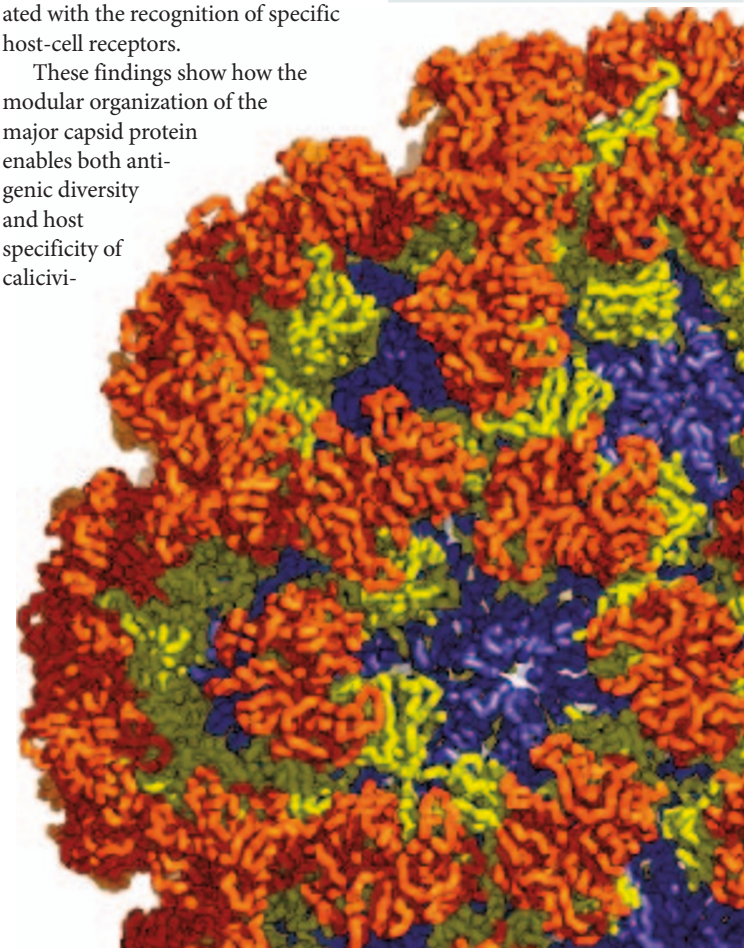
ORIGINAL RESEARCH PAPER Chen, R., Neill, J. D., Estes, M. K. & Prasad, B. V. V. X-ray structure of a native calicivirus: structural insights into antigenic diversity and host specificity. *Proc. Natl Acad. Sci. USA* **103**, 8048–8053 (2006)



X-ray structure of SMSV. Colours indicate the various domains of VP1, with the P2 subdomain shown in orange. Image courtesy of B. V. V. Prasad, Baylor College of Medicine, USA.