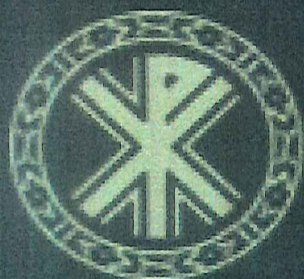
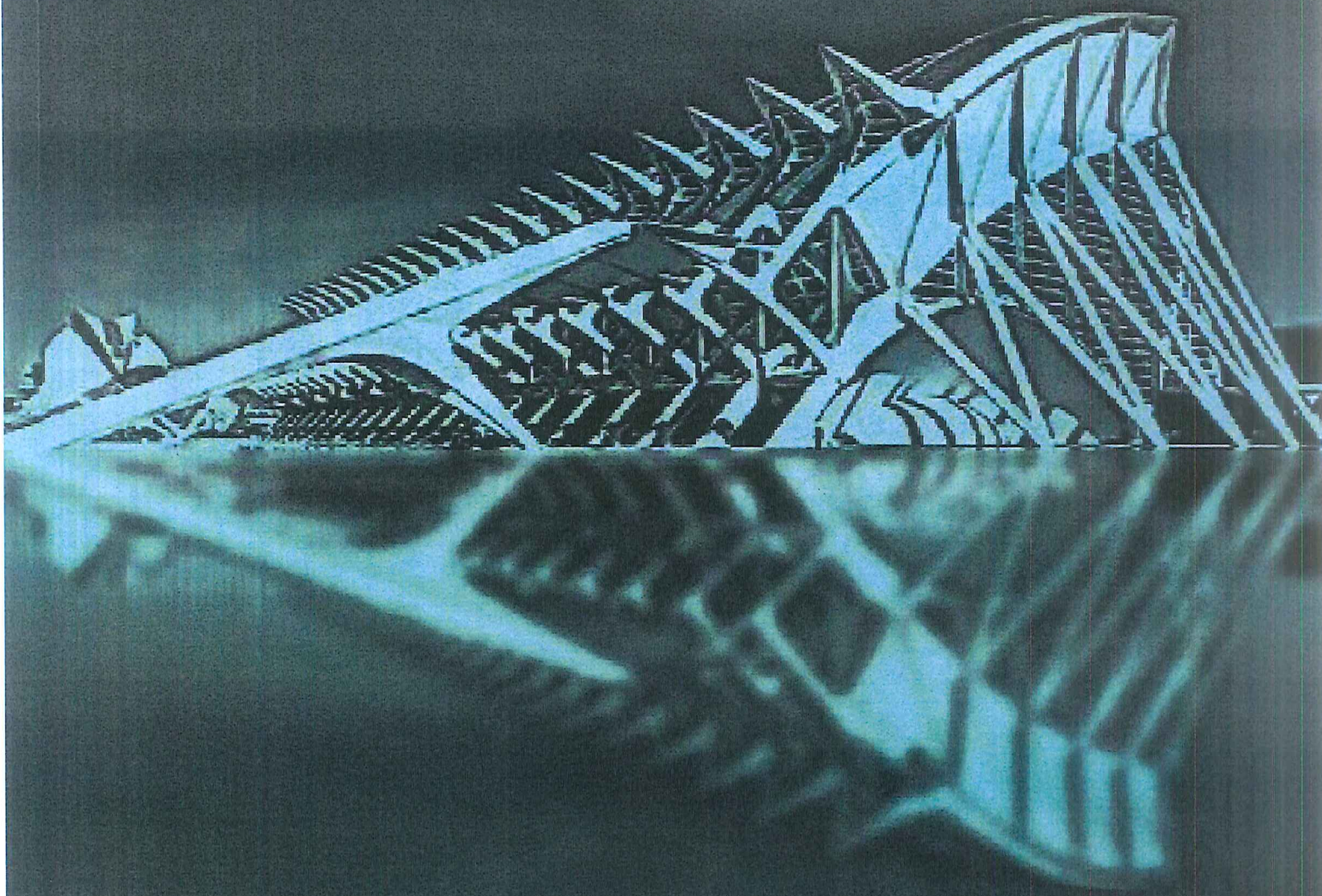


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(F)uridylated Peptides Linked to Vpg1 of Foot-and-Mouth Disease Virus (FMDV): Design, Synthesis and X-Ray Crystallography of the Complexes with FMDV RNA-dependent RNA polymerase

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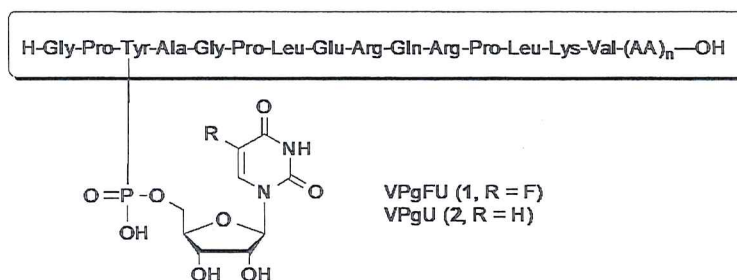
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VPg1 (viral protein genome-linked) is covalently attached to the 5' end of the positive RNA strand of foot-and-mouth disease virus (FMDV), a picornavirus responsible for the highly contagious foot-and-mouth disease of cloven-hoofed bovids¹. Uridylated VPg1 acts as a primer during RNA synthesis because it provides a free hydroxyl on a Tyr residue that is extended by the virally encoded RNA-dependent RNA polymerase (RdRp).^{2,3} Unlike other picornavirus, FMDV-RNA encodes three distinguishable copies of this protein (VPg1, VPg2, VPg3). Each of them attached to genomic RNA, and therefore believed to be functionally equivalent².

5-Fluorouridine triphosphate (FUTP) is a potent competitive inhibitor of VPg-1 uridylylation. By peptide analysis, a VPg fragment containing FUMP covalently attached to Tyr was identified. However, the molecular basis for this phenomenon is still unknown.

To investigate the role of FUMP, VPg-1 peptides of different lengths covalently linked to either U or FU through the hydroxyl group of Tyr3 were synthesized. The X-ray crystal structure of FMDV RdRp in complex with the 15-mer peptide VPg-FU (Figure) showed a significant distortion of the β 9- β 11 loop of the polymerase.



References

- 1 <http://www.fao.org/3/I9857EN/I9857en.PDF> (2018)
- 2 Foot-and-mouth disease virus: current research and emerging trends. F. Sobrino, E. Domingo (Eds). Caister Academic Press 2017 (ISBN: 978-1-910190-52-4)
- 3 C. Ferrer-Ortra, N. Verdaguer in Foot-and-mouth disease virus: current research and emerging trends. F. Sobrino, E. Domingo (Eds). Caister Academic Press 2017, chapt 6, pp137-146.