Crystal structure of the Porcine Circovirus 2 in complex with heparin-derived disaccharides

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Abstract

Procine circovirus type2 (PCV2), the small virus with a single-stranded 1.76-kb circular DNA and ~17 nm in diameter, the icosahedral non-enveloped virus, is a dominant causative agent of procine cirovirus associated disease (PCVAD) such as postweaning multisystemic wasting syndrome (PMWS) infecting 5- to 14-week-old piglets. The pig farms in many countries, including USA, Canada, Taiwan and etc., are highly threatened by the disease. Once PCV2 infects small pigs, the attachment of PCV2 on the host cell is a critical step. Glycosaminoglycans (GAGs), including heparan sulfate (HS), chondrotin sulfate (CS), and kerratan sulfate (KS), covalently conjugated with the core protein on the all adherent cells, are proposed as the attachment receptors to recruit PCV2 on the cell membrane. Structurally, GAGs are composed of repeating disaccharide units. These different GAGs differ in the composed repeating disaccharide units. HS and CS-B were identified as attachment receptors for PCV2 among GAGs in 2006 [1]. The predicted HS binding site, ^{98}IRKVKV^{103} on the PCV2 capsid protein, is located at the interior of PCV2 in search of the determined structure of PCV2 in 2011 [2]. Therefore, the structure of PCV2 in complex with HS is necessary to explore the exact HS binding site on the surface of PCV2 as well as the structurally functional role of GAG during the attachment process of PCV2 on the host cell. Herein, three crystal forms, A, B and C, were obtained while the crystals of PCV2 are soaked with the solution of heparin-derived disaccharide. The crystal forms A, B and C diffract to resolution of 3.4, 2.8 and 2.5 Å respectively. The space groups of forms A, B, and C are *P*2(1)2(1)2, *I222,* and *I*23 respectively with cell lengths (A) a=210, b=712, c=193 Å (B) a=199, b=206, c=211 Å (C) a=203, b=203, c=203 Å. Five sites of heparin-derived disaccharide were obtained. This five heparin bindings sites might be utilized to design the novel drugs for the PCV2-related disease of pigs. In addition, the development of the PCV2 vaccine based on the virus-like particle (VLP) of PCV2 is a safer and more efficient compared to live-attenuated or inactivated vaccines. The drug design and vaccine development based on our PCV2 and PCV2/disaccharide HS structures for solving the sever PCVAD problems in pig farms will be performed in the future.

Keywords – Procine cirovirus type2, procin cirovirus associated disease, heparan sulfate, Virus-like particle.

References

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