Characterizing the Structure of the Cutavirus Capsid-Glycan Complex via Cryo-EM and Comparing Its Structural Features With Oncolytic Protoparvoviruses

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Cutavirus (CuV) belongs to the genus Protoparvovirus, which includes important viruses such as H-1PV, MVMp, and LuIII, known for their applications in cancer therapies and as gene therapy vectors. CuV could have potential for these therapies, but its entry mechanisms into human cells remain poorly understood. To address this, CuV's structure was analyzed using cryogenic electron microscopy (cryo-EM), and a 3D reconstruction was generated to identify potential glycan binding interactions. These findings served as the foundation for comparative structural analysis with related protoparvoviruses. Structural comparisons were performed to evaluate percent structural similarity, root-mean-square deviation (RMSD), and conservation scores of binding sites. The analysis revealed that H-1PV, the most closely related to CuV evolutionarily, exhibited the highest structural similarity and shared high conservation of binding sites with CuV. MVMp and LuIII, which are equally but less closely related to CuV, demonstrated lower structural similarity. RMSD values showed that LuIII had the closest structural alignment with CuV, while MVMp displayed the largest deviation. Conservation scores further highlighted that MVMp exhibited the least conserved binding sites, whereas LuIII and H-1PV shared comparable levels of conservation with CuV. These findings suggest that structural similarities between CuV and related protoparvoviruses align with their evolutionary relationships. Understanding CuV's structural features and evolutionary context offers valuable insights for advancing its use in cancer and gene therapies.

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