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Structure analyze HIV-1 Gag-IP6 complexes using ambient-temperature X-ray crystallography and in-solution Small-angle X-ray scattering.

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AIDS caused by infection of human immunodeficiency virus (HIV) is one of the big issues in the world. Antiretroviral therapy (ART) using multiple drugs has developed, and suppression of HIV in a body is possible. However, latent HIV reservoirs can be found in body, and HIV can hide for years inside reservoirs. This reservoir is resistant to ART and leads to viral rebound once the treatment is stopped. To remove the reservoir and cure AIDS is the biggest goal. To achieve this goal, Otsuka group have recently developed a compound inositol hexaphosphate (IP6) named L-HIPPO targeted to suppress membrane localization of Gag and induce apoptosis of the host cell containing the un-budded viruses. The L-HIPPO was designed based on the fact that the MA domain of Gag mediates membrane binding through its interaction with inositol phospholipid PIP2 in the membrane.The main structural component of HIV-1 is the Gag polyprotein, which has five domains. By that, there is no structure of Gag that includes all of its five domains. We aim to first use home source XRD then use time-resolved Serial Femtosecond X-ray crystallography (SFX) to understand dynamic structure of HIV-1 Gag itselfs and with IP6 /L-HIPPO (or PIP2) complexes.

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