

Antivirals alter the kinetic assembly pathway and elastic properties of Hepatitis B virus capsids

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1. Abstract

Capsid assembly modulators (CAMs) are antiviral molecules that disturb the formation of icosahedral viral capsids, in particular, those of the Hepatitis B virus (HBV). We report an integrated, physics-driven study elucidating quantitatively the effects of two classes of CAMs on HBV capsid assembly. Time-resolved small-angle X-ray scattering measurements revealed accelerated self-assembly processes that implied the increase of subunit binding energy from 9- up to 18-fold the thermal energy due to CAMs. Cryotransmission electron microscopy images showed that both classes induce various changes in capsid morphology: from a slight elongation, unrecognized in previous work, to a strong deformation with a capsid size more than twice as large. The observed capsid morphologies were closely reproduced in coarse-grained simulations by varying the Föppl-von-Kármán number, thus pointing out the role of CAMs in altering the capsid elastic energy. Our results revise and extend previous knowledge on the mechanisms of action of CAMs, drugs that are currently developed towards HBV cure.