Effects of zinc ion on oligomerization and pH stability of influenza virus hemagglutinin

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During influenza infection, Zn^{2+} and Cu^{+2} are known to prevent the growth of viruses in mammalian cells, and viral titers decrease significantly onto a copper surface. However, the molecular mechanism of metal ion against influenza viruses is not well understood, only proposed as DNA damage by radicals, viral protease, M1 or neuraminidase inhibition, or morphological changes of virions. Fusion of the viral and host endosomal membranes is required for influenza virus entry into host cells, driven by large conformational changes of HA through its receptor binding. Here, we characterized the stability and determined the crystal structure of hemagglutinin (HA), derived from A/Thailand/CU44/2006, bound to a metal ion Zn^{+2}. Although the presence of Zn^{+2} induced the oligomerization of HA through the interaction of head domains in the crystal structure, the metal ion did not enhance the stability of HA. Rather, the binding of Zn^{+2} decreased the acid stability of HA so that the acid-induced conformational change of HA occurred at higher pH, showing resemblance to the role of receptor binding that shifted the dynamic equilibrium in favor of the conformational change upon acidification.

References

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