Poster Presentation

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Crystal structure of the Vif-interaction domain of the anti-viral APOBE3F

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Human cells express a family of cytidine deaminases, called APOBEC3 (A3) (A3A, B, C, D, F, G, and H). The family enzymes, especially A3G and A3F potentially inhibit replication of retroviruses including HIV-1. However, HIV-1 overcomes the A3-mediated antiviral system by expressing a virus-encoded antagonist, viral infectivity factor (Vif) protein. In HIV-1-infected cells, Vif specifically binds with A3 followed by proteasomal degradation of A3. Hence, inhibition of the interaction between A3 and Vif is an attractive strategy for developing novel anti-HIV-1 drugs. To date, we have determined the first crystal structure of A3 with Vif-binding interface, A3C (PDB ID: 3VOW). In addition, our extensive mutational analysis, based on the A3C structure, revealed that structural features of the Vif-binding interface are highly conserved among A3C, DE, and F [1]. However, more recently, Bohn et al. and Karen et al. have shown the crystal structures of mutant A3F C-terminal domain (CTD) which is responsible for the Vif interaction, and have predicted more extended area, including our identified residues, for the interface on the A3F CTD [2][3]. To clarify the Vif-binding interface of A3F, we sought to determine the crystal structure of the wild-type A3F CTD and evaluated contributions of the additional residues for the Vif-interaction interface by virological method. First, we have successfully determined the crystal structure of A3F CTD at 2.75 Å resolution. Furthermore, we have identified four additional residues unique on the A3F CTD but not A3C for Vif interaction, which are located in the vicinity of our previously reported interface. These results demonstrated that the structural features of Vif-binding interface are indeed conserved between A3C and A3F. Taken together, these results will provide the fine-tuned structure information to understand the binding between A3 and Vif and to facilitate a development of novel anti-HIV-1 compounds targeting A3 proteins.

[1] *S. Kitamura, H. Ode, M. Nakashima, et al., Nature Structural & Molecular Biology, 2012, 19, 1005-1010.,* ***[2]*** *M. Bohn, S. Shandilya, J. Albin, et al., Structure, 2013, 21, 1042-1050.,* ***[3]*** *K. Siu, A. Sultana, F. Azimi, et al., Nature Communications, 2013, 4, 2593.*

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