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Modulating ADAR-1 arm of innate immunity for HIV cure

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Our team has been studying an important arm of “versatile” innate anti-viral immunity, i.e., the adenosine deaminase acting on RNA-1 (ADAR-1)/interferon (IFN) pathway of the innate cytoplasmic immunity that mounts rapid responses to many viral infections. In particular, the ADAR-1 p150 isoform is IFN inducible. In the cytoplasmic compartment, it recognizes double-stranded RNA (dsRNA) intermediates of invading viruses and edits them by converting adenosine (A) residues to inosine (I)/guanosine (G). The A-to-I/G editing alters the structure of viral RNA genome and the encoded viral proteins to interfere with the infection. We report here progress in identifying orphan drug candidates to modulate ADAR-1/IFN arm of innate immunity and explore their potential use in treating HIV-1 infection. Our preliminary data indicates that an RNA-splicing modulating-based anti-cancer molecule significantly enhances expression of the ADAR-1 p150 isoform and effectively suppresses HIV-1 activation in the human T-cells harboring latent HIV-1. The mechanisms of actions (MOAs) of this new class of anti-viral drugs warrant further investigation.