

Chemistry and Molecular Biology Department
and NIH Center for Protease Research
Departmental Seminar
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3:45 pm in Dunbar 152

“The Role of VPAC1 and VPAC2 Neuroendocrine Receptors in HIV-1 Infection”

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Abstract

Despite after 26 years of research and the therapeutic advances in HIV treatment using combinations of reverse transcriptase, integrase and protease inhibitors, an urgent need still remains to develop new therapies aimed at novel targets within the HIV infection cycle. Resistance to such inhibitors is becoming more widespread and the rigorous regime combined with a number of significant side effects can compromise compliance. Our research has been focused on identifying novel targets involved in the pathogenesis of HIV infection. Possible targets are the 7-transmembrane G-protein-coupled neuroendocrine receptors known as VPAC1 and VPAC2. We have previously reported that gp120 of the HIV-1 envelope interacts with VPAC1 to provide a facilitation signal for HIV-1 infection. Blocking this signal by specific signal-blocking antibody or by strategies to knock-down or over-express VPAC1 protein confirmed the facilitatory effect of VPAC1. We also have preliminary results using Chinese Hamster Ovary (CHO) cells transfected to express VPAC1 that, after being infected to express HIV-1 cDNA mostly in the cytosol, can be induced to integrate the cDNA by stimulation of VPAC1. Published reports have claimed that VPAC1 and VPAC2 stimulation may have opposing effects. Recently, we have found that stimulation of VPAC2 using specific ligands results in strong inhibition of HIV-1 infection by a dramatic inhibition of HIV-1 integration and inhibition of formation of 2-LTR circular HIV-1 DNA. This effect correlates with increased activation of tyrosine phosphatase activity and CD45 specifically. Our current working hypothesis is that VPAC1 and VPAC2 can positively and negatively, respectively, regulate HIV-1 integration into the host cell genome.