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## Regulation of the innate cell response to HIV infection in lymphocytes

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pon viral entry in lymphocytes and monocytes, the human immunodeficiency virus (HIV)-1 triggers an innate cell response, which ultimately results in the induction of interferonstimulated genes. One of these genes encodes the Protein Kinase RNA-activated (PKR). Upon activation by double-stranded (ds)RNA, PKR becomes phosphorylated and then phosphorylates the eukarvotic initiation factor 2 (eIF2 $\alpha$ ). The consequence is the inhibition of protein synthesis and viral replication. In lymphocytic cells, HIV-1 replicates actively, suggesting that PKR is not activated or that its activation is reversed. We hypothesized that in HIV-replicating cells, PKR is within a ribonucleoprotein complex that regulates its activation to ensure high viral replication. Our results show that PKR is transiently activated in lymphocytic cell lines and in peripheral blood mononuclear cells early after HIV infection and that the activation is reversed during high replication. At the peak of HIV infection, we identified a ribonucleoprotein complex around PKR, which contains the dsRNA binding proteins adenosine deaminase acting on RNA (ADAR)1, TAR RNA Binding Protein (TRBP) and PKR Activator (PACT). In cells transfected with an HIV molecular clone, TRBP, ADAR1 and PACT inhibited PKR and eIF2 $\alpha$ phosphorylation and increased HIV-1 protein expression and virion production. In contrast to its previously described activity, PACT appears as a new PKR inhibitor in HIV-infected cells. HIV has evolved to replicate in cells that express high amounts of TRBP, to increase the expression of ADAR1 and to reverse the activity of PACT, which results in the inhibition of PKR activation and an enhancement of viral replication.

## Biography

Anne Gatignol has completed her Ph.D. from University of Toulouse (France) in 1988 and postdoctoral studies from the National Institute of Allergy and Infectious Diseases (Bethesda, MD, USA). She is a project director at the Lady Davis Institute for Medical Research and Associate Professor at McGill University in Montréal, QC, Canada where she coordinates a Viral Pathogenesis course. She has published 50 papers in highly-ranked journals and has written several book chapters. She serves as an editorial board member of virology and molecular biology journals. Her research relates to virus-cell interactions during HIV replication.