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## The HIV-1 Vpr and glucocorticoid receptor complex is a gain of function interaction that prevents the nuclear localization of PARP-1

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The Vpr protein of HIV-1 functions as a vital accessory gene by regulating various cellular functions including cell differentiation, apoptosis, NF- $\kappa$ B suppression and cell cycle arrest of the host cell. Several reports have suggested that Vpr complexes with the glucocorticoid receptor (GR), but it remains unclear whether the GR pathway is required for Vpr's effects. Here we report that Vpr utilizes the GR pathway as a recruitment vehicle for the NF- $\kappa$ B coactivating protein Poly(ADP-Ribose) Polymerase-1 (PARP-1). The glucocorticoid receptor interaction with Vpr is both necessary and sufficient to facilitate this interaction by potentiating the formation of a Vpr/GR/PARP-1 complex. The recruitment of PARP-1 by the Vpr/GR complex prevents its nuclear localization, which is necessary for Vpr to suppress NF- $\kappa$ B. The association of GR with PARP-1 is not observed with steroid (glucocorticoid) treatment, suggesting that the GR association with PARP-1 is a gain of function solely attributed to HIV-1 Vpr. These data provide important insight into Vpr biology and its role in HIV pathogenesis.