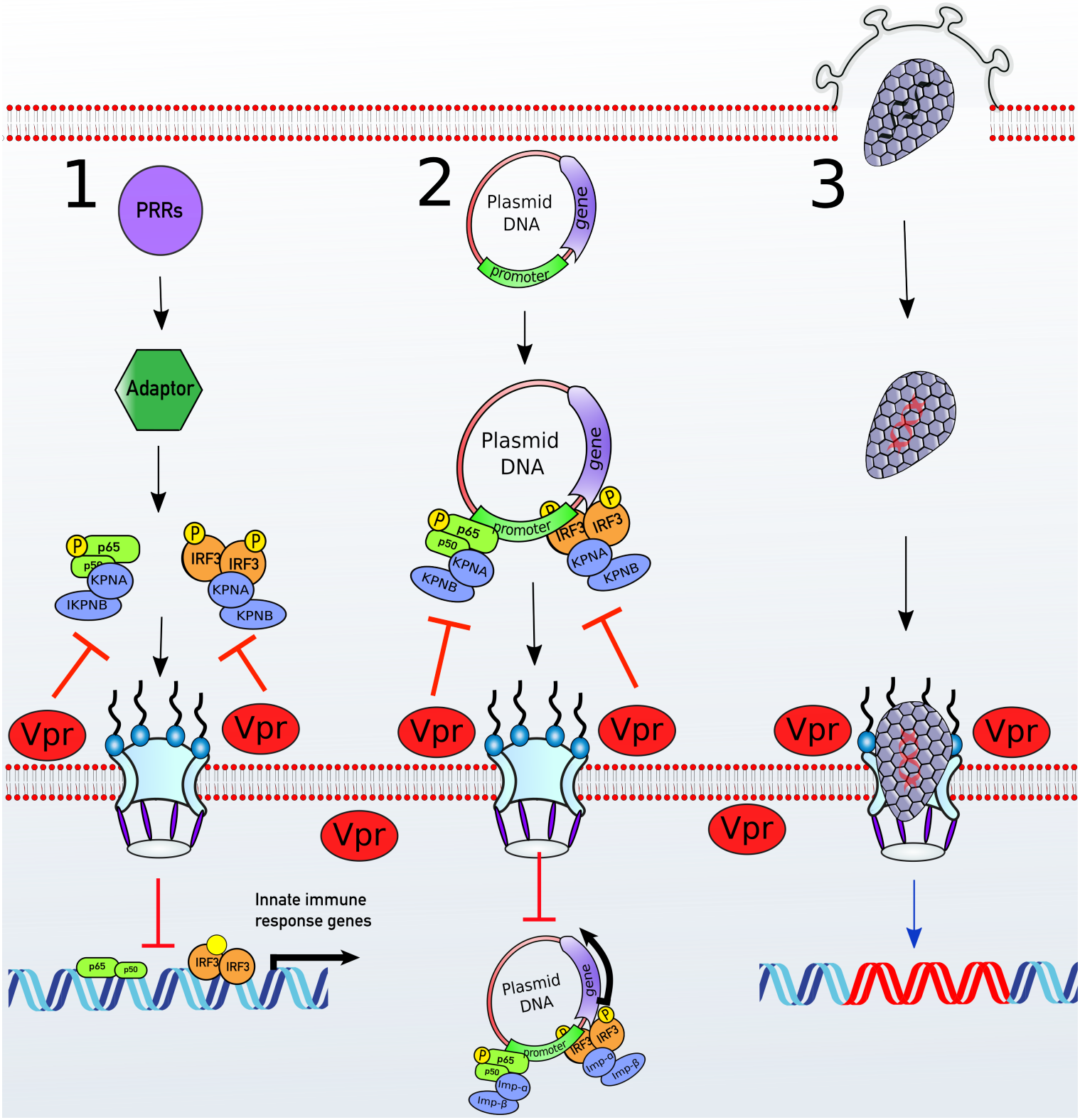

Figure 7 figure supplement 1 A unifying model of Vpr function

(1) Stimulation of various PRRs results in activation of transcription factors such as IRF3 and NF-κB. To activate ISGs or proinflammatory genes expression, NF-κB and IRF3 translocate to the nucleus via the classical Karyopherin-α/β dependent nuclear import pathway. **(2)** Nuclear import of a plasmid transfected into cellular cytoplasm is essential for gene expression. Transcription factors such as IRF3 and NF-κB bind to their cognate response elements present in the promoter of the plasmid and allow nuclear import via the classical karyopherin-α/β dependent pathway (Mesika et al., 2001) as well as transcription. **(3)** HIV-1 based vectors deliver genes to the nucleus in a karyopherin-α/β independent manner. Vpr localises to the nuclear pores and targets karyopherin-α dependent nuclear import in a DCAF1 E3 ubiquitin ligase dependent manner. This inhibits nuclear translocation of transcription factors such as IRF3 and NF-κB and subsequent antiviral ISG expression. This also inhibits IRF3 and NF-κB dependent plasmid expression or nuclear import but does not impact lentiviral gene delivery.