A series of experiments clearly indicate that RABV infection is sensitive to type 1 IFN signaling and that P and N protein-mediated IFN evasion is efficient to promote virus replication. Nevertheless, in the course of infection, the IFN induction in the whole RABV-infected nervous system, NS, is far from being abrogated. Indeed, after injection of RABV (Challenge Virus Standard, CVS strain) into the hindlimbs of mice, a progressive infection within the spinal cord and the brain is accompanied by a robust innate immune response characterized by a type 1 IFN response. It may not be surprising that IFN can be produced in the NS during infection because the mechanisms evolved by RABV to escape the IFN response are restricted to infected neurons, the only cell type expressing the P and N proteins. These mechanisms cannot operate in glial cells because they do not express any viral proteins, glial cells being rarely infected in vivo. Nevertheless, glial cells are innate-immuno-competent cells and they do not need to be infected to mount an innate immune response suggesting that non infected glial cells may be the source of heterocellular IFN in the RABV -infected NS. One can wonder what the function of the heterocellular IFN in RABV infection is. Beside intrinsic antiviral properties, IFN also controls the expression of a large number of IFN stimulated genes (ISG). The ligand of the Programmed death protein-1, (PD-L1) (also named B7-H1), is an ISG which expression is upregulated in RABV-infected NS and which has been demonstrated to be a critical factor for RABV neuroinvasiveness. Thus, it can be proposed that RABV evades the antiviral effect of IFN in the infected neurons, whereas RABV benefits from the heterocellular IFN to facilitate its progression in the NS.