

狂犬病市街毒之致死機轉

1. 狂犬病減毒株(TriGAS)對狗進行肌肉感染可誘導血清病毒中和抗體(VNA)的產生。在狗進行減毒株(TriGAS)的脊髓鞘內(intrathecal immunization, IT)免疫會在周邊和腦脊液(CSF)中誘導高力價的血清病毒中和抗體(VNA)，並暫時增強血腦屏障(blood-brain barrier, BBB)的通透性。
2. 反之，狂犬病市街毒株(wt) DRV-NG11的感染會產生抗狂犬病病毒(RABV)之抗體，但不含血清病毒中和抗體(VNA)和抗G蛋白之特異性抗體。結果，所有感染了市街毒株(wt)的狗都死於狂犬病。
3. 結論：未能激活保護性免疫是犬狂犬病市街毒發病機制的重要特徵之一。

Differential Host Immune Responses after Infection with Wild-Type or Lab-Attenuated Rabies Viruses in Dogs

Gnanadurai CW, Yang Y, Huang Y, Li Z, Leyson CM, Cooper TL, Platt SR, Harvey SB, Hooper DC, Faber M, Fu ZF. Differential Host Immune Responses after Infection with Wild-Type or Lab-Attenuated Rabies Viruses in Dogs. PLoS Negl Trop Dis. 2015 Aug 20;9(8):e0004023. doi: 10.1371/journal.pntd.0004023. PMID: 26292099; PMCID: PMC4546273.

Rabies virus (RABV) induces encephalomyelitis in humans and animals. One of the major problems with rabies is that the infected individuals most often do not develop virus neutralizing antibodies (VNA). In this study we have investigated the host immune response to RABV infection in dogs, using a live-attenuated (TriGAS) or a wild-type (wt) (DRV-NG11) RABV isolated from a rabid dog.

Methodology/Principal Findings

The experimental infection of dogs with TriGAS induced high levels of VNA in the serum, whereas wt RABV infection did not. Dogs infected with TriGAS developed antibodies against the virus including its glycoprotein, whereas dogs infected with DRV-NG11 only developed rabies antibodies that are presumably specific for the nucleoprotein, (N) and not the glycoprotein (G). We show that infection with TriGAS induces early activation of B cells in the draining lymph nodes and persistent activation of DCs and B cells in the blood. On the other hand, infection with DRV-NG11 fails to induce the activation of DCs and B cells and further reduces CD4 T cell production. Further, we show that intrathecal (IT) immunization of TriGAS not only induced high levels of VNA in the serum but also in the CSF while intramuscular (IM) immunization of TriGAS induced VNA only in the serum. In addition, high levels of total protein and WBC were detected in the CSF of IT immunized dogs, indicating the transient enhancement of blood-brain barrier (BBB) permeability, which is relevant to the passage of immune effectors from periphery into the CNS.

Conclusions/Significance

IM肌肉 infection of dogs with TriGAS induced the production of serum virus neutralizing antibodies (VNA). Whereas, intrathecal (IT) immunization of TriGAS in dogs induces high levels of VNA in the periphery as well as in the CSF and transiently enhances blood-brain barrier (BBB) permeability. In contrast, infection with wild-type (wt) DRV-NG11 resulted in the production of RABV-reactive antibodies but VNA and antibodies specific for G were absent. As a consequence, all of the dogs infected with wild-type (wt) DRV-NG11 succumbed to rabies. Thus the failure to activate protective immunity is one of the important features of RABV pathogenesis in dogs.