ImmunoTools *special* Award 2013

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Characterization of plasmacytoid dendritic cells infection by Junin virus, induction of type I interferon and its modulation by platelet

The *Arenaviridae* family, whose prototype is lymphocytic choriomeningitis virus (LCMV), contains more than 20 members with diverse geographical distributions. The arenaviruses are essentially rodent-borne viruses. LCMV infects *Mus musculus*, the common mouse, which explains why this virus is the only arenavirus with a worldwide distribution. In contrast, the other arenaviruses infect different types of rodents with circumscribed geographical distribution patterns that relate to the distribution of the associated viruses. In the rodent, arenaviruses usually establish a persistent chronic infection with few symptoms. However, arenaviruses may occasionally be transmitted to humans through material contaminated with an infected rodent's excreta. Historically, 5 types of arenavirus have been associated with hemorrhagic fever (HF): Junin virus (JUNV), the etiologic agent of HF in Argentina (AHF); Machupo virus (MACV), the etiologic agent of HF in Bolivia; Guanarito virus (GTOV), the etiologic agent of HF in Venezuela; Sabia virus (SABV), the etiologic agent of HF in Brazil; and Lassa virus (LASV), the etiologic agent of HF in west Africa (Lassa fever).

Viral hemorrhagic fevers (VHFs) caused by arenaviruses are acute diseases characterized by fever, headache, general malaise, impaired cellular immunity, eventual neurologic involvement, and hemostatic alterations that may ultimately lead to shock and death. The pathogenesis of the viral hemorrhagic fevers are still poorly understood. However, it is generally accepted that these causes are associated to some degree with impaired hemostasis, endothelial cell dysfunction and low platelet counts or function.

The dendritic cells (DC) are critical cells during viral infections. Many studies have shown that DCs are selectively target by several viruses, including arenavirus. The virus strategy consist to subvert the DC function in order to avoid or reduce the host immune response and consequently benefit its own replication and dissemination. As a result of the resulting immunosuppression, viral persistence may occur in the host. Recent research findings suggests a direct relationship between a particular subpopulation of DC named plasmacytoid dendritic cells (pDCs), and platelets that may decide if a viral infection became acute or persistent by mechanisms that involve type I interferon (IFN-I). However, the infection of pDCs by the arenavirus Junín (JUNV) have been not been studied before. In this project, we propose to

characterize the pDC infection by JUNV, its association with the IFN-I levels, and the eventual modulation of the pDC response by platelet interaction. Particularly, it will be study from the beginning of the infection, the levels of susceptibility to the infection with the degree of activation, function, viability, and production of IFN-I by murine pDCs infected with JUNV in function of time. In addition, it will be correlated the viral genic expression and the eventual modulation by platelets using in vitro models. The studies will be performed with 2 JUNV strains of different pathogenicity. The results obtained with the murine model will finally be compared with a similar human model.

The reagent mentioned in this application award will be extremely usefull in order this project may be successfully finished.

Selected bibliography

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