

Public Abstract

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The role of macrophages and anti-viral antibodies in West Nile virus pathogenesis

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Since the introduction of West Nile virus into the United States in 1999, the virus has spread throughout the continental territory of the United States and it is suspected that the virus has moved present into Mexico and Canada. The emergence of this flavivirus in North America has resulted in an intense interest in the virus, leading to research efforts focused on the pathogenesis and possible treatments or methods for prevention of the disease. In the present studies, we demonstrate the ability of WNV to productively infect horse monocytes, CD4<sup>+</sup> T lymphocytes as well as monocyte-derived macrophages. Along with these findings we report the ability of immune horse serum to induce antibody dependent enhancement of WNV infection of horse macrophages and mouse macrophages *in vitro*. The question of ADE *in vivo* was also addressed and we found that the sub-neutralizing dilutions of anti-WNV immune horse serum that induce ADE *in vitro* fail to induce the same effect *in vivo*. The serum induces protection, which is perhaps driven by the up-regulation of IL-12 in spleen during the earliest phase of infection. In brain the chemokines C-10 and MCP-5 are secreted earlier than other chemokines and cytokines, suggesting that those chemokines play an important role in the beginning of the encephalitis caused by WNV. High titers of virus in blood and spleen, as well as the ability of the virus to infect horse monocytes and CD4<sup>+</sup> lymphocytes suggest that this virus spreads from subcutaneous tissue to the brain by a hematogenous route.