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Successful treatment of Ebola virus infected nonhuman primates with monoclonal antibodies

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E bola virus can cause a fulminant infection and rapid progression to death in humans and nonhuman primates. Although of Frelatively low consequences to public health worldwide, Ebola virus infection has been one of the most challenging infectious agent to control through prophylaxis or therapeutic interventions. Recent strategies have succeeded in preventing acquisition of infection in nonhuman primates following vaccination; however, treatment of infected animals has shown some successes only minutes after infection. This study shows that a combination of three monoclonal antibodies directed against the Ebola envelope glycoprotein administered at 24 hours after a lethal infection of cynomolgus macaques with Zaire Ebola virus (ZEBOV) resulted in complete survival (4/4) with no apparent side effect. The same treatment of 25 mg of antibody per kilogram of body weight administered first after 48 hours resulted in 2 animals out of 4 fully recovering from the lethal infection with ZEBOV. These data complement and further support the important role of the humoral immune response in controlling Ebola virus replication in vivo. Recent experiments analysing cellular and humoral responses from 144 nonhuman primates show that certain antibody responses correlate with protection with the highest statistical significance. Overall, these studies support the use of monoclonal antibodies for the treatment of severe viral infection and the use of antibody responses as a reliable predictor of survival against Ebola virus.

Biography

Dr. Gary Kobinger has obtained his PhD research at the University Montreal which focused on the development of novel gene therapy with HIV-1 proteins and their mechanism in preventing HIV-mediated immunosuppression, where his first landmark scientific contribution was to demonstrate that the HIV Vpr protein could be used as a Trojan horse to deliver amino acid sequences capable of inhibiting HIV replication in CD4+ T cells.

Dr, Kobinger's post-doctoral training was completed at the University of Pennsylvania, where his research was focused on the application of lentiviral, adenoviral and adeno-associated viral vectors for gene therapy and vaccine development. His second landmark scientific contribution was to use pseudotyping as a strategy to target lentiviral vectors to specific cell types in vitro and in vivo). It is worth noting that his initial findings pioneered a since growing field of pseudotyping lentiviral vectors leading to in vivo transduction of organs such as muscle, lungs, brain and liver. It was highlighted as one of the "Best 100 Ideas of 2001" according to the Times Magazine, and to date there are more than 100 peer-reviewed articles published by different research groups around the world.

The National Microbiology Laboratory (NML) is one of a handful of laboratories around the world and the only one in Canada that can handle highly infectious containment level 4 (CL-4) pathogens with significant public health impact to which he is now the Chief, Special Pathogens Program. Dr. Kobinger has since made many more important research contributions, with the most significant being the development and characterization of human, chimpanzee and porcine adenoviral vectors for protection against Ebola virus, SARS coronavirus, H5N1 influenza virus and Hantaviruses in different animal models.

Dr. Kobinger has published over 60 peer-reviewed manuscripts, 4 book chapters or review articles and is the holder of 9 patents. It should be noted that over 35 of these peer-reviewed articles were published within the past 5 years, which strongly indicates the recent relevance of his work.

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