Genetic Engineering and Gene Cloning: Open Access
Received: Oct 29, 2015, Accepted: Nov 23, 2015, Published:Nov 27, 2015
Genet Eng Gene Cloning, Volume 1, Issue 1
http://crescopublications.org/gegcoa/GEGCOA-1-001.pdf
Article Number: GEGCOA-1-001

Editorial Review Open Access

Future Strategies for Rabies Control and Treatment

Shimao Zhu*

Shenzhen Weiguang Biological Products Co., Ltd, China

***Corresponding Author:** Shimao Zhu, Shenzhen Weiguang Biological Products Co., Ltd, China, E-mail: zhushimao1118@163.com

Citation: Shimao Zhu (2015) Future Strategies for Rabies Control and Treatment. Genet Eng Gene Cloning 1: 001.

Rabies is an ancient neurological disease caused mainly by Rabies Virus (RABV) and is almost invariably fatal once the clinical symptoms develop. Currently, rabies continues to present a public health threat in most areas of the world, especially in the developing countries of Asia and Africa. It has been estimated by the WHO that more than 55,000 human deaths are caused by rabies through bites from rabid animals annually worldwide.

The beginning of rabies starts from a bite of a rabid animal, such as stray dogs, in the periphery site followed by entry of virus into the Central Nervous System (CNS) via a motor neuron at the neuromuscular junction in a retrograde direction. Once in the CNS, the virus travels rapidly within the axons at a rate of 8 to 20 mm/d in rodents, and probably faster in humans (15-100 mm/d). Besides, virus infection causes neuronal dysfunction which probably the main cause of the fatal outcome of rabies.

Fortunately, rabies is preventable *per se* provided that Post Exposure Prophylaxis (PEP) is given promptly. As rabies virus may take days or weeks to reach the CNS, this time interval provides the valuable chance to limit and control virus infection. Most importantly, recent studies have demonstrated that rabies can be cured in theory through clearing virus infection from the CNS, at least in the mouse model. Due to the almost 100 % mortality of rabies, currently only inactivated vaccines have been approved for human use. However, once the infection has progressed into CNS, inactivated viral vaccines have no protection against virus infection. What makes thing worse, it has been stated that delayed treatment with inactivated rabies vaccines might actually accelerate the development of rabies. At this situation, live, highly attenuated, or even totally avirulent RABV strains which could trigger cellular as well as humoral immune responses, are more ideal candidates for future vaccine development.

Live-attenuated recombinant RABV has been shown to enhance the permeability of the blood-brain barrier, thus facilitating the infiltration of immune effectors from the periphery into the central nervous system (CNS) and the immune clearance of RABV from the CNS. To increase vaccine immunogenicity, several strategies have been employed such as insertion of innate immunity genes like cytokine/chemokine into vaccine candidates, expression of multiple copies of viral glycoprotein and direct insertion of interferon gene into the viral backbone. Through using live-attenuated recombinant RABV, it has been shown to elicit better immune responses against RABV infection, and excitingly, can even protect the recipient from rabies several days after inoculated with virus, shedding light on future clinical therapy for cases with delayed treatment. On the other hand, it has been shown that during the immune protection of rabies, functional T cell could only promote the survival of infected mice but cannot clear the virus from the CNS, and infiltration of Virus Neutralizing Antibodies (VNA) from the circulation, either naturally developing or intraperitoneally administered, into the CNS tissues has minimal role in clearing virus infection. These studies led to the conclusion that it is the VNA produced *in situ* by invading B cells rather than those produced in the periphery and then crossed into the CNS, that are pivotal in clearing RABV from the CNS.

However, recently, a study reported that intravenously administered VNA can help to clear an established RABV infection from the CNS given that the blood-brain barrier permeability was enhanced by Monocyte Chemotactic Protein-1 (MCP-1), suggesting that simultaneously administration of VNA and MCP-1 might be a way for developing VNA therapy for clinical rabies. However, considering that MCP-1 might negatively affect the function of CNS through uncontrolled enhancement of the blood-brain barrier, cautions should be taken to maximally mitigate the adverse effect of MCP-1.

Live-attenuated viruses have proven to be effective vaccines against many diseases, such as smallpox, yellow fever, and measles, and live-attenuated viruses are at some circumstances more effective than inactivated viruses in triggering host immune response. Due to high mortality of rabies, live attenuated RABV strain has been only approved for animal use. However, after systematically manipulating the RABV genome using reverse genetic technique, it would be desirable to obtain highly attenuated live RABV strains with elevated immunogenicity which promises to provide a novel approach for the development of vaccines against rabies as well as other numerous problematic viral pathogens.