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## Creation of highly efficient recombinant viral vectors for development of prime-boost vaccines: Matrix protein gene variants of two antigenically distinct serotypes of vesicular stomatitis virus are ideal vaccine vectors for viral, bacterial and parasitic diseases

In order to induce the maximum immune responses by vaccination, the priming recombinant viral vector should be antigenically distinct from the boost vaccine vector. A priming vaccine vector will most likely induce neutralizing antibodies which will neutralize the boosting vaccine vector if one uses the same vector for the prime-boost. One of the rhabdo viruses, the vesicular stomatitis virus (VSV), offers the ideal system for prime-boost vaccine vectors. We have generated safer and more highly efficient recombinant VSV vaccine vectors using two antigenically distinct Indiana serotype ($VSV_{Ind}$) and New Jersey serotype ($VSV_{NJ}$). The M51R mutation in the M gene of $VSV_{Ind}$ was combined with a temperature sensitive mutation of the $VSV_{Ind}$ Orsay tsO23 for priming vaccine vector [designated as $rVSV_{Ind}$ (GML)]. In addition, we have generated two new $VSV_{NJ}$ vaccine vectors by combining M48R+M51R mutation with G22E and L110F mutations in the M gene of $VSV_{NJ}$, [designated as $rVSV_{NJ}$ (GMM) and $VSV_{NJ}$(GMML)] for boosting. The combined mutations of G21E/M51R/L111A in the M protein of $VSV_{Ind}$ [$rVSV_{Ind}$(GML)] significantly reduced the burst size of the virus by up to 10,000 fold at a semi-permissive temperature of 37°C without affecting the level of protein expression. The $BHK_{21}$ cells and human neuroblastoma, SH-SY5Y cells infected with $rVSV_{Ind}$ (GML), $rVSV_{NJ}$(GMM) and $rVSV_{NJ}$(GMML) showed significantly reduced cytopathic effects in vitro at 37°C, and mice injected with one million infectious particles of the viruses into the brain showed no neurological dysfunctions or any other adverse effects. In contrast, only one thousand wild-type $VSV_{Ind}$ killed mice within four days. To examine the $CD8^+$ T cell and B cell responses against the protein of interest expressed from the new rVSV vectors, we generated rVSVs with HIV-1gag, pol and/or env genes. From the various vaccination regimens tested in mice, priming with $rVSV_{Ind}$ (GML)-HIV-1gag, pol, and/or env and boosting with $rVSV_{NJ}$(GMM)-HIV-1gag, pol, and/or env and $rVSV_{NJ}$(GMML)-HIV-1gag, pol, and/or env induced the strongest $CD8^+$ T cell immune responses against HIV-1 Gag, Pol, and Env proteins. The same vaccination regimen also induced strong humoral immune responses against HIV-1 Gag and Env proteins in mice. The best humoral immune responses against HIV-1 Gag and Env proteins were induced when two serotypes of rVSV were alternated for prime and boost vaccination. Increasing vaccination doses of $rVSV_{Ind}$ (GML)-HIV-1 gag, pol, and/or env, $rVSV_{NJ}$ (GMM)-HIV-1gag, pol, and/or env and $rVSV_{NJ}$ (GMML)-HIV-1gag, pol and/or env induced stronger immune responses against HIV-1 Gag, Pol and Env proteins in mice. As a boost vaccine vector, $rVSV_{NJ}$ (GMM), it induced better cellular and humoral immune responses against HIV-1 Gag and Env proteins compared to $rVSV_{NJ}$ (GMML) with the same vaccine dose. This is our unique platform technology and is useful for development of not only viral diseases but also bacterial diseases and even parasitic diseases.

### Biography

C Yong Kang, PhD, DSc, FRSC, is a Molecular Virologist and Professor of Virology in the Department of Microbiology and Immunology, Schulich School of Medicine and Dentistry at the University of Western Ontario in Canada (1992-Present). He carried out his Post-graduate studies at McMaster University where he received a PhD in Virology and his Post-doctoral training, Nobel Laureate in Physiology and Medicine at the University of Wisconsin-Madison. He went on to serve as a Professor of Virology in the Department of Microbiology at the University of Texas, Professor and Chairman of the Department of Microbiology and Immunology at the University of Ottawa, and Dean of Science at the University of Western Ontario. His research in molecular virology includes the development of viral-specific antiviral therapeutic agents and efficacious vaccines against various human viral diseases including AIDS, hepatitis and hemorrhagic fever with renal syndrome. He has published 135 peer reviewed research papers and 149 scientific proceedings and abstracts in the fields of virology, Immunology, molecular biology, and medicine. He holds nine international biotechnology patents that cover over 70 countries. He also serves as a reviewer for the Journal of Virology, Journal of Infectious Diseases, Virus Research, Virology, Journal of Biological Chemistry, Journal of Human Virology and Retrovirology, and Canadian Medical Association Journal.

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