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Engineering of highly efficient recombinant viral vectors for development of prime-boost vaccines against viral diseases

C Yong Kang
Western University, Canada

In order to induce the maximum immune responses, the priming recombinant viral vector should be antigenically distinct from the boost vaccine vector. We have engineered safer and highly efficient recombinant vesicular stomatitis virus (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 *ts*O23 for priming vaccine vector [$rVSV_{Ind}$ (GML)]. In addition, we have engineered VSV_{NJ} vaccine vector by combining M48R+M51R mutation with G22E and L110F mutations in the *M* gene of VSV_{NJ} [VSV_{NJ} (GMML)] for boosting vaccine vector. 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. Mice injected with one million infectious particles of $rVSV_{Ind}$ (GML) 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 proteins of interest expressed from the rVSV vectors, we generated rVSVs with HIV-1*gag*, *pol* and/or *env* genes. From the various vaccination regimens tested in mice, priming with $rVSV_{Ind}$ (GML)-HIV-1*gag, pol,* and/or *env* and boosting with $rVSV_{NJ}$ (GMML)-HIV-1*gag, 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. This is our unique platform technology and is useful for development of vaccines against many other viral diseases.

Biography

C Yong Kang has completed his PhD from McMaster University in Canada and Post-doctoral training at the University of Wisconsin-Madison. He served as a Professor of Virology at the University of Texas Southwestern Medical School, Professor and Chairman at the University of Ottawa Faculty of Medicine, and Dean of Science at the University of Western Ontario. He has published 137 peer reviewed research papers and 151 scientific proceedings and abstracts. He holds 9 international biotechnology patents. He received numerous awards including the Ho-Am Prize in Medicine. He is a Life-time Fellow of the Royal Society of Canada Academy of Science. He serves as a reviewer for 8 international journals.

cykang@uwo.ca

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