

Establishment of lipid-based immunogens for the development of novel subunit vaccines

Chih-Hsiang Leng

National Health Research Institutes, Taiwan

We have established a platform technology for high-yield production of recombinant lipoproteins. The lipid moiety of the produced lipoproteins is identical to that of bacterial lipoproteins, which are recognized as danger signals by the immune system. Thus, both innate and adaptive immune responses can be induced by lipoproteins. Ag473 (a lipoprotein from *N. meningitidis*) can be produced in high yields using *E. coli* strain C43 (DE3). After testing a non-lipoprotein (E3, from dengue virus) fused with different lipid signal peptides, we identified that a fusion sequence, D1, to express a recombinant lipoprotein, ripo-D1E3, at high level. Multiple-stage fragmentation and immunological analysis demonstrated that the structure of recombinant lipoprotein was different from that of synthetic tri-acylated lipopeptide and it elicited different immune responses from synthetic lipopeptide by inducing different levels of biological cytokines and chemokines. The ripo-D1E3 was found to elicit stronger virus neutralizing antibody responses than those from rE3 alone or rE3 formulated with alum adjuvant. Moreover, an inactive human papillomavirus (HPV) E7 (E7m) biologically linked to a bacterial lipid moiety (riipo-E7m) induced the maturation of mouse bone marrow-derived dendritic cells through toll-like receptor 2, skewed the immune responses toward the Th1 responses and induced E7-specific CTL responses. We further validated that the ripo-E7m was able to induce anti-tumor immunity against HPV associated tumors in a mouse model. The therapeutic efficacy of E7m was dramatically increased in its lipidated form. These results have successfully demonstrated the merit of lipo-immunogens for the development of novel subunit vaccines.

Biography

Chih-Hsiang Leng has completed his PhD from National Defense Medical Center, Taiwan and Postdoctoral studies from Division of Biotechnology and Pharmaceutical Research, National Health Research Institutes (NHRI). He is an Associate Investigator in National Institute of Infectious Diseases and Vaccinology, NHRI and is now working for the development of novel and effective recombinant subunit-based vaccines. He collaborated with his colleagues to develop novel polymer-based adjuvant for enhancing the potency of subunit vaccines and to establish a novel lipoprotein expression system to produce high potent lipo-immunogens for the development of novel subunit vaccines.

leoleng@nhri.org.tw