以家蠶為生物反應器生產禽流感 H5 次單位疫苗

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摘要

高病原性禽流感病毒H5N1自1997年爆發感染後，已在全球肆虐，造成歐亞及非洲地區 62個國家感染，並造成至少1億隻禽鳥因染病或撲殺而死亡。台灣鄰近中國大陸且是候鳥南遷必經之地，位處禽流感高危險地區。顧及對本國整體畜牧產業之保護及國人公共衛生安全之維護，因此必須開發緊急防疫用疫苗，做為防疫工具之一。已知利用經過重組的家蠶核多角體病毒，以家蠶幼蟲(silkworm larvae)或蠶蛹(pupae)做為生物反應器，可以大量表現所需的重組蛋白，進而降低抗原的生產成本。目前成功應用蠶蛹表現禽流感H5N1病毒株之血球凝集素HA（Hemagglutinin）抗原，並試製H5次單位疫苗，結果顯示以蠶蛹表現之H5重組抗原可以誘發雞隻產生良好之血球凝集抑制抗體反應，並且每顆蠶蛹平均可生產1mg之HA抗原。在疫苗安全性評估，雞隻無不良反應產生。基於上述實驗結果，此表現系統未來可做為禽流感疫苗之儲備抗原生產使用。

Development of Avian Influenza H5 Subunit Vaccine by Silkworm Bioreactor

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Abstract

Since the outbreak in 1997, the H5N1 highly pathogenic avian influenza virus (HPAIV) has been found in 62 countries in Asia, Europe and Africa, and over one billion birds has died or killed. As Taiwan is located on the flyway of migratory birds and close to the mainland China, these geographic characteristics lead to high risks for HPAIV infection. Therefore, for public health concern, it is important to develop an efficacious avian influenza (AI) vaccine for domestic poultry for emergency use. Using Bombyx mori nuclear polyhedrosis virus as vector, combining with silkworm larvae or pupae as bioreactor to obtain recombinant proteins, is known to be a low cost and efficient way to produce the vaccine on a large scale. We have successfully expressed the majority H5N1 H antigen, the hemagglutinin, to develop the subunit vaccine with this expression system. The results showed that the pupae-derivative rHA subunit vaccine can induce adequate hemagglutination inhibition (HI) antibody response in chicken. The HA antigen can be effectively produced by pupae with an average yield of 1mg per pupae in average. In addition, there is no side effect shown in chicken on the pilot vaccine test. Based on the above results, it suggests that the baculovirus-larvae recombinant protein system could be a reserved antigen production of AI vaccine in the future.