含新佐劑之牛流行熱疫苗研發

製劑研究組

李燕霖 助理研究員

摘要

牛流行熱是由桿狀病毒經吸血昆蟲媒介傳染的發熱性疾病，在台已成為常在性疾病，除使牛隻產生高熱、呼吸症狀、關節疼痛等臨床症狀之外，泌乳量遽減常造成重大經濟損失。為改善本所牛流行熱不活化疫苗以水質磷酸鋁膠作為佐劑，抗體高峰期不夠長的缺點，於104 年起著手研發含新佐劑之牛流行熱疫苗，陸續完成小鼠、兔子及牛的試驗，並於 107 年開始田間試驗，108 年完成兩試驗場第三次免疫後長達一年的效力評估，中和抗體力價不僅高且維持期相當長久；另外此疫苗對於小牛及懷孕牛安全性均高。3 批疫苗保存 21 個月之安定性試驗中，疫苗外觀性狀均無改變並通過無菌檢驗，以牛與兔子進行安全試驗，注射後均正常；效力部分，3 批疫苗保存 21 個月後與剛製造完 0 個月時相較，誘發中和抗體的能力並未降低，3 批疫苗彼此之間的效力也非常相近。攻毒試驗結果顯示，以野外病牛血攻擊之小牛出現病毒血症，同時體溫略高及呼吸次數增加並持續數天均可在血中偵測到病毒核酸；免疫後再攻毒之小牛則沒有出現任何病毒血症及其他臨床症狀。綜合各項試驗結果可發現此疫苗不僅安全，且免疫效果優秀，已於 108 年 7 月完成變更疫苗許可證使用之賦形劑，目前生產之牛流行熱疫苗已全面更改為新佐劑，希望可提供農民高免疫效益之疫苗按照免疫期程施打，藉此有效防治台灣牛流行熱疫病發生。

Development of a bovine ephemeral fever vaccine containing a new adjuvant

Yen-Lin Lee

Abstract

Bovine ephemeral fever (BEF) is an acute febrile illness affecting cattle and water buffaloes, caused by an arthropod-borne rhabdovirus. BEF has become an endemic and persistent infection disease in Taiwan affecting cattle. In addition to causing the the clinical symptoms such as high fever, respiratory syndrome and joint pain, this disease causes serious economic damage to the dairy industry, due to the potential reduction in milk production. Although the conventional aluminum phosphate (Al-gel) vaccine is safe, the high serum neutralizing (SN) antibody titer does not persist long enough to provide effective protection for cattle herds. To improve this, the development of the BEF vaccine containing a new adjuvant began in 2015. Animal trials were conducted on mice, rabbits, and cattle in succession and field trials started on two farms in 2018. Vaccine efficacy tests resulted in conferred immunity for one year after the 3rd immunization. The titers of SN antibodies remained high and had a long maintenance period. The vaccine was safe for both calves and pregnant cattle causing no adverse effects. Vaccine stability tests established that new vaccines from three different batches did not change in texture or color, and remained sterile after 21 months in storage. Safety tests conducted with rabbits and calves, demonstrated no adverse effects . Furthermore, efficacy test results demonstrated that the ability of the vaccine to elicit SN antibodies after long-term storage was almost the same as at the time of production, and that the results were very similar among the three batches. Calves exhibited viremia two days after challenges using the blood of infected cattle and viral nucleic acids were detected in calf blood for more than ten subsequent days. Meanwhile, calf body temperatures and respiratory rates also increased. In regard to the calves that were vaccinated prior to the challenge, no viremia or any other clinical signs were observed. In summary, this BEF vaccine displays an excellent ability to elicit a strong and enduring SN antibody response without significant safety concerns. The animal pharmaceutical license, with the change in adjuvant added to the BEF vaccine, was approved in 2019, and the current BEF vaccine manufactured by AHRI now contains this new adjuvant. This developmental result will hopefully provide a high efficacy vaccine to Taiwanese farmers by conferring increased immunological protection against BEF for cattle herds in Taiwan.