家蠶攻毒室之建構

製劑研究組
助理研究員 黃琦新

摘要

為改善疫苗製程、降低成本、提升疫苗效能，本所研發以家蠶生產平台製造豬瘟 E2 次單位疫苗。家蠶生產平台是運用核多角桿狀病毒(Bombyx mori nuclear polyhedrosis virus, BmNPV)作為基因載體，感染家蠶大量表現外來蛋白；在真核系統中，外來蛋白經過適當的醣基化、磷酸化等修飾，折疊產生正確的三級結構，因此具有高生物活性的優點。家蠶核多角體病毒僅只感染家蠶，即使被釋放至田間，也不會感染其它生物，所以不會造成生態污染。相較於發酵槽或組織培養，使用家蠶做為生物反應器，生產基因工程蛋白，具有成本低、效率高等優點。為落實研發成果能夠量產商品化，需建構家蠶攻毒室，作為疫苗抗原材料之生產供應線，且須符合 GMP 之規範。

利用本所已有空間資源，於 98 年規劃、整修出家蠶攻毒室之雛型，其室內環境控制在恆溫 25±2℃、恆濕 60±5%、正壓＞5Pa，並依「潔淨度」，分隔為三區：一級區－潔淨度 100 級，為無菌操作區；二級區－潔淨度 10,000 級，屬於操作室的範圍；三級區－潔淨度 100,000 級，包含飼養室、感染室等區域。此家蠶攻毒室具備二套獨立的空調系統，分別供應作業區及動物飼養區的空氣，並由單獨監控系統整合控管此二套空調系統。室內地面鋪設環氧樹脂（EPOXY），且底層經過玻璃纖維強化塑膠（FRP）之防水處理。這些規劃可做為家蠶系統小型量產之先導。未來計畫研發機械化設施，減少製程所需人力，期能達到自動化大量生產的目標。

Construction of a Silkworm Challenge Laboratory

Chyi-Sing Hwang

Abstract

In order to improve the process of vaccine production, reduce the costs, and increase vaccine efficacy, a silkworm production platform for E2 subunit vaccine of classical swine fever virus was developed. The platform utilized a baculovirus called Bombyx mori nuclear poly- hedrosis virus (BmNPV) as a vector to infect silkworms to overexpress foreign proteins. In the eukaryotic silkworm expression system, the overexpressed protein can be modified by glycosylation and/or phosphorylation to form the correct structure and possess high level of bioactivity. The BmNPV only infects silkworms and makes no biohazard if it was leaked into the field. Compared with the protein expression of fermentation tank and tissue culture, utilizing silkworms as bioreactors to overexpress the engineered protein is low-cost and high-efficiency. For large-scale production and commercialization of E2 subunit vaccine, construction of a silkworm challenge laboratory was in need.

Using the facilities and resources in AHRI, we renovated a room as the miniature of silkworm challenge laboratory in 2009. This laboratory was set up as a controlled environment in constant temperature 25± 2℃, constant humidity 60± 5%, air pressures ＞5Pa. According to the classes of air cleanliness levels in cleanrooms and clean zones, there are three classes clean zones. Zone 1－ a class 100 cleanroom, never allows more than 100 particles (0.5 microns or larger) per cubic foot of air, was designed to aseptically operate. Zone 2 and zone 3 were Class 10,000 and Class 100,000 cleanrooms, respectively. There were 2 air-conditioning systems and 1 supervisory control system in this laboratory. The laboratory floor was EPOXY with fiberglass reinforced plastics (FRP). These constructions were a model of small-scale production in silkworm system. We will develop mechanical facilities to decrease the manpower in process of vaccine production. Our aim is large-scale production automatically.