Abstract

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Development of in vitro and in vivo rabies virus neutralization assays based on a high-titer pseudovirus system

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Pseudoviruses are useful virological tools because of their safety and versatility; however the low titer of these viruses substantially limits their wider applications. We developed a highly efficient pseudovirus production system capable of yielding 100 times more rabies pseudovirus than the traditional method. Employing the high-titer pseudoviruses, we have developed robust in vitro and in vivo neutralization assays for the evaluation of rabies vaccine, which traditionally relies on live-virus based assays. Compared with current rapid fluorescent focus inhibition test (RFFIT), our in vitro pseudovirus-based neutralization assay (PBNA) is much less labor-intensive while demonstrating better reproducibility. Moreover, the in vivo PBNA assay was also found to be superior to the live virus based assay. Following intravenous administration, the pseudovirus effectively infected the mice, with dynamic viral distributions being sequentially observed in spleen, liver and brain. Furthermore, data from in vivo PBNA showed great agreement with those generated from the live virus model but with the experimental time significantly reduced from 2 weeks to 3 days. Taken together, the effective pseudovirus production system facilitated the development of novel PBNA assays which could replace live virus-based traditional assays due to its safety, rapidity, reproducibility and high throughput capacity.