STUDY OF RABIES VLPs EXPRESSION IN BHK-21 CELL LINE FOR VACCINE APPLICATIONS

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In the last decades, virus-like particles (VLPs) have played an essential role in the development of novel vaccines due the fact that they trigger robust and balanced immune responses and, as they lack viral genome, are biosafe. Nowadays, several VLPs are commercially available for human use and one veterinary product was licensed. Besides, other VLP-based vaccine candidates are in the stages of clinical trials or preclinical evaluation.

Our group had previously developed a rabies glycoprotein based-VLP (RV-VLPs) expressed in HEK293 cells. These RV-VLPs were fully characterized and their capacity to induce a protective response and neutralizing antibodies production was confirmed. As inactivated veterinary vaccines for rabies are usually produced using BHK-21, the goal of the present work was to develop a RV-VLPs expressing BHK-21 cell line to analyze the characteristics of the VLPs produced using this cell substrate.

Therefore, by lentivirus vector-mediated transduction, we generated a rabies virus glycoprotein expressing a stable cell line. The cellular expression of the recombinant protein was analyzed by flow cytometry and the membrane localization was confirmed by fluorescent microscopy. Later, RV-VLPs budding to the supernatant was analyzed by sandwich ELISA. After that, VLPs were purified by density gradient ultracentrifugation and the hydrodynamic diameter of the particles was analyzed by DLS. In a western blot assay, the particles were recognized by specific antibodies present in a rabies polyclonal serum. Finally, the recombinant cell line was cultured in 850 cm2 roller bottles producing RV-VLPs continuously during 25 days of culture. Thus, these results encourage further studies to confirm if BHK-21 is a good cell substrate for the production of RV-VLPs as a veterinary rabies vaccine candidate.