EXPRESSION OF RABIES VLPs IN ADHERENCE AND SUSPENSION CONDITIONS: A FLEXIBLE PLATFORM FOR RABIES VACCINE PRODUCTION

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Rabies is a zoonotic viral disease with a mortality by close to 100%. As there is not an efficacious treatment available, post-exposure vaccination is recommended for individuals in contact with the virus. On the other hand, the most common source of virus transmission is saliva of infected animals, mostly dogs, whereby mass vaccination of pets is the most cost-effective way to reduce human infections. In this context, availability of both human and veterinary vaccines is critical.

In previous works1-2, our group developed immunogenic rabies VLPs, expressing the virus glycoprotein in HEK293 cells. We obtained a producer clone capable of growing in adherence (adhP2E5) and then adapted to suspension conditions (sP2E5). In this work, we analyzed the production of VLPs in both conditions, using two different platforms.

On the one hand, adhP2E5 was cultured in 850 cm2 roller bottles (GBO) using medium with 5% FCS, that was exchanged every 48 h during the first 10 days and every 24 h during the last 5 days. RV-VLPs were continuously produced and the harvest obtained (2.5 L per bottle) was analyzed by sandwich ELISA, using the 6th International Standard for rabies vaccine that quantify the glycoprotein content (NIBSC), presenting a value of 19 IU.ml-1 in average. On the other hand, we cultured sP2E5 in a 5 L bioreactor during 15 days, using EX-CELL293 SFM (SAFC). The culture reached densities of 2x107 cel.ml-1 and VLPs were continuously secreted to the supernatant. The obtained harvest (28.5 L) presented a glycoprotein content of 28 IU.ml-1, a results that is comparable with the previous one taking into account the number of cells presents in both conditions.

These results showed that our clone could be cultured in both platforms depending on the objectives and characteristics of the desired product. For the production of the rabies veterinary vaccine, RV-VLPs can be produced in adherent conditions using medium supplemented with FCS and, for human vaccine production, RV-VLPs can be produced in bioreactors using SFM.

1 Fontana et al. Rabies virus-like particles expressed in HEK293 cells. Vaccine 32 (2014) 2799-2804.
2 Fontana et al. Immunogenic virus-like particles continuously expressed in mammalian cells as a veterinary rabies vaccine candidate. Vaccine 33 (2015) 4238-4246.