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Scaling up the biotechnological process of the recombinant rabies virus glycoprotein

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The rabies virus glycoprotein (RVGP) is the main antigen of vaccine formulations. A robust *Drosophila* S2 cell line (S2MtRVGPH-His) was engineered by our group for the expression of recombinant RVGP (rRVGP) using metal-inducible promoters. The objective of this work was to evaluate the potential of a WAVE Bioreactor™ in the initial steps of scaling-up the rRVGP production process by the S2MtRVGPH-His cell line to produce rRVGP in sufficient quantities for immunization and characterization studies. The WAVE bioreactor is an innovative approach for the cultivation of animal cells as it offers high process flexibility, as well as cost and time savings. For this purpose, we firstly established a Schott flasks procedure for culturing the S2MtRVGPH-His lineage. Using an inoculum of 5x10⁵ cells/mL in culture medium (Sf900-III) induced with CuSO₄, adequate pH range and parameter values such as time of induction (72 h) and temperature (28°C) to optimize rRVGP production could be defined. In the sequence, the procedure was reproduced in culture experiments conducted in a WAVE bioreactor 2/10 using a 2 L Cellbag. The results in Schott flasks and WAVE bioreactor were very similar, yielding a maximum titer of rRVGP above of 1 mg/L. After the rRVGP production process, the animals were immunized with rRVGP and submitted to rabies virus challenge. The rRVGP assessed in the immune system of the vaccinated animals showed high levels of anti-RVGP antibodies, statistically not different from the levels induced by a commercial vaccine. The animals immunized with rRVGP also survived the rabies virus challenge, whereas two negative group controls did not. This bioprocess enables an efficient scale-up of the production with high quality immunoactive glycoprotein and may be promising in terms of obtaining rRVGP in the near future in the order of grams for use in immunological, preclinical or clinical assessments.

Biography

Monize C Decarli is Biotechnologist. She has completed her Bachelor's and Master's degrees at Federal University of São Carlos, UFSCar, SP, Brazil and currently, she is developing her PhD Thesis in Chemical Engineering at the State University of Campinas (UNICAMP, SP, Brazil). She has expertise in Bioprocess, Biotechnology, Animal Cell Culture and Microbiology, and has been working in these fields since 2010. She has developed the bioprocess production of rRVGP in Wave Bioreactor for two years and half, in the course of her Master research work. This approach can be promising in terms of obtaining in the near future rRVGP in order of grams to use in preclinical assessments aiming the development of a recombinant rabies vaccine.

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