Poster

Recombinant baculovirus vector development for universal vaccine production against human common cold virus, Rhinovirus

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ABSTRACT

Motivation: HRV (Human Rhinovirus) is a pathogen member of the Picornaviridae virus family and the responsible for common cold. In addition, HRV takes a part in asthma and chronic obstructive pulmonary disease exacerbations. The costs associated with HRV infections -medical visits, treatments, job absentism- are about $60 billion per year only in the USA. There are more than 100 HRV serotypes, therefore creating an universal common cold vaccine supposes a great challenge. Another challenge for making a recombinant vaccine is that for preparation of well-conformed HRV capsid antigens, the processing of a viral polyprotein by a viral protease must be done within the hetelogous expression system. The fine tuning of expression of both the polyprotein and protease ORFs is key for getting an acceptable production yield. In this project, we investigated the properties of a dual insect expression vector with this purpose, using two types of baculovirus promoters, a very late and an early promoter, respectively.

Methods: Different working viral banks (WVB) for production of the HRV antigen in either insect cells or insect larvae were prepared by inserting several candidates for dual expression constructs into the genome of Bionaturis' Master Viral DNA, based on the Autographa californica nuclear polyhedrosis virus (AcNPV) genome. The constructs carried the ORFs encoding either (A) the HRV polyproteins M5 or M17, 2 previously optimized capsid sequences for raising a universal immune response against many HRV serotypes; (B) the HRV 3C protease, or (C) the reporter genes GFP and dTomato. The accumulation of the proteins of interest driven by the different WVBs in insect cells and larvae was analyzed.

Results: Eight WVBs comprising all combinations of promoters driving expression of either HRV- or reporter-ORFs have been successfully prepared and passed all quality-controls applied. In addition a control WVB with no insert has been prepared. Currently we are performing expression tests in both Sf21 insect cells and Trichoplusia ni larvae for analyzing the timing of expression and how that influences the yield of recovery of the HRV antigen in the best conformation. So far, the best recovery yields are in the range of 75-100 µg per larvae.

Conclusions: Optimization of recovery of a universal HRV antigen by manufacturing it in insect larvae might lead to development of the first economically sustainable vaccine against the common cold virus.

REFERENCES

1. Palmenberg, A. C., Spiro, D., Kuzmickas, R., Wang, S., Djikeng, A., Rathe, J. A., . . . Liggett, S. B. (2009). Sequencing and analyses of all known human rhinovirus genomes reveal structure and evolution. Science, 324(5923), 55-59. doi:10.1126/science.1165557
2. Felberbaum, R. S. (2015). The baculovirus expression vector system: A commercial manufacturing platform for viral vaccines and gene therapy vectors. Biotechnology Journal, 10(5), 702.
3. Son, J. H., Buchholz, R., Park, J., & Kim, S. K. (2006). Production of baculoviruses and expression of green fluorescent protein in immobilised Sf21 insect cell cultivation. Biochemical Engineering Journal, 29(1), 55-61. doi:10.1016/j.bej.2005.02.02