DEVELOPMENT OF A VACCINE PRODUCTION PLATFORM FOR POULTRY DISEASES IN AFRICA: NEWCASTLE DISEASE VIRUS NON-REPLICATIVE ADENOVIRUS-VECTORED VACCINE

Omar Farnos, Viral Vectors and Vaccine Bioprocessing Group, Department of BioEngineering, McGill University, Canada. omar.farnosvillar@mcgill.ca
Héla Kallel, Bioprocess Development Unit, Institut Pasteur de Tunis, Tunisia.
Martha Yami, National Veterinary Institute, Ethiopia.
Esayas Gelaye, National Veterinary Institute, Ethiopia.
Khaled Trabelsi, Bioprocess Development Unit, Institut Pasteur de Tunis, Tunisia.
Amine Kamen, Viral Vectors and Vaccine Bioprocessing Group, Department of BioEngineering, McGill University, Canada.

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Poultry are a vital village livestock playing an important economic and nutritional role in the livelihoods of poor rural households in developing countries, including the Sub-Saharan Africa. Poultry production in Africa is threatened by infectious diseases such as Newcastle Disease (ND), which is highly contagious and endemic, with recurrent outbreaks that provoke heavy losses every year. ND is caused by the Newcastle disease virus (NDV), a negative-sense single-stranded RNA virus from the genus Avulavirus, family Paramyxoviridae. In particular, ND is one of the major problems in village chickens in most parts of Ethiopia where commercial poultry is routinely vaccinated with inactivated or live vaccines. Available ND vaccines are produced in specific pathogen free chicken embryonated eggs, whose supply is expensive and imported from Europe.

The development and execution of the present project, funded by the Canadian International Development Research Center and presently in its initial phase, aims towards the implementation at the National Veterinary Institute (NVI), Ethiopia, of a technological platform for the production of veterinary vaccines based on the development of recombinant non-replicating adenoviral vectors, using the human adenovirus serotype 5 (Ad5). The ND adenovirus vaccine proposed, expressing protective antigens from ND virus (NDV), will provide an efficient and cost-effective system to address the limitations associated with the current vaccines such as efficacy and virus shedding in flocks of vaccinated birds.

The key success factor of the project relies on the development of a robust and cost-effective production platform using serum-free suspension HEK293 adapted cells expressing maximized rAd5 product yields. This will be achieved by augmenting the production cell mass and the cellular productivity beyond cell densities of 6 million cells per mL. Critical parameters and operating conditions impacting the yield and quality of the Ad vaccine will be identified and elevated in a rational process operating strategy that will lead to high-cell density productive infection in bioreactors. Process development and scale-up will be followed by a downstream processing, evaluation of immunogenicity, formulation and stability assays, and protective capacity assessments after viral challenge in the target animals.

Recombinant adenoviruses have been generated carrying the NDV coding sequences for the fusion (F) or the hemagglutinin-neuraminidase (HN) proteins, and also for co-expression of both genes in a bicistronic construction. Phylogenetic analyses were primarily conducted to ensure a high degree of sequence identity of the genes cloned with the genoype of locally circulating strains. Recombinant protein expression was also designed and analyzed under different regulatory sequences aiming for selection of the most immunogenic variant. Following the initial phases of project execution, the subsequent steps will define the final parameters for high-cell density infection and rAd5 production for the animal studies.

Here we discuss in detail the completed and upcoming project steps as well as the different strategies implemented to achieve the set objectives supporting the main goal of sustainable technology transfer and capacity building of the NVI in Ethiopia.