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ENHANCING ENVELOPED VIRAL PARTICLES PRODUCTION BY TARGETED SUPPLEMENTATION DESIGN: RELEASING BOTTLENECKS IN IC-BEVS

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Abstract

The increasing demand of Insect Cell-Baculovirus Expression Vector System (IC-BEVS) based biopharmaceuticals raises the interest in developing high-titer production processes. Previously, we addressed the impact of the baculovirus infection on the physiology of High Five and Sf9 host cell lines, stressing out key cellular features that support higher productivities. This information was applied to design tailored supplementation schemes to boost IC-BEVS production yields of three targets with increasing complexity: recombinant influenza neuraminidase (rNeur); enveloped influenza VLPs (Inf-VLP) and the baculovirus itself (BV). Higher rNeur productivities were achieved when supplementing High Five cultures with cholesterol. For Sf9 cells, GSH, antioxidants combined with polyamines and cholesterol yielded the best outputs during Inf-VLPs and infectious BVs production. The results also show that the viral load influence the cellular responsiveness to the supplements, with lower MOIs retrieving higher improvements of IC-BEVS specific productivity. The careful selection of the MOI in a batch infection process, along with the supplementation of culture medium with compounds altering cellular redox state and cholesterol, yielded an improvement of the systems' specific productivity up to 6 fold. The correlation between systems productivity, host cell line and target product was extensively analyzed. The resulting implications for the development of rational strategies for increased productivity are discussed.