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High cell density culture for VLP production in latent virus-free insect cell line

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HIGH CELL DENSITY CULTURE FOR VLP PRODUCTION IN LATENT VIRUS-FREE INSECT CELL LINE

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Continuous virus-like particle (VLP) production in insect cells with the baculo virus expression system faces numerous problems: The presence of defective interfering particles (DIPs) hinders continuous infection, cell growth is slower than virus replication, cell retention membranes and hollow fibres retain VLPs. High cell densities (HCD) can nevertheless enable VLP process intensification in small reactor vessels.
We were able to achieve a HCD with the Tnms42 insect cell line in both shaking flasks with pseudo perfusion and in the bioreactor utilizing an alternating tangential flow (ATF) filtration. Compared to some commercially available insect cell lines, this cell line has no persistent adventitious viral infection and is equally well suited to produce HA-GAG VLPs as HighFive™ cells. With daily medium exchange the exponential growth phase could be elongated and the total cell concentration (TCC) increased by a factor of two in the shaking flask (SF) and four in the bioreactor (BR) to ~40x10^6 cells/mL in comparison to reference batch processes (~9 Figure 1). Such HCD can be used to optimize and investigate cell concentration at infection (CCI), multiplicity of infection (MOI) and cell state at infection to reach higher volumetric VLP titers.

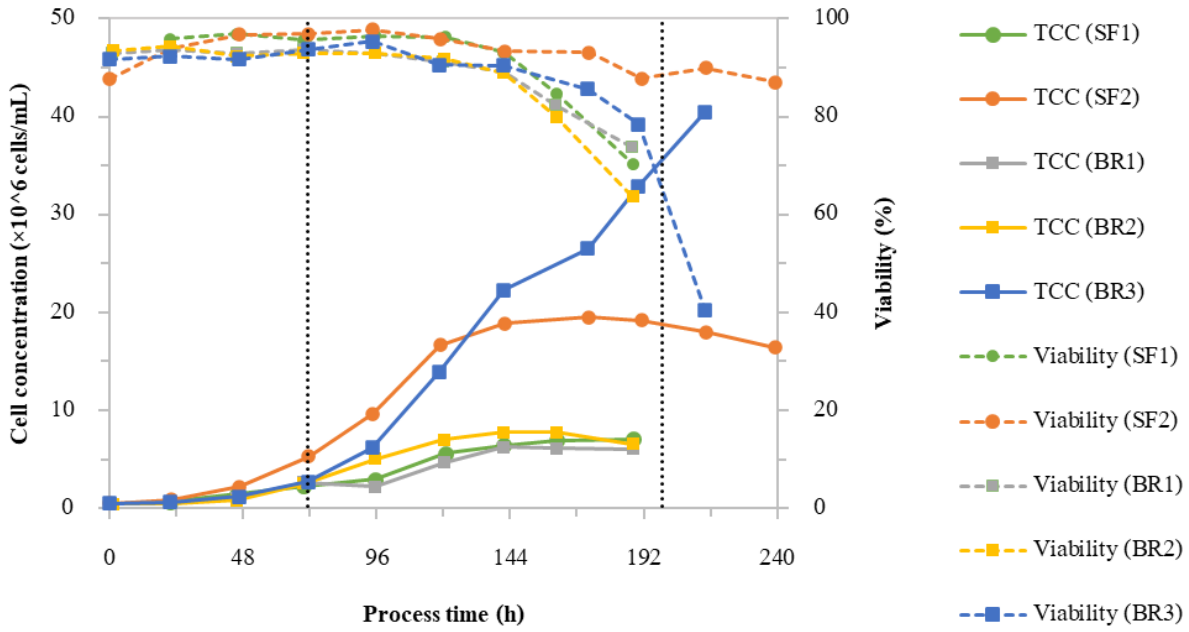

Figure 1: Total cell concentration (x10^6 cells/mL) and viability (%); SF1: batch culture SF, SF2: HCD culture SF, BR1: fed batch culture in BR with baculo virus infection after 96h, BR2: batch culture BR, BR3: HCD culture BR. The vertical lines indicate the start and end of the perfusion in the bioreactor.