ALTERNATIVE TRANSFECTION METHODS FOR SF9 CELLS IN VACCINE DEVELOPMENT

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Current CHO and HEK293 platform processes are suitable for a majority of gene-based and protein-based vaccine candidates, but do not always provide adequate production of virus-like particles (VLPs) as observed by inconsistent and low titers. Thus, alternative production platforms are being considered. One option that we are exploring is the use of insect cells as an alternative host, specifically Sf9, since they are biologically well suited to produce VLP's for mosquito-borne viruses.

We first considered a Baculovirus infection method, and successfully produced all components of two VLP's in our system. However, during initial studies of this process, we encountered issues with the assembly of the VLPs due to the low pH of Sf9 cultures (Figure 1). Thus, we pH adapted Sf9 cells to 7.0 and determined optimal bioreactor parameters to control pH throughout the process. With the capability to maintain cells at this higher pH, the Baculovirus/Sf9 platform looks promising. However, there are additional manufacturing complications to consider. There are concerns with Baculovirus contamination of dual-use equipment and more extensive and costly processing downstream to address viral inactivation and isolation. Thus, we are also considering a transient transfection process.

Several researchers have shown that PEI-based transient transfection of insect cells is a viable and reproduceable option.[1-4] Thus, we are evaluating whether a Sf9 platform process utilizing PEI would be more feasible with the current manufacturing capabilities of our organization. Using pH adapted Sf9 cells, we are presently determining optimal transfection and expression conditions using design of experiment (DOE). However, lower titers are anticipated in comparison to the Baculovirus system. As a result, productivity of transiently transfected Sf9 cells will be further investigated in a perfusion culture.

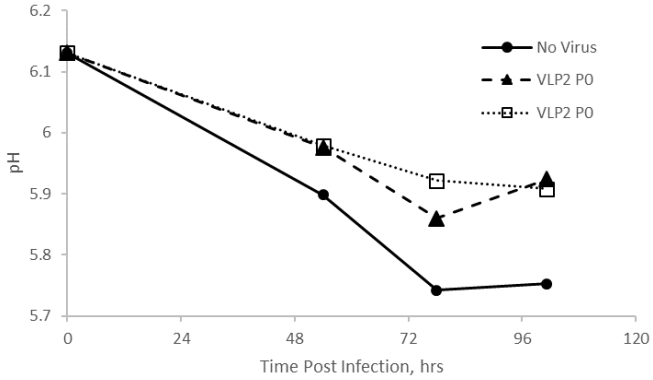

Figure 1 – pH of Sf9 cells post-infection.

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