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Development of a production and purification platform for virus like particles (VLP) and adenovirus vector vaccine candidates: Two case studies

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Case Study 1: Virus-Like Particles (VLP) have received increased attention following their success with marketed vaccines. Whilst clinical candidates have proven efficacy and protection, their large-scale production implies high titer production, high recovery and purity leading to constant process improvement to meet market demand. In this study, a Hepatitis C Virus VLP based vaccine candidate production and purification was evaluated in collaboration with Instituto de Biologia Experimental e Tecnologica (IBET), Portugal. The VLP vaccine candidate was produced in insect cell expression system in a disposable bioreactor technology and cell culture attributes were compared with those from glass stirred tank bioreactor culture. Both systems harvests were subsequently purified to assess the impact of upstream processing on the downstream and the product quality. The downstream train was improved through the selection of appropriate anion exchange resin to reach 70% recovery and a satisfactory Baculovirus log reduction. In addition, appropriate depth filtration and ultrafiltration technologies were assessed and selected. Altogether, this case study lays the foundation for a fully GMP production process that can be easily pilot transferred and implemented for clinical and subsequent commercial production of VLP vaccine candidates.

Case Study 2: Adenoviral vectors (AV) offer a promising new approach to vaccine development due to their easy transgenic coding manipulation, efficient infection of various mammalian cell types and the broad immune response against the target antigen in vaccine recipients. Furthermore, these vectors are known to offer excellent safety profile, in that they can be engineered to be non-replicating in the vaccine recipient and they lack the molecular mechanism for integration into the host genome. AV's are highly amenable to scalable manufacturing processes such as the use of stirred tank bioreactors, high capacity filtration methods, and chromatographic purification procedures. GenVec and Merck have collaborated to evaluate different technologies for potential use in Adenoviral vector (AV) vaccine production. We will present the filter options evaluated on GenVec's AV product candidates, along with the results and filter sizing estimates for the process steps of medium exchange, lysate clarification, post-clarification filtration, concentration/ diafiltration, and post-hold sterile filtration prior to column chromatography.

Biography

Youness Cherradi, PhD is a Process Development Scientist for Merck in EMEA since 2013. He is responsible for customer process development and optimization on various downstream technologies and recently took the responsibility of Global Lead for the Vaccine Process Development team at Merck. He completed Master's Degree in BioEngineering, specializing in Chemical Engineering, Biotechnologies and Applied Genetics from the Université Libre de Bruxelles (ULB, Belgium) as well as a PhD in Molecular Bacteriology from the Medicine Faculty of ULB where he worked and published on virulence mechanisms of Type-3 Secretions Systems.

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