AFFINITY RESIN SCREENING FOR OPTIMAL DSP – APPLICATION TO ROTAVIRUS VACCINE PRODUCTION

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A crucial step in the down-stream processing (DSP) of recombinant vaccine production is the correct choice of affinity chromatography resins for product purification. All too often vaccine DSP protocols are based on methodologies that worked to allow development of candidate products to proof of concept and clinical trial rather than being optimized for efficiency and cost. This “what worked” approach often leads to increased production costs. Our aim here, as part of a Bill and Melinda Gates funded ULTRA project, is a more systematic approach to resin choice and DSP development that will enable low cost of goods of 15cents/dose or less. Ideally, this approach should be incorporated into the early stages of vaccine development.

To achieve this we have implemented a resin screening protocol based on the use of 96 well filter plates where each well contains chromatography resins. This approach allows for the rapid screening of large numbers of potential affinity resins and bind/elute conditions. It has the advantage that it can be operated either fully automated (using TECAN robotic platforms) or manually using relatively simple laboratory equipment. It is therefore quite feasible to incorporate such an approach into DSP development irrespective of whether development is being carried out in a well-funded or resource-limited environment. This approach allows for a saving of many months in process development time along with significant savings in resources compared to a conventional resin and bind/elute condition screening using individual columns.

We have applied this approach to the screening of affinity chromatography resins for DSP of two non-replicative rotavirus (NRRV) vaccines. Bind/elute characteristics are determined by monitoring OD_{280nm} for total protein levels, OD_{260nm} for nucleic acid levels and specific product levels by antibody detection and finally SDS-PAGE. We have screened 19 potential resins for use in hydrophobic interaction (HIC), cation exchange (CIEX) and multimodal (MM) chromatography. Initial rounds of screening allowed exclusion of four HIC resins as completely unsuitable. Bind/elute conditions were further investigated for the remaining resins leading to the choice of optimal resin-bind-elution combination for each affinity class. These were scaled up to for use in column chromatography.

Using the data from the 96 well plate studies it proved possible to predict DSP protocols that can be used in NRRV purification by HIC, CIEX or MM chromatograph. These results further demonstrate which of these can potentially be incorporated into an integrated production process.