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ASTBURY CENTRE
UNIVERSITY OF LEEDS

Application Note

Production of an immunogenic trivalent poliovirus virus-like particle vaccine candidate in yeast using controlled fermentation

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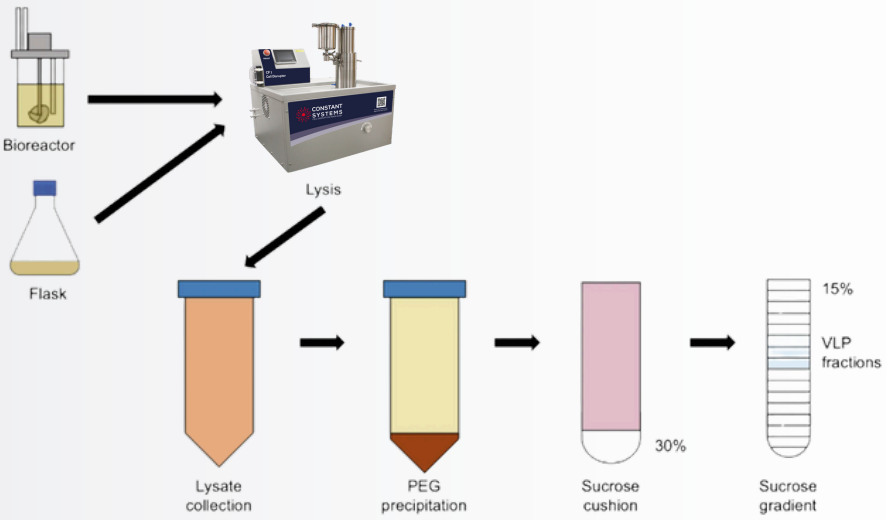
Introduction

The success of the poliovirus (PV) vaccines has enabled the near-eradication of wild PV, however, their continued use post-eradication poses concerns, due to the potential for virus escape during vaccine manufacture. Recombinant virus-like particles (VLPs) that lack the viral genome remove this risk. Here, we demonstrate the production of PV VLPs for all three serotypes by controlled fermentation using Pichia pastoris. We determined the cryo-EM structure of a new PV2 mutant, termed SC5a, in comparison to PV2-SC6b VLPs described previously and investigated the immunogenicity of PV2-SC5a VLPs. Finally, a trivalent immunogenicity trial using bioreactor-derived VLPs of all three serotypes in the presence of Alhydrogel adjuvant, showed that these VLPs outperform the current IPV vaccine in the standard vaccine potency assay, offering the potential for dose-sparing. Overall, these results provide further evidence that yeast-produced VLPs have the potential to be a next-generation polio vaccine in a post-eradication world.



"Not only has the CF-1 allowed us to move our science forward from a technical point-of-view, it was also a necessity from a scientific viewpoint. Our poliovirus VLPs are temperature sensitive, consequently if these VLPs are exposed to temperatures above 40°C, they undergo a conformational shift, increasing the size of the particles. This increase leads to these particles no longer being able to induce a long-term protective immunological response. Therefore, the CF-1's ability to cool samples during the cell disruption process meant that we were able to maintain the correct conformation of our VLPs, allowing us to test these VLPs in animal models. The success of these trials has led to these VLPs being transferred to industry for Phase I clinical trials."

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About The Continuous Flow Cell Disruptor

The CF Cell Disruptor offers Continuous Flow Processing with two models, the CF1 and CF2. Both models offer the same process and differ only by process speed.
The CF1 offers up to 6L per hour and the CF2 offers up to 24L per hour processing rates.

Both models benefit from a HMI control, a maximum process pressure of 40kpsi (2700 bar), integrated sample cooling jacket, 200mL inlet reservoir (hopper), auto shut down feature for when the process is complete and both models take advantage of Constant Systems precise and consistent hydraulic control which is fully scaleable through the whole product range from 0.5mL single preparation processing to large volume processing at 150L per hour. This precise control ensures that the entire sample is processed at the operators set pressure to ensure accurate and consistent results and in most cases a single process or pass is adequate meaning multiple passes are not required. Both models are capable of processing fluid or re-suspended sample types and are utilised for many sample types such as bacteria, yeast, algae and mammalian / Insect cell types.

CF1 Model
At approximately 700mm^2 the CF1 is small enough to bench mount if required but is best suited when used on its tailor made trolley. The CF1 trolley ensures that the equipment is situated at its optimum working height and is mounted on full swivel and lockable casters that enables safe and free movement of the equipment when needed. The CF1 is recommended for process volumes in the range of 15mL through to 10L. For those processing larger volumes in this range the CF1 can be offered with an integrated peristaltic pump fully controlled through the HMI which will ensure that the inlet reservoir is continually fed whilst recirculating the sample to help avoid any settling until the entire sample is processed.

CF2 Model
With a footprint of approx. 700mm^2 the CF2 is a floor standing model that is recommended for process volumes from 15mL through to 100L. The CF2 is offered with an integrated peristaltic pump as standard. The CF2 is mounted on full swivel and lockable castors that enables safe and free movement of the equipment when needed.

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