A TAILOR-MADE PURIFICATION STRATEGY FOR ONCOLYTIC MEASLES VIRUSES USING MEMBRANE-BASED PROCESSES

Daniel Loewe, Institute of Bioprocess Engineering and Pharmaceutical Technology, University of Applied Sciences Mittelhessen, Giessen
Daniel.loewe@lse.thm.de
Hauke Dieken, Institute of Bioprocess Engineering and Pharmaceutical Technology, University of Applied Sciences Mittelhessen, Giessen
Tanja A. Grein, Institute of Bioprocess Engineering and Pharmaceutical Technology, University of Applied Sciences Mittelhessen, Giessen
Tobias Weidner, Institute of Bioprocess Engineering and Pharmaceutical Technology, University of Applied Sciences Mittelhessen, Giessen
Denise Salzig, Institute of Bioprocess Engineering and Pharmaceutical Technology, University of Applied Sciences Mittelhessen, Giessen
Peter Czermak, Institute of Bioprocess Engineering and Pharmaceutical Technology, University of Applied Sciences Mittelhessen, Giessen

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Cancer patients can benefit from the Measles virus, since in the early 70s a relation between cancer remission and an infection with Measles was first mentioned (Bluming, Ziegler 1971). Further studies confirmed this oncolytic activity and therefore, the Measles virus became highly interesting for the application in cancer treatment.

However, for the widespread application as a therapeutic agent several bottlenecks have to be overcome in context of quantity and quality. For one therapeutic dose of oncolytic Measles viruses (OMV) at least 10^{11} infectious particles are needed (one vaccination contains ~10^3 $TCID_{50}$) (Russell et al. 2014).
Besides that, the impurities, such as host cell proteins (HCP) and host cell DNA (hcDNA), must be reduced to appropriate limits set by regulatory authorities. The full recovery of OMV infectivity must also addressed. This underlines the need of a tailor-made downstream processing.

After we established a high titer production process, achieving OMV titers of 10^{11} $TCID_{50}$ mL^{-1} (Grein et al. 2017), we are now focused on the downstream processing of OMV. For this purpose we characterized the OMV regarding process parameters used in DSP, such as stability towards ionic strength, osmolality, agglomeration and shear stress. Based on this, a clarification step was conducted, followed by the further purification with tangential flow filtration (TFF). By using polyether sulfone flat sheet membranes in concentration mode, we were able to recover the infectious virus and lowered the impurities by ~70% for hcDNA and ~80% for protein content. In the next purification step, we applied a discontinuous diafiltration and could deplete the impurities by ~95% in total. These results showed that TFF is an appropriate tool for the purification and formulation of OMV.

References

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