High-Throughput Manufacturing of Personalized Plasmid DNA Cancer Vaccines

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Personalized medicine is a progressive approach in the treatment of diseases, based on the genetic variability of each single patient, enabled by the ever-increasing knowledge in the field of genetic engineering and novel technologies. One of the most rapidly advancing areas of application has been individualized cancer therapy, where the mutational alterations found in each patient's tumor cells are evaluated and a customized therapeutic cancer vaccine specific for that individual's tumor antigensis developed.
Here we present our manufacturing platform for individualized plasmid DNA vaccines in compliance with GMP standards. A well-established production process with currently over 100 manufactured patient-specific batches provides a major contribution to a clinical trial with the objective to treat different types of cancer.
The whole manufacturing cycle from tumor biopsy over identification of tumor-specific biomarkers, neoepitope selection and sequence design, synthesis of pDNA starting material to the manufacturing of the individualized drug substance and drug product demands short turnaround times and robust processes. Our parallelized small-scale manufacturing process starts with the generation of a personalized *E. coli* cell bank followed by a fed-batch fermentation, harvest and lysis. Purification is accomplished by a two-step chromatography process using monoliths, followed by formulation via UF/DF and concluded by low-bioburden filling. In-process and batch release testing accompany the whole manufacturing process.
Our presentation will give insight on facility design, process optimization strategies (e.g. DoE) and approaches to the continuous monitoring of process performance to ensure a small footprint, rapid turnaround times and cost effective manufacturing of high-quality personalized plasmid DNA.