DEVELOPMENT OF SCALABLE MANUFACTURING PROCESS AND GMP-COMPATIBLE FORMULATION FOR A NOVEL RECOMBINANT SCHISTOSOMIASIS VACCINE

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Schistosomiasis is a parasitic disease spread by fresh water snails. After malaria, schistosomiasis is the deadliest parasitic disease, plaguing an estimated 200 million people worldwide, and causing up to 280,000 fatalities in Africa. This neglected tropical disease has also emerged as an important co-factor in Africa's HIV/AIDS epidemic, especially among women and adolescent girls. Together with hookworm disease and leishmaniasis, it ranks as the neglected tropical disease with the highest disease burden as defined by disability-adjusted life years (DALYs)[1]. Although treatments exist, such as praziquantel chemotherapy, a vaccine will likely be needed to prevent infection and re-infection, interrupt disease transmission, and ultimately establish long-term control and elimination of the disease. No such vaccine currently exists, but a promising candidate is currently under development at Texas Children's Hospital Center for Vaccine Development (TCH-CVD).

The *Sm*-TSP-2 schistosomiasis vaccine comprises a 9 kDa recombinant protein corresponding to the extracellular domain of a unique *S. mansoni* tetraspanin found in the parasite's tegumental surface. *Sm*-TSP-2 was expressed as a recombinant protein secreted by the yeast *PichiaPink™* and purified in a two-step process, which resulted in a protein recovery yield of 31% and a protein purity of 97%.[2] The developed processes were suitable for production of purified protein for subsequent formulation and Phase 1 clinical studies. However, improvements in process yield and efficiency, as well as transition of the formulation to GMP-compatible materials, are desirable for the advancement of this candidate through subsequent clinical phases and large-scale manufacturing.

TCH-CVD and MilliporeSigma are conducting a collaborative project to optimize the efficiency and scalability of the *Sm*-STP-2 schistosomiasis vaccine manufacturing process. The overall goal of this work is to develop a safe and low-cost process for the purification of the vaccine antigen. This was accomplished by redesigning the original process, which utilized 750kD hollow fiber and 3kD cellulose membrane tangential flow filtration (TFF) devices for the clarification and concentration of the *Pichia pastoris*-based vaccine lysate process feed. The level of solids in the fermentation broth (30%) had required a dilution to enable processing through the hollow fiber device, which led to decreased product yield and increased complexity.

MilliporeSigma assisted TCH-CVD with studies to eliminate the dilution prior to lysate clarification and to also streamline the process to enable Texas Children's to simultaneously clarify and concentrate the yeast lysate. 0.1um, open-channel, stacked plate, membrane sheet TFF devices were successfully used to clarify the undiluted lysate. The TFF operating parameters (specifically the feed and permeate flow rates) were optimized to enable the downstream 3kD concentration process to run concurrently in a cascade TFF. Enhancement of the chromatography operations is currently underway as well. This presentation will detail the optimized clarification and concentration process and highlight the economic and process simplification benefits.
Work was also performed to optimize the vaccine formulation. Extensive studies were previously conducted to identify excipients and conditions to maximize the stability of soluble recombinant *Sm*-TSP-2.[3] Additional components were tested to find alternative GMP-grade reagents that maintained or improved the stability of the vaccine.

REFRENCES

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