JOURNEY TO COMMERCIALIZATION OF A COMPLEX, BIOLOGICAL ANCILLARY MATERIAL

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Raw materials used in the manufacture of cell therapies require robust qualification and characterization studies to ensure safety and understanding of material variability and function, and their effects on the manufacturing process and final product. Many commercially available cell therapy ancillary materials are complex, proprietary materials which challenge a user's understanding of how to control and evaluate these materials. T cell activation is a critical step in the manufacture of cell therapies such as CAR-T cells, which require precise control over the initiation and termination of the activation stimuli imparted to achieve high level of T cell transduction, as wells as ideal T cell phenotypes and function. We have developed a novel, modular activation reagent named Expamers to provide a more precise control over the timing of T cell activation stimuli compared to current proprietary T cell activation reagents on the market. Expamers are comprised of anti-CD3 and anti-CD28 Fab fragments that are multimerized with the aid of a *Strep*Tactin backbone for efficient CD3 and CD28 crosslinking on the T cell surface.

Expamers can be rapidly bound and removed from the cell surfaces, allowing nearly instantaneous initiation and termination of activation stimuli. Expamers are versatile reagents that are intended for both research and clinical use. Similar to drugs in development, Expamers have been developed and qualified using a phase appropriate approach. The commercialization process included a scale up effort, a material configuration change, and significant supply chain complexity. The focus of this talk is to both describe this novel T cell activation reagent and its contribution to advancing T cell therapy manufacturing, and to capture a drug product manufacturer's journey to commercialization of a complex ancillary biological material.

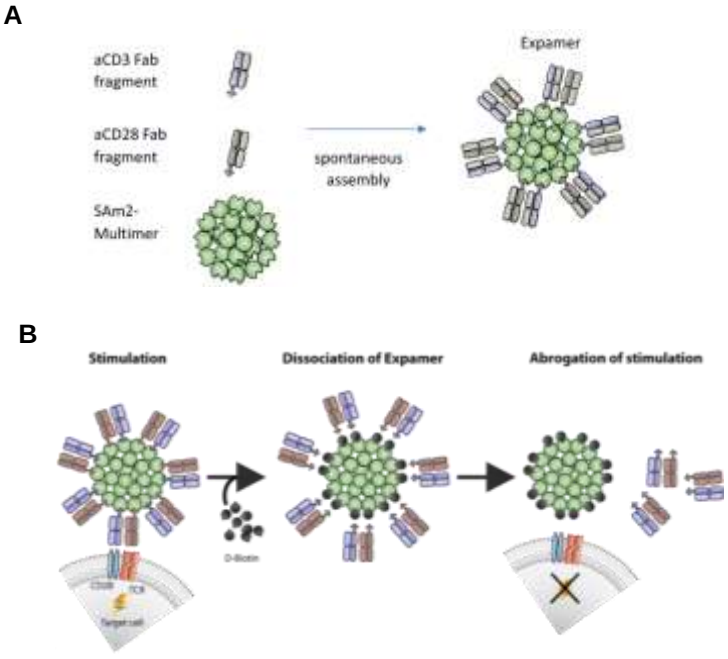

FIGURE: Schematic visualization of Expamers mode of action. A) Expamers spontaneously assemble form single components (anti-CD3 and anti-CD28 Fab fragments as well as StrepTactin multimer backbone). B) Assembled Expamers bind to target T cells by binding to and cross-linking CD3 and CD28 surface receptors, triggering activation signaling downstream of the TCR complex. Subsequently, Expamers can be rapidly dissociated upon addition of D-biotin. Dissociation results in removing of Expamers from the T cell surface and termination of the activation signal.

Poltorak, M.P., Graef, P., Tschulik, C. et al. Expamers: a new technology to control T cell activation. Sci Rep 10, 17832 (2020). https://doi.org/10.1038/s41598-020-74595-8