Engineering of Fusion Protein Constructs to Efficiently Combat Neurological Damage Caused by E. coli K1 Meningitis

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Bacterial meningitis is the inflammation of the meninges and subarachnoid cerebrospinal fluid caused by bacterial infection. E. coli K1 is a major cause of neonatal meningitis, which has been strongly linked to neurological damage later in life for surviving victims, including a higher risk for cognitive and behavioral brain diseases, and necrosis of the hippocampal dentate gyrus. Traditional treatments of antibiotics and corticosteroids are ineffective, and a novel treatment is needed. Therefore, a conjugate protein construct consisting of endosialidase-N (Endo-N) and interleukin-10 (IL-10) has been proposed. In the first stage of research, in silico studies were performed in order to choose the optimal crosslinker. The heterobifunctional crosslinker Mal-PEG4-NHS was chosen because of its flexible nature and ability to increase solubility. Antibacterial properties of the conjugate were analyzed through a capsule stain and an assay to measure the ability to expose bacteria to killing by complement. Anti-inflammatory properties were analyzed using a murine IL-1β ELISA kit. The conjugate did not significantly improve bacterial killing by human blood serum, nor did it reduce IL-1β production by activated macrophages. The results indicate that possible causes of ineffectivity include steric hindrance between the two proteins and nonspecific binding of the crosslinker, impeding biological activity. These problems may be able to be solved by a recombinant fusion protein in future research.

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