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TITLE

IMMUNE PROFILE OF CHIMERIC ELASTASE CONTAINING T-CELL EPITOPES (SMCET) FROM SCHISTOSOMA MANSONI

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ABSTRACT

The hygiene hypothesis supports the increased prevalence of allergies in developing countries. Such diseases, characterized as the most common chronic immune disorders, lack definitive cures, making the development and availability of treatments essential. Among the major causes of allergies, dust mites, such as Blomia tropicalis, stand out as significant sources of aeroallergens in the Brazilian population. In this context, allergen-specific immunotherapy has gained relevance as a viable alternative to pharmacotherapy due to its ability to modulate the immune response and potentially alter the natural course of allergic diseases. Since helminth infections activate immune mechanisms similar to allergic responses—promoting Th1 response polarization and modulating Th2 responses through immune evasion strategies—recombinant molecules from S. mansoni present a promising treatment option. Molecules from the cercarial stage, such as cercarial elastase (SmCE), can regulate inflammatory mediators and influence both Th1 and Th2 responses, depending on the phase of infection. This study aimed to evaluate the immunoregulatory and immunomodulatory profile of a chimeric protein, SmCET, designed with T-cell epitopes from SmCE, using in vitro stimulation of PBMCs from allergic and non-allergic individuals sensitized to B. tropicalis. PBMCs offer a comprehensive representation of immune responses, covering various immune cell types, such as T and B cells, involved in allergic reactions and regulatory mechanisms. The chimeric protein was designed based on T-cell epitope predictions from different isoforms of SmCE, with peptide ligands incorporated into the construct. The three-dimensional structure of the protein was predicted using modeling tools. For protein expression, the cDNA sequence encoding the chimeric protein was synthesized into plasmids and transformed into E. coli strains (Star and Rosetta). The recombinant protein was purified, dialyzed, and quantified. Mite extract was also prepared. Venous blood samples were collected from both allergic and non-allergic individuals sensitized to B. tropicalis. To assess IgE reactivity to mite proteins, an indirect ELISA was performed. PBMCs were isolated and stimulated with the chimeric protein SmCET for 48 and 72 hours. Following incubation, cell viability was assessed, and the culture supernatant was analyzed for cytokine production, including IL-1β, IL-4, IL-5, IFN-γ, IL-10, IL-13, and TNF-α. Results showed that SmCET significantly stimulated IL-1β production and inhibited IL-13 levels in both allergic and non-allergic individuals, while other cytokine levels remained at basal levels. No changes were observed in cell viability tests, indicating that the protein did not affect cell culture growth. These findings suggest that the chimeric protein SmCET could provide a favorable proposal for specific immunotherapy, potentially replacing or complementing traditional corticosteroid-based treatments in the future.

KEYWORDS

Immunology; Chimeric Proteins; Allergy; Biotechnoloy

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