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Developing novel antigen specific therapies as autoimmune disease treatments

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Autoimmune diseases are conditions in which the body's natural immune system can't differentiate between self and foreign cells, resulting in inadvertent damage to healthy tissues. One such autoimmune dysregulation, anti-neutrophilic cytoplasmic antibodies (ANCA)-associated vasculitis (AAV), is a rare group of heterogeneous disorders with key subtypes defined by the presence of antibodies targeting proteinase-3 (PR3) or myeloperoxidase (MPO). In MPO-positive disease, pathogenic antibodies bind to the MPO protein found in healthy neutrophils, initiating an inflammatory response to the vascular endothelium. Research has identified an immunogenic hot spot within the MPO heavy chain (MPO435-465), which contains epitopes recognized by CD4+and CD8+ T cells, as well as anti-MPO-IgG, highlighting the potential for exploring disease-related epitopes for immune-based therapeutic strategies.

Given the heterogeneity inherent in autoimmune diseases, our research is dedicated to developing more effective, targeted, and less toxic therapeutic options for prevention, diagnosis, and treatment. We are currently exploring the development of antibody fragment-based therapeutics, specifically "Nanobodies" (or Variable Heavy domain of Heavy chain, VHHs), directed against an immunogenic hot spot within the MPO heavy chain (MPO435-465). Our aim is to uncover whether blocking this "hot-spot" results in changes in the disease-associated signaling pathways.

Nanobodies are exquisitely specific targeting moieties that have the potential to provide powerful tools for dissecting and understanding the intricate pathways of immune regulation, revealing novel targets and mechanisms of action. Additionally, Nanobodies may offer advantages over conventional antibodies, including enhanced antigen-binding capacity, high stability, reduced immunogenicity, and lower production costs. Thus, the development of Nanobodies represents a promising strategy for therapeutic intervention and diagnostic applications in MPO-ANCA and related autoimmune diseases.

Biography

Aparajita Dubey has more than 17 years of experience in pharmaceutical research, mainly in drug discovery and development. As a biologist she has broad experience in the field of cell line development for various biosimilar molecule and novel fusion proteins along with medical writing and consulting experiences. She is M.Sc. in Life Sciences and a PG Diploma in IP from National Law School University, Bangalore, India. Currently pursuing her PhD form University of Queensland, Australia in the field of Antibody fragment-based therapeutic for a rare autoimmune disease. A self-motivated, enthusiastic, cheerful, result-oriented and integrity driven healthcare professional. Highly adaptable and open to new challenges and like to take initiative to work with the best of abilities in a dynamic and demanding work environment.

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