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The Role of Linear Epitopes in Anthrax Toxin Neutralization

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Neutralization of anthrax toxicity can be achieved by disrupting several steps in the intoxication pathway. An early step in this pathway is the binding of anthrax protective antigen (PA) to its cellular receptor, Anthrax Toxin Receptor (ATR) via the C-terminal domain of the protein. Binding disruption has previously been demonstrated using a conformational dependant monoclonal antibody, 14B7, which binds to the C-terminal domain of PA. We have developed and characterized several novel monoclonal antibodies which are distinct from 14B7, are capable of disrupting toxicity in vitro, and bind to the C-terminal domain of PA. Of these novel monoclonal antibodies several are conformational dependant, however a subset are capable of recognizing 12 amino acid linear peptide sequences. Using this sequence data we have mapped the binding of the antibodies to anthrax protective antigen which enhances our understanding of the binding of this protein to ATR. Protective monoclonal antibodies that recognize linear sequences are extremely useful in furthering our understanding of vaccine efficacy, individual immune responses and key neutralizing epitopes required to effectively overcome the fatal consequences of anthrax intoxication.