Unraveling the Binding Mode of the Neutralizing Neuroantibody αD11 to NGF

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The monoclonal neuroantibody αD11 is a potent antagonist that prevents the binding of the neurotrophin NGF (nerve growth factor) to its receptors, TrkA and p75, in a variety of systems, most notably in two *in vivo* systems linked to crucial pathological states (*i.e.* Alzheimer disease and AIDS). To elucidate the mechanism of neutralization, structural and functional studies were performed.

The potential therapeutical interest of the antibody was confirmed, demonstrating that it binds both mouse and human NGF with similar affinity. Its epitope was mapped by Sandwich Elisa assay with a pool of mutants. Its Fab fragment was crystallized [1] and the structure was solved at 1.80Å resolution. This structure, that may assist in the humanization without loss in affinity, was docked to NGF on the basis of epitope mapping results.

The present structural investigation along with the crystallographic analysis of the two complexes between NGF and its receptors [2], [3] should provided important insights in the molecular basis of antibody specificity for the NGF antigen and its mode of interaction with the full-length receptor TrkA.

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