Directed selection of a conformational antibody domain that prevents mature amyloid fibril formation by stabilizing Abeta protofibrils.

Habicht G, Haupt C, Friedrich RP, Hortschansky P, Sachse C, Meinhardt J, Wieligmann K, Gellermann GP, Brodhun M, Götz J, Halbhuber KJ, Röcken C, Horn U, Fändrich M (2007) Directed selection of a conformational antibody domain that prevents mature amyloid fibril formation by stabilizing Abeta protofibrils. *Proc Natl Acad Sci U S A* 104(49), 19232-19237.

Details

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Abstract

The formation of amyloid fibrils is a common biochemical characteristic that occurs in Alzheimer's disease and several other amyloidoses. The unifying structural feature of amyloid fibrils is their specific type of beta-sheet conformation that differentiates these fibrils from the products of normal protein folding reactions. Here we describe the generation of an antibody domain, termed B10, that recognizes an amyloid-specific and conformationally defined epitope. This antibody domain was selected by phage-display from a recombinant library of camelid antibody domains. Surface plasmon resonance, immunoblots, and immunohistochemistry show that this antibody domain distinguishes Abeta amyloid fibrils from disaggregated Abeta peptide as well as from specific Abeta oligomers. The antibody domain possesses functional activity in preventing the formation of mature amyloid fibrils by stabilizing Abeta protofibrils. These data suggest possible applications of B10 in the detection of amyloid fibrils or in the modulation of their formation.

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Camelid VHH-antibodies

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