THE ABETA PROTEIN OF ALZHEIMER’S DISEASE PROTECTS AGAINST MICROBIAL INFECTION

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Introduction: Two decades of findings from cell biology, genetic, neuropathological, biochemical and animal studies overwhelmingly point to the beta-amyloid peptide (Abeta) as the key protein in Alzheimer’s disease (AD) pathology. However, the normal in vivo function of Abeta remains unclear. Indeed, the Abeta peptide is often presented as a disease-associated product of abnormal catabolism with no normal physiological role.

Aims: We recently reported that Abeta and the archetypal human antimicrobial peptide (AMP) LL--37 share striking physiochemical and biological activities, including potent cytotoxicity towards microbial organisms in standard in vitro assays for antibiotic activity. In this study we present data that further characterizes the antimicrobial activities of oligomeric Abeta and the peptides AMP actions in vivo.

Results: In in vitro experiments soluble low molecular weight oligomeric Abeta species have potentiated antimicrobial activity compared to monomeric forms. This finding is consistent with the cytotoxic mechanisms of membrane--disrupting AMPs, including LL--37. Data from experiments using cell culture and animal models confirm Abeta expression is protective against pathogenic microbial infection.

Conclusions: Our data suggest that the normal role for Abeta in vivo is protective and that oligomerization may mediate the peptides normal AMP activity. If confirmed, our findings have significant implications for how AD pathology is viewed and suggests new therapeutic strategies that target the innate immune should be considered.