THE AMYLOID HYPOTHESIS FOR ALZHEIMER'S DISEASE REMAINS UNCHALLENGED

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The amyloid hypothesis for Alzheimer's disease is based simply on genetic findings... APP and presenilin mutations which lead to increased Aβ. No other hypothesis has been put forward which explains the genetic findings in the few, autosomal dominant kindreds. Animal models based on these findings, and on the identification of MAPT mutations in Pick's disease, have become the testbed for therapies for the disease. It is, however, a matter of debate as to whether findings from the little autosomal dominant kindred can be applied to the 99% of cases which do not have mutations.

I will argue that the amyloid hypothesis is certainly correct in the families with autoosmal dominant disease and is likely to be part of the problem in late onset disease. However, for us to understand fully the disease process in late onset disease, I will argue we need to understand what the function of APP (and Aβ?) is so that we develop a more clear idea of why it is deposited.