OBJECTIVE: We propose to utilize a human cerebrovascular endothelial cell line to determine which enzymatic activities that degrade Abeta are present and whether these enzymes are tightly bound to the cell surface or secreted.

RESEARCH DESIGN: We will utilize an experimental model and determine whether specific enzymatic inhibitors alter Abeta concentrations.

METHODOLOGY: We will employ specific inhibitors of the putative Abeta degrading enzymes: insulin degrading enzyme, neprolysin, and an elastase-like serine protease. We will measure changes in Abeta concentrations in the media of human cerebrovascular endothelial cells incubated with specific inhibitors.

FINDINGS: We have found evidence that insulin degrading enzyme and neprolysin are expressed in human endothelial cells. Insulin degrading enzyme is also highly expressed in blood vessels removed from the intact brain at autopsy. We have a paper in press describing these results.

CLINICAL RELATIONSHIP: These studies should provide new information on the role of Abeta degradation and may suggest new therapeutic agents to block Abeta deposition.