NACC Project #8
Identification of Atypical Dementias from Neuropathology to Molecular Etiology

Principal investigator
Bernardino Ghetti, Indiana University

Collaborating centers
Case Western Reserve University, Johns Hopkins University, Northwestern University, Rush-Presbyterian-St. Luke's Medical Center, University of Kentucky, University of Michigan, University of Pittsburgh

Project description
In the past few years, following the discoveries of numerous mutations in the APP, PS1 and PS2 genes, the spectrum of AD phenotypes has widened. In addition, the discovery of the Tau gene mutation has contributed information revealing a wide range of clinical and pathological phenotypes in FTD with Tauopathy. Recently, other dementing illnesses have been found to be associated with the accumulation of previously unknown abnormal gene products. The aim of this study is to analyze a large of familial dementias with atypical neuropathological features in order to determine the possible biochemical and genetic mechanism operating in those disorders. The study uses immunohistochemistry, protein chemistry, and DNA analyses in order to further carry out the characterization of cases already available, as well as prospective ones in the future. There are 213 familial dementia cases available at these nine Centers, of which 81 are non-AD dementias. The specific aims of this study are to: 1) Characterize cases of familial atypical dementia currently available to participating Centers by tracing the illness through a family tree, immuno-staining protein-associated dementia, identifying new protein components of amyloid, other protein aggregates or other inclusions, and sequencing candidate genes; 2) Carry out similar studies on new families with hereditary dementia; and 3) Isolate the putative protein and molecular characterization when sporadic cases present clear evidence of intracellular proteinaceous inclusions through neuropathological analysis.

Contact information
For further information regarding the results of this study, please contact:
Bernardino Ghetti, MD
Indiana University School of Medicine
Alzheimer’s Disease Center
phone: (317) 278-2030
http://www.pathology.iupui.edu/ad/

Rev. 02/07/2005