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 Work Dates
1999-2004

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.

Publications to Date
Tsutsui M, Spillantini MG, Crowther RA, Goedert M, Koto A. Early-onset dementia with
Vidal R, Delisle MB, Ghetti B. Neurodegeneration caused by proteins with an aberrant carboxyl-
Vidal R, Ghetti B, Takao M, Crefel-Courbon C, Uro-Coste E, Glazier BS, Siani V, Benson MD,
Calvas P, Miravalle L, Rascol O, Delisle B. Intracellular ferritin accumulation in neural and
extraneural tissue characterizes a neurodegenerative disease associated with a mutation in the
Powers JM, Byrne NP, Ito M, Takao M, Yankopoulou D, Spillantini MG, Ghetti B. A novel
leukoencephalopathy associated with tau deposits in white matter glia. Acta Neuropathologica


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
website: http://www.pathology.iupui.edu/ad/