“Clinical, Pathologic, and Genetic Characteristics of Dementia with Lewy Bodies”
(NACC Project #2003-03)

Principal Investigator
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Collaborating Centers
Oregon Health and Science University, University of California San Diego,
University of Pennsylvania, University of Pittsburgh

Project Work Dates
2003-current

Project Description
Approximately 30-60% of neuropathological Alzheimer’s disease (AD) cases have concomitant
Lewy body (LB) pathology using alpha-synuclein immunostaining and extra-nigral sampling.
However, the clinical and pathophysiological significance of LB pathology in the setting of AD is
unclear.

Although consensus clinical and neuropathologic diagnostic criteria for dementia with Lewy
bodies (DLB) have been established, heterogeneity exists even within LB cases with concomitant
AD pathology (AD/DLB).

Genetic susceptibility in subsets of AD/DLB may differ from that found in AD alone.
Identification of distinct subtypes is critical to future clinical-neuropathological and molecular
 genetic studies.

A separately funded (NIA R01) multi-Center collaborative effort will collect and systematically
review postmortem brain tissue and clinical characteristics from 250 AD cases with and 250 AD
cases without concomitant LB pathology. Utilizing DNA, clinical and neuropathological
characteristics collected as part of the R01, this project will conduct ApoE haplotype and Nurr1
genotyping of AD with and without concomitant LB pathology. We will conduct genotype-
phenotype correlations in these cases.

Furthermore, we will also ascertain families with multiple autopsies available from the
collaborating Alzheimer’s Disease Centers to investigate whether LB pathology segregates into
families. Differentiation of AD/DLB from AD will allow us to better define each phenotype, as well
as to elucidate the underlying pathophysiologie of these disorders.

Publications to Date
Hamilton RH, Tsuang DW, Wilson RK, Lopez OL, Luedecking-Zimmer EK, Leverenz JB,
DeKosky ST, Kamboh MI. Genetic Association Between the APOE ε4 Allele and Lewy Bodies
in Alzheimer’s Disease. Neurology. (submitted 7/04)

Tsuang D, Riekse R, Bird T, Muilenberg M, Steinbart E, McCutcheon M, Purganan K, Leverenz J.

Tsuang DW, Murray I, Lee V, Trojanowski JQ, Ishikawa A, Idezuke J, Wakabayashi M, Toda T,
Bird TD, Leverenz JB, Tsuji S, La Spade AR. Beta-synuclein gene alterations in dementia with
Lewy bodies. Neurology. (in press)
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