**NACC Project #2003-03**  
*Clinical, Pathologic, and Genetic Characteristics of Dementia with Lewy Bodies*

**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 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 pathophysiology of these disorders.

**Contact information**  
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Rev 10/11/04