SAGE-Hindawi Access to Research
International Journal of Alzheimer's Disease
Volume 2011, Article ID 284728, 2 pages
doi:10.4061/2011/284728

Editorial

Genetics and Genomics of Late-Onset Alzheimer's Disease and Its Endophenotypes

Christiane Reitz,[1] Ekaterina Rogaeva,[2] Tatiana Foroud,[3] and Lindsay A. Farrer[4, 5, 6, 7, 8, 9, 10]

[1]*Department of Neurology, G. H. Sergievsky Center, Taub Institute for Research on Alzheimer's Disease and the Aging Brain, Columbia University, New York, NY 10032, USA*
[2]*Department of Medicine, Tanz Centre for Research in Neurodegenerative Diseases, University of Toronto, Toronto, Canada M55 1A8*
[3]*Department of Medical and Molecular Genetics, Indiana University, Indianapolis, IN 46202, USA*
[4]*Department of Medicine, Schools of Medicine and Public Health, Boston University, Boston, MA 02118, USA*
[5]*Department of Biomedical Genetics, Schools of Medicine and Public Health, Boston University, Boston, MA 02118, USA*
[6]*Department of Neurology, Schools of Medicine and Public Health, Boston University, Boston, MA 02118, USA*
[7]*Department of Ophthalmology, Schools of Medicine and Public Health, Boston University, Boston, MA 02118, USA*
[8]*Department of Genetics & Genomics, Schools of Medicine and Public Health, Boston University, Boston, MA 02118, USA*
[9]*Department of Epidemiology, Schools of Medicine and Public Health, Boston University, Boston, MA 02118, USA*
[10]*Department of Biostatistics, Schools of Medicine and Public Health, Boston University, Boston, MA 02118, USA*

Correspondence should be addressed to Christiane Reitz, cr2101@columbia.edu

Received 23 February 2011; Accepted 24 February 2011

Late-onset Alzheimer's disease is the most common cause of dementia in western societies. Despite remarkable achievements in human genetics over the years, in particular, techno-logical advances in gene mapping and in statistical methods, to date only a small proportion of the genetic contribution to Alzheimer's disease can be explained. One reason for the difficulty in gene identification is that Alzheimer's disease is a complex disorder in which multiple genes with small individual effects as well as environmental factors are likely to contribute to disease risk as well as the various quantitative traits associated with the disease such as age-of-onset, cognition, neuropsychiatric symptoms, amyloid/tau pathology, or structural brain changes. Identifying the genetic factors modulating changes in these individual endophenotypes would help elucidate disease pathogenesis. In this special issue on genetics and genomics of Alzheimer's disease and its endophenotypes, we have invited a few papers that address this issue.

The first two articles address the impact of APOE genotype, the best established Alzheimer's disease susceptibility gene, on neuropsychiatric endophenotypes associated with Alzheimer's disease including psychosis, late-life depression, anxiety, apathy, hallucinations, agitation, and aggressiveness. The third paper examines the effect of an intron 7 polymorphism in the amyloid precursor protein (APP) on the age of onset of Alzheimer's disease in persons with Down syndrome. The fourth and fifth papers explore mechanisms modulating components of the amyloid cascade pathway, focusing, in particular, on the APP intracellular domain (AICD), which is an end product of the proteolytic cleavage of APP by β- and γ-secretase. In the first of these two papers, Ansaloni et al. evaluated the effect of *NTRK2* which encodes the TrkB receptor on APP metabolism and AICD levels. TrkB is a member of the tyrosine kinase receptor family and binds specifically to brain-derived neurotrophic factor (BDNF). The paper reports on the effects of different TrkB isoforms on APP metabolism in the human neuroblastoma cell line. In the other paper, Raychaudhuri et al. examined the impact of overexpression of AICD on expression of proteins that are part of pathways involved in neurodegeneration and neuroregeneration. Finally, the sixth paper reviews the findings of genome-wide association studies (GWAS)

that tested whether SNPs in the top-ranked Alzheimer's disease-related candidate genes were associated with various brain imaging endophenotypes including the volumes of the temporal lobe, hippocampus, amygdale, and frontal lobe, as well as grey matter density, entorhinal cortex thickness, and white matter integrity. In addition, this article discusses multigene and more complex genetic models as a means to identify genetic contributions to Alzheimer's disease.

Christiane Reitz
Ekaterina Rogaeva
Tatiana Foroud
Lindsay A. Farrer