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**Degree Objective:** Ph.D. Endocrinology and Reproductive Physiology

**Background:** BS Biology Shinshu University, Nagano, Japan, MS Human Sciences Shinshu University, Nagano, Japan

**Current Research Project:**

Apolipoprotein E (APOE)  $\epsilon 4$  allele is reported as the major risk factor for late-onset Alzheimer's disease (AD), though ~50% of AD patients do not carry the allele. The function of APOE is to transport cholesterol for luteinizing hormone (LH)-regulated steroidogenesis, and both LH and neurosteroids have been implicated in the etiology of AD. In our previous study, we scored AD DNA samples and age-matched control samples for APOE genotype and 14 single nucleotide polymorphisms (SNP) of LHB and LHCGR. Thirteen gene-gene interactions between the loci of LHB, LHCGR, and APOE were associated with AD. The most strongly supported of these interactions was between an LHCGR intronic polymorphism (rs4073366; *lhcr2*) and APOE in males, which was detected using all three interaction analyses: linkage disequilibrium (LD), multifactor-dimensionality reduction, and logistic regression (LR).

Recently, SORL1, a cell membrane protein of the LDLR family that adjusts the flow of amyloid- $\beta$  precursor protein (A $\beta$ PP) in neurons has been identified as an AD risk factor. Since SORL1 may influence cholesterol metabolism and steroid synthesis, we examined two AD-associated SORL1 polymorphisms (rs2298813 and rs2282649) in DNA samples from our case-control cohort. We did not identify any main effects of SORL1 with AD, however, there was an interaction between SORL1 (rs2282649) and gender, such that females with this SORL1 SNP were 1.4 fold more likely to have AD [OR = 2.2667 (0.9882, 5.1993);  $p=0.017$ ]. A significant gene-gene interaction between rs2282649 and GnRH1 ( $p = 0.0134$ ,  $D' = 0.3913082$ ) in the AD population was detected by LD analysis. Although rs2298813 was not associated with AD ( $p = 0.494$ ), a significant gene-gene interaction between rs2298813 and LHCGR ( $p = 0.0002$ ,  $D' = 0.9967663$ ) was detected by LD analysis. A gene-gene interaction also was detected between rs2282649 and FSHR ( $p = 0.00176$ ) by logistic regression. Our results suggest interactions between SORL1, gender and other hormone-related SNPs as increasing the risk of AD.

**Honors:**

**Grants Received:**

**Publications:**

**National Presentations:**



## **Other Presentations:**

Hayashi, K. and Atwood C.S. (2010) Identification of SNPs in Genes of the Steroidogenic Pathway that Predict Alzheimer's Disease. 22nd Annual Colloquium for the Institute on Aging

Hayashi, K. and Atwood C.S. (2010) Identification of SNPs in Genes of the Steroidogenic Pathway that Predict Alzheimer's Disease. ERP Research Symposium.

Hayashi, K. and Atwood C.S. (2010) Identification of SNPs in Genes of the Steroidogenic Pathway that Predict Alzheimer's Disease. Department of Medicine Research Day.

## **ERP Service:**