Title: Alzheimer Disease Overview *GeneReview* – Genes of Research Interest
Author: Bird TD
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Note: The following information is provided by the author and has not been reviewed by *GeneReviews* staff.

Other potential genes/loci under investigation

- *A2M* on chromosome 12 [Dodel et al 2000, Gibson et al 2000, Depboylu et al 2006]

- *ABCA7*; when suppressed, results in an elevation of amyloid production [Chen et al 2015, Vardarajan et al 2015]

- *AKAP9*, a kinase anchor protein 9 (PRKA) that regulates NMDA channel activity and is associated with long QT syndrome 11. AD association has only been found in African Americans [Logue et al 2014].

- There is evidence both for [Kim et al 2009] and against [Cai et al 2012] *ADAM10* being a risk factor.

- *BIN1*, a tumor suppressor protein [Vardarajan et al 2015]

- *CALHM1* on chromosome 10q24; *CALHM1* influences calcium homeostasis and has a single nucleotide polymorphism (SNP) associated with late-onset AD [Dreses-Werringloer et al 2008].

- *CD2AP*, an adaptor molecule involved in dynamic actin remodeling and membrane trafficking [Vardarajan et al 2015]

- A SNP in *CD33* has been implicated as a risk factor in AD [Bertram et al 2008]; Griciuc et al [2013] have shown that CD33 inhibits microglial uptake of amyloid beta.

- Clusterin (*CLU, APOJ*), a molecular chaperon present in senile plaques that has been shown to modulate Aβ oligomer assembly [Lambert et al 2009]

- *CR1* and *PICALM*, implicated in two genome-wide association studies (GWAS) [Harold et al 2009, Lambert et al 2009]

- Dysferlin (encoded by *DYSF),* associated with several limb-girdle muscular dystrophies; has been shown to accumulate in endothelial cells near multiple sclerosis lesions and with Aβ plaques of patients with AD [Chen et al 2015]

- *EPHA1* (encoding a protein that belongs to the ephrin receptor subfamily); plays a role in cell and axonal guidance and synaptic plasticity [Vardarajan et al 2015]

- *GAB2* on chromosome 11q14 interacting with the *APOE* e4 allele [Reiman et al 2007]

- *GST01* and *GST02* on chromosome 10 [Li et al 2003]

- *PAX1P1*, which encodes for a nuclear protein that may function in DNA repair pathways [Chen et al 2015]

- *PLD3* on chromosome 19q13.2 [Cruchaga et al 2014]

- *SORL1* on chromosome 11q23, a protein involved with *APP* protein trafficking [Rogaeva et al 2007]

- *TOMM40,* located on chromosome 19q very close to the *APOE* locus,*TOMM40* has been implicated in late-onset AD both by linkage analysis [Potkin et al 2009] and by the presence of a variable length poly-T repeat within the gene [Roses et al 2010].

- *UNC5C* is enriched in neurons of the hippocampal pyramidal layer [Wetzel-Smith et al 2014].

- In a large GWAS meta-analysis [Lambert et al 2013] variants in or near the following candidate genes (including several previously reported) were identified as risk factors for AD: *HLA-DRB5*/*HLA-DRB1*, *SLC24A4*, *SORL1*, *PTK2B*, *ZCWPW1*, *CELF1*, *FERMT2*, *CASS4*, *INPP5D*, *MEF2C*, and *NME8*.

- Several other potential loci under investigation on the following chromosomes:

    - 12 [D'Introno et al 2006]

    - 10 [Bertram et al 2000, Ertekin-Taner et al 2000, Myers et al 2000, Grupe et al 2006, Riemenschneider et al 2006]

    - 2q, 9p, and 15q [Scott et al 2003, Li et al 2006]

    - 19p13 [Wijsman et al 2004]

    - 7q36 [Rademakers et al 2005]

    - 9q22 *(UBQLN1*) [Bertram et al 2005, Bensemain et al 2006, Kamboh et al 2006, Smemo et al 2006]

- Studies of LOAD in a genetically isolated Dutch population suggesting linkage of AD to markers on chromosome 1q22, 3q23, 10q22 and 11q25 [Liu et al 2007]

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