Objective: Apolipoprotein E (APOE) is the only confirmed susceptibility gene for late-onset Alzheimer disease (AD). A recent study concluded that there are up to four additional genes with an equal or greater contribution to the disease. Our goal is to identify more genes contributing to AD. Methods: We performed 3.6cM chromosome screen of 132 families with late-onset AD on chromosome 10 (spanning 84 cM from D10S674 to D10S187) and 12 (spanning 56 cM from D12S1623 to D12S1632). Meanwhile, we genotyped 78 gene-based SNPs. We not only performed parametric and non-parametric linkage analyses to evaluate linkage to risk gene of AD, but also applied variance component linkage analysis to evaluate linkage to age-at-onset (AAO) of AD. Results: We obtained positive evidence of linkage to AD with 3 markers on chromosome 12 and with one marker on chromosome 10. The strongest evidence for linkage was at D12S1695 (nonparametric linkage [GHPLOD] score 3.94) on chromosome 12 at position 19.68 cM; a second peak (nonparametric linkage [GHPLOD] score 2.07) with D12S1632 at position 71.61 cM. Variance component analysis of AAO revealed suggestive evidence for linkage on both chromosomes 10 and 12, at D10S1227 (LOD score 1.88), at D12S1695 (LOD score 1.46). Several SNPs showed association with AD including those at positions at 92.1Mb (p-value 0.003), 92.03Mb (p-value 0.005), and 94.45Mb (p-value 0.01). Conclusions: We have obtained strong evidence for linkage on chromosome 12 near the alpha-2 macroglobulin gene locus with genes influencing disease risk, AAO of late-onset familial AD. Evidence for linkage to a second more distal location on chromosome 12 is consistent with results from previous studies including ours. We did not find evidence of linkage on chromosome 10; however, we found strong associations with several SNPs on this chromosome. We are evaluating additional gene-based SNPs in these regions to further narrow the intervals that harbor the variants conferring risk of AD.