Supplementary Materials

Neuroimaging Methods:

At the UCSF MAC, MRI of the brain was performed on a 1.5 Tesla Magnetom VISION system (Siemens, Iselin, NJ). At UCLA, a1.5 Tesla Siemens Avanto scanner was used. At Dokuz Eylül University, MRI of brain was performed on a 1.5 Tesla Magnetom Phillips system.

Two patients underwent PET imaging with the beta-amyloid ligand [11C] PiB[1] at Lawrence Berkeley National Laboratory. Images were acquired, processed and analyzed as previously described.[2] PiB distribution volume ratio (DVR) images were classified as positive or negative for cortical tracer uptake based on visual inspection and using a quantitative threshold empirically derived from cognitively normal controls (DVR-1.20).[3]

Genetic Testing Methods:

Genotyping of the sequence variant in *MAPT* exon 7 NM_005910.5:c.454G>A (p.A152T), and APOE (rs429358 and rs7412) and MAPT H1/H2 (rs1560310) defining variants was conducted using a TaqMan Allelic Discrimination Assay on an ABI 7900HT Fast Real-Time PCR system (Applied Biosystems, Foster City, CA) according to manufacturer's instructions. Sanger Sequencing was used to confirm identified variant carriers. All primer and probe sequences are available on request.

For progranulin mutations, DNA was sent from a stored sample.[4] All 12 coding exons of PGRN and the noncoding exon 0 were amplified from genomic DNA by PCR

using primers designed to flanking intronic sequence. The presence of expanded GGGGCC hexanucleotide repeats in *C9ORF72* was detected using a 2-step protocol. First, in all samples, the hexanucleotide repeat was PCR amplified using 1 fluorescently labeled primer followed by fragment length analysis on an automated ABI3730 DNA analyzer as previously described.[5] All patients who appeared homozygous in this assay were further analyzed using a repeat primed PCR method.[5] A characteristic stutter amplification pattern on the electropherogram was considered evidence of a pathogenic repeat expansion.

References:

1. Klunk WE, Engler H, Nordberg A, et al. Imaging brain amyloid in Alzheimer's disease with Pittsburgh Compound-B. *Ann Neurol.* Mar 2004;55(3):306-319.

2. Rabinovici GD, Furst AJ, O'Neil JP, et al. 11C-PIB PET imaging in Alzheimer disease and frontotemporal lobar degeneration. *Neurology.* Apr 10 2007;68(15):1205-1212.

3. Rabinovici GD, Rosen HJ, Alkalay A, et al. Amyloid vs FDG-PET in the differential diagnosis of AD and FTLD. *Neurology.* Dec 6 2011;77(23):2034-2042.

4. Baker M, Mackenzie IR, Pickering-Brown SM, et al. Mutations in progranulin cause tau-negative frontotemporal dementia linked to chromosome 17. *Nature.* Aug 24 2006;442(7105):916-919.

5. DeJesus-Hernandez M, Mackenzie IR, Boeve BF, et al. Expanded GGGGCC hexanucleotide repeat in noncoding region of C9ORF72 causes chromosome 9p-linked FTD and ALS. *Neuron.* Oct 20;72(2):245-256.