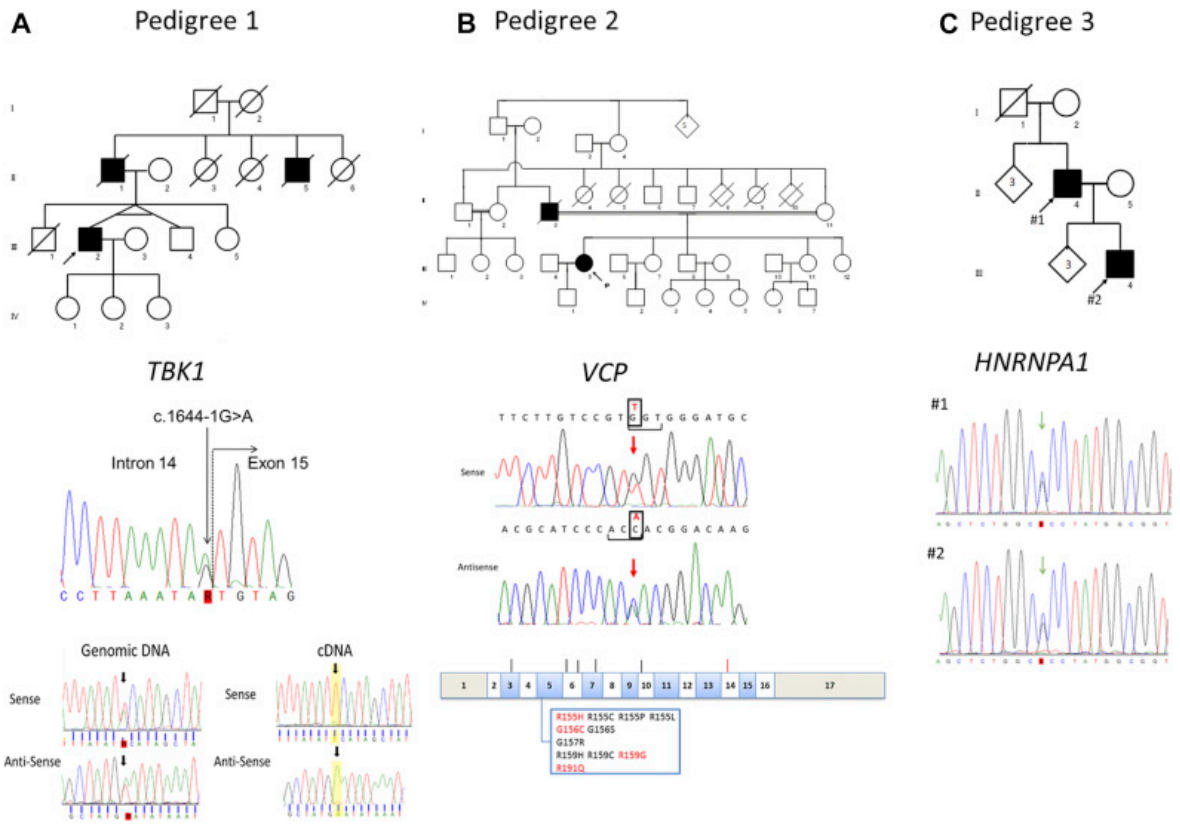
From Laboratory of Neurology

Molecular epidemiological study of familial amyotrophic lateral sclerosis in Japanese population by whole-exome sequencing and identification of novel *HNRNPA1* mutation.



Identification of novel mutations of ALS-related genes in FALS patients. In the pedigree charts, ALS-affected individuals are indicated by filled symbols. Unaffected individuals are indicated by open symbols. Slashed symbols indicate the deceased individuals. Squares denote the male family members and circles denote the female family members. (A) In pedigree 1, the novel splice site mutation (c.1644-1G>A) in *TBK1* was identified. The electropherogram shows heterozygous *TBK1* c.1644-1G>A splice site point mutation (arrow) in the index patient (III-2). Electropherograms of SNP (rs7486100) (arrows) in exon 8 of *TBK1* in the genomic DNA and cDNA sequences in the index patient (III-2) are shown. (B) In pedigree 2, the novel mutation p.G156C in *VCP* was identified. The electropherogram shows heterozygous *VCP* p.G156C mutation (arrows) in the index patient (III-5). At the bottom, distribution of *VCP* mutations detected in FALS or IBMPFD patients are summarized. The 17 exons of *VCP* are numbered. Mutations detected in FALS cases are indicated in red, whereas mutations reported to cause IBMPFD are shown in black. The amino acid changes in exon 5, which is a mutational hotspot, are also presented. (C) In pedigree 3, the novel mutation (p.P288A/340A) in *HNRNPA1* was identified in the 2 affected individuals. Electropherograms of heterozygous *HNRNPA1* p.P288A/340A mutation (arrows) in the affected individuals [#1 (II-4) and #2 (III-4)] are presented. Abbreviations: ALS, amyotrophic lateral sclerosis; cDNA, complementary DNA; FALS, familial amyotrophic lateral sclerosis; IBMPFD, inclusion body myopathy with Paget disease of bone and frontotemporal dementia.

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