

**P036** Angiogenin Gene Mutations in Amyotrophic Lateral Sclerosis  
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Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disease characterised by progressive destruction of motor neurons.

Transgenic mice with specific deletions of the vascular endothelial growth factor (*VEGF*) promoter result in an ALS phenotype. At-risk haplotypes have been identified in *VEGF* which confer double the risk for the development of ALS. Angiogenin is similar in function to VEGF. *ANG* was sequenced in 800 individuals with sporadic ALS and 383 controls taken from the Irish, Scottish and North American populations. Screening of the angiogenin gene has identified an at-risk SNP ( $p > 0.001$ ) and 5 novel disease-specific mutations in 9 individuals with sporadic ALS and not in controls ( $p = 0.034$ ). The overall mutation frequency in individuals with ALS was 1.13% with little inter population variation (1.07-1.18).

Although subject to confirmation, these mutations are predicted to interfere with angiogenin function. More specifically, the K40I mutation as seen in 3 individuals is strongly predicted to completely abolish angiogenin function.

Our study suggests that angiogenin and other genes with similar function to VEGF are important in the pathogenesis of ALS.