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The A20210 Allele of the Prothrombin Gene Is Not Frequently Associated With the Factor V Arg 506 to Gln Mutation in Thrombophilic Families

To the Editor:

A genetic variation in the 3′-untranslated region of the prothrombin gene was recently linked to an increased risk for venous thrombosis. In 28 families selected for hereditary thrombophilia, 5 (18%) of the probands carried the G to A transition at nucleotide 20210 of the factor II gene, whereas the A20210 allele was found in 1% of 100 healthy subjects.[1] Two (40%) of the A20210 carriers also had the factor V (FV) Arg 506 to Gln mutation. This prompted us to look for an association of the two risk alleles in 26 families carrying the FV mutation in two French centers. As recently underlined,[2] the selection of such families is based on the severity of clinical expression that motivates the laboratory background. It is thus concevable that several genetic risk factors might account for the expression of the thrombotic phenotype.

We screened 288 subjects belonging to the 26 families; 151 carried the FV Arg 506 to Gln mutation and 66 had had thromboses. The G to A transition at position 20210 was identified after amplification with primer A (5′-TTACAAGCCTGATGAAGGGA-3′) and primer B (5′-CCATGAATAGCACTGGGAGCATTGAAGC-3′). The latter was designed with a C to A substitution at position 20214 to create a restriction site for *Hin*dIII when the G to A transition is present. None of the probands or family members had the prothrombin gene mutation. We also screened 400 apparently healthy subjects and found the mutation in 2.8% of them. The frequency in the normal population was therefore comparable to that found in the Dutch population (1% in healthy subjects and 2.3% in a population-based case/control study). We conclude that the newly identified prothrombin gene mutation does not frequently contribute to thrombosis in individuals with the FV Arg 506 to Gln mutation.

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