



[haematologica reports]  
2005;1(4):20

## Genetic characterization of von Willebrand disease type 1: tracing the evolutionary history of the von Willebrand factor gene region

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A B S T R A C T

The study investigates the evolutionary history of the VWF gene region in patients with von Willebrand disease (VWD) type 1 and normal individuals. To identify single nucleotide polymorphisms (SNPs) that are relevant in our population, we have sequenced the promoter region, all 52 exons and flanking intronic sequences in 54 VWD type 1 individuals. A total of 106 polymorphisms have been detected in this effort. Seven of these are listed as known disease causing mutations and 50 as polymorphisms in the VWF database. Of the 57 coding SNPs, 15 are in first, 17 in second and 25 in third codon position. These result in 38 non-synonymous changes, of which some are obvious candidate mutations. Out of the 106 polymorphisms, 33 are found in a single individual only. In addition, more than 200 polymorphisms are reported from this region in the public databases. We will analyze a scaffold of 250 quality SNPs in 190 individuals. This collection contains small pedigrees from a large set of type 1 families. In parallel with this effort, all candidate mutations will be screened in all index cases, in all family members where the index case has the mutation and in a normal control population. These data will be used to determine the extent of linkage disequilibrium and to describe the evolutionary history of this region.