

Cloning of factor XI mRNA of a patient with inherited factor XI deficiency

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INTRODUCTION

Factor XI deficiency was described by Rosenthal et al in 1953 as a third type of haemophilia, distinct from haemophilia A and B. This disorder, which is described as haemophilia C or PTA deficiency is caused by a lack of coagulation factor XI.

Haemophilia C is regarded as a rare disorder restricted to isolated cases and families, occurring at a frequency of between 1:500.000 to 1:1.000.000 in the general population.

However, it is common in people of Jewish descent, in particular in persons of Ashkenazi origin. Recently, PTA deficiency has also been reported in the French Basque population and persons of African ancestry. Through the discovery of more and more new mutations it's importance has increased.

The Factor XI deficiency is an inherited autosomal bleeding diathesis, associated with injury-related bleeding disorders of variable severity. The lack of factor XI leads to variable factor XI-activities in coagulation assays. These are often visible in prolonged APTT. The bleeding risk is not always influenced by the severity of the FXI-deficiency, especially in individuals with partial deficiency – not all affected patients show symptoms.

Factor XI is located on Chromosom 4, it has 15 exons and 14 introns. Males and females are therefore equally affected.

MATERIAL

• F11-Forward Primer:

5'-CAC ACC AAG CGC CAA GTA CT- 3'

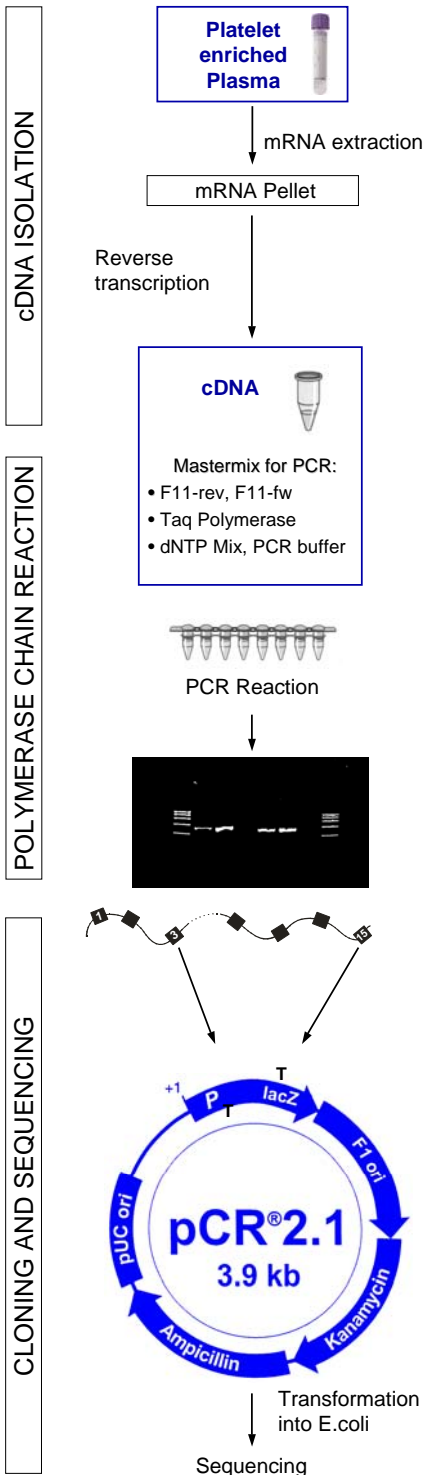
• F11-Reverse Primer:

5'-GTG AGC GGC TGT TAA TAT CC- 3'

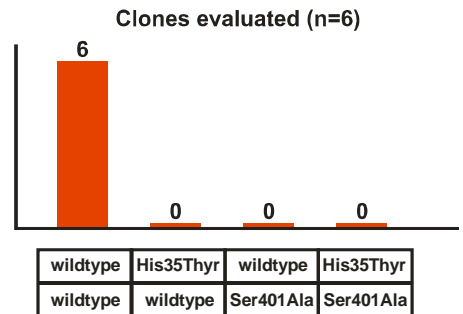
METHODS

- Evaluation of the patient by standard coagulation assays
- Isolation of the mRNA
- cDNA synthesis
- PCR with cDNA
- Ligation
- Cloning of recombinant DNA into E. coli
- PCR out of clones
- Sequencing
- Interpretation of the analysed results in relation of the coagulation assay results

ANALYSIS



RESULTS



Neither the His 35 Thyr nor the Ser 401 Ala mutation were found in the analyzed clones (n=6), suggesting the mutation in *cis* on the opposite allele.

CONCLUSION

The effect of two pointmutations and their genomic position – *cis* / *trans* – in a double heterozygotic female patient were described.

We have evaluated 6 clones derived from PCR amplified cDNA of platelet mRNA of a patient showing two mutations (His 35 Thyr, Ser 401 Ala) on germline DNA.

Both of the mutations were located on the same allele of the factor XI gene. The 26 year old woman shows no signs of a bleeding disorder.

These results were analysed in relation to the coagulation assay results of this patient.

This finding is in good correlation with the finding of moderately decreased FXI plasmatic activity.

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