



### Introduction

Phenylketonuria (PKU) is an autosomal recessive inborn error of metabolism caused by deficiency of phenylalanine hydroxylase (PAH) enzyme, which converts phenylalanine to tyrosine.

Phenylketonuria can result in impaired postnatal cognitive development resulting from a neurotoxic effect of hyperphenylalaninemia.

### Methods

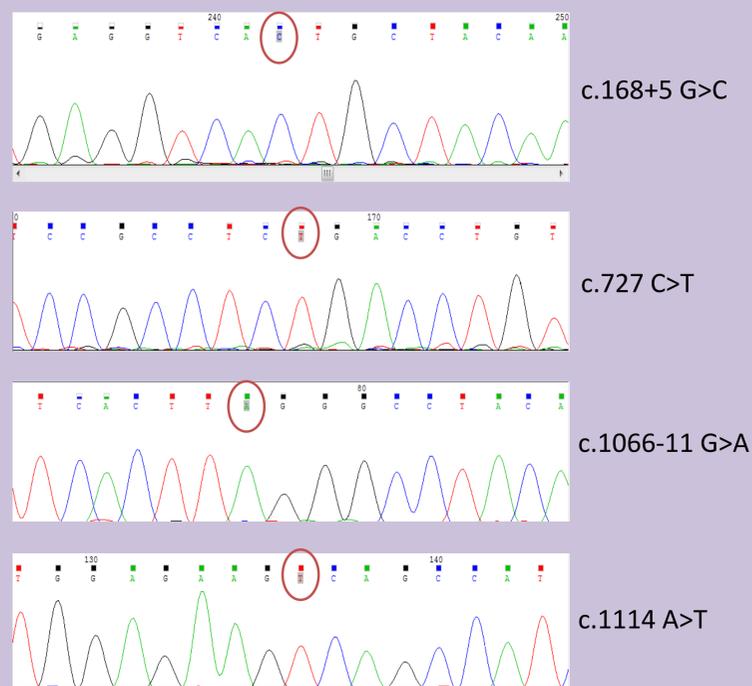
Five individuals were referred to our center for carrier detection of PKU. The PAH gene was studied using STR markers and direct sequencing. Their family history was studied, paternity and maternity test was conducted and a large pedigree was drawn up. In all of these pedigrees at least one affected individual with severe phenotype is observed who carries the same mutation in a homozygous form.

### Conclusion

These results suggest that adults with PKU may seem normal completely without receiving any phenylalanine-restricted diet; however, the two last mutations lead to "mild" PKU with little or perhaps no mental retardation. Although the causes are not always clear, these observations may be due to the effect of genetic and environmental factors result in both incomplete penetrance and variable expressivity.

### Results

Although c.168+5 G>C, c.727 C>T (p.R243X), c.533 A>G (p.E178G), c.1066-11 G>A, and c.1114 A>T (p.P281L) mutations were previously known to be associated with the severe form of PKU, we observed undetected phenylketonuria (PKU) in affected adults homozygous for the above mutations; except for c.533 A>G (p.E178G) mutation which was found as a compound heterozygote with c.1066-11 G>A mutation. Furthermore, high level of phenylalanine was observed in the patients but they all have normal intelligence, and normal lives.



### References

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