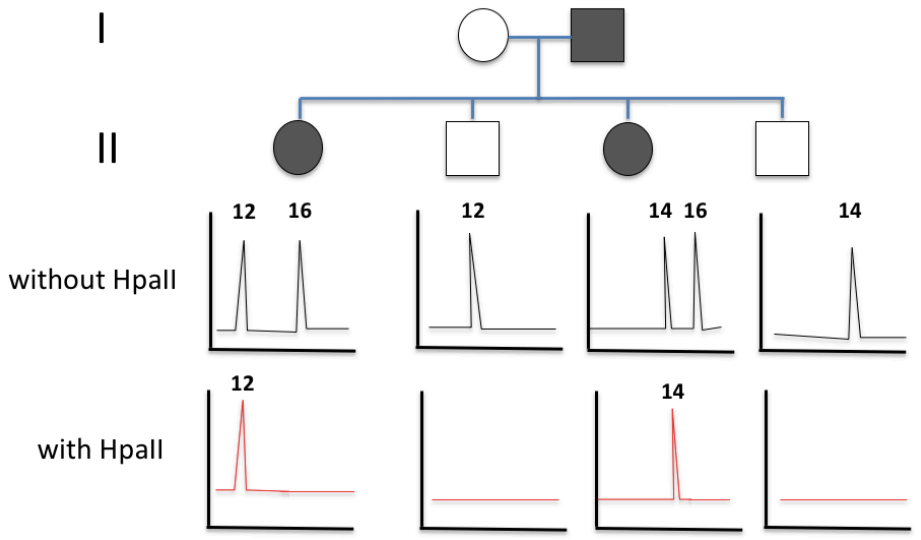
Question 5

A couple has 2 daughters and 2 sons. The father is colorblind (does not distinguish green from red), the mother distinguishes green from red.
Their 2 sons distinguish red from green but their 2 daughters are colorblind!
According to textbooks, colorblindness is transmitted by the X chromosome:
- males are colorblind when their X chromosome is mutated
- carrier females (1 X chromosome mutated) are not colorblind;
- homozygote females (2 X chromosomes mutated) are colorblind.
The family presented here is exceptional.



The HUMARA assay has been done for all 4 children.
Results without digestion by HpaII are given.

Genotype of the mother: __ 12, 14_____ mother gave 12 to 1rst son and 14 to 2nd son

Genotype of the father: ___ 16 _____ father gave 16 to both daughters

Is the mother carrier for colorblindness? YES NO
The 2 sons have received different X from their mother, but none is affected; the two daughters have inherited different X from their mother but both are affected. This make the mother very unlikely to be carrier.

Draw the most likely results of the HUMARA assay with digestion by HpaII before the PCR. Explain your reasoning.
Both daughters received the mutated X from their father but they would not be affected if X inactivation is random. Let's therefore assume **non random** X inactivation: the paternal X remains always (100%) active and the maternal X is always inactivated. This is explained by a **loss-of-function** mutation of **XIC** on the paternal X chromosome; the paternal X cannot do the inactivation and the maternal X compensates by being always inactivated. The loss-of-function is not detrimental in the father (no X inactivation in men !)