MULTIPLEX LIGATION DEPENDENT PROBE AMPLIFICATION AS FIRST TIER SCREENING FOR TURNER SYNDROME DETECTION

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Turner syndrome (TS) is one of the most common genetic conditions affecting females, with an incidence of one in 1500–2000 live births. TS occurs when an entire X-chromosome or a portion of it is deleted in all the cells or in a subset of them (TS mosaicism).

Patients affected by Turner syndrome show abnormalities in reproductive function as well as a number of other clinical manifestations such as renal abnormalities, structural cardiac problems, and short stature. It has been estimated that one in 50–100 girls with short stature have TS; as reported in literature, short girls have to be tested for this condition.

The early diagnosis allows the initiation of GH therapy, so that an improvement of adult stature can be achieved.

At the moment, cytogenetic analysis by karyotype is the standard test used to diagnose TS. Karyotype analysis is labor intensive and is impractical for large-scale population. In contrast, multiplex ligation-dependent probe amplification (MLPA) based on relative quantification of different DNA target sequences in a single reaction is a quantitative method, faster and cheaper.

MLPA technique for X quantification and conventional karyotyping have been compared in order to verify if classical cytogenetic analysis could be replaced by MLPA as the first tier screening.

Up to now a cohort of females were analyzed in a double blind manner by MLPA and conventional cytogenetics. The MLPA kit (SALSA P106), includes 47 MLPA probes with amplification products between 130 and 481 nucleotide on 16 different X genes (MRC-Holland, Amsterdam, The Netherlands).

All the samples analyzed show concordant results and until now only in one case a normal karyotype corresponded to a doubtful MLPA result. Sensitivity of MLPA was 100% and specificity 95.6%.

In conclusion our data suggest that MLPA represent a rapid, economic, automated, reliable and accurate method to diagnose Turner syndrome in girls with short stature, not requiring culturing cells.