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Rapid aneuploidy detection of chromosome 21 by segmental duplication – high resolution melting analysis for prenatal diagnosis

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Abstract

Chromosomal aneuploidy causes a number of syndromes and the most common is Down Syndrome (trisomy 21). These syndromes cause severe intelectual disability, and many abnormalities for lifetime. Thus, prenatal diagnosis is important to predict these aneuploidy. Karyotyping has been known as a gold standard for chromosomal abnormality detection. However, it has some disadvantages such as time consuming, culture failure, external contamination, and labour intensive. Molecular methods have been developed for rapid aneuploidy detection, such as *Segmental Duplication-High Resolution Melting Analysis* (SD-HRM). The purpose of this study was to propose and investigate a SD-HRM as screening method for rapid aneuploidy detection. This study used 1 primer set containing 2 pairs of primer for segmental duplication, which are similar sequences located on different chromosomes (chromosome 21,7, and 12). Dosage of segmental duplication targeted on aneuploidy (trisomy) will affect the melting profile and produce different melting curve compare to the euploid sample (normal) when amplified. This study used peripheral blood DNA of unaffected control (n=30) and Down syndrome individuals (n=57) which had been confirmed as classic trisomy (n=53), and mosaic (n=4) with karyotyping. SD-HRM attained high sensitivity (100%) and specificity **(**100%) (CI 95%=1.0), equal accuracy with karyotyping as diagnostic gold standard. Trisomy 21 samples were clearly differentiated with unaffected control. Mosaic trisomy 21 also was detected as positive with SD-HRM. Quantification analysis using mixed mosaic samples approach showed that SD-HRM could detect mosaic sample until 20% abnormal DNA. SD-HRM enables to detect aneuploidy with fast, sensitive, and cost-effective thus meet the demand to be used as method for prenatal diagnosis screening.

Keywords: Aneuploidy*;* karyotyping*;* prenatal diagnosis; SD-HRM

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