A non-invasive prenatal DNA screening test for Down Syndrome

Thilakavathy Karuppiah, Rozita Rosli

Clinical Genetics Unit, Department of Human Growth and Development, Faculty of Medicine and Health Sciences, 43400 UPM Serdang, Selangor Darul Ehsan, Malaysia.
E-mail: thilathy@medic.upm.edu.my

Down syndrome or Trisomy 21 is the most commonly occurring genetic disorder that stems from the failure of chromosome 21 to segregate normally during meiosis, resulting in an individual carrying an extra copy of chromosome 21. The aim of this study was to develop a relatively non-invasive prenatal DNA screening test for Down syndrome using maternal blood. As an initial step, the presence of foetal cells and DNA in the maternal blood was firstly determined by foetal haemoglobin (HbF) staining and polymerase chain reaction (PCR). It was found that the ratio of the nucleated foetal cell to maternal cell increased from 2 in $10^6$ to 3 in $10^6$ and 5 in $10^6$ at the first, second and third trimester, respectively. By using Y chromosome specific primers, DNA from male foetuses could be detected as early as 6 weeks of gestation in 200 µl maternal blood obtained from fingertip. This is in line with the current technology in non-invasive screening methods of foetal aneuploidies, which is focused on detecting Y chromosomal sequences which is impossible to be used for female foetus pregnancies. Therefore, the superoxide dismutase 1 (SOD1) gene sequence, which is located on the Down Syndrome Critical Region, was used to overcome this situation by using real-time quantitative PCR. The level of SOD1 sequences in maternal blood was found to be significantly elevated in the third trimester normal pregnancies (mean = 11728 copies/µl) when compared to the second trimester (mean = 5705.6 copies/µl), $p<0.005$ and non-pregnant normal women (mean = 3580.2 copies/µl), $p<0.0001$. Down syndrome pregnancies have the greatest elevation compared to all the three trimesters of normal singleton pregnancies and twin pregnancies, $p<0.05$. In conclusion, non-invasive prenatal diagnosis at first trimester using Y chromosomal sequence is feasible for diagnosis of foetal-derived paternally inherited polymorphism/mutations or genes. Quantitative analysis using gene associated with a disorder has a potentially significant advantage over the invasive techniques currently used widely for prenatal diagnosis.