

## INTRODUCTION

Preeclampsia is a disorder specific for human pregnancy of unknown etiology. It is characterized by hypertension and associated proteinuria late in pregnancy of previously normotensive women. The underlying pathology is suspected to occur early in pregnancy, perhaps even at time of implantation and is known to involve a failure in trophoblast differentiation and migration. It is likely that a cascade of events triggered by these early events lead to the eventual manifestation of the disorder, leading to an over maternal inflammatory immune response, widespread damage of maternal endovasculature and development of the characteristic symptoms (*Sibai et al., 2005*).

Current prenatal diagnostic techniques, chronic villous sampling, amniocentesis, and cordocentesis are invasive, carry a risk of miscarriage and are gestational age specific. These tests are usually aimed at detecting abnormal karyotypes, and can test for specific fetal DNA using polymerase chain reaction (PCR) techniques on chorionic villi or amniocytes (*Siva et al., 2003*).

Non-invasive diagnostic tests would be more desirable for prenatal use. Interest is focused on the isolation of fetal cells or, a more recent discovery, free fetal DNA from the maternal circulation. Fetal cells have been shown to persist in some women for decades after delivery (*Bianchi, 1999*). In contrast fetal DNA in maternal plasma is undetectable one day after delivery. The rapid turnover of circulating DNA suggests that it may be less susceptible to false positive results (from previous pregnancies) than the detection of fetal cells in maternal

blood. Fetal DNA is found in much large quantities in the maternal circulation are readily detectable using PCR techniques and cleared quickly from the maternal circulation after delivery.

Fetal DNA has been detected as early as 7 weeks' gestation and constitutes between 0.4 and 11% of fetal plasma DNA (*Lo et al., 1997*).

The source of fetal DNA is not established, however, it may arise directly from the syncytiotrophoblast, from shed apoptotic placental cells or results following lysis of fetal cells transferred across the placenta (*Bianchi et al., 1999*).

Previously *Lo et al., (1999)*, have shown that women with established preeclampsia have a five fold increase in circulating fetal DNA concentrations in their plasma compared with control pregnant subjects.

Since it is likely that the underlying changes leading to preeclampsia occur early in pregnancy before manifestation of the symptoms, the next question that wanted to address was whether this abnormal increase in circulating fetal DNA concentrations occurs early in those pregnancy that later develop preeclampsia.

The development of sensitive and reliable quantitative real-time PCR methods has permitted the precise determination of the quantity of PCR template in the sample being examined (*Zhong et al., 2001*). By the use of such methods it has been shown that significant elevations in cell free fetal DNA are present in pregnancies affected by preeclampsia, even before onset of the disorder (*Chan, et al., 2003*).