Areas of Excellence Scheme – Highlights of Achievements
Centre for Research into Circulating Fetal Nucleic Acids

The most impactful research achievement of the project, titled "Centre for Research into Circulating Fetal Nucleic Acids", was the successful development of non-invasive prenatal screening of Down syndrome based on cell-free DNA analysis in maternal plasma. Conventional screening methods for Down syndrome, such as maternal serum biochemical markers and fetal ultrasonography, are associated with relatively high false-positive rates. This has led to a high number of invasive prenatal diagnostic procedures being performed, such as amniocentesis, which far exceeded the number of fetuses with Down syndrome. In this project, we have successfully developed maternal plasma cell-free DNA tests that offered 99% sensitivity at 0.1% false positive rate for the screening of Down syndrome. The efficacy of the test approach was recognised by professional organisations, such as the American College of Obstetricians and Gynecologists, American College of Medical Genetics and the International Society of Prenatal Diagnosis, which recommended the incorporation of non-invasive prenatal testing (NIPT) into routine prenatal practices. Technology transfer arrangements between CUHK and companies such as Sequenom and Illumina were established. To date, NIPT for fetal chromosomal aneuploidy screening is practised in over 90 countries and has led to a worldwide reduction in the number of invasive prenatal procedures performed. The team has also developed maternal plasma DNA-based approaches for the non-invasive screening of other fetal chromosomal and subchromosomal aneuploidies.

The World Health Organisation (WHO) has estimated that the collective incidence of single gene diseases is about 10 in 1,000 pregnancies. The non-invasive detection of single gene disease mutations by cell-free fetal DNA analysis is challenging because there is a large number of single gene diseases and each disease may be associated with a myriad of gene mutations. Point mutations in particular are challenging to detect in maternal plasma. The team proposed that much of the technical challenges could be overcome by using single molecule counting strategies. The team developed a number of strategies which have been adopted for clinical use in centres around the world.

To maximise the amount of information of the fetus that could be extracted from maternal plasma analysis, the team has successfully developed non-invasive strategies to decipher the fetal genome, the placental transcriptome and the placental methylome. These data have far-reaching implications that would stimulate many further studies.

The approach for the NIPT of fetal chromosomal aneuploidies has not only been successfully licensed or sublicensed to many companies overseas, the project coordinator has successfully founded a company, Xcelom Ltd, which is located in the Hong Kong Science Park for the development and provision of NIPT services in Hong Kong. The company's service was launched in late 2014 and soon thereafter became a reputable name in the diagnostic industry in Hong Kong.

The fruits of this research project has led to a worldwide transformation of how prenatal testing is conducted.

**The above summary is written mainly by the project team. The views expressed in the summary do not necessarily represent those of the University Grants Committee/ Research Grants Council.*