Isolation and genetic characterisation of circulating cell-free fetal DNA for non-invasive prenatal diagnosis of haemoglobinopathies and monitoring of pre-eclampsia

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Overview: The overall objective of this master proposal is to develop an integrated microsystem for the separation of plasma from maternal blood sample, isolation of circulating cell free foetal DNA and its qualitative and quantitative characterisation to be used as a minimally-invasive tool for the early, primary diagnosis/monitoring of various diseases.

Background and State of the Art:

Prenatal diagnosis of chromosomal anomalies is based on invasive procedures, which carry a risk of approximately 1%–2% for loss of pregnancy. An alternative to these inherently invasive techniques is to isolate fetal DNA circulating in thepregnant mother's plasma. It is known that free circulating fetal DNA in maternal plasma is ascribed to be mainly less than 500 bp, with a majority being 300bp and can be separated by size distribution from the larger maternal DNA (>1000 bp). Separating these fragments by size facilitates an increase in the ratio of fetal to maternal DNA.

Project Contribution and Methodology:

The overall objective of this study is to exploit breakthroughs at the confluences of micro, nano- and bio-technologies to create a low-cost minimally-invasive intelligent diagnosis system using a nanotechnology-based device for the separation of plasma from a maternal blood sample, isolation of circulating cell free fetal DNA and its qualitative and quantitative characterization to be used as a minimally-invasive tool for the early, primary diagnosis/monitoring of various diseases. Advances in molecular biology and biosensor technology and the integration of nanostructured functional components in macro- and microsystems will facilitate the isolation of cell free circulating fetal DNA on the basis of the size of fetal DNA fragments using chip-capillary electrophoresis followed by biosensor based genetic characterization.In this study, we will focus specifically on beta-thalassaemia, as an example of non-invasive prenatal diagnosis and screening and preeclampsia, as an example of monitoring.

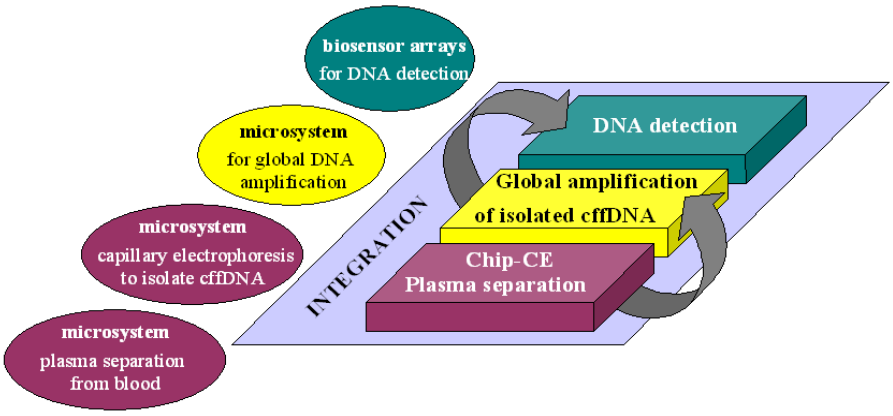

Figure 1: *Platform for the isolation and characterization of circulating cell free fetal DNA from maternal blood*

Educational value of the project: The graduate of this master will learn the fundamentals of molecular biology, topics in the field of medical diagnostics and microchip manipulation. The student will have a high background on the laboratory due this project suppose the contact with a lot of techniques. This fact will allow to the graduate the possibility to find work both in academia and industry, especially in research positions.

References:

1.- Hahn T, O'Sullivan CK, Drese KS. Microsystem for field-amplified electrokinetic trapping preconcentration of DNA at poly(ethylene terephthalate) membranes. Anal.Chem.2009;81:2904 –11.

2.- Hahn T, Drese KS, O'Sullivan CK. Microsystem for isolation of fetal DNA from maternal plasma by preparative size separation. Clin Chem 2009;55:2144–52.

3.- Chan KC, Zhang J, Hui AB, Wong N, Lau TK, Leung TN, et al. Size distributions of maternal and fetal DNA in maternal plasma. Clin Chem 2004; 50:88 –92.