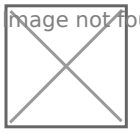
**Docket #:** S10-416

# Noninvasive Determination of the Fetal Genome

Researchers in Prof. Stephen Quake's laboratory have developed a method to measure the entire fetal genome noninvasively using materials from maternal blood. This technique involves knowing the whole-genome molecular haplotypes of either or both parents, followed by high-throughput shotgun sequencing of maternal cell-free DNA that contains a small portion of DNA from the fetus. To achieve whole-genome haplotyping of the parents, the researchers have also built a microfluidic device that can separate and analyze individual copies of each human chromosome from a few single blood cells.

The ability to determine fetal genotypes (including all SNPs and CNVs) across the entire genome enables testing for all inherited genetic disorders that currently require an invasive procedure to diagnose. The microfluidic device for haplotyping could also facilitate high-throughput, individualized haplotype analysis for personalized medicine, diagnostics and research applications.




*Microfluidic device designed for the amplification of metaphase chromosomes from a single cell.*

**Stage of Research**

The inventors have used the microfluidic device to analyze SNPs in a single human metaphase cell from four individuals. These assays determined alleles with 99.8% accuracy. They have applied the haplotyping technique on blood cells from two pregnant women and shotgun sequenced their cell-free plasma DNA and confirmed that the fetal genome could be revealed using their proposed technique.

# Applications

- **Noninvasive prenatal testing** - determination of the entire inherited fetal genome, including typing of fetal SNPs and CNVs
- **Personalized medicine** - individual genomic haplotype analysis to guide therapeutic options (device)
- **Diagnostics** - single cell genomics for preimplantation genetics, cancer and other diseases (device)
- **Research** - statistical genetics studies using haplotype analysis (device)

# Advantages

- **Comprehensive:**
  - can analyze the entire fetal genome
  - enables noninvasive prenatal analysis for all genetic conditions beyond current aneuploidy testing
- **Scalable and high-throughput:**
  - device can be used with standard metaphase cells, does not require chromosome microdissection or construction of somatic cell hybrids
  - device can be adapted for processing multiple cells simultaneously
- **Single cell analysis** - enables application to preimplantation genetics and other clinical settings that require single-cell sensitivity (device)

# Publications


- U.S. Patent Application No. 13/313,909
- H. Christina Fan, Jianbin Wang, Anastasia Potanina & Stephen R. Quake, Whole-genome molecular haplotyping of single cells, Nature Biotechnology, published online Dec. 19, 2010.
- Ingfei Chen, Separating Chromosomes: A more precise way to read DNA will change how we treat disease, Technology Review: Magazine: TR10, May/June 2011.
- H. Christina Fan, Wei Gu, Jianbin Wang, Yair J. Blumenfeld, Yasser Y. El-Sayed, Stephen R. Quake, Non-invasive prenatal measurement of the fetal genome, Nature 2012, published online July 4, 2012, doi:10.1038/nature11251.

- Sequencing of Fetal Genomes Using Only Maternal Blood Sample, Science Daily, July 4, 2012.
- New method enables sequencing of fetal genomes using only maternal blood sample, Stanford News, July 4, 2012.

## Patents

- Published Application: 20120196754
- Published Application: WO2012078792
- Published Application: 20160024579
- Issued: 8,877,442 (USA)

## Innovators

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