Abstract Of Clinical Research

The Feasibility study of Non-Invasive Fetal Trisomy 18 and 21 Detection with Semiconductor Sequencing Platform

Study Design

1. Research purpose: A performance parameter of Non-Invasive Prenatal Test using Ion Torrent system
2. Research subject: 155 pregnant women with fetuses of 12 weeks or more at high risk of defects who visited Xiamen Maternal & Child Health Care Hospital (Xiamen, Fujian, China) during 2012 and 2013 year.

Demographic Data

Table 1. Demographic characteristics of study subjects.

| Demographic characteristics | T18 (n=5) | T21 (n=11) | Combined detection (n=16) |
|-----------------------------|----------|-----------|--------------------------|
| Maternal age (year)          | 37 (35-39) | 37 (35-39) | 37 (35-39) |
| Male (%)                     | 20.0%     | 100.0%    | 80.0%                    |
| Female (%)                   | 80.0%     | 0.0%      | 20.0%                    |
| Total (n=155)                | 100.0%    | 100.0%    | 100.0%                   |

Sensitivity and Specificity

Table 2. Detection sensitivity, specificity in this study.

| Aneuploidy                  | T18 (n=5) | T21 (n=11) | Combined detection (n=16) |
|-----------------------------|----------|-----------|--------------------------|
| Detection sensitivity (95% CI) | 100.0% (47.8% - 100.0%) | 100.0% (71.5% - 100.0%) | 100.0% (79.4% - 100.0%) |
| Detection specificity (95% CI) | 100.0% (97.6% - 100.0%) | 100.0% (97.5% - 100.0%) | 100.0% (97.4% - 100.0%) |

Interactive dot diagrams for fetal trisomy 18 and 21
Abstract Of Clinical Research

Comparison of two high-throughput semiconductor chip sequencing platforms in noninvasive prenatal testing for Down syndrome in early pregnancy

Study Design

1. Research purpose: Developing an accurate and cost-effective method for measuring fetal fraction using SNP imputation.
2. Research subject: A total of 84 samples were sequenced via semiconductor sequencing using identical samples.

Demographic Characteristics

Table 1. Demographic characteristics of 101 pregnant women in Mirae & Heemang, Numujungwon, and GN hospitals in Korea.

| Characteristic          | Value                      |
|-------------------------|----------------------------|
| Maternal age, years    | 35 (30.21) ; 60 (39.41)    |
| Pregnancy trimester     | 1 drill: 1-13 week gestation | 2 drill: 14-25 week gestation | 3 drill: 26-40 week gestation |
| Range                   | 137 (43) ; 300 (100)       |
| Gestational age, week   | 20 ± 4.3                   |
| Mean                    | 15                         |
| Range                   | 11-49                      |
| Pregnancy outcome (%)   | 6.20, 8.86                 |
| Total No of patients    | 100.0% (96.2%–100.0%)      |
| Euploid (n=96)          | 35.45±3.64                 |
| Turner Syndrome (XO)    | 3 (3.07)                   |
| Male sex - no (%)       | 240 (24.5)                 |
| Female sex - no (%)     | 220 (21.5)                 |
| Table 1. Demographic characteristics of 101 pregnant women in 12 hospitals in Korea.

Positive and negative predictive values

Table 2. Predictive and negative predictive values of the NIFTI test results for fetal trisomy 21 for the PGIM and Proton sequencers used in the study.

| Test            | Positive predictive value (%) | Negative predictive value (%) |
|-----------------|------------------------------|-------------------------------|
| SNPimputed      | 100.0% (97.0% - 100.0%)      | 99.2% (96.9% - 100.0%)        |
| PGIM sequencing | 100.0% (97.0% - 100.0%)      | 99.2% (96.9% - 100.0%)        |
| Proton sequencing | 100.0% (97.0% - 100.0%)    | 99.2% (96.9% - 100.0%)        |

Abstract Of Clinical Research

An adaptive Detection method for fetal chromosomal aneuploidy using cell-free DNA from 447 Korean Women

Study Design

1. Research purpose: Developing a new algorithm to predict the risk of trisomies 13, 18, and 21 using the set of extracted reference samples.
2. Research subject: A total of 447 pregnant women at high risk for fetal aneuploidy were enrolled at 12 hospitals in Korea.

Demographic Characteristics

Table 1. Demographic characteristics of 447 pregnant women in 12 hospitals in Korea.

| Characteristic          | Value                      |
|-------------------------|----------------------------|
| Maternal age, years    | 35                         |
| Pregnancy trimester     | 1 drill: 1-13 week gestation | 2 drill: 14-25 week gestation | 3 drill: 26-40 week gestation |
| Range                   | 137 (43) ; 300 (100)       |
| Gestational age, week   | 20 ± 4.3                   |
| Mean                    | 15                         |
| Range                   | 11-49                      |
| Pregnancy outcome (%)   | 6.20, 8.86                 |
| Total No of patients    | 100.0% (96.2%–100.0%)      |
| Euploid (n=96)          | 35.45±3.64                 |
| Turner Syndrome (XO)    | 3 (3.07)                   |
| Male sex - no (%)       | 240 (24.5)                 |
| Female sex - no (%)     | 220 (21.5)                 |

Figure 2. 2 score comparison between PGIM and Proton platforms using identical samples.

Abstract Of Clinical Research

Cost-effective and accurate method of measuring fetal fraction using SNP imputation

Study Design

1. Research purpose: Developing an accurate and cost-effective method for measuring fetal fractions using single-nucleotide polymorphisms (SNPs).
2. Research subject: A total of 84 samples were sequenced via semiconductor sequencing using a 0.3X sequencing coverage.

Table 1. Mean number of SNPs in the 84 samples before imputation and increased mean number of single-nucleotide variants (SNVs) after SNP imputation using HRC v1.1 and 1000GP3.

| Test            | Mean number of SNPs | Increased mean number of SNVs |
|-----------------|---------------------|-------------------------------|
| SNPimputed      | 247,596             | 6,204                         |
| PGIM sequencing | 239,596             | 6,204                         |
| Proton sequencing | 239,596              | 6,204                         |

Figure 1. Coefficient of variations (CV) for chromosome 21 with and without adaptive sample selection using the representative samples with a GC = 0.2-0.4. The baseline bar represents the coefficient of variation used to measure the PI change of the representative samples (n=30) among reference samples (n=30) without adaptive sample selection.

Figure 2. Z-scores obtained in the A, B, C, D, E, F, and G of adaptive reference samples generated using the Adaptive method. 2 scores obtained for each sample along with the unambiguous thresholds using the adaptively selected reference samples represented in Figure 1 are shown.

Abstract Of Clinical Research

Typical chromosomal disorders

| Chromosomal Disorder | Chromosome | Description |
|----------------------|------------|-------------|
| Down syndrome (DS)   | 21         | Trisomy of chromosome 21, typically associated with physical growth delays, characteristic facial features, and intellectual disability. Occurs in about one in 600 babies each year. In DS, Down syndrome was prevalent in 6.4 million individuals and resolved in 27,000 deaths due to from 2000 to 1998. |
| Edwards syndrome (ED) | 18         | Trisomy of chromosome 18, typically associated with physical growth delays, characteristic facial features, and intellectual disability. Occurs in about one in 5,000 babies each year. In ED, Edwards syndrome was prevalent in 6.4 million individuals and resolved in 27,000 deaths due to from 2000 to 1998. |
| Turner syndrome (TS)  | X          | Trisomy of chromosome X, typically associated with physical growth delays, characteristic facial features, and intellectual disability. Occurs in about one in 2,000 babies each year. In TS, Turner syndrome was prevalent in 6.4 million individuals and resolved in 27,000 deaths due to from 2000 to 1998. |