▶ INSPECTION EQUIPMENT

Ion Proton™

The Ion Proton™ System makes affordable, high-quality next-generation sequencing accessible to scientists around the world. The Ion Proton™ System is a reliable sequencing platform that combines simple sample preparation and data analysis solutions with flexible chip output for ultimate project flexibility.

Human disease researchers can perform applications such as exome sequencing to elucidate variants important for the heritability of cancer as well as Mendelian and complex disorders.

Exome sequencing is a targeted sequencing approach that is restricted to the protein-coding region of genomes. The exome is estimated to encompass approximately 1% of the genome, yet contains approximately 85% of disease-causing mutations.For genetic researchers trying to unravel the disease-causing genes of over 6,800 rare diseases,exome sequencing enables the identification of common single-nucleotide variants (SNVs) and small insertions or deletions (indels), as well as rare de novo mutations that may explain the heritability of Mendelian and complex disorders.

▶ TEST DESCRIPTION

The test is a screening method for detecting certain specific chromosomal abnormalities in a developing baby.
This test will provide an evaluation of the fetal risk influenced by Trisomy21, Trisomy18, Trisomy13 and sex chromosome aneuploidies using noninvasive technology.

▶ DISCLAIMERS

- A 'high risk' result should not be considered a diagnosis. The result should be confirmed by conventional tests such as fetal karyotyping.
- A 'low risk' result does not exclude the possibility of fetal trisomy.
- This report is not intended for a clinical diagnosis, but is intended for guidance for doctors.

Genome Care

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GENOMOM
Non-Invasive Prenatal Test

FOR YOUR
HEALTHY BABY!!

SAFE
NIPT
EASY
ACCURATE

NON-INVASIVE
PRENATAL TEST **NIPT**

What is NGS?

NGS stands for "Next Generation Sequencing", the advanced technology of DNA sequencing with fast, accurate and high output performance.

NIPT Method

NIPT is a screening method for detecting certain specific chromosomal abnormalities in a developing baby.After 10 weeks of pregnancy, NIPT can detect whether your baby is at risk of fetal Trisomy21,18,13 and sex chromosome aneuploidies.
(Down syndrome, Edwards syndrome, and Patau syndrome) accurately.

List of Test in NIPT

*Down syndrome, Edwards syndrome and Patau syndrome with 99% sensitivity
*X0, XXY, XXX, XYY with 95% sensitivity

NIPT Process

Who we are

Genome care published the clinical results of NIPT in PLOS ONE & BMC Medical Genomics (October 2014. April 2016, October 2016) worldwide authoritative scientific journal. Through these experiments, Genome Care became the first sacrificially verified NIPT service provider in Korea with world-class level of NGS and data analysis competency.

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.

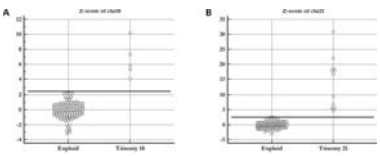
Demographic Data

Table 1. Demographic characteristics of study subjects

Demographic characteristics	Euploid (n=139)	T18 (n=5)	T21 (n=11)	Total (n=155)
Maternal age, year, mean±SD	30.61±5.22	27.60±5.51	33.90±3.35	30.73±5.20
≥35 years (%)	37 (26.6)	1 (20.0)	5 (45.5)	43 (27.7)
NIPT during 12-27 gestational weeks (%)	107 (77.0)	5 (100.0)	8 (72.7)	120 (77.4)
NIPT during 28-33 gestational weeks (%)	32 (23.0)	0 (0.0)	3 (27.3)	35 (22.6)
Male fetus (%)	65 (46.8)	4 (80.0)	9 (81.8)	78 (50.3)
Female fetus (%)	74 (53.2)	1 (20.0)	2 (18.2)	77 (49.7)

T18, Trisomy 18; T21, Trisomy 21; SD, standard deviation.

Interactive dot diagrams for fetal trisomy 18 and 21



Sensitivity and Specificity

Table 2. Detection sensitivity and specificity in this study

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

T18, Trisomy 18; T21, Trisomy 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 :** Noninvasive prenatal testing for Down syndrome in early pregnancy.
2. **Research subject :** 101 pregnant women aged between 25 and 42 years were enrolled under an Institutional Review Board protocol in three hospitals (Mirae & Heemang, Namujungwon, and GN in Korea) after high-risk group screening.

Demographic Characteristics

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

Demographic characteristics	Euploid (n=96)	T21 (n=5)	P value	Total (n=101)
Maternal age, years, mean±SD	35.55±3.63	33.40±3.64		35.45±3.64
≥ 35 years (%)	59 (61.46)	1(20.00)		60 (59.41)
NIPT during gestational week 11–13 (%)	67 (69.79)	3 (60.0)		70 (69.31)
NIPT during gestational week 14–18 (%)	29 (30.21)	2 (40.0)		31 (30.69)
PGM, z-score of chr21 (min, max)	-3.46, 2.07	5.50, 9.43	< 0.0001†	-3.46, 9.43
Proton, z-score of chr21 (min, max)	-2.32, 2.10	6.20, 8.86	< 0.0001†	-2.32, 8.96

Figure 1. Interactive dot diagrams of trisomy 21 for PGM and Proton sequencers showing the minimal z-scores.

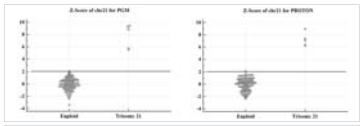
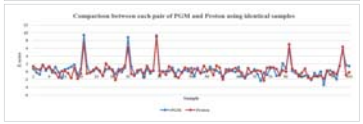


Figure 2. Z-score comparison between PGM and Proton platforms using identical samples.



Positive and negative predictive values

Table 2. The positive and negative predictive values of the NIPT results for fetal trisomy 21 for the PGM and Proton sequencers used in this study

Chip	Positive predictive value (95% CI)	Negative predictive value (95% CI)
318 of PGM	100.0% (47.8%–100.0%)	100.0% (96.2%–100.0%)
PI of Proton	100.0% (47.8%–100.0%)	100.0% (96.2%–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 sets of extracted reference samples.
2. **Research subject :** A total of 447 pregnant woman 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
No. of patients	447
Maternal age - year	
Mean	35
Range	20 ~ 46
Gestational age - week	
Mean	15
Median	16
Range	11 ~22
Pregnancy trimester - no. (%)	
First: 1-13 week gestation	137 (30.6)
Second: 14-26 week gestation	310 (69.4)
Male fetus - no. (%)	249 (52.5)
Female fetus - no. (%)	225 (47.5)

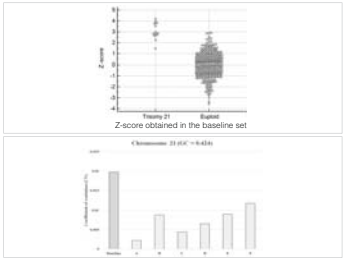


Figure 1. Coefficient of variation (CV) for chromosome 21 with and without adaptive sample selection using the representative sample with a GC =0.424. The baseline bar represents the coefficient of variation used to measure the genomic representation of chromosome 21 among reference samples (n=396) without adaptive sample selection.

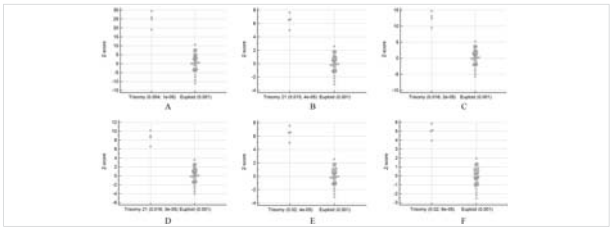


Figure 2. Z scores obtained in the A, B, C, D, E, and F sets of adaptive reference samples generated using the adaptive method. Z scores obtained for each sample along with the unambiguous thresholds using the adaptively selected samples represented in Figure 1 are shown.

Abstract Of Clinical Research

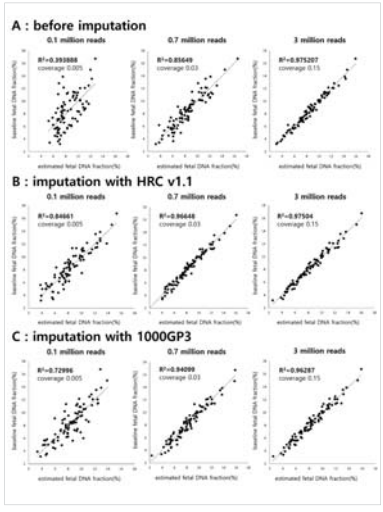
Cost-effective and accurate method of measuring fetal fraction using SNP imputation

Study Design

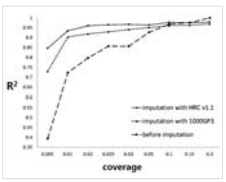
1. **Research purpose :** Developing an accurate and cost-effective method for measuring fetal fractions using single-nucleotide polymorphisms (SNPs).
2. **Research subject :** A total of 84 samples were sequenced via semiconductor sequencing using a 0.3X sequencing coverage.

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 HRCv1.1 and 1000GP3

	Before imputation	HRC v1.1	1000GP3
Average number of SNVs (84 samples)	247,596	10,254,299	11,319,299



◀**Figure 1.** Graphs depicting the correlation between the fetal fractions estimated at 0.005x. 0.03x, and 0.15x sequencing coverage and baseline. (A) The fetal fractions were measured using 250K genotyped SNPs before SNP imputation. (B) SNP imputation was performed using a HRC v1.1 reference panel. (C) SNP imputation was performed using a 1000GP3 reference panel.



▲**Figure 2.** Graph of correlation between the fetal fractions estimated at each sequencing coverage and baseline. The solid line indicates the correlation between fetal fractions with HRC v1.1 and baseline, dotted line indicates the correlation with 1000GP3, and broken line indicates the correlation without imputation.

Typical chromosomal disorders

Down Syndrome - Trisomy 21

Down syndrome, also known as trisomy 21, is a genetic disorder caused by the presence of all or part of a third copy of chromosome 21. It is typically associated with physical growth delays, characteristic facial features and mild to moderate intellectual disability. Down syndrome is one of the most common chromosome abnormalities in humans. It occurs in about one per 1000 babies born each year. In 2015, Down syndrome was present in 5.4 million individuals and resulted in 27,000 deaths down from 43,000 deaths in 1990.

Edwards Syndrome - Trisomy 18

Edwards syndrome, also known as trisomy 18, is a genetic disorder caused by the presence of all, or part of a third copy of chromosome 18. Many parts of the body are affected. Babies are often born small and have heart defects. Other features include a small head, small jaw, clenched fists with overlapping fingers, and severe intellectual disability. Edwards's syndrome occurs in around one in 5,000 live births. Some studies suggest that more babies that survive to birth are female. Many of those affected die before birth. Survival beyond a year of life is around 5–25%

Patau syndrome - Trisomy 13

Patau syndrome is a syndrome caused by a chromosomal abnormality, in which some or all of the cells of the body contain extra genetic material from chromosome 13. The extra genetic material disrupts normal development, causing multiple and complex organ defects. Like all nondisjunction conditions (such as Down syndrome and Edwards syndrome), the risk of this syndrome in the offspring increases with maternal age at pregnancy, with about 31 years being the average. Patau syndrome affects somewhere between 1 in 10,000 and 1 in 21,700 live births.

JACOBS syndrome - XYY

XYY syndrome is a genetic condition in which a male has an extra Y chromosome. Symptoms are usually few. They may include being taller than average, acne, and an increased risk of learning problems. The person is generally otherwise normal, including normal fertility. Treatment may include speech therapy or extra help with schoolwork. Outcomes are generally good. Prevention is not possible. The condition occurs in about 1 in 1,000 male births. Many people with the condition are unaware that they have it. The condition was first described in 1961.

Turner syndrome - XO

Turner syndrome (TS), also known as X or XO, is a condition in which a female is partly or completely missing an X chromosome.- Signs and symptoms vary among those affected. Often, a short and webbed neck, low-set ears, low hairline at the back of the neck, short stature, and swollen hands and feet are seen at birth. Typically, they develop menstrual periods and breasts only with hormone treatment, and are unable to have children without reproductive technology. Heart defects, diabetes, and low thyroid hormone occur more frequently. Turner syndrome occurs in between one in 2000 and one in 5000 females at birth. All regions of the world and cultures are affected about equally. Generally people with TS have a shorter life expectancy, mostly due to heart problems and diabetes.

Klinefelter Syndrome - XXY

Klinefelter syndrome (KS) also known as XXY or XXY, is the set of symptoms that result from two or more X chromosomes in males. The primary features are sterility and small testicles. Often symptoms may be subtle and many people do not realize they are affected. Sometimes symptoms are more prominent and may include weaker muscles, greater height, poor coordination, less body hair, breast growth, and less interest in sex. Often it is only at puberty that these symptoms are noticed. Intelligence is usually normal; however, reading difficulties and problems with speech are more common. Symptoms are typically more severe if three or more X chromosomes are present. Klinefelter syndrome is one of the most common chromosomal disorders, occurring in 1:500 to 1:1,000 live male births.

TRIPLE syndrome - XXX

Triple X syndrome, also known as trisomy X and 47, XXX, is characterized by the presence of an extra X chromosome in each cell of a female. Those affected are often taller than average. Usually there are no other physical differences and normal fertility. Occasionally there are learning difficulties, decreased muscle tone, seizures, or kidney problems.
Treatment may include speech therapy, physical therapy, and counseling. It occurs in about one in every 1,000 female births. It is estimated that 90% of those affected are not diagnosed as they either have no or only few symptoms. It was first identified in 1959.