PIMS
The next generation of PGT

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The Next Generation of PGT

Groundbreaking and Innovative
Embryo Screening Technology

What is PIMS?

Preimplantation DNA Methylation Screening (PIMS) is a groundbreaking and innovative embryo screening technology that can test ***both chromosomal aneuploidy and DNA methylomes*** including whole-genome methylation level, DMRs (Differential Methylation Regions), and imprinted genes. It is the ***first and only*** technology in the world that can test ***both molecular genetics and epigenetics*** information from an embryo within a ***single*** PIMS run.

How PIMS was established?

The founder of PIMS --- ***Dr. LIU Jiang*** collaborating with clinical scientists invented PIMS. It took more than ten years in epigenetics-related scientific and clinical research to establish PIMS method.

- Early stage embryo of zebra fish inherits methylome mapping from sperm[1]
  —— Jiang, L., et al. (2013). Cell

- Active methylome reprogramming at paternal and maternal genes of mammals[2]
  —— Wang, L., et al. (2014). Cell

- Methylome reprogramming related to assisted reproductive technology (ART)[3]
  —— Li, G., et al. (2017). J Genet Genomics

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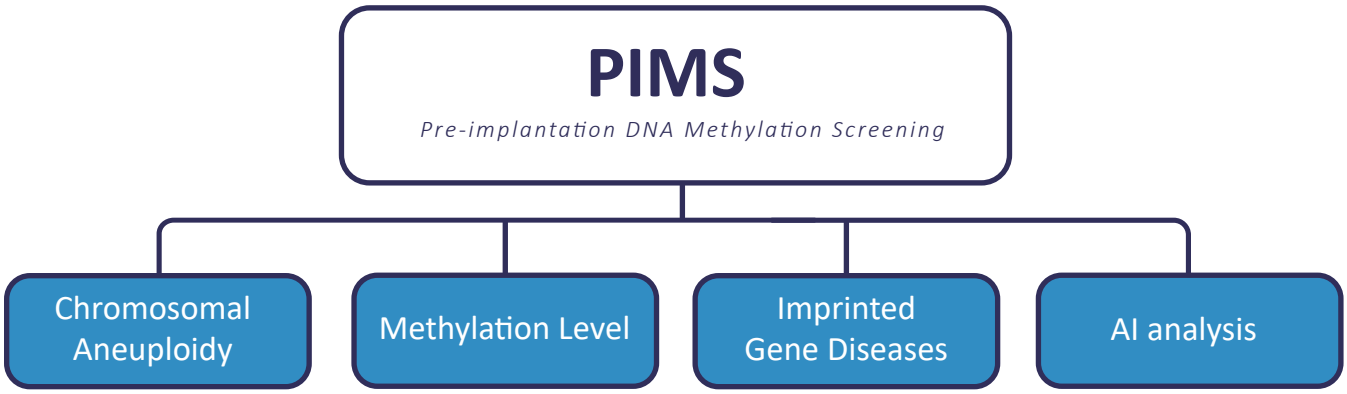
How does PIMS work?



Chromosomal Aneuploidy: Check if the embryos are euploid (normal), mosaic (partially abnormal) or aneuploid (abnormal)

Methylation Level: Test the methylation level to determine if embryos fall into the optimal range

Imprinted Gene Diseases: Test the methylation status of the specific imprinted genes to determine the risks of obtaining related diseases

Embryo Selection: Analyze all the parameters by using proprietary AI algorithm to predict which embryo has the best potential

Why PIMS^4?

- Improve first live birth rate by at least ***10%***
- Provide higher resolution in CNV Calling to ***avoid false positive & false mosaic*** (100x data compared with a world leading company)
- Improve IVF outcomes for ***all*** age groups of women
- ***Lower*** birth defect risk by analyzing key imprinting control regions (ICRs)
- Help select the ***healthiest*** embryo to transfer

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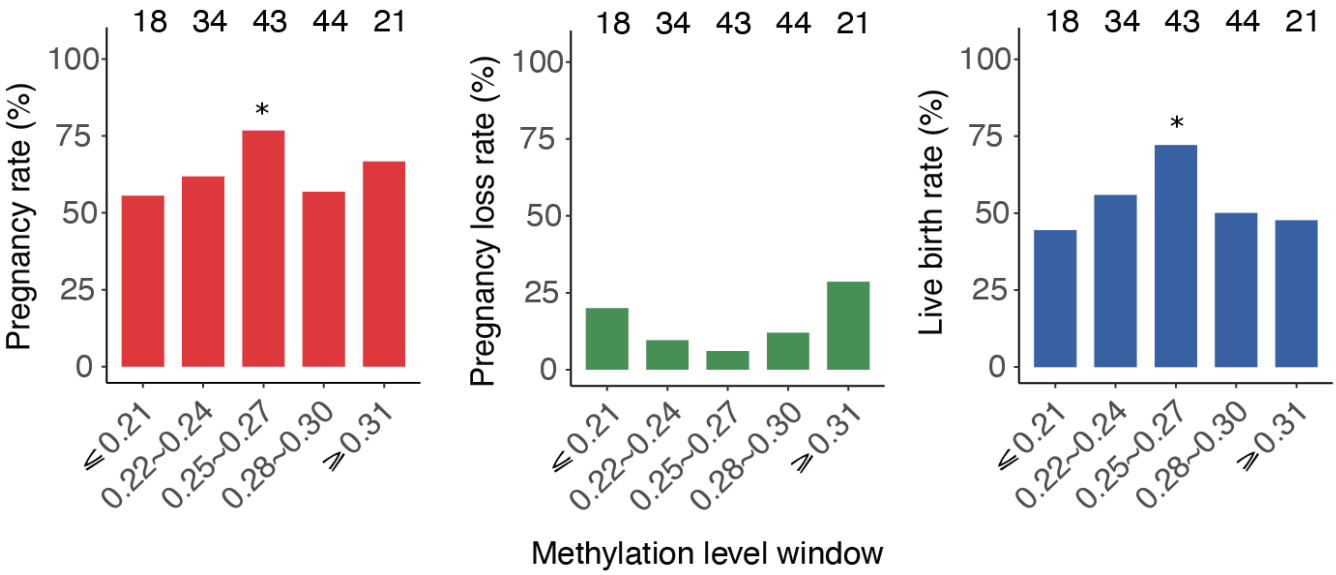
PIMS Clinical Study[4,5]

Design of the clinical study

- Focus Group: Patients with potential genetic disease that requires PGT screening
- More than 800 embryos in 182 families with PIMS
- 160 PGT cycles Conducted
  - 90 cycles live birth
  - 57 cycles pregnancy failure
  - 13 cycles pregnancy loss

DNA methylation is associated with ART outcome



- The embryos are divided into different groups according to their global methylation level
- Embryos with methylation level within 0.25-0.27 have the highest pregnancy rate, the highest birth rate, and the lowest pregnancy loss rate
- Methylation level closer to 0.25-0.27 results in higher birth rate as well

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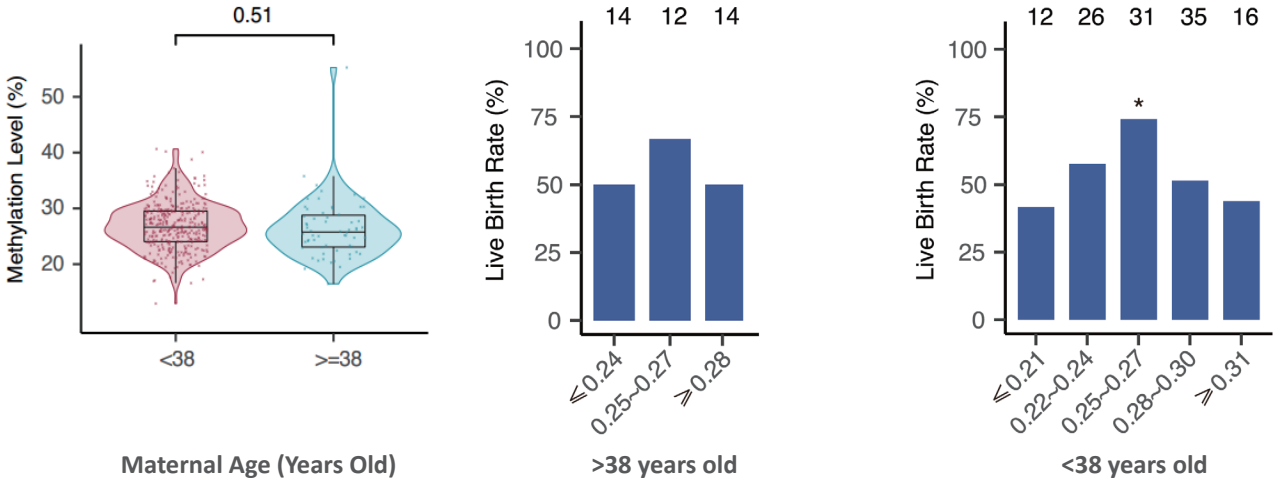
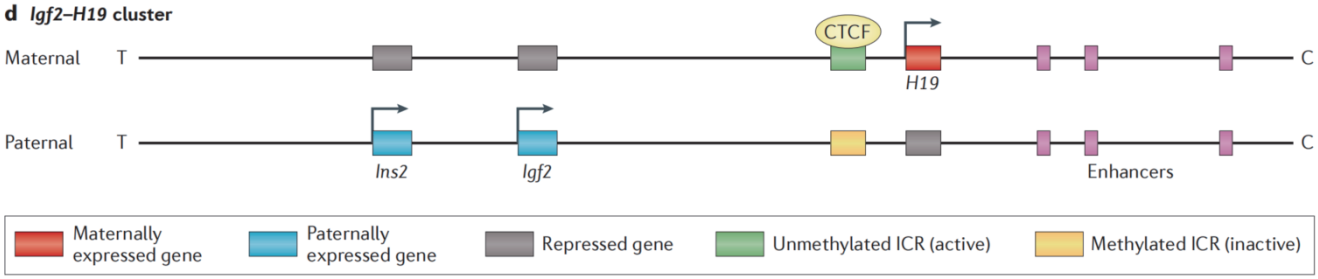
The overall distribution of methylation level is similar among different aged women groups



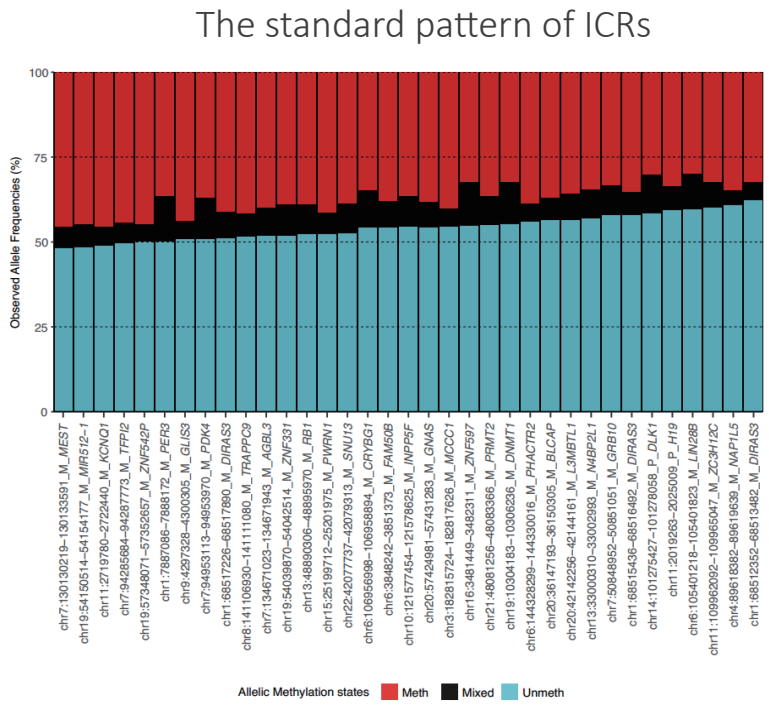
- Methylation level distribution is not significantly different among different aged women
- For both young and AMA females, the birth rate for the embryos with the methylation levels within 0.25-0.27 is the highest



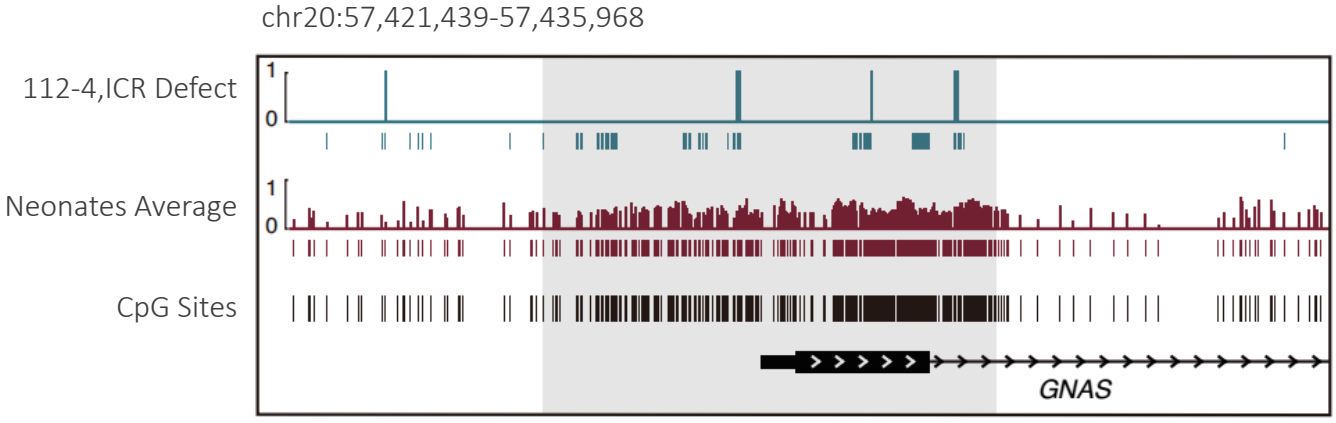
Genomic imprinting is a normal form of gene regulation that causes a subset of mammalian genes to be expressed from one of the two parental chromosomes. Some imprinted genes are expressed from the maternally inherited chromosomes and others from the paternally inherited chromosomes. The monoallelic parent of origin-specific expression of imprinted genes in mammals is regulated by differentially DNA methylated imprinting control regions (ICRs).

As French National Heath Data showed, incidence rate of imprinted gene disease was 1.4‰ for infants from normal conception and 3‰ for IVF infants. It was mostly caused by abnormal DNA methylation. However, there is no specific method to diagnose, screen or even cure the imprinted gene disease.

Imprinted gene defects can be identified by PIMS[5]



- The standard methylation patterns of ICRs (Imprinting Control Regions) are established according to the embryos with healthy live birth



- A gene named GNAS is linked to the birth defect of Pseudohypoparathyroidism[5]

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How to distinguish PIMS?

PGT-A

▼

Biopsy 3-5 TE Cells from D5 blastocysts

▼

Next Generation Sequencing (NGS)

▼

Results:
· Copied number variations (CNV)

PIMS

▼

Biopsy 3-5 TE Cells from D5 blastocysts

▼

Micro Enzymatic Methyl-seq (MEM-seq)

▼

Results:
· **Copied number variations (CNV)**
· **Methylation level**
· **Imprinted genes**
· **AI analysis**

Product	Chromosomal Aneuploidy	Methylation Level	Imprinted Gene Diseases	AI Analysis	Customized Report
PIMS Premium	●	●	●	●	●

Reference:

1. Jiang, Lan et al. “Sperm, but not oocyte, DNA methylome is inherited by zebrafish early embryos.” Cell vol. 153,4 (2013): 773-84. doi:10.1016/j.cell.2013.04.041

2. Wang, Lu et al. “Programming and inheritance of parental DNA methylomes in mammals.” Cell vol. 157,4 (2014): 979-991. doi:10.1016/j.cell.2014.04.017

3. Li, Guoqiang et al. “Genome wide abnormal DNA methylome of human blastocyst in assisted reproductive technology.” Journal of genetics and genomics = Yi chuan xue bao vol. 44,10 (2017): 475-481. doi:10.1016/j.jgg.2017.09.001

4. Gao, Yuan et al. “A clinical study of preimplantation DNA methylation screening in assisted reproductive technology.” Cell research vol. 33,6 (2023): 483-485. doi:10.1038/s41422-023-00809-z

5. Mendes de Oliveira E, Keogh JM, Talbot F, Henning E, Ahmed R, Perdikari A, Bounds R, Wasiluk N, Ayinampudi V, Barroso I, Mokrosiński J, Jyothish D, Lim S, Gupta S, Kershaw M, Matei C, Partha P, Randell T, McAulay A, Wilson LC, Cheetham T, Crowne EC, Clayton P, Farooqi IS. Obesity-Associated GNAS Mutations and the Melanocortin Pathway. N Engl J Med. 2021 Oct 21;385(17):1581-1592. doi: 10.1056/NEJMoa2103329. Epub 2021 Oct 6. PMID: 34614324.

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Spectrum Fertility Group Inc.

Email: support@spectrumfertility.com
Address: 867 Boylston St, 5th Floor-#1984, Boston, MA 02116, USA

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