Critical Review of Mertens et al. (2024): Mitochondrial DNA Variability and Birthweight in ART-Conceived Children

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INTRODUCTION

Assisted Reproductive Technologies (ART) represent one of the most important medical revolutions of the 20th century, making pregnancies possible in infertile couples. Since the birth of Louise Brown in 1978, the first child conceived using in vitro fertilization (IVF), the field of ART has experienced tremendous development, continuously improving the techniques and increasing the number of children that were born using these methods. However, despite the remarkable clinical success, concerns regarding the long-term safety and health levels of children born through ART persist. They are based and fueled by scientific evidence gathered in recent decades.

Epidemiological and clinical studies have shown that there are significant differences between children conceived spontaneously (SC) and those conceived through ART, in terms of increased risk for congenital anomalies, low birth weight, and other adverse perinatal outcomes. Particularly, children born from freshly transferred embryos after ART procedures have a 2 to 3 times higher risk of having low birth weight or suffering from other neonatal complications compared to SC children. Surprisingly, children resulting from frozen embryos are at an increased risk of being overweight for their age. This excess weight at birth may carry additional health risks, such as an increased predisposition to cardiometabolic diseases (such as obesity or diabetes) and possibly certain types of pediatric cancers.

Given this context, numerous studies have been done in the attempt to identify the causes for these differences, concentrating on three main factors: maternal subfertility, ovarian stimulation (OS), and in vitro embryo manipulations, including the type of culture medium used. However, the often contradictory results of previous studies have compli-

cated clarifying the specific role of each factor. For example, maternal subfertility itself has been correlated with an increased risk of adverse perinatal outcomes, regardless of whether the pregnancy was achieved through ART or naturally, suggesting a pre-existing maternal genetic influence. At the same time, the OS procedure was associated with changes in the uterine environment that can affect embryonic development, and the different culture media used in the laboratory have demonstrated influences on the birth weight of children, although the exact effects are difficult to generalise due to variability between assisted reproduction centers.

At the molecular level, most of the research focused on the epigenetic effects of ART, investigating possible DNA methylation changes at both the placenta and embryonic genome levels. However, the studies that have been done on humans have returned inconsistent results: some reported subtle differences, whilst others have not found significant epigenetic alterations, despite clear evidence from animal models. Recent studies actually denied even the hypothesis that stated that in vitro fertilisation could increase the incidence of chromosomal abnormalities in the fetus or placenta, thus highlighting the need to explore other biological mechanisms potentially involved.

Against this complex and controversial background, the study analysed proposes an innovative hypothesis: the role of mitochondrial DNA (mtDNA) variants in determining the birth weight of children born through ART. Mitochondria, organelles essential for cellular metabolism and energy production, possess their own distinct genetic material, mutations of which can directly influence critical biological functions. In fact, there is already strong evidence linking mitochondrial dysfunction to metabolic abnormalities, obesity, insulin resistance, and even low birth weight in the general population. Furthermore, inherited defects in mtDNA are known to predispose individuals to severe metabolic disorders and to influence fetal development in a crucial way.

The hypothesis the authors proposed says that maternal subfertility could be partially caused by the presence of some mitochondrial variants that affect the efficiency of oxidative phosphorylation, thus affecting natural fertility and reproductive results. Moreover, ovarian stimulation, used in ART to obtain an increased number of oocytes in a menstrual cycle, could induce de novo mutations in the mtDNA of oocytes, therefore amplifying the negative effects on future embryos.

In order to test these hypothesis, the authors have conducted a complex analysis of the mitochondrial genome, using deep sequencing on a large number of samples: 451 children (270 conceived through ART, and 181 conceived spontaneously), 157 mother-child pairs, and 113 individual oocytes, collected both in natural cycles, and after OS. The main purpose was to determine if there are significant differences between mitochondrial genetic profiles of ART and SC children, if these differences correlate with birth weight, and to

identify the possible origins of these variants (inherited or de novo).

Preliminary results have shown that, even though the distribution of major mitochondrial haplogroups does not differ significantly between the ART and SC groups, children born after ART show a higher incidence of de novo nonsynonymous variants and rRNA variants – changes that are known for their potential to affect mitochondrial function. These variants were also associated with lower birth weight percentiles, independent of the mode of conception. Interestingly, these differences appear to be the result of a combination of inherited mutations (reflecting the maternal genetic background) and de novo mutations arising in the context of OS and maternal aging.

Furthermore, the data obtained from oocyte analysis indicated that the number of de novo mtDNA variants is correlated with both increased maternal age and the size of oocyte samples obtained after OS. This result suggests that, in addition to inherited genetic factors, specific ART procedures and individual patient characteristics contribute to modifying the mitochondrial genetic profile of the offspring.

This work represents an important step in understanding the subtle molecular mechanisms with which ART may influence the long-term health of children, going beyond previous paradigms focused exclusively on epigenetic changes or chromosomal abnormalities. The authors' findings add a new level of complexity to the discussion of the safety of ART, highlighting the need to assess the impact of mitochondrial mutations in preconception genetic counseling and in optimizing infertility treatment protocols.

This research also raises crucial questions about how reproductive medicine should approach oocyte selection and manipulation, given that seemingly neutral factors, such as the size of oocyte samples or maternal age, can have important genetic consequences on future children. There is, thus, a need for future studies to explore the long-term impact of these mitochondrial variants on the metabolic and cardiac health of individuals born through ART, as well as determine whether there are ways to reduce the incidence of these mutations by adapting ovarian stimulation and embryo culture techniques.

Therefore, the reviewed work not only has an original contribution to the field of bioinformatics and reproductive genetics but also opens new directions of interdisciplinary research, with major practical implications for modern reproductive medicine. A deep understanding of the role of mitochondrial DNA in embryonic and perinatal development could lead, in the long term, to improving the quality of ART procedures and reducing risks to the health of future generations.

RESULTS

Characteristics of the studied groups and analysis methodology

In this study, the authors analyzed 451 participants, of whom 270 were children conceived through assisted reproductive technologies (ART) and 181 were conceived spontaneously (SC). In addition, 157 mother-child pairs and 113 individual oocytes, collected from both natural cycles and after ovarian stimulation (OS), were analysed. The primary aim was to assess differences in mitochondrial DNA (mtDNA) between ART and SC children, examining the potential impact on birth weight and exploring the origin of these mitochondrial variations.

Biological samples included peripheral blood, placenta, saliva, buccal cells, and urinary tract samples. For mitochondrial DNA sequencing, deep-coverage next-generation sequencing (NGS) technology was used for sensitive detection of homoplasmic and heteroplasmic variants, including low-frequency ones. To avoid errors, 1037 base pairs corresponding to regions susceptible to sequencing artifacts were excluded.

The distribution of mitochondrial haplogroups was similar between the ART and SC groups, with no significant differences. Therefore, any differences observed later in the analysis of mtDNA variants could not be attributed to ancestral differences in mitochondrial genetic background.

Profile of mtDNA variants: homoplasmic and heteroplasmic

Comprehensive analysis of mitochondrial DNA (mtDNA) from the studied samples allowed the identification of a total of 430 distinct heteroplasmic variants, of which 66% were unique to a single individual. This high proportion of unique variants indicates significant mitochondrial diversity in the analyzed population and emphasizes the importance of examining each variant in detail in the context of perinatal health. To systematically understand the biological impact of the identified variants, they were functionally classified into several relevant categories:

- Hypervariable regions (HV): areas of mtDNA known for their high mutation rate, often used in phylogeny and personal identification studies.
- Non-coding regions: sequences that are not translated into proteins, but may have important regulatory roles in mtDNA replication and expression.
- Origin of heavy chain replication (OHR) and Termination associated sequences (TAS): regions directly involved in the replication and transcription processes of mitochondrial DNA.
- rRNA genes: encode ribosomal RNA required for mitochondrial protein synthesis.

- tRNA genes: encode transfer RNA molecules, essential for mitochondrial protein translation
- Protein-coding genes include variants that can be:
  - Synonymous (do not change the amino acid sequence).
  - Nonsynonymous (change the amino acid sequence, with potential major functional impact).

Comparison between ART and SC groups:

1. Proportion of individuals carrying homoplasmic variants
The analysis showed that the proportion of individuals carrying homoplasmic variants (mutations present in all copies of mtDNA in a cell) was similar between the ART and SC groups. This observation indicates that, regarding mutations fixed completely in mitochondria, assisted conception does not introduce major variations compared to natural conception.

2. Total number of heteroplasmic variants per individual
In what concerns the total number of heteroplasmic variants (mutations present only in a proportion of mitochondrial genomes in a cell), there have not been identified significant statistical differences between ART and SC groups. This finding suggests that the ART procedure itself does not induce a generalized increase in heteroplasmy in mitochondria.

3. Frequency of nonsynonymous variants in coding genes
A notable observation was that individuals conceived through ART showed a slightly higher frequency of nonsynonymous variants in coding genes compared to SC children. Although this difference did not reach the classical threshold of statistical significance ($p < 0.05$), the trend is biologically relevant, as nonsynonymous variants have an increased potential to affect the functionality of mitochondrial proteins essential for cellular energy production.

4. The percentage load of variants in the hypervariable (HV) regions
The analysis revealed that the percentage load of variants in HV regions was lower in ART individuals compared to SC individuals. This observation may reflect either a different natural selection on neutral variants in the context of ART or an indirect effect of laboratory procedures on mitochondrial genome stability.

Integrating and reducing data complexity: exploratory factor analysis

Given the extreme complexity of the data generated, the authors used an advanced statistical method (exploratory orthogonal factor analysis) to reduce the dimensionality of the information and identify underlying patterns. This analysis generated four main factors, each reflecting coherent combinations of variant types. Factor 2 was by far the most relevant for differentiating between the ART and SC groups.

Factor 2 was characterized by:

- An increased abundance of variants in protein-coding regions
- An increased abundance of variants in rRNA genes
- A decreased number of variants in hypervariable and non-coding regions

This composition of Factor 2 suggests that alterations relevant to mitochondrial health (and implicitly to clinical phenotypes such as birth weight) are concentrated in functional variants of mtDNA, not in neutral regions.

Moreover, the scores for Factor 2 were significantly higher for ART individuals than for the SC ones. This implies that, within ART, there is a strong tendency for mutations to accumulate in regions critical for mitochondrial function.

Interpreting the identified differences

Overall, these results support the hypothesis that:

- Assisted reproductive technologies do not significantly alter the global distribution of mitochondrial mutations
- ART is specifically associated with a qualitative change in the mutation profile, increasing the incidence of mutations with functional potential for cellular bioenergetics.
- This altered profile could contribute to the clinical risks observed in children conceived through ART, including the increased incidence of low birth weight and subsequent metabolic complications.

This conclusion is particularly important because nonsynonymous mutations in protein-coding mtDNA genes are well known for their ability to alter the efficiency of the mitochondrial respiratory chain, ATP production, and oxidative stress control, all being key factors in fetal development.

Correlation of mtDNA profile with birth weight

In the study, the authors wanted to study if there was any link between mutations in mitochondrial DNA (mtDNA) and the birth weight of children. To be fair in their analysis, they adjusted the data for both gestational age (how many weeks the pregnancy lasted) and the sex of the child, because these factors can influence weight.

Then they split the children into two big categories:

- Those who had a weight below the 10th percentile (P10) - among the lowest 10% in weight.
- Those who were below the 25th percentile (P25) - the smallest 25%

In other words, P10 and P25 are thresholds used in medicine to see if a baby has a normal weight or if it is considered "small for gestational age".

What did they discover?

When they compared genetic profiles:

- Naturally conceived (SC) babies who were under P10 or under P25 had higher scores on Factor 2. (Factor 2, in the factor analysis, represented mainly mutations in protein-coding genes and rRNA genes)
- These small SC babies at birth were more likely to have nonsynonymous mutations (which can affect protein function) and mutations in rRNA genes (which affect protein synthesis in mitochondria).
- The cumulative burden (the sum of the percentages of nonsynonymous and rRNA mutations that each baby had) was higher in the low-birth-weight SC babies.

In other words, naturally conceived babies who had more of these mutations also had lower birth weights, supporting the idea that poor mitochondrial function due to mutations may affect how the baby develops in the womb.

What happened with children conceived through ART?

Interestingly, these correlations were not found in children born through ART. In them, whether they had similar mutations or not, birth weight did not seem to be influenced by their mitochondrial mutation profile. This led the authors to propose that, in ART children, other mechanisms are probably involved in affecting birth weight. These may be factors specific to assisted reproductive procedures, such as:

- Embryo culture medium
- In vitro manipulation procedures

- Hormonal stimulation during oocyte retrieval

Overall, in SC babies, mitochondrial mutations seem to play a role in how big or small they are born, while in ART babies, the same relationship was not found, suggesting that in these children, low birth weight is not directly cause by mutations in the mitochondria, but probably by other factors related to the ART process.

Analysis of the impact of the culture medium on the results

In this part of the study, the authors wanted to see if the type of embryo culture medium used in the laboratory had any influence on the link between mitochondrial DNA (mtDNA) mutations and birth weight. In assisted reproduction (ART), after an egg is fertilized in the laboratory, the embryo is grown for several days in a special medium (a nutrient solution) before being implanted in the uterus. The exact type of medium can influence how the embryo develops. The authors looked at three different media:

- **Cook** – a culture medium used in many fertility clinics.
- **UZB** – another type of medium used in some hospitals or assisted reproduction centers
- **Vitrolife** – a newer medium and considered more "standardized" in assisted reproduction

This led to discovering that:

- Children conceived through ART and raised in the Cook and UZB environments had a higher rate of birth weight below the 25th percentile (P25), especially for boys.
- When Vitrolife medium was used, this problem was considerably reduced. In Vitrolife, such a clear link between culture medium and low birth weight was no longer observed. Thus, Vitrolife allowed a "cleaner" analysis of the effect of mitochondrial mutations on weight, without so much "noise" caused by the medium.

To make sure that their result concerning mDNA was not artificially influenced by the culture medium, the authors chose to exclude from final statistical analyses the children who were raised in Cook or UZB media. Therefore, only children raised in Vitrolife were included in final analyses; in this way, they were able to analyze more accurately whether mutations in mitochondrial DNA influence birth weight, without being confused with the effects of the culture environment.

Why is this important:

If they had not removed the influence of the culture medium, it would have been difficult to clearly say whether the low birth weight is due to mitochondrial mutations or whether it is, in fact, due to the way the embryo was grown in the laboratory.

Therefore, standardization on a single type of medium (Vitrolife) was essential to draw correct conclusions in this study.

Applied statistical models: logistic regression and discriminant analysis

To better understand how certain genetic factors (such as mtDNA mutations) and clinical factors (such as smoking or hypertension) influence birth weight, the authors used two main types of statistical models:

- Binary Logistic Regression
- Discriminant Analysis

These methods are frequently used in bioinformatics and medicine to analyze relationships between variables and build predictive models.

1. Binary Logistic Regression

This is a method used when we want to predict a variable that can take only two values. The authors built logistic regression models to identify which factors are most important in predicting whether a child will have a weight below the 10th percentile (P10) or below the 25th percentile (P25).

Results for predicting weight <P10:
The model showed that the following factors were significant:

- **Smoking during pregnancy**: Mothers who smoked during pregnancy were more likely to have very low birth weight babies.
- **Hypertension during pregnancy**: Mothers with high blood pressure during pregnancy had an increased risk of having low birth weight babies.
- **Presence of homoplasmic tRNA variants**: If there were homoplasmic mutations in mitochondrial tRNA genes, the risk was increased.
- **Maternal age**: Older mothers were more likely to have babies below P10.

Results for predicting weight <P25:
Other factors were important for the less severe threshold (<P25):

- **Maternal age** (similar to P10).
- **Presence of nonsynonymous heteroplasmic and rRNA variants**: Children who had more such mutations in mitochondrial DNA had an increased risk of being below P25.
- **Membership in haplogroup I**: some mitochondrial haplogroups (especially haplogroup I) were associated with lower weights.

2. Discriminant analysis

Discriminant analysis is another statistical technique used to see how well we can separate two groups (for example, children <P10 vs children >=P10) based on multiple factors.

- Initially, when they used only clinical data (smoking, hypertension, etc.), the models had a classification accuracy of 40% for children under P10.
- After they added information about mtDNA variants (nonsynonymous mutations, rRNA, etc.), the accuracy increased to 70%.

This means that mitochondrial mutations are strong additional factors in predicting which babies will have low birth weight. The models became much better when into account were taken both clinical and genetic data.

Conclusions

Using logistic regression and discriminant analysis, the authors demonstrated that:

- Certain genetic factors in mtDNA influence the risk of low birth weight.
- Genetic data adds significant value to predictive models, significantly improving their accuracy.
- This combined approach (clinical + genetic) is better than using either data set separately.

Analysis of de novo variants in mother-child pairs

A very important part of the study was the analysis of de novo variants. "De novo variants" are new mutations that appear in the child and are not present in the mother. These mutations are important because they can occur due to natural processes or can be influenced by assisted reproductive technologies (ART).

Technique used

They analyzed mother-child pairs and compared the mitochondrial DNA of each mother with that of the child:

- If they found a variant in the child that was not present in the mother at all, they considered it a de novo variant.
- Then they compared how many such de novo variants appeared in children conceived naturally (SC) versus those conceived through ART.

What they discovered:

1. Increased number of de novo variants in ART children

- Children born through ART had more de novo variants in mtDNA than children conceived spontaneously.
- This suggests that the assisted fertilization process (with all the manipulations involved: egg collection, in vitro fertilization, embryo culture) could introduce or favor the emergence of new mutations in mitochondria.

2. Type of de novo variants The de novo variants that emerged in ART children were predominantly nonsynonymous. Those are mutations that change the amino acid sequence of mitochondrial proteins. This type of mutation can affect the normal function of proteins and can impact cellular metabolism.

3. Load of de novo nonsynonymous heteroplasmy The total load of de novo nonsynonymous mutations (the sum of the percentages of these mutations in the child's cells) was higher in ART children than in SC children. In other words, not only were there more mutations, but their relative level (how "present" they were in the mitochondrial population) was also higher.

All these results mean:

- ART procedures, even if very advanced and controlled, can directly or indirectly contribute to the emergence of new mutations in mitochondria.
- These mutations can have long-term implications for children's health, given the essential role of mitochondria in energy, metabolism, and development.

This finding adds new insight into the potential genetic risks associated with assisted reproduction and supports the idea that ART technologies must be continuously optimized to minimize these effects.

Influence of maternal age and ovarian stimulation

In further analysis of new (de novo) mutations, the authors wanted to understand which factors influence the occurrence of these mutations in children conceived through ART.

They focused on two main factors:

- Maternal age (the mother's age at the time of oocyte retrieval).
- Number of oocytes retrieved after ovarian stimulation procedure (OS).

1. Correlation with maternal age
The authors found a significant positive correlation between maternal age and the total number of de novo variants identified in mtDNA.

The older the mother was, the more new mitochondrial mutations were observed in the child. This association is logical, as with increasing maternal age, oocytes accumulate more DNA damage, and mitochondria become more susceptible to mutations due to the cumulative effects of oxidative stress over time.

2. Correlation with ovarian stimulation (OS)
A correlation with ovarian stimulation (OS) was also observed. More specifically, the number of oocytes retrieved after hormonal stimulation was positively correlated with the number of de novo variants identified. Precisely, in oocytes obtained through intensive OS protocols, where a large number of oocytes are collected in a single cycle, a higher number of new mutations was detected. This correlation was particularly strident in protein-coding genes and rRNA genes within the mtDNA, which are essential regions for proper mitochondrial function.

What do these results mean?

In short, oocyte aging with increasing maternal age leads to a higher risk of mitochondrial mutations. Intensive ovarian stimulation protocols, where more oocytes are forced to mature than would occur naturally, can also favor the appearance of new mutations in mtDNA. Therefore, not only maternal age but also hormonal manipulation during ART procedures contributes to the genetic alteration of mitochondria inherited by the offspring. This suggests that, in the future, these factors should be carefully considered when optimizing ART protocols in order to minimize genetic risks. In summary, oocyte aging combined with ovarian stimulation leads to a higher burden of mitochondrial mutations, potentially impacting the health of children conceived through ART.

Summary of the Main Findings

At the end of their analysis, the authors synthesized the most important results obtained throughout the study. These findings clearly demonstrate that assisted reproductive technologies (ART) impact mitochondrial genetic inheritance and can influence newborn development.

The main conclusions are as follows:

- Children conceived through ART exhibit a distinct mtDNA mutation profile compared to spontaneously conceived (SC) children.
- ART-conceived children presented a higher number of nonsynonymous variants (mutations that alter amino acid sequences in proteins) as well as mutations in rRNA genes, which are crucial for mitochondrial protein synthesis.
- These mutations are significant because they can disrupt normal mitochondrial function, affecting cellular metabolism and overall organismal development.
- Low birthweight among spontaneously conceived children is associated with specific mtDNA mutations.
- In SC children, certain heteroplasmic variants in mtDNA were linked to reduced birthweight. Thus, impaired mitochondrial function due to these mutations may play a critical role in normal fetal development.
- ART procedures promote the appearance of de novo mutations in mitochondria. Children conceived via ART exhibited a higher burden of new (de novo) mtDNA mutations compared to SC children.

These de novo mutations appear to arise mainly through two mechanisms:

- Increased maternal age, as older oocytes are more prone to genetic damage
- Intensive ovarian stimulation, where hormonal treatments to retrieve multiple oocytes may favor the accumulation of mitochondrial mutations.

Finally, the embryo culture medium further influences developmental outcomes. The type of culture medium used during embryo growth in vitro (Cook, UZB, or Vitrolife) can modify the impact of mitochondrial mutations on offspring development. Notably, the use of Cook and UZB media was associated with a higher incidence of low birthweight, particularly among male infants.

CONCLUSIONS

Impact and Relevance of the Study

The study conducted by Mertens et al. has a major impact in the fields of reproductive medicine and genetic bioinformatics, offering an original contribution to the understanding of the molecular effects of assisted reproductive technologies (ART) on the long-term health of offspring. By highlighting the role of mitochondrial DNA (mtDNA) variants in association with low birthweight, the study proposes a new paradigm for investigating ART-related risks, moving beyond the traditional focus on epigenetic alterations.

Although published relatively recently, in 2024 in *Nature Communications*, the study has already accumulated six citations according to Google Scholar, reflecting the growing interest of the scientific community in this innovative topic. Given the importance of the subject and the opening of new interdisciplinary research directions, it is expected that the number of citations will increase significantly in the coming years.

The findings can be directly utilized by:

- Specialists in reproductive medicine (embryologists, gynecologists) to improve the selection and manipulation of oocytes.
- Researchers in molecular genetics and bioinformatics interested in the dynamics of mitochondrial mutations and their effects on embryonic development.
- Clinicians involved in preconception genetic counseling, who must provide people undergoing ART procedures with information based on the latest scientific evidence.
- Authorities, or entrusted people, that aim to establish optimized and safer protocols for in vitro fertilization procedures.

Moreover, the study opens valuable perspectives for future research on the cumulative impact of mitochondrial mutations on cardiometabolic health, suggesting the potential for new predictive biomarkers in the field of personalized reproductive medicine.

General Conclusion

The study analysed offers a new and important perspective on how assisted reproductive technologies (ART) can influence not just the success of fertilization, but also the genetic quality of the mitochondrial inheritance passed on to children.

By carefully studying mitochondrial DNA variants, the authors showed that children conceived through ART have:

- A distinct mutation profile, with a higher number of potentially functional variants

(nonsynonymous and rRNA mutations),

- And a higher number of de novo mutations, influenced by both maternal age and the intensity of ovarian stimulation.

In addition, the study found that:

- In spontaneously conceived (SC) children, certain mitochondrial mutations are associated with low birthweight,
- While in ART-conceived children, the effect of mutations on birthweight seems to be masked or changed by factors related to laboratory procedures, including the type of embryo culture medium used.

Overall, these findings highlight that ART is not just a simple technical tool, but a process with important genetic and biological implications for the health of future generations. Therefore, to maximize the benefits of ART and reduce possible risks:

- Continuous improvement of fertilization, embryo culture, and manipulation techniques is necessary
- Personalized genetic counseling should be offered to people considering ART
- And careful long-term monitoring of clinical outcomes is essential.

This research opens the way towards a more responsible and informed approach to modern reproductive medicine, combining advanced technology with an understanding of the complexity of human biology.

From my point of view, the study represents an essential step in understanding the complex impact of assisted reproductive technologies on the health of offspring, by focusing on a relatively unexplored area - mitochondrial DNA variability. I believe the study is impressive because of its rigorous methodology, the large amount of data analyzed, and the use of modern sequencing and advanced statistical analysis techniques.

However, there are some limitations that could be improved in future research. One important limitation is the lack of long-term monitoring of the children, which would help assess the real effects of the mitochondrial mutations over time. Additionally, it would be useful to expand the study to include a wider variety of culture media used in ART, to better pinpoint specific risk factors.

In conclusion, I believe this study has significant potential to influence clinical practice in reproductive medicine and to open new directions for bioinformatics research in the field of perinatal health.

References

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