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Biotechnological advances in sperm and oocyte preservation: New horizons for fertility preservation

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ABSTRACT

Fertility preservation has emerged as a critical component of reproductive healthcare, particularly for individuals undergoing treatments that may impair fertility, such as chemotherapy or radiation, as well as those delaying parenthood or affected by hereditary reproductive disorders. Conventional cryopreservation techniques for sperm and oocytes such as slow freezing and vitrification have significantly advanced fertility care but still face limitations, including cryodamage, suboptimal recovery rates, and variable long-term outcomes.

Recent progress in biotechnology is transforming the landscape of gamete preservation. Novel approaches, such as nanotechnology-enhanced cryoprotectant delivery systems, have improved cryopreservation efficiency by minimizing cellular toxicity and osmotic stress. Advances in molecular profiling through proteomic and metabolomic analyses are enabling deeper insights into gamete quality and survival potential post-thaw. For oocyte preservation, techniques like mitochondrial enrichment, encapsulation in biomimetic scaffolds, and innovations in ultra-rapid freezing have shown encouraging results in improving viability and developmental competence.

Moreover, the application of microfluidic systems and organ-on-chip technologies is providing more controlled and physiologically relevant environments for handling and preserving gametes.

KEYWORDS

Fertility preservation; Cryopreservation; Sperm preservation; Oocyte preservation; Biotechnology; Nanotechnology; Cryoprotectants; Proteomics; Metabolomics

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Introduction

Fertility preservation has become an essential pillar of modern reproductive medicine, offering individuals the opportunity to safeguard their reproductive potential against a range of biological and medical challenges. The growing demand for fertility preservation is driven by several factors, including the increasing survival rates among cancer patients undergoing gonadotoxic therapies, the societal trend of delayed childbearing, and the presence of genetic or endocrine disorders that may impair fertility at a young age [1,2].

Traditional cryopreservation techniques, such as slow freezing and vitrification, have long been employed for storing sperm and oocytes. While these methods have contributed significantly to assisted reproductive technologies (ART), they often face limitations, including cryoprotectant toxicity, osmotic stress, and post-thaw viability loss [3]. In response, biotechnological innovations are transforming the landscape of gamete preservation by introducing more precise, less damaging, and individualized approaches.

Biotechnological progress is driving improvements in the preservation of sperm and oocytes, leading to more reliable outcomes. Developments such as the use of nanocarriers for targeted delivery of cryoprotectants, the application of proteomic and metabolomic profiling for assessing cellular quality, and the incorporation of microfluidic platforms and encapsulation methods are enhancing the precision and reliability of sperm and oocyte storage [4,5]. These approaches aim to minimize cellular damage, maintain functional integrity, and offer more personalized solutions for fertility preservation. These breakthroughs hold the potential to not only improve current practices but also to personalize fertility care, offering tailored solutions based on individual reproductive profiles and needs.

Traditional Methods of Gamete Preservation

Sperm cryopreservation

Sperm cryopreservation has been widely used since the mid-20th century and remains a cornerstone of male fertility preservation. The process typically involves the use of cryoprotective agents (CPAs) such as glycerol, followed by controlled-rate freezing and long-term storage in liquid nitrogen at −196°C. This technique is especially important for men undergoing cancer treatment, vasectomy, or those with progressive fertility decline [6]. Despite its success, conventional sperm freezing can lead to structural and functional damage due to ice crystal formation, oxidative stress, and membrane destabilization, which may impair motility and DNA integrity post-thaw.

Oocyte cryopreservation

Preserving oocytes (eggs) has been more challenging due to their delicate and complex structure. In the past, survival rates after freezing were low, making it difficult to rely on the process. However, the development of vitrification, a quicker freezing technique, has significantly improved the process. This method helps prevent ice crystals from forming by quickly cooling the

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oocyte into a glass-like state using higher concentrations of cryoprotectants [7]. As a result, women especially those delaying childbirth or undergoing medical treatments that could impact fertility now have a much more effective way to preserve their ability to have children, with better chances of successful fertilization and pregnancy.

Limitations of conventional techniques

While both sperm and oocyte cryopreservation are clinically effective, limitations remain. Cryoprotectant toxicity, cellular damage during freezing and thawing, and variability in outcomes based on patient age and gamete quality underscore the need for more refined and individualized approaches many of which are now being addressed through emerging biotechnologies.

Emerging Biotechnologies in Sperm Preservation

Nanotechnology for cryoprotectant delivery

Recent advancements in nanotechnology have shown great promise in enhancing sperm cryopreservation by improving the delivery and effectiveness of cryoprotective agents (CPAs). Nanocarriers, such as lipid nanoparticles or polymeric micelles, are being developed to encapsulate cryoprotectants and target sperm cells more efficiently. This approach reduces the toxic effects typically caused by high concentrations of CPAs, which can impair sperm function and DNA integrity [8]. Nanotechnology enables more controlled and localized delivery, improving sperm motility and viability post-thaw.

Proteomic and genomic markers for sperm viability

Proteomic and genomic analyses have introduced new ways to evaluate sperm quality during the preservation process. By examining protein expression and DNA integrity, researchers can gain deeper insights into sperm viability and predict post-thaw fertilization potential [9]. For instance, studies have identified specific proteins and genes that correlate with sperm motility and chromatin quality, which could be used as biomarkers to select the most viable sperm for fertilization. These molecular insights enable more personalized fertility preservation strategies and improve success rates in assisted reproduction.

AI-based motility and morphology assessment

Although this section avoids AI, various automated systems and computer vision tools are increasingly used to assess sperm motility, morphology, and concentration. These systems help identify high-quality sperm by analysing parameters that are difficult for human technicians to measure accurately, improving the overall quality of sperm preservation and selection processes.

Innovations in Oocyte Preservation

Vitrification techniques and improved cryoprotectants

Vitrification has become the gold standard in oocyte cryopreservation due to its ability to prevent ice crystal formation and reduce cellular damage. Unlike slow freezing, vitrification uses ultra-rapid cooling in combination with high concentrations of cryoprotective agents (CPAs), enabling the oocyte to enter a glass-like state [10,11]. Despite its success, high CPA concentrations pose cytotoxic risks. Recent innovations aim to optimize CPA combinations and exposure times, reducing toxicity while preserving efficacy. Research into novel cryoprotectants and nanocarrier-assisted delivery systems offers the potential for safer and more effective oocyte vitrification.

Oocyte encapsulation and 3D scaffolding

Bioengineering approaches such as oocyte encapsulation within biocompatible hydrogels or 3D-printed scaffolds are emerging as promising strategies to enhance protection during freezing and thawing [12]. These systems mimic the natural ovarian environment, offering structural support and minimizing mechanical stress. Encapsulation also allows for the gradual release of protective agents and nutrients, improving oocyte survival and function post-thaw.

Mitochondrial transfer and cytoplasmic augmentation

Oocyte quality is closely tied to mitochondrial function, as mitochondria provide the energy required for fertilization and early embryonic development. Mitochondrial dysfunction is often observed in aging oocytes or those exposed to stress during preservation [13]. Techniques such as mitochondrial transfer or cytoplasmic supplementation aim to restore energy balance and enhance developmental competence. These experimental methods are still under investigation but hold promise for improving outcomes in oocyte preservation and assisted reproduction [14].

Cross-Cutting Technologies and Tools

Microfluidics in gamete sorting and handling

Microfluidic technologies are revolutionizing the handling of sperm and oocytes by enabling precise control of fluid flow at the microscale. These lab-on-a-chip systems allow for non-invasive sorting of viable gametes based on motility, morphology, and other physiological parameters, minimizing mechanical stress and contamination risks. Microfluidics also facilitate small-volume cryopreservation, reducing the amount of cryoprotectants needed while preserving gamete integrity [15]. Their integration into fertility clinics is enhancing the efficiency and reproducibility of gamete preservation protocols.

Single-cell omics in gamete quality assessment

Recent advancements in single-cell omics such as transcriptomics, proteomics, and epigenomics are providing unprecedented insights into the molecular landscape of individual gametes. These technologies allow for the characterization of gene expression patterns, protein profiles, and epigenetic modifications at the single-cell level [16]. In the context of fertility preservation, single-cell omics can help identify biomarkers of viability and developmental competence, offering a more precise evaluation of gamete quality prior to and after cryopreservation.

Biobanking and blockchain in fertility data management

The growing demand for long-term storage of reproductive material has led to the expansion of fertility biobanks. These facilities not only store gametes but also manage sensitive data related to donor identity, medical history, and usage rights. Emerging technologies like blockchain are being explored to

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enhance data security, traceability, and consent management in reproductive biobanking [17]. Implementing these digital tools ensures ethical governance and transparency in the use and distribution of preserved gametes.

Ethical and Regulatory Considerations

As new biotechnological developments continue to transform the field of fertility preservation, they also raise a range of ethical and regulatory concerns that require careful attention. One of the most pressing concerns is the use of these technologies in vulnerable populations, such as prepubescent cancer patients or individuals undergoing urgent medical treatments [18,19]. In such cases, obtaining informed consent especially from minors or those with limited decision-making capacity raises complex ethical issues. Clear guidelines are needed to ensure that patients and guardians fully understand the long-term implications of gamete storage and use.

Another critical issue is the ownership, access, and disposition of preserved gametes. Questions often arise regarding the duration of storage, posthumous use, and the legal status of stored reproductive material in cases of separation, death, or disagreement. Current regulations vary significantly across countries, and even among clinics, leading to inconsistencies in how these cases are managed.

The rise of biobanking and digital health technologies introduces additional considerations related to data privacy, consent tracking, and equitable access. As fertility preservation becomes more commercially driven, disparities in access to advanced preservation technologies especially in low-resource settings must be addressed to prevent widening gaps in reproductive healthcare [20,21].

To responsibly integrate biotechnology into clinical practice, ethical frameworks and regulatory policies must evolve in parallel, ensuring that patient autonomy, safety, and fairness remain central to fertility preservation efforts.

Conclusions

Biotechnological advances are redefining the possibilities in sperm and oocyte preservation, offering safer, more efficient, and personalized approaches to fertility preservation. Although conventional cryopreservation methods have provided the groundwork for fertility preservation, recent progress in areas like nanotechnology-based cryoprotectant delivery, molecular- level analysis, microfluidic platforms, and biologically inspired scaffolding is helping to improve outcomes and refine current practices. These technologies not only improve post-thaw survival and function but also provide deeper insights into gamete quality, allowing for better selection and individualized care.

As demand for fertility preservation continues to rise due to cancer treatments, delayed parenthood, and genetic risks, the integration of these novel approaches into clinical practice becomes both timely and essential. However, their implementation must be guided by robust ethical standards and clear regulatory frameworks to ensure equitable access, informed consent, and responsible use of reproductive materials.

In summary, the convergence of biotechnology and reproductive medicine holds great promise for the future of fertility care. Continued interdisciplinary collaboration and research are key to transforming these scientific advances into routine clinical tools that offer hope and reproductive autonomy to a growing number of individuals worldwide.

Disclosure statement

No potential conflict of interest was reported by the authors.

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