

Review

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Review

CRISPR, AI, and Omics in Animal IVF: Narrative mini-review on emerging Tools for Precision Breeding and Reproductive Success

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Abstract

In vitro fertilization (IVF) has long been a cornerstone of assisted reproductive technologies (ART) in animals, widely used in livestock breeding, endangered species conservation, and biomedical research. Traditional IVF techniques, while effective, often rely on trial-and-error protocols and are influenced by various biological and environmental factors. Recent innovations in biotechnology are revolutionizing this field. The integration of CRISPR-based genome editing, artificial intelligence (AI), and multi-omics technologies is propelling animal IVF into a new era of precision, efficiency, and predictability. In this review, the potential and recent researches of IVF in animals advancing with CRISPR, AI and omics were discussed before including future directions of this valuable field.

Keywords: CRISPR; artificial intelligence; omics; animal IVF

Introduction

In vitro fertilization (IVF) has long been a cornerstone of assisted reproductive technologies (ART) in animals, widely used in livestock breeding, endangered species conservation, and biomedical research. The integration of CRISPR gene editing, artificial intelligence (AI), and omics technologies is rapidly transforming *in vitro* fertilization (IVF) in animals, offering unprecedented opportunities for precision breeding, genetic improvement, and fertility enhancement. Traditionally, animal IVF has faced challenges such as low embryo viability, inefficient fertilization, and limited understanding of reproductive biology at the molecular level [1]. However, with the advent of multi-disciplinary tools, these barriers are being overcome through data-driven, targeted approaches [1].

CRISPR-Cas systems allow precise genome editing in embryos or germline cells, enabling the correction of genetic defects, insertion of desirable traits, and generation of transgenic animals with improved performance or disease resistance [2,3]. This is particularly valuable in livestock breeding programs aiming to enhance productivity, as well as in wildlife conservation and biomedical research involving animal models. AI enhances IVF efficiency by automating embryo assessment, predicting developmental outcomes, and optimizing protocols using machine learning [4,5]. Through image analysis and pattern recognition, AI tools outperform traditional subjective evaluations, increasing the reliability of embryo selection. Omics technologies including genomics, transcriptomics, proteomics, and metabolomics provide deep insight into the molecular landscape of reproduction [6]. These datasets help identify biomarkers of fertility, understand oocyte and sperm quality, and fine-tune culture conditions [6]. Together, CRISPR, AI, and omics are setting the stage for the next generation of animal IVF. In this review, the potential and recent researches of IVF in animals advancing with CRISPR, AI and omics were discussed before including future directions of this valuable field.

CRISPR: Precision Gene Editing for Reproductive Improvement

The introduction of CRISPR-Cas systems into reproductive biology has unlocked new avenues in animal IVF. This gene-editing tool enables precise modifications in gametes and embryos, allowing for the correction of genetic defects, introduction of desirable traits, and improved embryo viability. In livestock breeding, CRISPR has been employed to enhance traits such as disease resistance, meat quality, and growth efficiency. For example, gene editing in cattle and pigs has successfully knocked out genes linked to susceptibility to viral infections, thereby reducing production losses and the need for antibiotics. In the IVF context, CRISPR can be used to edit embryos post-fertilization or even gametes prior to fertilization, enabling the propagation of elite genetics across generations [7]. Moreover, germline editing in model organisms like mice and zebrafish supports functional genomic studies to understand reproductive mechanisms [8]. However, ethical considerations, regulatory frameworks, and off-target effects still pose challenges that must be addressed before widespread implementation.

Recent studies have highlighted successful applications of CRISPR-Cas technology in IVF. Briski et al. [9] compared three CRISPR-Cas9 delivery approaches for generating genetically modified pigs: introduction before fertilization via IVF, during fertilization using ICSI-mediated gene editing (ICSI-MGE), and post-fertilization through *in vivo* methods. ICSI-MGE demonstrated high efficiency in producing homozygous biallelic mutations in pig embryos, comparable to oocyte microinjection followed by IVF [9]. Successful live births were achieved only from *in vivo*-derived embryos, showing effective simultaneous editing of multiple genes, including GGTA1 and GHR [9]. Du et al. [10] assessed three methods for delivering CRISPR-Cas9 RNPs into bovine zygotes. As a result, they unearthed that NEPA-21 and Neon systems were more effective in generating blastocysts with homozygous genetic edits [10]. These findings offer important guidance for optimizing gene editing protocols in cattle and could support the broader adoption and advancement of genome editing technologies in livestock production [10]. Zhang et al. [11] generated high fecundity Merino sheep mutants via CRISPR-Cas9 technology. They deduced that CRISPR-Cas9 gene editing provided notable advantages over traditional sheep breeding methods, enabling genetic improvement without negatively impacting the fine wool characteristics of Merino sheep, which are commonly altered by conventional crossbreeding approaches [11]. Pirali et al. [12] performed CYP19 gene editing on goat embryos via somatic cell nuclear transfer and CRISPR-Cas9 techniques. The knockout efficiency reached 78.4% in cells and 68.9% in goat blastocysts, confirming effective CYP19 gene disruption [12]. By integrating cell electrotransfection with somatic cell nuclear transfer (SCNT), a high yield of CYP19-edited embryos was obtained without compromising normal embryonic development [12]. These embryos are suitable for implantation to produce knockout goats, laying the groundwork for future research into CYP19's role in male fertility and production-related traits [12].

AI: Enhancing IVF Efficiency and Embryo Selection

Artificial intelligence has found powerful applications in animal IVF, particularly in image-based embryo assessment, gamete quality evaluation, and predictive analytics. Traditional embryo grading relies on morphological assessment by embryologists, which is subjective and varies across labs. AI models trained on large datasets can now evaluate embryo development patterns using time-lapse imaging, yielding higher predictive accuracy for embryo viability and implantation potential. For instance, AI algorithms can analyze minute features in oocytes, sperm motility patterns, or embryo cleavage rates, these parameters are often overlooked by the human eye [6]. These models provide real-time, automated, and non-invasive assessment, reducing operator bias and improving consistency. In livestock, this translates to better embryo selection, higher pregnancy rates, and reduced costs per offspring. Furthermore, AI-driven optimization of culture conditions and hormonal stimulation protocols allows for individualized IVF strategies tailored to specific species, breeds, or even animals [6]. Combined with robotics and automation, AI is laying the foundation for scalable and highly efficient IVF labs in both research and agriculture.

Recent research has showcased the effective use of artificial intelligence in enhancing IVF outcomes. Marques et al. [13] have developed a more precise method for predicting the optimal time for dairy cow conception by using automated activity monitoring (AAM) systems. These systems continuously track a cow's movement and behavior, providing vital insights into the best timing for artificial insemination [13]. Using data from over a thousand Holstein cows, the study built a mathematical model that factors in not only activity levels but also individual health, environmental conditions, and the specific bull used for AI [13]. The findings showed that integrating on-farm data with AAM data significantly improved the accuracy of pregnancy predictions compared to relying on activity data alone [13]. Among the methods tested, the random forest model proved especially effective in minimizing prediction errors [13]. Their study demonstrates that combining real-time monitoring with detailed farm-level information can significantly enhance reproductive management in dairy herds [13]. Nagahara et al. [14] developed an AI-based diagnostic approach to accurately determine the ideal timing for artificial insemination in cows. The findings showed that when the pregnancy probability diagnostic model predicted a pregnancy probability of 70% or more, it proved highly reliable, achieving accuracy and precision rates of 76.2%, a perfect recall of 100%, and an F-score of 0.86 [14]. These results highlight the effectiveness and practical value of AI-driven tools in forecasting optimal insemination timing, offering significant advantages for breeding management [14]. Sananmuang et al. [15] established a hybrid deep learning model combining one-dimensional convolutional neural networks (1DCNN) and gated recurrent units (GRU) to classify the fertility potential of goat granulosa cells based on single-cell transcriptomic data. The refined hybrid model demonstrated excellent classification performance, achieving an accuracy of 98.89%, precision of 100%, recall of 97.83%, and an F1 score of 98.84% [15]. Their study marks the first use of deep learning for classifying goat granulosa cells using single-cell RNA sequencing data [15]. The 1DCNN-GRU hybrid model provides a reliable and measurable approach to assess GC fertility, showing potential to enhance reproductive selection in livestock breeding [15]. Further validation with larger datasets and in different species may position this model as a scalable molecular tool for precision livestock management [15].

Omics: A Systems Biology Perspective in Reproduction

Multi-omics approaches, encompassing genomics, transcriptomics, proteomics, and metabolomics, provide a systems-level understanding of reproductive biology. In the context of animal IVF, omics technologies help identify biomarkers that correlate with gamete competence, embryo health, and fertility potential. For instance, transcriptomic profiling of oocytes and embryos can reveal gene expression signatures associated with successful development, guiding more accurate selection of viable embryos [6]. Metabolomics has been used to analyze embryo culture media, offering non-invasive insights into metabolic activity and embryo viability [16]. These data-driven insights help optimize culture conditions and refine selection criteria. In livestock and aquaculture species, genomic selection powered by high-throughput sequencing has improved the genetic merit of donor animals used in IVF programs [6]. Integrating omics with AI tools allows the handling of large, complex datasets to extract actionable insights. For instance, machine learning models trained on omics data can predict reproductive outcomes or identify key regulatory networks influencing fertility.

Recent studies have demonstrated the successful application of omics technologies in improving IVF success rates. Rabaglino et al. [17] employed integration of multi-omics data with machine learning techniques to uncover epigenetic and transcriptomic variations between bovine embryos produced *in vitro* and those developed *in vivo*. Their findings indicate that early conceptuses from IVP embryos undergo epigenomic and transcriptomic alterations that influence their elongation and focal adhesion, ultimately reducing their survival after embryo transfer [17]. Marrella et al. [18] utilized a multi-omics approach to discover molecular signatures related to fertility in heifers (*Bos taurus*). Their multi-omics analyses reveal the intricate complexity of female fertility [18]. Notably, their findings emphasize fertility-related molecular differences in heifers that go beyond breed-

specific genetic backgrounds [18]. Finnerty et al. [19] combined multi-omics analysis with machine learning to predict human oviductal responses when gametes and embryos are present. They confirmed that the multi-omics profiling, followed by *in vivo* validation of proteins and RNAs, demonstrates that the oviduct adapts and responds to the presence of sperm and embryos in a spatially and temporally regulated way [19].

Integration and Future Directions

The true power of these technologies lies in their integration [20,21]. CRISPR offers a tool for functional validation of genes identified through omics. AI can analyze high-dimensional omics data and guide CRISPR targeting strategies. Together, they create a feedback loop where predictive insights inform experimental edits, which in turn refine the models. This integrated approach is already beginning to transform commercial livestock breeding. High-value animals can be selected and edited for desirable traits, assessed via AI-enhanced embryo screening, and supported by omics-informed reproductive management [6]. In conservation, these tools offer hope for restoring fertility in endangered species, preserving genetic diversity, and even rescuing traits lost through inbreeding or habitat stress [22]. However, challenges remain. Cross-species applicability of AI models, ethical considerations in germline editing, and the high cost of omics platforms can limit adoption, particularly in low-resource settings. Future work must focus on improving model generalizability, ensuring regulatory compliance, and reducing technological costs.

Conclusion

The convergence of CRISPR, AI, and omics technologies is reshaping animal IVF into a precise, data-driven field. These tools are improving our ability to manipulate, monitor, and enhance reproductive outcomes across species. From advancing livestock productivity to supporting wildlife conservation and fundamental reproductive science, this triad offers unprecedented possibilities. As these technologies mature and become more accessible, the future of animal reproduction will be smarter, safer, and far more efficient than ever before.

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