The role of cytoplasmic movements during the first 24-72 hours of human preimplantation development: an innovative AI-based assessment for predicting blastulation

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Introduction

Previous studies have highlighted the potential of AI-driven systems in optimizing human preimplantation embryo selection within IVF laboratories ^[1], demonstrating high predictive accuracy when trained on datasets derived from cultures maintained for a minimum of five days. A single study employing Time-Lapse Technology (TLT) explored the association between Cytoplasmic Movements (CMs) in early preimplantation embryos and their developmental viability ^[2]. These movements, governed by specific cytoskeletal mechanisms, represent key indicators of blastocyst formation. By utilizing computational methods, the study analysed CMs during the initial two days post-fertilization, identifying them as valuable indicators of zygote competence. Nonetheless, constraints related to limited sample size and reliance on manual data extraction underscored the necessity for large-scale, automated analyses.

Objectives

Predict embryo development into blastocyst by analysing CMs within the first 24-72 hours of culture by applying AI models to optical flow data obtained from time-lapse videos of human embryos both normally fertilized and those with an anomalous number of ProNuclei (PN).

Results

AI models (ROCKET, LSTM-FCN, ConvTran), trained on embryonic CMs data extracted through optical flow algorithms (Farneback and Lucas- Kanade), predict blastocyst development by analysing the first 24-72 hours of culture with similar performance. The analysis of the first 24 hours showed a balanced accuracy of 64% for ROCKET, 63% for LSTM-FCN, 67% for ConvTran; a sensitivity of 67% for ROCKET, 78% for LSTM-FCN, 89% for ConvTran; and a F1 score of 62% for ROCKET, 64% for LSTM-FCN, 69% for ConvTran. Extending the analysis period to the first 72 hours significantly improved performance, with a balanced accuracy of 74% for ROCKET, 76% for LSTM-FCN, 77% for ConvTran; a sensitivity of 89% for ConvTran; and a F1 Score of 74% for ROCKET, 76% for LSTM-FCN, 76% for ConvTran. These results suggest that the AI models demonstrate high sensitivity, reliably identifying developmentally competent embryos while maintaining high classification performance. Clinically, this is particularly valuable as it minimizes the risk of discarding embryos that have the potential to reach the blastocyst stage, including those with an anomalous PN number, such as 1PN embryos. In fact, stratified analysis confirmed that the models perform well in predicting blastocyst formation in these abnormal embryos as well as they do in normally fertilized (2PN) embryos.

Conclusions

These preliminary results demonstrate potential for both clinical applications, such as predicting blastocyst development, and academic research, particularly in elucidating previously unrecognized cytoplasmic and cytoskeletal dynamics that influence developmental competence. These findings are promising, as the models were developed exclusively using automatically extracted data from CMs, without the incorporation of additional predictive features, manual interventions, or annotations, and utilizing only a single median focal plane.

Bibliography

1 Khosravi P et al. Deep learning enables robust assessment and selection of human blastocysts after in vitro fertilization. NPJ Digit Med. 2019;2:21.

² Coticchio G, Fiorentino G, Nicora G, et al. Cytoplasmic movements of the early human embryo: imaging and artificial intelligence to predict blastocyst development. Reprod Biomed Online 2021;42(3):521-8.