Integrated Framework for Human Embryo Ploidy Prediction Using Artificial Intelligence

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Background & Unmet Need

- The success of in vitro fertilization (IVF) is limited by challenges in selecting the most viable embryos.
- As women age, the incidence of euploid embryos (normal chromosome number) decreases while that of aneuploids (embryos with chromosomal abnormalities that may cause miscarriages or birth defects) increases.
- The current standard methods for embryo selection, morphological quality and morphokinetic analyses, suffer from intra- and inter-observer variability.
- A third method, pre-implantation genetic testing for aneuploidies (PGT-A), is less variable but has its own notable limitations, including invasiveness and cost.
- Machine-learning approaches for assessment of embryo quality based on morphology have not demonstrated a clear benefit over current methods.
- **Unmet Need:** A non-invasive, reliable, and high-throughput method to predict ploidy of candidate embryos prior to implantation in order to increase the success of IVF.

Technology Overview

- **The Technology:** A machine-learning based method, called STORK-A, to non-invasively predict embryo ploidy status.
- Uses time-lapse microscopy images of embryos and clinical information (e.g., maternal age & morphological assessments) as inputs and outputs a probability of euploid vs aneuploid for each embryo.
- **PoC Data:** The STORK-A algorithm was trained using a dataset of images and clinical information for >10k embryos with confirmed ploidy status and was then also tested on two independent external datasets.
- STORK-A classified embryo ploidy status with accuracies of ~70% for both the training and independent datasets.
- IVF transferred embryos that were predicted to be euploid by STORK-A exhibited a livebirth rate of 48%, which is very similar to that of the transferred embryos classified as euploid by PGT-A (49%).

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Patents:
PCT Application Filed

Publications:

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**Technology Applications**

- Supplement traditional methods of embryo selection and prioritization by assigning ploidy predictions to embryos in a high throughput and unbiased manner
- Assist embryologists in determining on which embryos the more invasive and costly PGT-A should be performed in IVF cases that are complex and/or unlikely to be successful (advanced maternal age, low embryo count, etc.)

**Technology Advantages**

- Not subject to observer variability
- Non-invasive and less expensive than PGT-A
- High-throughput and can easily be adopted by fertility clinics for use in the IVF process
- Machine-learning algorithm has ability to improve accuracy as more image data is accrued
- Accuracy can be further increased by integrating with spatiotemporal data (video)

**Supporting Data / Figures**

*Figure 1*: Example STORK-A interface and ploidy predictions for use in clinical settings as a support tool for embryologists.

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Supporting Data / Figures

1. Collect raw images from time-lapse microscopy and relevant clinical information including PGT-A results, patient age, and morphokinetics.
2. Preprocess data by removing overexposed images and imputing missing morphokinetics.
5. Evaluate model performance.

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Figure 2: Top: Study Design for STORK-A development Bottom: STORK-A Schematic.
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Figure 3: STORK-A classified aneuploids vs. euploids in two independent datasets with similar accuracies to that of its training test dataset.

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