O-13: A novel non-invasive metabolomics approach to screen embryos for aneuploidy

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1. Objective:

The aim of this study was to develop a novel non-invasive technique for embryo selection. This was performed by identification of metabolomics biomarkers of euploidy and aneuploidy in spent culture media after embryo culture.

2. Design:

Samples (n=80) consist of spent culture media collected in IVF clinics after embryo culture from day 3 to day 5. After collection, samples were frozen and shipped to analysis lab. Samples were analyzed using a high-resolution accurate mass (HRAM) mass spectrometer. After appropriate data processing and analysis, several critical biomarkers were identified, leading to the development of a new non-invasive technique for embryo selection based on these specific molecules.

3. Materials and Methods:

After embryo culture between days 3 and 5, spent culture media was collected from 80 samples with known PGT results. These samples were processed using an ultrafiltration technique to separate high-molecular weight molecules from the metabolites fraction, the relevant ones for this study.

After this step, samples were analyzed using HRAM mass spectrometer. Resulting chromatograms were aligned and processed to identify and quantify different metabolites in the culture media.

Several statistical and machine learning techniques were applied to identify the most important metabolites to use as biomarkers. To test the performance of the model built, half of the samples (50%) were used to build the prediction model and the other half were used in the validation phase.

4. Results:

A total of 7,523 metabolites were detected in spent media samples. Several dimension reduction techniques were applied and, eventually, selection was performed using PLS-DA (Partial Least Squares – Discriminant Analysis), which gave the best results. Sixty (60) metabolomics

biomarkers were identified as the most significant ones and a model was built using PLS-DA algorithm.

The model was tested using the other half of the dataset (27 aneuploid and 13 euploid), for validation purposes. The results gave a concordance with PGT results of 97.5% accurate prediction, with only one misclassified instance: one euploid embryo was classified as aneuploid.

5. Conclusions:

Differences in metabolites concentration in spent culture media between euploid and aneuploid embryos were highlighted, confirming that we are able to infer metabolic status of the embryo by analyzing the compounds in culture media. In addition, a set number of metabolites were identified as potential biomarkers, facilitating its use in clinical practice instead of the total data, which is highly dimensional and difficult to handle.

This research demonstrates the power of metabolomics in IVF as a non-invasive tool for accurate selection of euploid embryos.