Abstract title:

Metebolomic Biomarker Profile of Human Oocyte Culture is Predictive to Embryo Development and Viability

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Introduction: Assisted reproduction outcomes demonstrate a relatively low pregnancy and relatively high multiple implantation rates. According to the SART statistics, the average number of embryos transferred per cycle ranged between 2.4 (<35 years of maternal age) and 3.3 (41-42 years) in the U.S. At the same time, pregnancy rates ranged from 43% to 18% and multiple gestations ranged between 37.3% and 15.7% in the same age categories, respectively. These results clearly demonstrate our current impaired ability of evaluating oocyte/embryo potential and show the need for a new viability assessment technology. Recently, a novel, non-invasive embryo viability tests have been proposed to use that is based on near-infrared spectroscopy. In the current study, we aimed to evaluate, if using the same technique, metabolomic data obtained from oocyte culture may correlate with derived embryo development and implantation potential

Materials & Methods: Patient treatment and laboratory conditions were standardized during the study. Patient inclusion criteria: <38 years of age with 10 or more retrieved oocytes assigned for ICSI. A total of 148 MII stage oocyte culture medium samples were collected from 11 patients. Oocytes were retrieved 36 hours after HCG administration. Following enzymatic and mechanical cleansing (Cumulase or Sigma Fraction IV), nuclear maturity was recorded and MII oocytes were allocated into individual culture media drops of 60 µl. Three hours later mature oocytes were injected and spent oocyte media was collected representing the different maturation stages. Fertilized eggs were cultured until day-3 or day-5 when selected embryos were transferred and/or frozen. Individual profiles were obtained from 5 µl media samples using Near Infrared (NIR) spectroscopy. Resulting metabolomics data were correlated with embryo morphological development and viability of the corresponding oocytes using multivariate analyses with a P level of 0.05.

Results: Intracytoplasmic sperm injection was performed on all mature oocytes, and 107 of them fertilized normally (72.3%). There were 31.9% grade-A (excellent quality); 34.1% were grade-B (good quality); 23.1% were grade-C (medium quality) and 10.9% were grade-D (poor quality) embryos. NIR spectroscopic analysis of culture medium of oocytes that developed to grade-A embryos on day-3 demonstrated significantly higher viability indices (0.62 ± 0.23) than those that developed to grades-C/D on the same day (0.42 ± 0.26; P<0.006). NIR spectroscopic examination of culture medium of oocytes that developed to grade-A embryos (12%) on day-5 demonstrated significantly higher viability indices (0.37 ± 0.20) than those that developed to grades-C/D (41%) on the same day (0.14 ± 0.21; P<0.02). NIR spectroscopic determination of spent culture media of oocytes that resulted in HCG positive pregnancy (8 of the 11 patients) demonstrated significantly higher viability indices (0.87 ± 0.27) than those that did not (0.44 ± 0.17; P<0.0001).

Conclusions: The results of the current study have demonstrated that metabolomic profiling from spent culture media of the oocyte is able to predict embryo development at day-3 and day-5 stages (even though that there were fewer embryos present on day-5, as some excellent-quality embryos were already transferred/frozen on day-3). It has also been shown that oocyte metabolomic profile may also predict embryo viability. Strikingly, just three hours of individual culture of oocytes proved to be sufficient to produce clearly detectable metabolomic "fingerprints" that is predictive to embryo development and viability. These data also demonstrate that metabolomic profiling may serve as a useful methodology for rapid, non-invasive gamete assessment that, together with a similarly descriptive embryo viability test, may favorably impact outcomes of assisted reproduction by enhancing gamete and embryo selection procedures. These results are promising, however, further studies are warranted to verify the consistency and reliability of this novel approach.

Authors:

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Keywords:

oocyte; metabolism; embryo; implantation; spectroscopy; pregnancy;

Overview page

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