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Unique Biomarkers of Human Oocyte Maturation Assessed by Non-Invasive Metabolomic Profiling

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Objective: It has been recently proposed that biospectroscopy-based metabolomics can be used to assess biomarkers of oxidative metabolism (OM), from culture medium of embryos. Our objective was to evaluate, if it is possible to establish novel metabolomic data from culture medium obtained from different maturational stage oocytes. Furthermore, we wanted to assess how metabolomic profiles, obtained for each group of maturational stage oocytes, correlate with levels of oxidative metabolism.

Design: Prospective collection and evaluation of oocyte culture medium by infrared spectroscopy.

Materials and Methods: ICSI patients with more than 10 eggs and under age of 37 were included. After three hours of incubation of eggs in individual drops, oocyte media was collected representing the different maturation stages. Selected embryos were transferred on Day3 or 5. Individual profiles were obtained from 5 l media samples using Near Infrared (NIR) spectroscopy. Specific biomarkers, corresponding to unique functional groups (NH₂, aromatic -CH, -OH, -SH) were identified yielding exclusive metabolomic profiles which were then quantified using a wavelength selective algorithm (Molecular Biometrics, LLC, Chester, NJ). Resulting metabolomics data were correlated with morphological assessed nuclear maturity of the corresponding oocytes using multivariate analyses with a P level of 5%.

Results: A total of 264 oocyte culture samples were collected from 32 patient cycles. Unique metabolomic profiles of the specific OM biomarker populations were consistently identified in all samples by NIR spectroscopy. Profiles of Metaphase I and II oocytes were significantly different from each other and from profiles of Prophase I (GV) oocytes (P<0.001 at the 95% confidence interval). NIR analysis of biomarkers required a minimum of three wavelength regions, and resulted in a specificity of 83% and a sensitivity of 85% for GV versus MI oocytes; and 93% specificity and 100% sensitivity between MI and MII oocytes.

Conclusions: The results of this study demonstrate that a detectable and significant difference exists in the metabolomic profiles of OM biomarkers found in culture media obtained from oocytes with the different maturational stages. These data confirm that NIR analyses can serve to assess metabolomic status also at the gamete level with high sensitivity (only 3 h of incubation). Further studies are planned to evaluate if gamete metabolomic profiling can also correlate with corresponding embryo development.