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Novel approach to viability testing by non-invasive metabolomic profiling (MetPro) of biomarkers of oxidative metabolism (OM) from blastocysts used for single embryo transfer (SET)

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Objective: MetPro of biomarkers of OM has been used successfully to identify the reproductive potential of embryos following IVF and multiple ET. In this study we applied metabolomics, based on Near Infrared (NIR) spectroscopy, to ascertain the reproductive potential of day-5 embryos in SET.

Materials and Methods: Infertile women (n=23) and oocyte donors (n=11) were down-regulated and stimulated with gonadotropins. IVF embryos were cultured individually in 80μl drops of sequential media. Embryos were graded and selected for SET on day-5 based on morphology. Following ET 25μl of spent-medium was collected and stored at -80C. Pregnancy was determined by ultrasound detection of fetal cardiac activity (FCA) at 6.5 weeks. NIR measurements of samples were conducted using an InGaAs spectrometer (vol. = 7μl; analysis time <1min). Media controls were used to compensate for signal drift. Sample properties were quantified from the resulting mean centered NIR spectra by determining the most parsimonious combination of variables in selected wavelength domains using genetic algorithm optimization. Selected wavelength regions were weighted by coefficients calculated by inverse least-squares regression. Each sample's pregnancy viability was estimated in a continuous reproductive potential index by a leave-one-out cross validation method. Notch box plots were used to plot resulting viability indices, and statistical significances were determined by t-tests.

Results: Overall pregnancy rate was 56%. NIR spectral analysis reproducibly defined 4 to 5 OM biomarker regions associated with changes in ROH, C=C, -SH, -CH and -NH functional groups that were used to distinguish a statistically significant difference between FCA+ vs FCA- samples. Metabolomic profiles of donor embryos showed greater differences between FCA+ and FCA- results than did profiles of embryos produced by infertile women; the latter had considerably more variation in OM in the FCA+ group. Morphology score did not correlate with pregnancy outcome.

Conclusions: In this SET study, non-invasive MetPro revealed statistical differences between all FCA+ embryos compared to all FCA- embryos. FCA+ embryos of infertile women were more variable and had lower predictive scores than those of donors. Morphology was not correlated with embryo implantation. MetPro appears to offer an exciting new paradigm for selecting embryos with the greatest reproductive potential, beyond conventional morphological grading, for optimization of day-5 SET.