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Non-invasive method for embryo selection in single embryo transfer (SET) using metabolomic profiling (MetPro) of oxidative metabolism (OM).

**Vergouw, C.G.; Lambalk, C.B.; Lens, J.W.; Schats, R.; Hompes P.G.A; Botros, L; Roos, P; Burns, D.
Vrije Universiteit Medical Centre, Reproductive Medicine, Amsterdam, the Netherlands and
McGill University, Montreal, Quebec, Canada**

Objective: SET is an effective method to minimize risks of multiple pregnancies in IVF. Since morphology has limited predictive value, new selection tools are needed to ensure success rates are maintained. Previous studies have shown that non-invasive MetPro may be useful in predicting reproductive potential of embryos. The purpose of this study was to investigate the efficiency of MetPro of biomarkers of OM in patients undergoing SET compared to morphological selection.

Material and Methods: 274 patients scheduled for IVF with SET received standard gonadotropin stimulation protocols with agonist down-regulation. Embryos were cultured individually in 25 µl media drops (HTF, Cambrex, Belgium and 10% GPO) alongside embryo-free media drops as controls. Embryos were selected for transfer by strict morphological criteria. After transfer, spent media were immediately frozen (-196°C). Pregnancy was defined by positive fetal cardiac activity (FCA) at 12 weeks. 7 µl media samples were analysed by Near Infrared (NIR) spectroscopy; analysis time was < 1 min. OM biomarkers of ROH, -SH, C=C, -CH, -OH, and -NH groups were identified yielding unique metabolomic profiles that were quantified using a wavelength selective genetic algorithm, proprietary bioinformatics and leave-one out cross-validation, in conjunction with logistical regression, to create a relative “embryo viability score” that correlated to pregnancy outcomes. The resulting metabolomics data were compared to strict morphological assessment and pregnancy outcomes.

Results: NIR spectral analysis of discarded culture media samples produced unique metabolomic profiles of OM that correlated to an embryo's reproductive potential as determined by FCA. Differences in metabolomic profiles between FCA+ and FCA- groups were statistically significant (>95% confidence interval); sensitivity and specificity was 87% and 93%, respectively. Greater than 86% of all embryos transferred were classified as Grade A or B embryos by strict morphological criteria while 27% resulted in an ongoing pregnancy. Conversely, significant numbers of poorer quality embryos (Grade C and D) actually resulted in FCA+ outcomes.

Conclusion: MetPro of discarded embryo culture media by NIR was effective in distinguishing between viable and non-viable embryos in SET irrespective of embryo morphology. MetPro targeting biomarkers of OM may provide a strong addition for rapid, non-invasive selection of embryos with high reproductive potential in SET.