Take the survey

Micro-Magnetic Resonance Spectroscopy of individual mammalian embryos: a safe and non-invasive diagnostic tool for embryo screening in assisted reproduction

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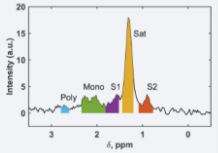
What is known already: Non-invasive selection of the best embryo to transfer is a great challenge for ART professionals. The chemical sensitivity, resolving power, and, more importantly, the non-invasive nature of Magnetic Resonance Spectroscopy (MRS) makes it an excellent candidate to investigate the building blocks of complex organisms. Although MRS is a well-established technique for the biochemical profiling of large organisms, handling small samples such as embryos and 3D cell cultures alongside sensitivity issues has prevented its adoption for clinical and research applications. Our group has overcome these limitations with a microchip-based sensors to leverage non-invasive MRS technology down to the embryo scale.

Study question: Is micro-magnetic resonance (micro-MRS) a safe tool to non-invasively unravel the metabolic fingerprint of single mammalian embryos?



Summary answer: We successfully tested the safety of micro-MRS in a mouse model. No long or short-term adverse effect was found in vitro and in vivo. Furthermore, we successfully utilized MRS on single mammalian embryos of different species to identify universal metabolic biomarkers.

Study design:

This safety study was divided into two main phases to test all aspects involved in operating the micro-MRS analysis. In phase 1 we tested materials, radiofrequency and magnetic field exposure in-vitro. In phase 2 we confirmed in-vivo that MF exposure was not affecting live animals over 3 generations of mice by assessing different IVF outcomes: i.e. natural mating, live parameters and histopathology. Furthermore, as a proof of efficacy of the method several biomarker studies were done on in-vitro produced samples, sorted in different cohorts of interest.

Methods:

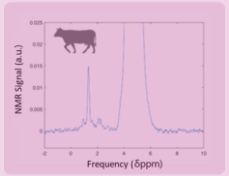
The safety study phase 1 was performed via standard MEAs on >800 2-cell stage embryos to assess blastocyst rates. In phase 2 embryos were exposed to magnetic field in a 9.4T Magnet for 1h at 37°C, then surgically transferred to surrogate mothers. Both mothers and progeny were tracked up to F3. For MRS biomarker analyses the individual embryos were loaded into a miniaturized proprietary MRS device previously prepared with a culture medium of choice. The MRS device was loaded into a spectroscopy magnet and measurements were performed to collect raw data and to quantify metabolic biomarkers. Statistical significance was set at p<0.05.

Limitations, reasons for caution: Our method is ready for further preclinical validation ahead of human clinical trials.

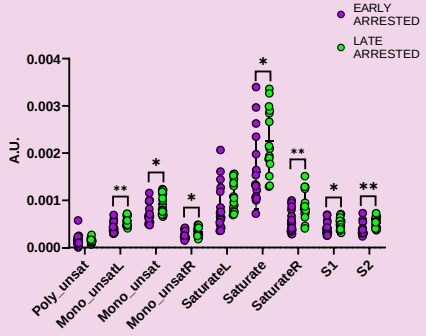
Wider implications of the findings: A non-invasive and quick embryo analysis would provide the means to reveal the role of pre-implantation metabolic pathways. Micro-MRS can further develop into a safe embryo assay for selection and quality control before embryo transfer. This would apply to both human and animal ART, whose success rate is relatively low.

EMBRYO DEVELOPMENT CORRELATION

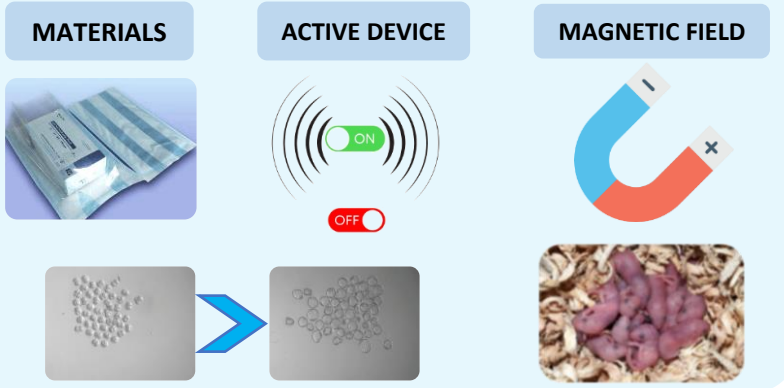
2022



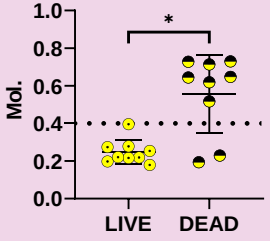
*The abundance of **7/9 markers** was significantly higher (p<0.05) in late arrested embryos when compared to early arrested embryos (n=32 embryos). Two-tailed unpaired t-test with Welch's correction for each marker.*



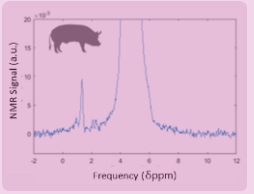
NO ADVERSE EFFECTS



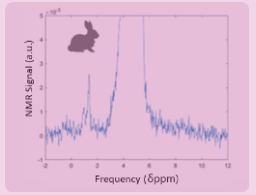
CRYORESISTANCE CORRELATION



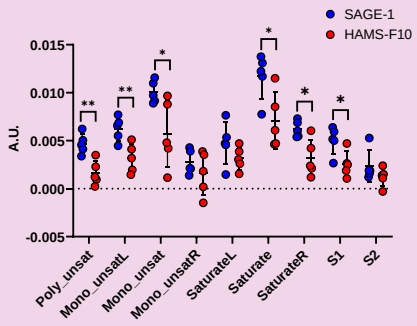
*Furthermore, delipidated embryos are correctly classified as alive and dead post thawing through **Saturate lipid marker** (n=18). Mann-Whitney test.*



MEDIA CORRELATION



*The abundance of **6/9 markers** was significantly higher (p<0.05) in embryos cultured in SAGE-1 medium when compared to embryos cultured in HAMS-F10 medium (n=10 embryos). Two-tailed unpaired t-test with Welch's correction for each marker.*



Keywords: Magnetic Resonance Spectroscopy, metabolism, embryo screening, non-invasive