Unveiling Biomarkers of Human Embryo Quality: Interplay Between Metabolomics and Sperm-Borne microRNAs in Assisted Reproduction

Soraia Pinto[1], António Rocha[2] Alberto Barros[1, 3, 4], Marco G. Alves[1, 2], Pedro F. Oliveira[3]

1 – Centre for Reproductive Genetics Professor Alberto Barros, Porto.
2 – ICBAS—School of Medicine and Biomedical Sciences, University of Porto.
3 – Department of Pathology, Faculty of Medicine, University of Porto.
4 – i3S – Instituto de Investigação e Inovação em Saúde, University of Porto.
5 – Ibimed & Department of Medical Sciences, University of Aveiro.
6 – LAQV-REQUIMTE & Department of Chemistry, University of Aveiro.

Human embryo quality evaluation is critical for successful assisted reproductive technologies (ARTs). Traditional morphological assessments can be subjective, highlighting the need for new biomarkers for gamete quality and fertility potential. To improve the accuracy of embryo selection, we integrated metabolomics and sperm-borne microRNA analysis alongside morphokinetic evaluation. Metabolomic profiling of embryo culture media revealed that specific metabolite differentials (pyruvate, alanine, glutamine, and acetate) are discriminative of embryo quality. Good and Lagging embryos export and accumulate pyruvate and glutamine, suggesting more active metabolic activity compared to Bad embryos. Furthermore, sperm-borne microRNAs play a role in embryo development, with an impact on its metabolism. Specifically, higher levels of miR-34c-5p in spermatozoa were strongly associated with the consumption or release of key metabolites by developing embryos, particularly those linked with lipid and glucose metabolism, suggesting enhanced metabolic performance. Moreover, the abundance of miR-34c-5p in spermatozoa correlates not only with embryo developmental competence, but also with total sperm motility. Higher levels of miR-34c-5p were found in sperm samples that originated good embryos. These studies highlight the potential of combining metabolomics and sperm-borne microRNA analysis to provide a more comprehensive evaluation of human embryo quality, potentially leading to improved embryo selection and increased success rates in ARTs. Further research is needed to confirm these findings in larger groups and to understand the molecular mechanisms underlying microRNA effects on reproductive outcomes.

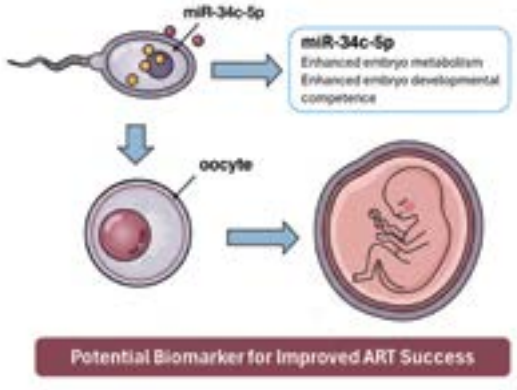

FIGURE 1
miR-34c-5p in spermatozoa links to better embryo metabolism and development – potential ART biomarker.