Analysis of deubiquitinating enzyme (DUBs) expression in blastocoel fluid from IVF-generated embryos may serve as a biomarker to aid in reducing miscarriages

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As the prevalence of infertility cases continue to increase, the use of in vitro fertilization (IVF) has become more frequent. Therefore, the importance of selecting viable IVF-generated embryos for uterine transfer has become paramount. This study aims to identify molecular markers in blastocoel fluid that could serve as potential biomarkers for reducing miscarriage rates. Blastocoel fluid was collected from day-5 human IVF-generated embryos immediately following trophectoderm biopsy. Media from 25 embryos with known implantation outcomes were analyzed for gene expression levels of selected DUBs (MYSM1, USP22, USP28, and USP34) and an additional 17 samples were also analyzed for USP34 alone. Aggregate DUB mRNA expression levels were compared in embryos associated with positive vs. negative implantation outcomes via a Welch's t-test. Additionally, DUB activity was assessed in an additional 21 individual blastocoel fluid-conditioned media samples with a fluorescent DUB Activity Assay Kit (Cayman Chemicals). This analysis revealed expression for DUBs MYSM-1, USP-22, USP-28, & USP-34 was increased in blastocoel fluid from implanted embryos vs nonimplanted embryos ($p < 0.05$). mRNA detected in the blastocoel fluid likely originates from the cytoplasm of embryonic cells that underwent apoptosis. A potential mechanism for increased DUB levels could be that more viable preimplantation embryos exhibit tighter regulatory control thereby increasing apoptosis of cells with upregulated DUBs, which are known to be pathogenic. In conclusion, this study shows that analysis of mRNA expression of DUB genes in blastocoel fluid could be used as an additional tool when selecting the most viable embryos in IVF patients.