Association of GPR30 transcript abundance in human spermatozoa with outcomes of assisted reproduction

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The DNA of spermatozoa is highly condensed, leading to the arrest of almost all transcription activity. Interestingly, mature spermatozoa carry into the oocyte a pool of mRNAs, which origin and function remain to be understood. Among these, the presence of G protein-coupled receptor for estrogen 30 (*GPR30*) mRNA in human spermatozoa has already been reported, although its relevance to sperm function and early embryo development remains unclear. This receptor mediates on-genomic rapid effects of estrogens. We hypothesized that *GPR30* mRNA abundance in human spermatozoa is associated with sperm quality and with the outcome of medical assisted-reproduction treatments (ART). We collected sperm samples of men from couples seeking for ART. Sperm quality was accessed by conventional methods following World Health Organization guidelines. *GPR30* mRNA abundance in spermatozoa was also accessed. Early pregnancies were evaluated by assessing serum β-human chorionic gonadotropin levels and clinical pregnancies determined by fetal heartbeat detection. Overall, our data indicate that even though *GPR30* mRNA abundance does not appear to be correlated with sperm quality, it may have an important role during pregnancy development. There is no correlation between the abundance of *GPR30* with paternal BMI, age nor with sperm quality parameters. Interestingly, we observed that higher levels of *GPR30* mRNA abundance in spermatozoa were correlated to the achievement of biochemical pregnancy and clinical pregnancy (P <0.05) by couples under treatment. Our results highlight the role of sperm RNA cargo in offspring development, suggesting that spermatozoa mRNA content can influence ART success.

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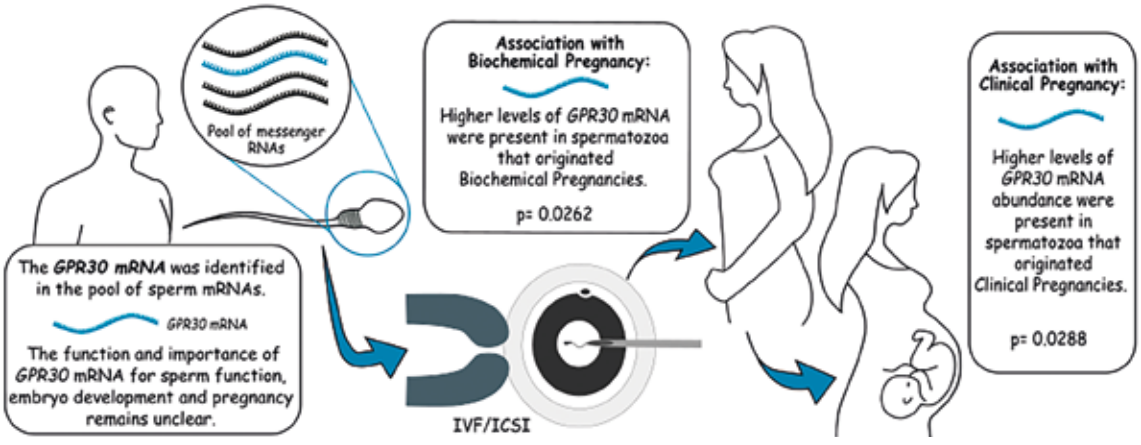

FIGURE 1

From the initial 81 couples that participated in this study, embryo transfer was performed in 60 women. 28 women were classified with a Biochemical Pregnancy, when serum βHCG concentration surpassed the value of 20 mIU/mL, 12 day after embryo transfer. Higher levels of *GPR30* transcript were present in spermatozoa that originated biochemical pregnancies (1.63 ± 0.27 arbitrary units). Accordingly, lower levels of *GPR30* transcript were found in spermatozoa whose embryos failed to implant in the uterus (1.13 ± 0.17 arbitrary units), p=0.0262. 22 biochemical pregnancies evolved to clinical pregnancies (identified by the fetal heartbeat). The spermatozoa that originated clinical pregnancies had a higher abundance of *GPR30* mRNA (1.68 ± 0.33 arbitrary unit). Spermatozoa associated with no-pregnancy (failed embryo implantation and abortions) had lower levels of *GPR30* mRNA abundance (1.13 ± 0.16 arbitrary units), p=0.0288, than the clinical pregnancy group. Statistical analysis was performed by two-tailed Student's t-teste for parametric data (confidence interval of 95%). Values of *P<0.05 were considered as statistically significant. Values are represented as mean ± SEM.