P-242 Gene expression profiles of SARS-CoV-2-associated receptors and proteases in human early embryonic development and follicular cells

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Study question: Are the oocytes, embryos, granulosa and cumulus cells, used during ART, susceptible to the SARS-CoV-2 infection?

Summary answer: Transcriptomic analyses of SARS-CoV-2-associated receptors and proteases strongly suggest that blastocysts are most permissive to SARS-CoV-2 compared with mature oocytes and day 3 embryos.

What is known already: Very few studies analyzed the gene expression profiles of SARS-CoV-2-associated receptors and proteases, mainly focusing on *ACE2* and *TMPRSS2* expression, resulting in partial knowledge in different specimens from female genital tract. To date, the gene expression profile of SARS-CoV-2 host entry candidates in the entire preimplantation embryos is scarcely available. Moreover, reports on oocyte and granulosa cells susceptibilityto SARS-CoV-2 are very sparse.

Study design, size, duration: To address this question, we retrospectively examined the gene expression profiles of SARS-CoV-2-associated receptors and proteases in human granulosa cells (GCs), cumulus cells (CCs), mature oocytes, day 3 embryos, blastocysts and trophectoderm cells obtained from our previously described Affymetrix microarray data.

Participants/materials, setting, methods: Human GCs and CCs (n=17), mature oocytes (n=6), and preimplantation embryos (n=20) were analyzed. The comparison of gene expression levels of receptors and proteases closely related to SARS-CoV-2 infection. For each gene, the number of samples with the probe set 'present', based on the detection call, was analyzed. Each probe set was classified according to the signal intensity value median, as low (<100), medium (100-200) or high expression level (>200).

Main results and the role of chance: *ACE2*, *BSG*, *CTSL*, *CTSA* were detectable at high expression level in all mature oocyte samples, while only *CTSL* was strongly expressed in all day 3 embryos. The most representative dual co-expression of SARS-CoV-2-associated receptor and protease (60% of samples) during the embryonic genome activation stage (EGA) was *ACE2-CTSL* and *BSG-CTSL*. In blastocysts, *ACE2*, *BSG*, *CTSL*, *CTSA* and *FURIN* were detectable in the entire cohort at high expression level, and the prevalence of the different dual co-expression of SARS-CoV-2-associated proteases and receptors was optimal (100% of samples). Interestingly, only *CTSL* was detectable in all trophectoderm samples and a prevalence of 60% was found for the *BSG-CTSL* co-expression. *ACE2*, *BSG*, *CTSL* and *CTSA* were present at high expression level in CCs samples. In contrast, *ACE2* and *BSG* expression was very low while *CTSL* and *CTSA* showed a high expression level in GCs.A prevalence of 100% was reported for *ACE2-CTSL*, *ACE2-CTSA* co-expression for both cell types. In addition, *BSG-CTSL* and *BSG-CTSA* co-expression were also present in all CCs against ~70% in GCs samples. This data suggest a potential risks of SARS-CoV-2 infection either GC or early embryo development.

Limitations, reasons for caution: Analyses of Affymetrix microarray gene expression data were performed in non-COVID-19 patients. Whether the SARS-CoV-2 infection change the gene expression profile of SARS-CoV-2-associated receptors and proteases is under investigation.

Wider implications of the findings: Specimens from female genital tract may be considered as potential targets for SARS-CoV-2.

Trial registration number: not applicable