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Probing Human Oocyte Heterogeneity by Single Cell Proteoform Imaging Mass Spectrometry

Ovarian tissue cryopreservation (OTC) is utilized by clinics to preserve oocytes and immature eggs for pediatric patients who are at increased risk of becoming infertile due to a diagnosis or treatment. Late-stage oocytes, that are not yet mature, are often released during OTC. We are interested in identifying proteoforms that may improve in vitro maturation of oocytes into eggs for these patients as an additional fertility preservation strategy. We are utilizing single cell proteoform imaging mass spectrometry (scPiMS), which is a nanoDESI direct sampling approach coupled to individual ion mass spectrometry (I2MS) detection, to profile human oocytes to identify and assess the intact proteoform population between single oocytes. We have used this scPiMS approach to analyze 24 denuded oocytes from 6 different participants/donors aged 1.71 years old to 33. We have also utilized the high spatial resolution afforded by the scPiMS probe (~100 μM) to selectively sample oocytes and cumulus granulosa cells within 4 cumulus oocyte complexes (COCs) from two participants to identify proteoforms that are cell-type specific. We have identified ~78 proteoforms on average across the 28 oocytes sampled, with an average identification rate of THRASH proteoform features of ~55%. We have identified several proteoforms that are highly specific to oocytes rather than cumulus granulosa cells, including oocyte expressing protein homolog (OOEP), KH-domain containing protein 3 (KHDC3), and ferritin light chain. We utilized this data to further understand the proteomic heterogeneity of single oocytes between patients and between multiple oocytes from the same donor. Finally, we demonstrate the utility of scPiMS for analyzing patient specific proteoform landscapes by identifying OOEP and KHDC3 proteoforms with SNPs and variable modifications across the cohort. We ultimately aim to expand our analysis to quantify the abundance of these proteoforms and understand how proteoform landscapes change in the context of age.

User consent

yes

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