Comet assay reveals a high level of cumulus cells DNA damage in females sharing a phenotype of ovulatory dysfunction

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Ovulatory dysfunction phenotypes include disturbances in menstrual cycles and hormonal impairments. Females with ovulatory dysfunction show irregular or absent ovulation commonly causing infertility. Cumulus cells (CC) are used to explore biomarkers for this reproductive health burden due to their proximity to the oocyte and their role in its development and maturation. CC DNA damage has been associated with oocyte status; however, the existing studies present contradictory results.

Our aim was to assess DNA damage in infertile females undergoing intracytoplasmic sperm injection (ICSI). The alkaline comet assay was performed on whole blood and CC from 42 females. Among them, 20 exhibited ovulatory dysfunctions, while the remaining 22 experienced mostly male-related infertility. The age range was matched to ensure similar hormonal secretory patterns. The CCs were obtained after oocyte denudation during the common ICSI procedure. Significant differences were obtained in the DNA damage levels of the two tissues ($p < 0.001$). Furthermore, the levels of DNA damage were higher in CC when compared to blood and were significantly different between females with ovulatory dysfunction and those experiencing male-related infertility ($p = 0.034$). An interesting positive correlation was obtained between CC DNA damage levels and the number of oocytes with two pronuclei (2PN) ($p = 0.026$). Following other studies, we speculate that the level of blood DNA damage reflects that of heterogeneous cell types, is dependent on several exogenous factors, and therefore does not mirror the level of damage of CC. The differences in the DNA damage levels obtained between the two tissues and the higher levels observed in CC prompt us to explore its potential utility in addressing fertility. The positive correlation with the number of oocytes in 2 PN suggests that CC damage level underlies a success of fertilization in females with an ovulatory dysfunction phenotype.

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