ASRM Abstract
学会名
ASRM 2025
Poster Presentation(ポースタ発表)
都市, 国名, 日程(西暦.月.日)
The Henry B. González Convention Center, 900 E Market St, San Antonio, TX.USA
(2025.10.27~2025.10.29)
題名

Regulatory T Cells in Ovulatory Follicular Fluid May Play a Critical Role in Embryo Developmental Competence

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Objective
The immune cell composition of ovulatory follicular fluid (FF) is heterogeneous, and its role in oocyte developmental competence remains poorly understood. This study investigates the variation of immune cell populations within individual FF samples in relation to patient background and their impact on oocyte developmental potential.

Material and Methods
This prospective observational study analyzed FF of the first punctured dominant follicle (18-25 mm) containing cumulus oocyte complexes, collected from 92 patients between June 2024 and March 2025. Immune cell populations were characterized using fluorescent antibody markers (CD45, CD68, CD80, CD11c, CD56, CD3, CD4, CD25) to identify macrophages, dendritic cells, NK cells, NKT cells, T cells, and Tregs. Flow cytometry was used to quantify immune cell proportions, which were then analyzed for identify the correlation with patient characteristics, oocyte quality, fertilization, and embryo development. The oocytes underwent ICSI and subsequent embryo evaluation via morphological assessment and AI-based time-lapse scoring (iDAScore).

Results
The percentage of CD45+ immune cells in FF showed a significant negative correlation with patient age ($R = -0.12$, $P = 0.02$). BMI exhibited a non-significant negative tendency, while AMH levels trended positively with FF immune cell proportions. Notably, CD45+ cell percentages correlated positively with day 5 embryos iDAScore values ($R = 0.18$, $P = 0.02$), particularly in morphologically high-quality embryos, independent of patient age. While macrophage, dendritic cell, NK cell, and NKT cell proportions were not significantly associated with patient characteristics or embryological outcomes. However, the percentage of Treg cells within $CD4^+$ T cells (CD3+ CD4+ CD25+) was significantly correlated with iDAScore values on both day 3 ($R = 0.46$, $P = 0.001$) and day 5 ($R = 0.21$, $P = 0.01$). Interestingly, Treg cell percentages did not correlate with patient age but were significantly higher in follicles showing normal fertilization and developing good quality transferable embryos.

Conclusion
The average immune cell and Treg percentage in FF significantly correlate with pre-implantation embryo quality, and Tregs may influence on fertilization and embryo development capacity.

Impact statement
These results suggest that FF immune cells play a pivotal yet unknown role in regulating oocyte maturation, fertilization, and embryo development, likely through their inter- and intra-cellular interactions and associated secreted factors. Notably, the Treg cell percentage in FF may appear as a promising biomarker for predicting embryo developmental competence.