The investigation of the presence of telocyte cells in the human ovarian stroma

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Background:
Telocytes (TCs) have been identified as a rather new and fascinating type of interstitial cell. Previously known as interstitial Cajal-like cells (ICLCs), these cells are now distinguished in the literature by their extremely long and thin telopods (Tp) and by the various sized vesicles they secrete into their environment. To date, these cells have been detected in several organs of humans and many other species. TCs are also found in female reproductive organs, although no data on the existence or morphological characterisation of TCs in human ovaries have been identified in the literature to yet. Furthermore, studies on human ovaries have shown the existence of many stromal cell clusters. However, there is still a significant lack of detailed research describing these cell types. This emphasizes the need for more research into understanding and identifying ovarian stromal cells, including the possible discovery of telocytes (TCs) in human ovaries. The ability of TCs for cell-to-cell signaling, plays an essential role in the regulation of homeostasis, immune surveillance and tissue morphogenesis. It has also been shown that these cells play important roles in angiogenesis, embryogenesis, and various pathologies or even tumorigenesis, under the guidance of tissue-resident stem/progenitor cell self-renewal and differentiation. Expressions or co-expressions of different markers of TCs have been reported in certain organs, but in general, CD34, vimentin, PDGRF-α and PDGRF-β, c-kit and α-SMA are primarily used in TC studies and these are so far considered as reliable TC markers. A combination of double immunofluorescence and electron microscopy is the definitive approach for identifying these cells, setting the gold standard in terms of accuracy and precision.

Aims:
This research aims to advance our understanding of ovarian stromal cells and detect the presence of TCs by employing techniques such as immunohistochemistry and electron microscopy. Through the investigation of their morphology and identification of telocytes in the human ovarian stroma, this study endeavors to provide novel insights into ovarian architecture and its implications for reproductive health.

Methods:
Tissue samples were obtained from women aged 18 to 65 undergoing Total Hysterectomy and Bilateral Salpingo-Oophorectomy (THBSO) for uterine reasons, excluding those who had received chemotherapy. After tissue preparation procedures for light microscopy, immunohistochemical and double immunofluorescence staining used CD34/c-kit, CD34/vimentin, CD34/PDGFR-β, and CD34/α-SMA markers for telocyte identification. Transmission electron microscopy and the immunogold technique, utilizing the CD34 marker, facilitated precise telocyte identification. This comprehensive approach aimed to illuminate telocyte presence and distribution in the ovarian stroma, offering future insights into ovarian physiology and pathophysiology.

Results:
Our study confirms the presence of telocyte cells within the human ovary, characterized by their distinctive morphology. We detected telocyte cells in the ovarian stroma through

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immunohistochemical analysis, labeling specifically with CD34 which is the most commonly used telocyte marker. Additionally, we utilized immunofluorescence analysis, employing double labeling with CD34/c-kit, CD34/vimentin, CD34/PDGFR-β, and CD34/α-SMA to further characterize these cells and distinguish them from fibroblasts and pericytes. We found out that TCs were strongly positive for CD34, PDGFR-β, vimentin, and weakly positive for α-SMA. On the other hand fibroblasts were found to be CD34 negative, while strongly positive for vimentin and PDGFR-β. Lastly pericytes were found to be CD34 negative and strongly positive for α-SMA and PDGFR-β. Notably, our findings delineate telocyte cells from fibroblasts and pericytes, underscoring their unique cellular identity within the ovarian microenvironment. Moreover, transmission electron microscopy provided detailed insights into the ultrastructural features of these cells, enriching our understanding of their morphology. TCs were recognized for their long and thin prolongations and small cell bodies primarily situated around blood vessels and dispersed throughout the ovarian stroma. Additionally, the use of the immunogold technique in conjunction with the CD34 marker facilitated the precise identification of telocyte cells, increasing the validity of our findings.

Conclusion:
Overall, our study significantly contributes to the understanding of telocyte biology within the context of the ovarian stroma, shedding light on their presence, distribution, and morphological attributes, thus paving the way for further exploration of their functional significance in ovarian physiology and pathology.

Keywords:

Human Ovary, Telocytes, Immunofluorescence, TEM.