

Histological and Ultrastructural Identification of Telocytes in Canine Uterine Tissue

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Abstract

Telocytes, characterized by slender cell bodies and elongated cytoplasmic processes known as telopodes, are distinct interstitial cells identified in various mammalian organs, including the heart, lung, fallopian tube, and kidney. This study investigated the presence, morphology and ultrastructure of telocytes in the uterine tissue of the dog. Samples from the uterine horn of adult Spitz dogs were collected and processed for histological, histochemical, and transmission electron microscopic examinations. Under light microscopy, telocytes were observed as elongated cells possessing a slender nucleus and numerous thin cytoplasmic processes extending from the cell body. They were in proximity to secretory units of uterine glands, blood vessels, collagen bundles of the connective tissue, and, smooth muscle cells throughout all layers of the uterine wall. The complete morphology of telocytes and telopodes, including their close associations with glandular, smooth muscle, and endothelial cells, as well as collagen fibers, was clearly visualized by transmission electron microscopy. Collectively, the findings of this study provide the first evidence of telocyte presence in the canine uterus and describe their morphology.

Key words: Telocyte, Uterus, Dog, Histology, Cell structure

Introduction

Telocytes are mesenchymal-derived cells characterized by their exceptionally long and thin cellular processes. They are distinct from neurons, fibroblasts, and smooth muscle cells, yet they possess the remarkable ability to interact with all these cell types. Telocytes are consistently found in close proximity to nerve endings, smooth muscle cells, blood vessels, and other interstitial cells (Awad and Ghanem, 2018; Dolbnya et al, 2025).

Despite their identification in numerous tissues, a universally accepted consensus on the defining characteristics of telocytes remains elusive. Their morphology and

protein composition exhibit considerable variability across different tissues, which can pose challenges for their precise immunohistochemical identification (Cretoiu, 2016; Hanan et al, 2025).

Telocytes engage in intricate interactions with various cell types, playing a pivotal role in regulating tissue functions through intercellular communication, immune response modulation, and the maintenance of homeostasis (Crețoiu, et al, 2012; Kondo and Kaestner, 2019). Serving as master regulators, telocytes maintain tissue homeostasis and guide stem cells toward proliferation and differentiation, thereby

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facilitating tissue repair (Popescu and Fausson-Pellegrini, 2010; Shoshkes-Carmel, et al, 2018). Furthermore, these cells actively modulate the immune response by providing essential information that enables the immune system to efficiently combat pathogens (Aleksandrovych et al, 2022; Sanches et al, 2024).

As specialized cells dispersed throughout uterine tissue, telocytes are subject to changes in response to the extensive hormonal fluctuations that occur during the estrous cycle and pregnancy. Numerous studies have investigated these changes in telocytes across various reproductive stages to better understand their role in regulating uterine function (Salama, 2013). Telocytes appear to interact with virtually all cell types within an organ. This arrangement suggests a vast array of potential integrative and regulatory roles, akin to a rudimentary yet crucial neuronal network at the cellular level, implying a surveillance function (Smythies and Edelstein, 2014). Given the significant role of telocytes in tissue repair and regeneration, a comprehensive understanding of their function in organ regeneration will soon become a major challenge, ultimately leading to potential advancements in clinical applications (Bei, et al, 2015).

The study of telocytes not only enhances our understanding of the physiology of various tissues but can also lead to the discovery of novel therapeutic approaches. Identifying telocytes in different body tissues and examining their functions can significantly improve our comprehension of diseases and facilitate the development of new treatments, particularly in the context of uterine pathologies (Kondo and Kaestner, 2019). To the best of our knowledge, no existing studies have examined the presence, structural and ultrastructural characteristics of telocytes within canine uterine tissue. Additionally, research on uterine tissue in other animal species is quite limited. Therefore, this

study was conducted with the aim of identifying telocytes in canine uterine tissue, describing their structural and ultrastructural characteristics within the canine uterus.

Materials and Methods

Light Microscopy

Uteri from three adult female Spitz dogs, of defined and homogeneous mean age, were immediately removed following ovariohysterectomy at a small animal clinic. The owners of the dogs provided informed consent for this procedure. The uterine horns were divided into three parts, and the middle portion was further subdivided into smaller pieces. Uterine samples (5 mm × 5 mm) were immersed in 10% buffered formalin for histological and histochemical studies. The samples were then processed using standard histological techniques for light microscopic examination. After fixation and washing, tissues were dehydrated, cleared, and embedded in paraffin wax using an automated processor. Subsequently, thin (5 µm) and semi-thin (1 µm) sections were cut from the paraffin blocks and stained with hematoxylin-eosin (HandE), periodic acid-Schiff (PAS), Giemsa, Masson's trichrome (MT), methylene blue (MB), and toluidine blue (TB) (Bancroft and Gamble, 2008). The sections were observed under light microscope (Olympus CX23, Japan) and images were captured using a digital camera (KEView, China).

Transmission Electron Microscopy (TEM)

A 1 mm³ piece from the mid-section of the uterine horn was excised and fixed in 2.5% glutaraldehyde in phosphate buffer (pH 7.4, 0.1 M) for 48 hours. The samples were then post-fixed in 1% osmium tetroxide for one hour and subsequently dehydrated in ascending concentrations of ethanol (50%, 70%, 90%, and 100%). Finally, the samples were embedded in Epon resin. Semi-thin sections (0.5–1 µm) were prepared from the resulting blocks and

stained with toluidine blue. A light microscope was used to select the area of interest. In the next step, ultrathin sections (60 nm) were obtained and stained with saturated uranyl acetate and lead citrate. The sections were examined using a Philips CM10 transmission electron microscope (Eindhoven, The Netherlands) at an accelerating voltage of 80 kV in Aria Rastak company TEM laboratory (Tehran, Iran).

Results

Histological Study

Based on HandE and MT staining results, the canine uterine tissue, when viewed in cross-section, exhibited three distinct layers. The innermost layer, the endometrium, comprised a single layer of columnar cells lining a thick bed of connective tissue. Embedded within this connective tissue were uterine glands. The middle layer, the myometrium, displayed a dual muscular arrangement with an inner circular layer and an outer longitudinal layer. Sandwiched between these muscular layers was a layer rich in blood vessels. The outermost layer, the perimetrium, comprised a thin layer of loose connective tissue (Figure 1).

Light microscopic examination of uterine tissue sections stained with Giemsa, MT, and PAS unveiled small, elongated cells within the uterine wall. These cells, possessing spindle or oval-shaped nuclei, were characterized by the presence of two prominent, thread-like extensions at each end. Their distribution was notable, with a predilection for locations surrounding endometrial glands, blood vessels, and within the interstitial spaces between stromal and smooth muscle cells. These morphological features led to the identification of these cells as telocytes. A distinguishing characteristic of telocytes is their limited cytoplasmic volume, which tapers into the aforementioned thread-like extensions, aptly termed telopodes (Figures 2 and 3).

Semi-thin sections of the uterus stained with TB and MB clearly demonstrated the typical characteristics of these cells, including an elongated oval body and long, thin cytoplasmic processes. These cells were particularly abundant around endometrial glands and blood vessels. Within the myometrium, small cell bodies with distinct telopodes were observed interspersed among smooth muscle cells (Figure 4).

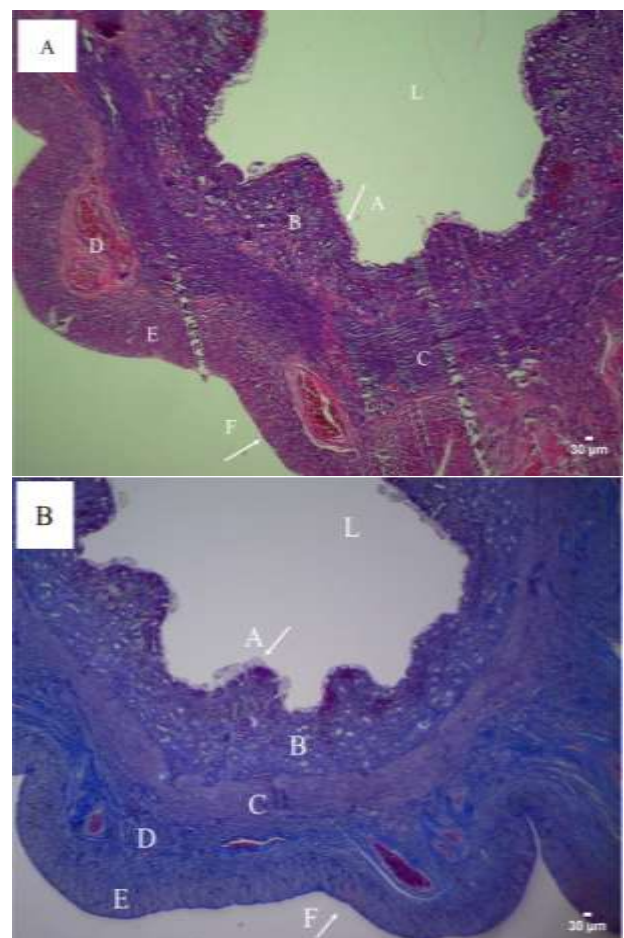


Figure 1: Cross section of uterine tissue representatives general histology of the Spitz's uterus; Uterine lumen (L), Endometrial epithelium (A), Endometrial propria-submucosa connective tissue (B), Myometrium inner muscle layer (C), Vascular layer (D), Myometrium outer muscle layer (E), Epimetrium (F), (A: HE staining, and B: MT staining).

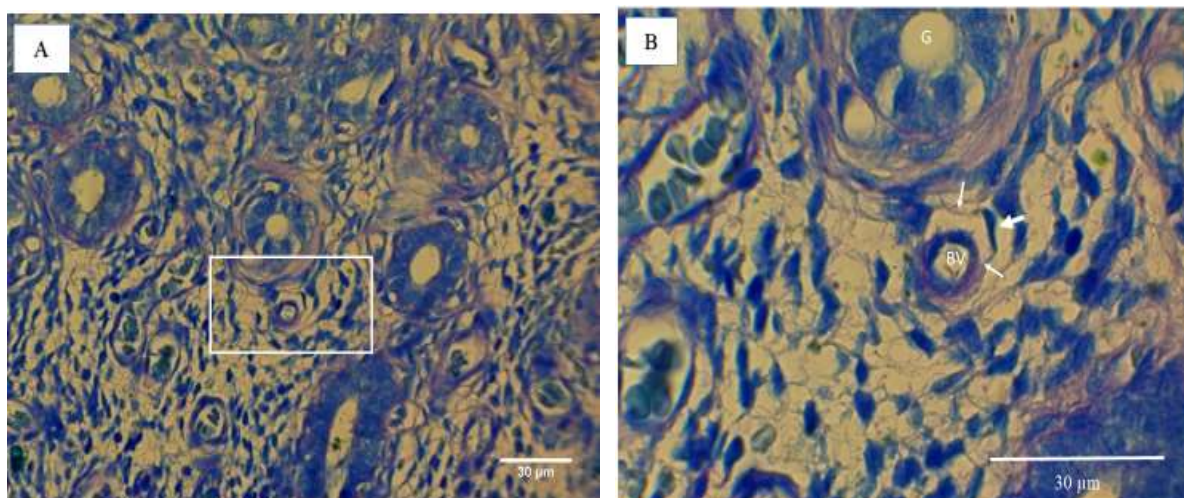


Figure 2: Light micrographs of the endometrium, (A) representatives photomicrograph of Geimsa -stained endometial tissue sections, (B) representatives a higher magnification of the box area in (A) to indicate telocyte with a large nucleus and very small cytoplasm (thick arrow) and telopodes as moniliform cytoplasmic processes (thin arrows). Telocyte are particularly in the vicinity of blood vessels (BV) and endometrial glands (G).

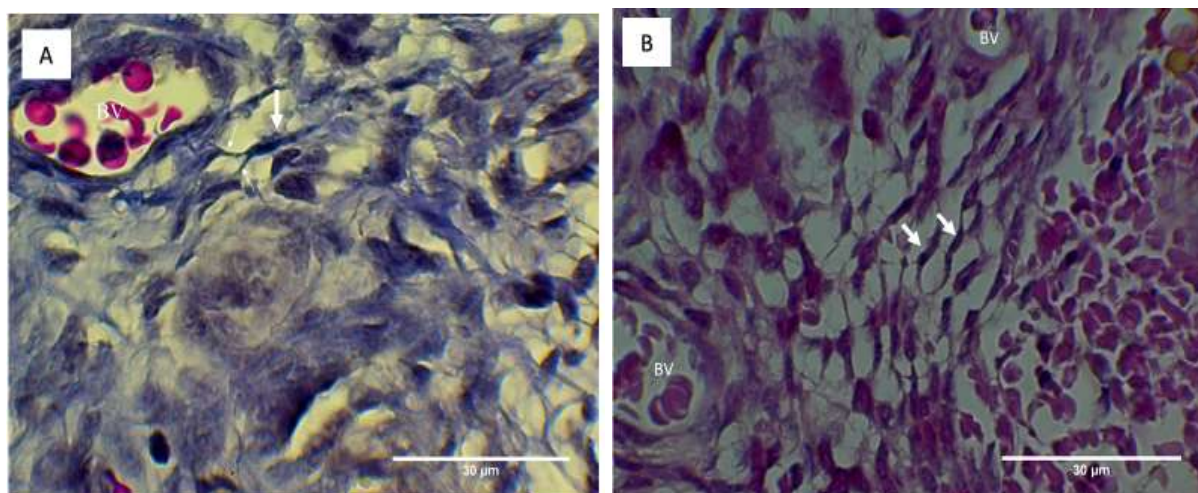


Figure 3: Light micrographs of the endometrium representatives photomicrograph of MT (A) and PAS (B)-stained endometial tissue sections to indicate telocyte with a large nucleus and very small cytoplasm (thick arrows) and telopodes as moniliform cytoplasmic processes (thin arrows).

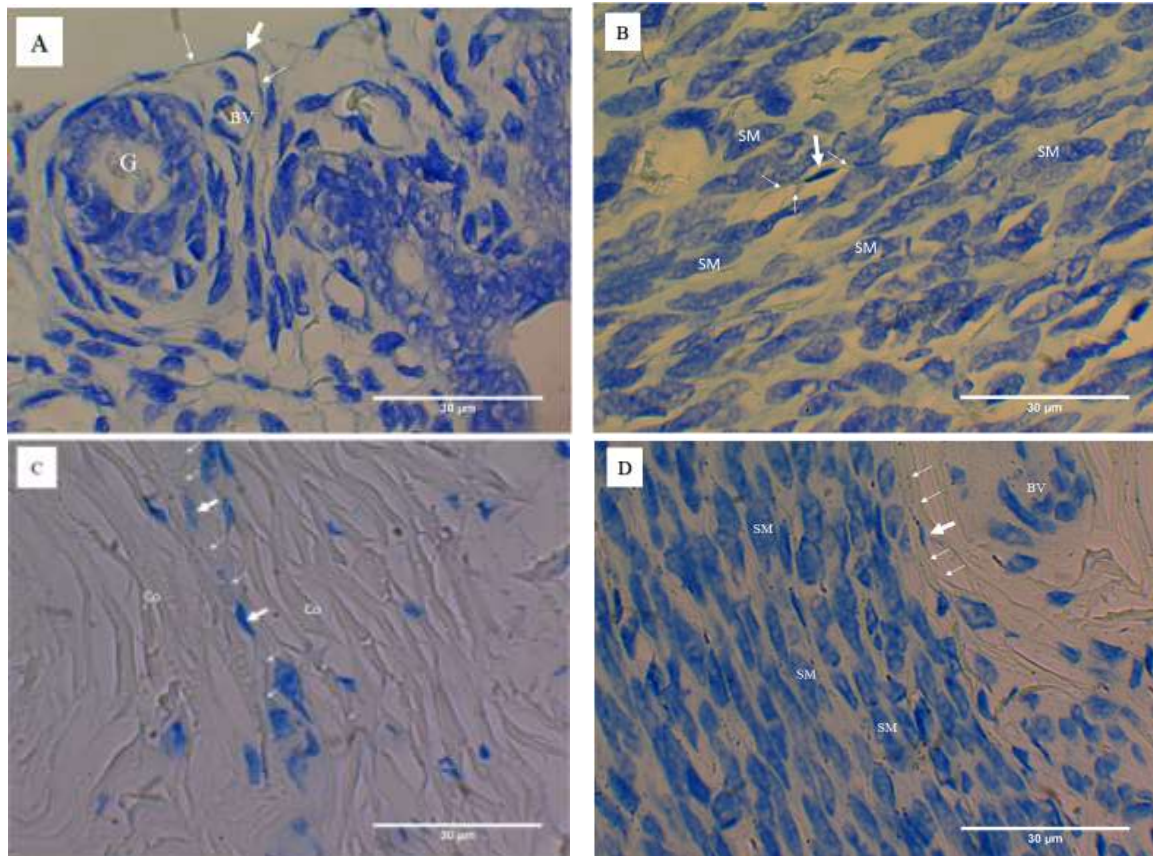


Figure 4: Light micrographs of the endometrium representatives photomicrograph of TB and MB-stained endometrial tissue semi thin sections to indicate telocyte with a large nucleus and very small cytoplasm (thick arrows) and telopodes as moniliform cytoplasmic processes (thin arrows). (A), (B), (C): (TB staining) and (D): (MB staining). Telocytes are particularly in the vicinity of blood vessels (BV) and endometrial glands (G). SM shows smooth muscle cells and Co shows collagen fibers.

Telocyte Ultrastructure (Transmission Electron Microscopy)

Transmission electron microscopy images of canine uterine tissue in this study revealed that telocytes exhibited a small, spindle-shaped or pyramidal cell body surrounded by a scant amount of cytoplasm. Notably, they were smaller than their neighboring cells. Several extremely long cytoplasmic processes (telopodes) extended from the cell body as thin cytoplasmic protrusions. A basal lamina was not observed in telocytes. Exosomes were found in the vicinity of the telopodes; specifically, exosomes detached from the telopodes were also observed. The cell body contained a centrally located nucleus, organelles such as mitochondria and rough

endoplasmic reticulum, polyribosome aggregates or glycogen granules, and other electron-dense bodies. Telocytes were identified in the paracrine region surrounding endometrial glands and in the myometrium. Telocytes were often found between collagen fibers and were in close contact with them. A close association between telopodes and longitudinal and transverse sections of collagen fibers was observed along their course. Telopodes were in very close proximity to each other and were in close contact with neighboring cells. The nucleus of telocytes was indented and conformed to the general outline of the cell body. Electron-dense heterochromatin masses were observed attached to the nuclear membrane (Figure 5).

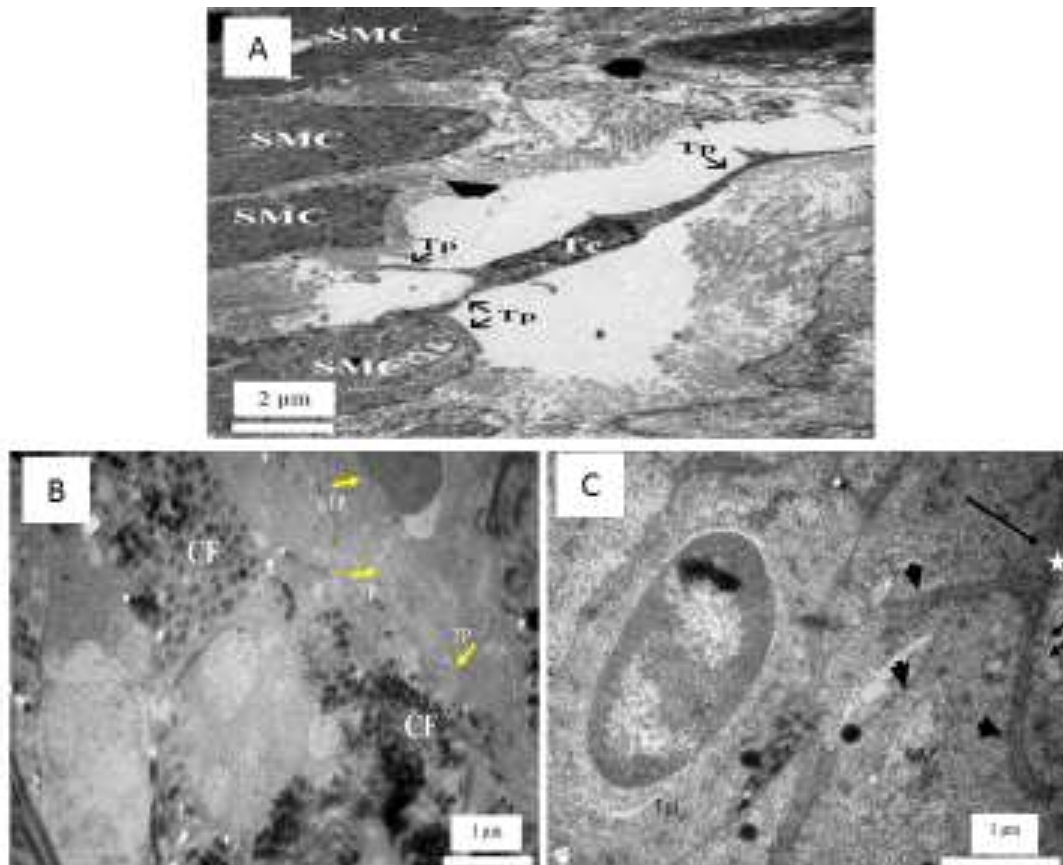


Figure 5: TEM micrograph of uterine tissue, (A) A telocyte (TC) is situated adjacent to a smooth muscle cell (SMC). The telocyte's telopodes (TP) extend to make close contact with the SMC. (B) shows telopodes (TP) as long, thin processes in contact with the cross-section of collagen fibrils (CF), (C) A telocyte is shown, with its cell body indicated by a long arrow. Three slender telopodes (arrowheads) extend from the cell body, one of which contacts a neighboring cell. Short arrows highlight exosomes budding from a telopode. The telocyte nucleus is marked with an asterisk, and a blood capillary (Cap) is also visible.

Discussion

This study investigated the morphology and distribution of telocytes in the uterus of the Spitz dog, providing detailed information on their light and electron microscopic features and their distribution within the organ. Using light microscopy and various staining techniques, we identified telocytes as long, thread-like cells with a small, spindle-shaped cell body containing a nucleus. These cells possess very long, thin processes, termed telopodes, which form an extensive network-like structure in the endometrial connective tissue and the vascular layer of the uterus. They were also present, albeit in smaller numbers, among the smooth muscle cells of the myometrium. Telocytes frequently formed close associations with capillaries,

nerve endings, and immune cells. Similar to telocytes found in other tubular organs in mammals, telocytes in the canine uterus exhibited a strong affinity for PAS staining. Since this staining highlights neutral polysaccharides, this indicates the presence of this carbohydrate group within these cells (Soliman, 2021). Additionally, telocytes in semi-thin sections of uterine tissue demonstrated a strong affinity for MB and TB staining techniques, which target cellular proteins, including cytoskeletal proteins (Zheng et al, 2014).

Semi-thin sections of tissue specimens stained with TB and MB are generally useful for determining the overall distribution of telocytes within a tissue. The observation of a small cell body with a few

thin cytoplasmic processes is often considered sufficient for defining a telocyte. However, the most accurate method for identifying telocytes remains transmission electron microscopy (TEM) (Etcharren et al, 2023).

Despite limitations in accessing samples preserved in epoxy resin, which hindered a comprehensive electron microscopic analysis of all telocytes within the entire uterine wall, we successfully confirmed their presence. We employed ultrastructural criteria specific to telocytes for this confirmation. Our observations revealed that uterine telocytes exhibit a distinctive ultrastructure characterized by a prominent nucleus occupying a significant portion of the cell, while the cytoplasm remains relatively limited. Long, slender, and intricately branched cytoplasmic extensions, known as telopodes, extended abruptly from the cell body. Electron micrographs further demonstrated close interactions between these telopodes and surrounding structures, including collagen fibers, glandular epithelial cells, and smooth muscle cells. While the sample size in this study restricted a thorough examination of all uterine wall regions, we conclusively identified cells possessing the characteristic structural features of telocytes within a subset of the analyzed tissue. In the present study, telocytes were more frequently observed in the endometrium and vascular layer, which is consistent with the findings of Hatta and colleagues (2012)

who hypothesized that telocytes are often found in tissues with low cell density and significant space between neighboring cells (Hatta et al, 2012). As previously reported for telocytes in the human exocrine pancreas, parotid gland, and sublingual salivary glands, we observed, in this study, that telocytes surrounded the secretory units of the uterine glands. This finding may indicate their involvement in regulating glandular function along with the adjacent myoepithelial cells in the walls of the secretory units (Nicolescu et al, 2011; Nicolescu et al, 2012; Alunno et al, 2015). Research on the distribution of telocytes in the uterine myometrium is likely to have practical or clinical value. The various functions of uterine telocytes, such as the coordination of myometrial contractility, have been discussed (Hutchings et al, 2006).

Based on histological, histochemical, and ultrastructural features, telocytes were definitively present in the canine uterine tissue. Although ultrastructural characteristics provide the most reliable method for identifying telocytes, by conducting more extensive research, especially immunohistochemical analyses, and performing in-depth ultrastructural studies of cells in various regions of the uterine wall, we can expect to gain a more comprehensive understanding of the distribution, potential roles of telocytes, and their intricate interactions within the uterine tissue of dog.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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شناسایی بافتی و فراساختاری تلوسیت‌ها در بافت رحم سگ

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چکیده

تلوسیت‌ها، که با بدنه‌های سلولی باریک و زوائد سیتوپلاسمی کشیده معروف به تلپود مشخص می‌شوند، سلول‌های بینابینی متمایزی هستند که در اندام‌های مختلف پستانداران، از جمله قلب، ریه، رحم، لوله‌های فالوپ و کلیه، شناسایی شده‌اند. این مطالعه به بررسی وجود، مورفولوژی، فراساختار و توزیع تلوسیت‌ها در بافت رحم سگ پرداخته است. نمونه‌هایی از شاخ رحم سگ‌های بالغ نژاد اشپیتز جمع‌آوری و برای بررسی‌های بافت‌شناسی، هیستوشیمی و میکروسکوپ الکترونی عبوری آماده شدند. تحت میکروسکوپ نوری، تلوسیت‌ها به صورت سلول‌های کشیده‌ای مشاهده شدند که دارای یک هسته باریک و زوائد سیتوپلاسمی نازک متعددی بودند که از بدنه سلول منشأ می‌گرفتند. در مجاورت نزدیک با واحدهای ترشحی غدد رحمی، عروق خونی، دسته‌های کلاژن یافت می‌شدند و سلول‌های ماهیچه صاف در سراسر تمام لایه‌های دیواره رحم قرار داشتند. مورفولوژی کامل تلوسیت‌ها و تلپودها، شامل ارتباطات نزدیک آن‌ها با سلول‌های غده‌ای، ماهیچه صاف و اندوتلیال، و همچنین فیبرهای کلاژن، به وضوح توسط میکروسکوپ الکترونی عبوری مشاهده شد. در مجموع، یافته‌های این مطالعه اولین شواهد مبنی بر حضور تلوسیت در رحم سگ را فراهم می‌کند و مورفولوژی و توزیع تقریبی آن‌ها را شرح می‌دهد.

کلمات کلیدی: تلوسیت، رحم، سگ، هیستولوژی، فراساختار

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