THE SCIENCE WORLD
A Monthly e Magazine
ISSN:2583-2212
Review Article
August, 2026 Vol.6(8), 2443-2448

Biology of Ovarian Interstitial Gland Cells: From Development to Clinical Relevance

Pratik N. Rathod[1], Hemant Y. Pawar[1], Bhavesh B. Parmar[1], Anil Sharma[1], R. Menaka[2]
[1]Department of Veterinary Anatomy, College of Veterinary Science and Animal Husbandry, Kamdhenu University, Navsari (Gujarat) - 396450.
e-mail: pratiknanjibhai1311@gmail.com
[2]Department of Veterinary Anatomy,College of Veterinary Science and Animal Husbandry, Kamdhenu University, Bhuj (Gujarat).
doi.org/10.5281/ScienceWorld.22256213

Introduction

The ovaries are the principal female reproductive and endocrine organs responsible for oogenesis and the synthesis of steroid and peptide hormones essential for reproductive homeostasis. Anatomically, each ovary is distinctly organized into a richly vascularized inner medulla and a structurally complex outer cortex, the latter housing follicles at successive stages of growth, maturation, and regression (Eurell *et al.*, 2007). Despite extensive research on follicles and corpora lutea, ovarian interstitial gland cells remain one of the most under-recognized and under-researched endocrine cell populations in the ovaries.

The term interstitial denotes cells that are strategically positioned within the intercellular spaces separating the principal functional elements of an organ, and a gland refers to specialized cellular assemblies capable of synthesizing and secreting biologically active substances, particularly hormones. Similarly, ovarian interstitial gland cells (IGCs) are a specialized steroidogenic cell population embedded in the ovarian stroma that play crucial roles in androgen production and the regulation of follicular dynamics.

History

The scientific history of interstitial gland cells is deeply rooted in the mid-nineteenth century, a period marked by rapid advances in histological techniques and microscopic anatomy. The first definitive recognition of ovarian interstitial gland cells occurred in 1863,

when investigators identified specialized interstitial cells in the rabbit ovary. In the same year, Pfliiger and Schron independently described similar cells in the ovary of a cat, documenting their location and distinctive cytological features within the ovarian stroma of the cat ovary. Alferd (1906) described interstitial gland cells in the human ovary and introduced the term "hilus cells" to denote morphologically distinct interstitial cells located near the ovarian hilum. Resko (1992) quantified steroid output from isolated IGCs in primates, providing direct evidence of endocrine competence in higher mammals. In 2005, Young and McNeilly elucidated the regulation of LH receptors in interstitial gland cells, thereby helping to elucidate their hormonal responsiveness.

Cell location and arrangement

Ovarian interstitial gland cells are not organized into discrete glands but occur as scattered individual cells, small clusters, cords, or diffuse aggregates embedded within the ovarian connective tissue matrix. Their abundance, size, and arrangement vary with species, age, reproductive status, and degree of follicular activity or atresia (Guraya, 1985).

Cell morphology

Ovarian interstitial cells appeared as large, polyhedral, or rounded cells with clearly defined boundaries. They are commonly located in the cortical stroma, particularly in proximity to atretic follicles, but may also extend into the medullary region, especially in species with extensive stromal development (Guraya, 1985). In younger animals, the cells tend to be smaller and more sparsely distributed, whereas in mature or aged animals, they may form conspicuous masses that occupy large areas of the stroma (Erickson, 1983). The cells are typically spherical, oval, or polygonal and measure approximately 15–30 μm in diameter, although size variations are common within the same ovary (Guraya, 1985). In well-developed interstitial cells, the nucleus is euchromatic, with finely dispersed chromatin and one or more prominent nucleoli, suggesting high metabolic activity (Maximow and Bloom, 1957).

The eosinophilic cytoplasm is abundant, contains numerous lipid droplets, and is finely granular in appearance. These features distinguish these cells from the surrounding stromal fibroblasts, which possess a scant, elongated cytoplasm. The cytoplasm contains numerous mitochondria, which are typically round or elongated and possess tubular or vesicular cristae, which are hallmarks of steroid-producing cells (Guraya, 1985). A prominent smooth endoplasmic reticulum (SER) forms an extensive network throughout the cytoplasm, often appearing as interconnected tubules and vesicles. In contrast, the rough endoplasmic reticulum is relatively sparse. The Golgi apparatus is moderately developed and usually located near the

Official Website
www.thescienceworld.net
thescienceworldmagazine@gmail.com
Published 30/08/2026

nucleus, consisting of flat cisternae and associated vesicles. Lysosomes and residual bodies may be observed, particularly in cells derived from degenerating follicles (Diaz Hernandez *et al*., 2018).

Types of IGCs

Based on their developmental appearance, structural organization, and histomorphological characteristics, ovarian interstitial gland cells are traditionally classified into primary and secondary ovarian interstitial gland cells.

Primary ovarian interstitial gland cells are observed early in ovarian development, particularly during the fetal and neonatal stages. These cells arise independently of follicular atresia and are located within the ovarian stroma, predominantly in the ovarian cortex. Morphologically, they appear as loosely arranged cellular groups or diffuse cellular fields, often occupying extensive stromal areas in immature ovaries (Corner, 1919). Their size generally ranges from 10–20 μm in diameter, making them slightly smaller than the later-developing interstitial cells (Guraya, 1970). The nucleus of a primary interstitial cell is usually centrally located, round to oval, and occupies a relatively large proportion of the cell's volume. The cytoplasm of primary interstitial cells is moderately abundant and lightly eosinophilic in routine H&E-stained sections. Lipid inclusions are few or absent, resulting in a compact cytoplasmic appearance without marked vacuolization. Cytoplasmic granules are fine and uniform, and the cells closely resemble undifferentiated stromal cells in the early developmental stage (Corner, 1919). These possess moderately developed organelles. Mitochondria are relatively small and spherical, with less conspicuous cristae. The smooth endoplasmic reticulum is present but limited in extent, and the rough endoplasmic reticulum may be observed more frequently than in secondary interstitial cells. Lipid droplets are scarce, and the Golgi complexes are small and inconspicuous (Christensen and Gillim, 1969).

Secondary ovarian interstitial gland cells appear later in postnatal life and are closely associated with follicular atresia. Morphologically, they are more prominent and form the major interstitial cell population in the adult ovaries. These cells are widely distributed throughout the cortical and medullary stroma, often forming clusters, cords, or sheets around regressing follicles and blood vessels (Guraya, 1985). The nucleus is typically eccentrically placed, round to oval in shape, and relatively larger in size. In some cells, nuclear indentation or irregular nuclear contours may be observed, particularly in older ovaries (Erickson, 1983). Secondary interstitial cells exhibit a well-developed smooth endoplasmic reticulum, forming an extensive tubular network throughout the cytoplasm. Mitochondria are numerous,

Official Website
www.thescienceworld.net
thescienceworldmagazine@gmail.com
Published 30/08/2026

elongated, and contain tubular or vesicular cristae, which are characteristic of steroidogenic-type cells. Lipid droplets are abundant and are often closely associated with mitochondria and smooth endoplasmic reticulum membranes (Christensen and Gillim, 1969).

Function

Ovarian interstitial gland cells represent a pivotal, yet historically underappreciated, endocrine component of the mammalian ovary. Early investigators frequently grouped these cells with the theca interna, leading to ambiguity regarding their independent physiological relevance (Corner, 1919). Ovarian interstitial gland cells are derived primarily from the theca interna of degenerating follicles and play a significant role in ovarian steroidogenesis through androgen secretion (Shen *et al*., 2023). Interstitial gland cells function as a steroidogenic reserve (Clarke and Brook, 2001), ensuring endocrine continuity during physiological and pathological stress.

Clinical significance

Polycystic ovary syndrome (PCOS) is a complex endocrine disorder in which ovarian interstitial cells play a central role in the development and maintenance of hyperandrogenism (Spaczynski *et al*., 1999). In PCOS ovaries, interstitial cells undergo marked hyperplasia and hypertrophy, leading to expansion of steroidogenically active stromal tissue. These cells exhibit upregulation of the CYP17A1 gene, which encodes the key steroidogenic enzyme complex possessing 17α-hydroxylase and 17, 20-lyase activities. The enhanced activity of these enzymes increases androgen biosynthesis, particularly of androstenedione and testosterone, independent of normal follicular regulation (Franks, 2008). Morphologically, PCOS ovaries exhibit a dense cortical stroma rich in lipid-laden interstitial cells with enlarged euchromatic nuclei, reflecting increased steroidogenic activity. Functionally, excessive androgen production by interstitial cells disrupts the intrafollicular hormonal milieu, inhibiting granulosa cell aromatase activity and impairing estrogen synthesis. This androgen-dominant environment arrests follicular growth at the preantral or early antral stage, resulting in the accumulation of multiple small cystic follicles, which are characteristic of PCOS (Dumesic *et al*., 2015). Persistent anovulation further exacerbates stromal androgen production due to the absence of cyclic progesterone feedback, creating a self-perpetuating endocrine imbalance. Clinically, hyperactivity of ovarian interstitial cells contributes directly to hyperandrogenism, manifesting as chronic anovulation, infertility, irregular menstrual cycles, hirsutism, and acne on the skin.

Histological studies of buffalo ovaries have demonstrated significant alterations in interstitial gland cells (IGCs) under cystic ovarian conditions. Mohammed *et al*. (2013) reported a marked

Official Website
www.thescienceworld.net
thescienceworldmagazine@gmail.com
Published 30/08/2026

reduction in IGC numbers in both follicular and luteal cystic ovaries compared with normal ovaries. In healthy buffalo ovaries, interstitial glands are composed of epithelial cells ranging from cuboidal to polyhedral in shape, with large oval nuclei and clear, lipid-rich cytoplasm, indicative of active steroidogenic function. In contrast, ovaries affected by follicular and luteal cysts exhibit pronounced degenerative and apoptotic changes, including interstitial cells with fragmented, faded, and pyknotic nuclei, suggesting functional impairment of these glands (Amin *et al*., 2025). Despite the reduction and degeneration of IGCs observed histologically, cystic ovarian syndrome in cattle and buffaloes is generally associated with structural remodelling of the ovarian stroma, including periods of interstitial cell hyperplasia and hypertrophy, which contribute to excess androgen production. Elevated androgen levels disrupt normal follicular maturation and ovulation, promoting follicular persistence, cyst formation, prolonged anoestrus, and reduced fertility (Roberts, 2004).

Ovarian interstitial gland tumors are rare neoplasms in domestic animals that arise from steroidogenic interstitial cells in the ovarian stroma. These tumors are most commonly reported in cattle, mares, and bitches (Farjanikish *& Oryan*, 2017) and are often classified as sex cord–stromal tumors. Histologically, they consist of sheets or cords of polygonal cells with abundant lipid-rich cytoplasm and round to oval nuclei, resembling normal interstitial gland cells. Functionally, these tumors may be hormonally active, leading to excessive androgen or oestrogen secretion, which can result in anoestrus, nymphomania, masculinization, or infertility. Due to their slow-growing nature and nonspecific clinical signs, interstitial gland tumors are frequently incidental findings during post-mortem or reproductive examinations, highlighting the need for detailed histopathological evaluation in cases of unexplained reproductive disorders (Kennedy *et al*., 1998).

References

Amin, Y. A., Nour, A. H. M., & Mohamed, R. H. (2025). Effects of follicular and luteal cysts on reproductive organs, interstitial glands, and mast cell distribution in buffalo ovaries. *Scientific Reports*, *15*(1), 12837. https://doi.org/10.1038/s41598-025-94941-y

Christensen, A. K., & Gillim, S. W. (1969). The correlation of fine structure and function in steroid-secreting cells, with emphasis on those of the gonads. *Journal of Cell Biology*, *43*, 1–24.

Clarke, J. R., & Brook, F. A. (2001). Effect of gonadotrophins on the ovarian interstitial tissue of the wood mouse, Apodemus sylvaticus. *Reproduction*, *121*(1), 123–129. https://doi.org/10.1530/rep.0.1210123

Corner, G. W. (1919). On the origin of the interstitial cells of the ovary. *American Journal of Anatomy*, *25*, 117–183.

Official Website
www.thescienceworld.net
thescienceworldmagazine@gmail.com

Published 30/08/2026

Díaz Hernández, V., Marmolejo Valencia, A., Montiel de la Cruz, C., Piñón Zárate, G., & Montaño, L. (2018). Ultrastructural features of ovarian interstitial cells during follicular atresia. *Microscopy Research and Technique, 81,* 1209–1218.

Dumesic, D. A., Oberfield, S. E., Victorin, E. S., Marshall, J. C., Laven, J. S., Legro, R. S. (2015). Scientific statement on polycystic ovary syndrome. *Endocrine Reviews, 36*(5), 487–525.

Erickson, G. F. (1983). Morphological aspects of ovarian interstitial tissue. *Biology of Reproduction, 29*, 475–486.

Eurell, J. A., & Frappier, B. L. (2007). *Dellmann's textbook of veterinary histology* (6th ed., pp. 256–262). Blackwell Publishing.

Farjanikish, G. & Oryan, A. (2017). Leydig cell tumor in ovary of a German shepherd bitch: An immunohistopathological study. Veterinary Research Forum, 8(1), 81–84.

Franks, S. (2008). Polycystic ovary syndrome in adolescents. *International Journal of Obesity, 32*, 1035–1041.

Guraya, S. S. (1970). *Histochemical and morphological studies on the interstitial gland of the mammalian ovary.* Springer.

Guraya, S. S. (1985). *Biology of ovarian follicles in mammals*. Springer.

Kennedy, P. C., Cullen, J. M., Edwards, J. F., Goldschmidt, M. H., Larsen, S., Munson, L., & Nielsen, S. (1998). Histological classification of tumors of the genital system of domestic animals. *Atlas of tumor pathology, 2*(4).

Maximow, A. A., & Bloom, W. (1957). *A textbook of histology*. W. B. Saunders.

Mohammed, A. H. S., Ali, T. J. & Naki, Z. J. (2013). Histological study of ovarian interstitial lands in IRAQI buffaloes at six and nine years old. *Journal of US China Medical Science, 10*, 170–173.

Roberts, S. J. (2004). *Veterinary obstetrics and genital diseases*. CBS Publishers.

Shen, L., Liu, J., Luo, A., & Wang, S. (2023). The stromal microenvironment and ovarian aging: Mechanisms and therapeutic opportunities. *Journal of Ovarian Research, 16*, 237. https://doi.org/10.1186/s13048-023-01300-4.

Spaczynski, R. Z., Arici, A., & Duleba, A. J. (1999). Tumor necrosis factor-α stimulates proliferation of ovarian theca-interstitial cells. *Biology of Reproduction, 61*(4), 993 998. https://doi.org/10.1095/biolreprod61.4.993.