

Telocytes are still unknown regulatory, supporting, and the source of other cells of the interstitial tissue of various organs in animal and the human body. They are characterized by projections reaching 200  $\mu\text{m}$ , which form a three-dimensional network surrounding other interstitial tissue cells (controlled microenvironment). In the ultrastructure of these cells, e.g. lipid droplets and cell membrane caveolae are present. Telocytes interact between cells through intercellular junctions, release secretory microvesicles or directly interact *via* e.g. proteins or lipids. Telocytes can be regulated by hormones. They have progesterone and estrogen receptors, which enable them to regulate e.g. extracellular matrix, neurotransmission, immunomodulation, and apoptosis. In heart, liver, testes, and prostate diseases, changes in telocyte number and distribution related to remodeling, damage, and dedifferentiation/differentiation or tissue hyperplasia have been observed. In the study of digestive tract cancer, the participation of telocytes was demonstrated and the term telocytopathy was introduced. Until now, it is not known whether telocytes are present and are involved in pathological processes: cryptorchidism (undescended testis) and tumorigenesis in the dog gonad. The tissues of these animals constitute an excellent research model in reference to human research. Hormonal mechanisms underlying these pathologies include signaling by classical androgen receptors (AR). AR, through interaction with caveolin, contributes to prostate hyperplasia. It is also known that androgens can also lead to the rapid, gene-omitted signal transmission through the newly discovered membrane androgen receptor ZIP9, the zinc ion transporter. ZIP9 has been studied in the tumorigenesis of the prostate and mammary gland as well as in canine gonad after blocking gonadoliberin secretion. The action of androgens in the reproductive system, apart from regulating spermatogenesis, also applies to the production of steroid hormones. Lipid homeostasis is paramount for the testis function, but also lipids are involved in pathological processes, e.g. cancer as structural and energetic units of proliferating cells. Adipose tissue fatty acids are an important source of cholesterol for the steroidogenesis process. Adipocyte-like cells have been shown in the testicular tumor. Leptin is produced by adipose tissue and influences metabolic homeostasis, regulating body weight, which is directly related to the proper function of the reproductive system. Abnormal development of the testis may be a result of hormonal imbalance, which results in e.g. disturbances of Leydig and Sertoli cells (nourishing spermatogenic cells) and leads to cryptorchidism or cancer. There is little data available on the physiology of the dog gonad, and the incidences of testicular cancer in these animals, in the last few years, is increasing. Cryptorchidism may predispose to cancer of Sertoli cells. In the canine gonad, overexpression of survivin and the vascular endothelial growth factor is associated with the tumor malignancy. We have shown that estrogen receptors and p16 protein can be additional markers of canine Leydig tumorigenesis. Insulin-like protein 3 together with androgens is known to mediate the descent of the testes into the scrotum. Therefore, here experiments were designed to demonstrate the role and interaction of telocytes under the control of androgen-ZIP9 signaling and the interaction of proteins and lipids in the canine gonad under physiological conditions and cryptorchidism/tumor. Comprehensive studies will be performed in *in vitro* and *ex vivo* systems using: (i) canine (first time), Leydig, Sertoli, and spermatogenic cells and/or appropriate human/mouse cell lines, (ii) testicular tissues (Clinic UCVM JU-UA in Krakow; mixed breed dogs in various age groups that are routinely castrated). In cells/tissues: - telocytes will be examined with the use of light, confocal, and transmission microscopes and expression markers, e.g. CD34, -ZIP9 will be blocked by siRNA and AR pharmacologically *via* hydroxyflutamide (anti-androgen), -secretory microvesicles from cell co-cultures will be isolated. The data will be compared to healthy testicular and pathological tissues of the dog, laboratory animals, and humans. This will allow us to check whether and how telocytes are involved in maintaining testis homeostasis, whether androgen signaling *via* ZIP9 is important in the control of telocytes and other testicular cells, and which genes are involved in e.g. interstitial tissue hyperplasia in the cryptorchid and tumor (Leydig cell cancer) in the dog. Molecular techniques will be used: NGS, qRT-PCR, MALDI-TOF, chromatography, and immunohistochemistry. The results will be important for reproductive biology, veterinary medicine, animal breeding, and andrology. Due to the multilateral approach of specialists from an international team, innovative solutions will be achieved and new biological phenomena will be discovered.