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SPECIFIC FEATURES OF THE RAT AND HUMAN PROSTATE GLAND

Karimov Hakimjon Rayimberdiyevich
Assistant, Department of Pathological Anatomy, Bukhara State Medical Institute

Annotation: This article presents information from local and foreign sources on the anatomical structure, histology, morphogenesis of the rat prostate gland and the specific features of the anatomy of the rat and human prostate.

Keywords: Rat prostate gland, coagulation glands, anterior, posterior, ventral and lateral sections.

Introduction. The prostate has a major impact on men's health, as it is involved in a number of clinically important diseases, including prostate cancer, benign prostatic hyperplasia, and prostatitis. The prostate is an accessory gland of the male reproductive system that is found only in mammals, making it logical to use mammalian animal models to study the mechanisms of these diseases. However, despite the similarities found in prostate morphogenesis across species, the variability in its anatomy among mammals is remarkable. For example, while the prostate gland in rats and mice consists of discrete lobes, in humans and dogs it is a compact, single structure. Furthermore, some prostate diseases that are common in humans are only observed in certain species and not in others. For example, the dog is the only animal known to develop spontaneous prostate cancer that can metastasize to bone, as seen in humans. Despite these differences, the mouse remains the most widely used animal model for studying the biological and pathological aspects of the prostate gland because of its small size, easy reproduction, short gestation period, cost-effectiveness, similarity to the human genome (approximately 95% identical), and, most importantly, ease of genetic manipulation. Indeed, the mouse has been used as a model to study prostate morphogenesis, prostatitis, and prostate cancer. In this manuscript, we describe the anatomy and histology of the rat and human prostate, and attempt to provide a concise but comprehensive guide for primary researchers and clinical pathologists who use this species to study prostate development and function, as well as the underlying molecular mechanisms leading to prostate diseases.

Rat Prostate Biopsy Preparation

To achieve optimal tissue quality, the rat prostate gland should be dissected together with the urethra, bladder, seminal vesicles, ampullary glands, and proximal vas deferens (a.k.a. ejaculatory ducts). This should be performed immediately after euthanasia of the mouse using institutionally approved methods. After securing the mouse on its hindlimbs, the fur is moistened with 70% ethanol to prevent the rat from becoming dislodged during dissection. The skin is then incised along the ventral midline with fine scissors. The incision should begin anterior to the urethra, using forceps to lift the skin so that it can be exposed without damaging the abdominal muscle wall. The midline incision is continued with a blunt-tipped scissor divulsion to the xiphoid process, followed by additional incisions to reinforce the surgical fields. After securing the skin flaps to a cutting board, an incision is made through the linea alba using Metzenbaum scissors to gain access to the abdominal cavity. At this point, the urogenital tract is exposed. The bladder is elevated with the help of cutting forceps, and the ureters, vas deferens, and urethra can be cut. In this way,

the bladder and genital tract (except the testicles) are collected as a single unit. Biopsies from the organs are then transferred to a Petri dish containing phosphate buffer solution for examination under a microscope.

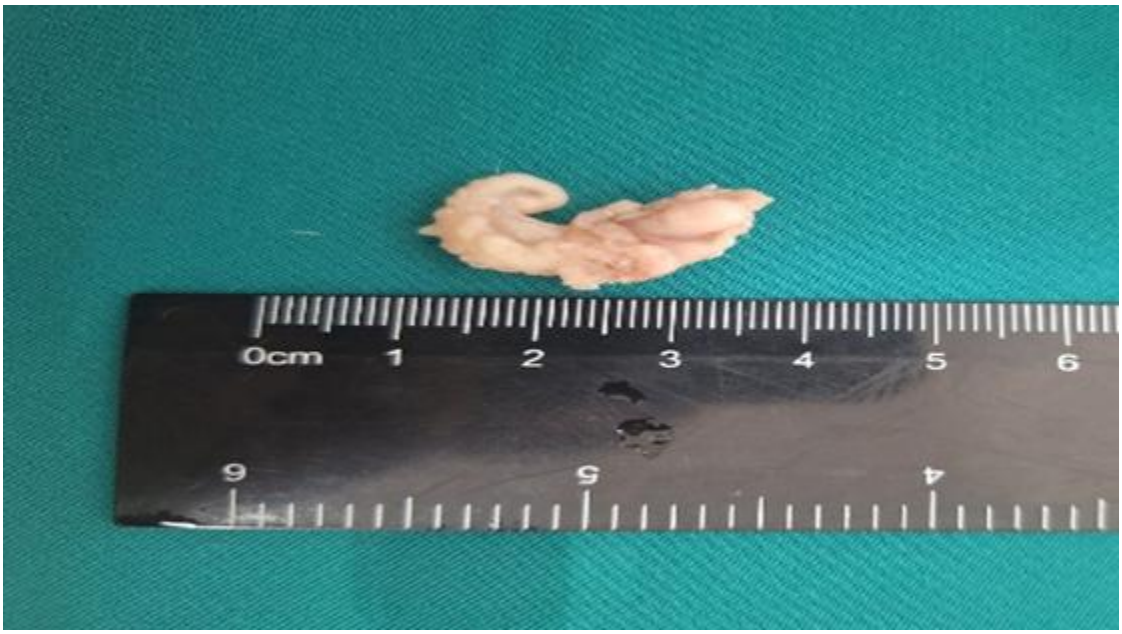

Figure 1. Macroscopic view of the anatomical structures of the rat prostate.

Rat and human prostate anatomy

In rats, the prostate is not a single anatomical structure, but an organ consisting of four lobes arranged in a circle around the urethra. These lobes, named for their spatial orientation, are the anterior, posterior, ventral, and lateral lobes, which can be distinguished from each other using a dissecting microscope. Anterior to the urethra and caudal to the bladder, the ventral prostate (VP) can be recognized as a gelatinous pink structure that partially surrounds the urethra and its ducts are empty. The VP is joined by two lobes located on either side of the urethra to form the lateral prostate (LP). The butterfly-shaped dorsal prostate (DP) is located bilaterally at the base of the seminal vesicles and is easily recognized as two white horn-shaped, coiled anatomical structures located dorsolateral to the bladder. The LP and DP are often referred to as the dorsolateral prostate (DLP), but they have some differences in histology (see "Histology of the Rat Prostate"). The anterior prostatic lobes (AP), also known as the "coagulation glands", are transparent and bilaterally attached to the lesser curvature of the seminal vesicles cranial to the other prostatic lobes. Unlike the human prostate gland, which is attached to the pelvic cavity and anterior to the rectum, the distal ends of each of the mouse prostatic lobes float freely in the pelvic cavity. A schematic drawing showing lateral views of the different mouse prostatic lobes and their spatial relationship to other adjacent organs can be seen in the following diagram. Additional views can be found in the "Visible Mouse Project" developed by the UC Davis Center for Comparative Medicine.

Unlike the rat, the male prostate gland lacks an outer lobe and is divided into distinct glandular regions, including the peripheral zone (PZ), central zone (CZ), transitional zone (TZ), and a nonglandular anterior fibromuscular stroma region. with characteristic histology. The PZ is the region surrounding the proximal part of the prostatic urethra. Based on anatomical and cross-species comparisons of mRNA expression patterns, the DL lobes of the rat prostate are homologous to the human PZ, where 75–85% of prostate adenocarcinomas occur in patients. The CZ, considered the human counterpart of the rat AP lobes, is a cone-shaped region surrounding the vas deferens and occupies approximately 25% of the prostate volume. The TZ, which has no rat homolog and is where benign prostatic hyperplasia develops in patients, is the

smallest zone (5–10% of prostate volume) and surrounds the distal urethra of the prostate. So, while in humans the urethra is completely surrounded by the prostate, in mice this is not the case.

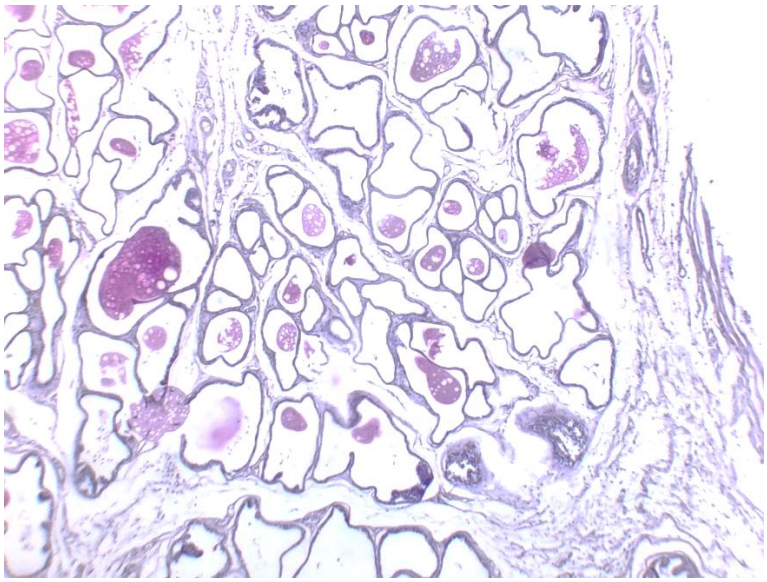

Figure 2. Microscopic features of a normal rat prostate gland. A median transverse section of the prostate gland shows the prostatic urethra, which is lined with coagulating secretions (also called seminal plugs or copulatory plugs), and the prostatic ducts and ductus ejaculatorii, which are surrounded by smooth muscle. and are surrounded by the lateral prostate.

The prostate gland of both species is embryologically derived from the urogenital sinus (UGS), an endoderm-like structure present in embryos at the ambisexual stage. UGS epithelial cells form rigid buds that penetrate the surrounding UGS mesenchyme in different directions by 10 weeks of gestation in humans and 17 days of gestation in rats. These distinct locations define the bases of the different lobes of the mouse prostate gland and the different zones of the human prostate described above. In humans, the prostatic buds elongate, undergo branching morphogenesis, form a lumen, and show signs of secretory differentiation by 14 weeks of gestation, and the prostate is almost fully developed at birth. In contrast, branching morphogenesis occurs postnatally in rats, and the lobe-specific branching patterns are complete by 15 to 20 days. In both species, the prostate grows and matures rapidly, with blood androgen levels rising at puberty (25–40 days in mice).

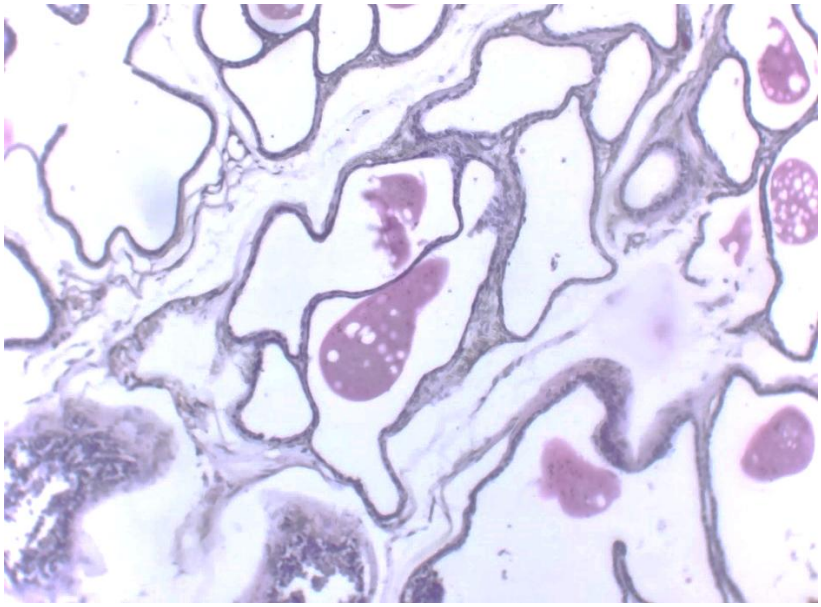

Figure 3. Microscopic features of the rat prostate gland: Dorsal and lateral prostate segments with surrounding tissue. Dorsal prostate: small acini surrounded by a fibromuscular layer. Dorsal prostate: cuboidal to columnar cells with cytoplasmic vesicles, lateral prostate showing a median epithelial fold.

Histology of the rat prostate gland

As in humans, the rat prostate gland contains glands (acini) and ducts with epithelial cell types, including columnar luminal secretory cells, basal cells (fewer and more discontinuous in mice), and neuroendocrine cells. In both humans and mice, luminal cells are characterized by the expression of low molecular weight cytokeratins (CK) 8 and 18 and androgen receptor (AR), while basal cells express high molecular weight CK5 and p63 in both species. It is noteworthy that prostate-specific antigen (PSA [kallikrein3 protein; KLK3, gene]) is expressed and secreted by human but not mouse luminal prostate cells, which secrete other proteins that are specific to the lobe. Neuroendocrine cells have both neural and epithelial properties, are found in very small numbers interspersed with basal cells present in the ducts and acini, and express chromogranin A and synaptophysin. The most striking histological difference between the two types of prostate is the stromal component, which is very well developed as a fibromuscular region in humans, and sparse with minimal smooth muscle cells in mice. Based on publications describing the normal histology of the rat prostate, here we summarize the main histological features necessary to identify the different mouse lobes under the microscope. All rat prostate lobes are surrounded by a thin capsule lined with mesothelium and are separated from each other by fibrous and fatty connective tissue. The acini that make up the prostatic lobes are surrounded by a fibromuscular tunic and are embedded in loose connective tissue with few stromal cells and collagen fibers. Nerve bundles and associated ganglia are often located in the connective tissue of the DLP. Each of the mouse prostate lobes has a unique histology and can be visualized under the microscope based on its location relative to the urethra and seminal vesicles (Figure 3). The VP has medium to large acini, which are composed mainly of cuboidal or simple columnar epithelial cells with nuclei containing small nuclei. The lumens of the VP glands are lined by a smooth mucosa, which shows minimal infolding or some focal epithelial tufting compared to the other lobes. Each gland of the VP is surrounded by a thin fibromuscular layer. The lumens of the glands contain homogeneous pale serous secretions. The rat VP has no human counterpart.

Conclusions. The rat prostate gland, although similar in embryological development, cellular composition, and molecular features to the human prostate, has distinct anatomy and histology. A comprehensive understanding of the normal anatomy and histology of the rat prostate is therefore essential for drawing definitive conclusions from studies conducted with this species. While the prostate gland in rats and mice consists of discrete lobes, in humans and dogs it is a compact, single structure. Furthermore, some prostate diseases that are common in humans are only observed in certain species and not in others. For example, the dog is the only animal known to develop spontaneous prostate cancer that can metastasize to bone, as seen in humans. Despite these differences, the mouse remains the most widely used animal model for studying biological and pathological aspects of the prostate gland because of its small body size, easy reproduction, short gestation period, cost-effectiveness, similarity to the human genome (approximately 95% identical), and, most importantly, ease of genetic manipulation.

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