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THE ROLE OF CELLS IN THE INNATE IMMUNITY OF ANIMAL REPRODUCTION ORGANS (review and own research)

Immune system of reproductive organs of animals is represented by a number of cellular and humoral protection factors. Recently, the attention of scientists was attracted by the role of immunocompetent cells, which integrally provide immune homeostasis at all stages of the reproductive function. More and more information is being published about the role of epithelial cells that form the first evolutionarily created natural barrier [1, 2]. Some types of epitheliocytes at the same time are able to secrete a number of antimicrobials, as well as participate in the launch of the immune response through specific initiation of the reaction of phagocytic cells [2, 3].

Epithelial cells provide a first line of defense that confers continuous protection, by providing a physical barrier as well as secretions containing bactericidal and virucidal agents. In addition to maintaining a state of ongoing protection, these cells have evolved to respond to pathogens, in part through Toll-like receptors (TLRs), to enhance innate immune protection and, when necessary, to contribute to the initiation of an adaptive immune response. The overall goal of this review is to focus on the dynamic role of epithelial cells in the upper reproductive tract, with special emphasis on the uterus, to define the unique properties of these cells as they maintain homeostasis [3, 4]. By understanding the nature of this protection and the ways in which innate and adaptive immunity are regulated by sex hormones, these studies provide the opportunity to contribute to the foundation of information essential for ensuring reproductive health.

Although not classically considered to be bona fide cells of the innate immune system, intestinal epithelial cells are equipped with an extensive repertoire of innate immune receptors 9. Expression of these receptors and active signal transduction on microbial recognition is pivotal for intestinal homeostasis because their epithelial-specific deletion leads to breaches in the epithelial barrier, which compromises the spatial separation between commensal bacteria and the lamina propria of the intestines, thereby predisposing the tissue to spontaneous inflammation [4-7]. This has been demonstrated for components that are involved in TLR signalling, including myeloid differentiation primary response protein MyD88, TNF receptor-associated factor 6 (TRAF6), and NF-κB essential regulator (NEMO)4,10–12, as well as for orchestrators of cell death such as receptor-interacting serine/threonine-protein kinase 1 (RIPK1), FAS-associated death domain protein (FADD) and caspase-8 (refs 13–16). NOD-containing protein 2 (NOD2), which is highly expressed in the Paneth cells of the small intestine, is activated by microbial [3, 5-8].

There are numerous bacteria that normally reside in the vaginal canal in the bitch and the preputial cavity in the dog. These bacteria are normal inhabitants and their presence in low to moderate numbers ensures a healthy mucosal environment. When these bacteria invade the higher reproductive tract (i.e. uterus, prostate, testicles), if the animal's immune system does not function properly and remove them in a timely manner, they can proliferate and cause disease (i.e. inflammation of the lining of uterus called endometritis which can turn into a full blown uterine infected called pyometra; infection of the prostate called prostatitis; or inflammation of the testicles and tubular sperm storage system called orchitis/epididymiditis). If the body's innate defense systems work properly, these bacteria are quickly cleared and do not cause disease [4, 6-8]. An example of this innate immunity would be when a bitch is bred naturally and all of the bacteria from the dog's penis and the bitch's vagina are forced up into the uterus along with the ejaculate. In a normal bitch, these bacteria are cleared from the uterus within 24 hours of breeding, resulting in a sterile environment in the uterus when the cervix closes at the end of the fertile period. If uterine defenses are inadequate, bacteria remain become trapped within the uterus during the high progesterone phase of the cycle (diestrus) and they proliferate in this environment, first causing endometritis and then eventually progressing to the production of pus in the uterus or pyometra [3, 5, 7].

Because bacteria are normal inhabitants of the lower reproductive tract it is very difficult to determine if they are potentially pathologic or not, simply based on their presence. The enter through the body orifices (vulva and prepuce) and are in highest numbers closest to the external opening and lesser numbers as one moves up the reproductive tract due to immune clearance mechanisms [6-9]. Cultures of the vaginal canal or preputial cavity will almost always result in growth of bacteria and interpretation of this growth is very difficult in terms of determining the need for treatment. In fact, a negative culture would be reason to suspect inadequate sampling

and not actually a true negative culture (except during anestrus when vaginal bacterial numbers are usually very low).

Our studies have found that in different stages of the sexual cycle cats, along with cytological changes in epithelial cells, changes occur in phagocytic protection [3]. In particular, in the post-infusion period there was an increase in the number of intermediate and basal epithelial cells on the surface of which were adhered to coccal and rod-shaped microorganisms. Along with epithelial cells, activated phagocytes were grouped. Neutrophils showed cytochemical reactivity in the NBT- test, and also formed NETs [10, 11]. At the same time, activated phagocytes absorbed microorganisms, and some epithelial cells formed specific cytoplasmic inclusions, which obviously also has an important role in the antimicrobial immunity of the mucosa. Some neutrophilic granulocytes were in a state of apoptosis [12].

Obviously neutrophil phagocytes take part not only in antimicrobial defense, but also provide maintenance of immune homeostasis. At present, antimicrobial reactivity of phagocytes under normal and pathological conditions and the participation of epithelial cells in the formation of local genital immunity are studied.

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