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COMPARATIVE CHARACTERISTIC OF INNATE AND ADAPTIVE IMMUNITY

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Comparative data about innate and adaptive immunity and activation of former by pattern-recognition receptors are briefly presented in this review.

KEY WORDS: *innate immunity, adaptive immunity, pattern-recognition receptors, pathogen- and damage-associated molecular patterns (PAMP and DAMP).*

Immunity is the mode of organism's protection against harmful genetically alien information of either exogenous (microbes, viruses, toxins), or endogenous (modified tumor cells) origin. It supports genetic homeostasis of the organism.

At present, specific immunity, which responds to one specific antigen and acts through lymphoid system, T-lymphocytes (cellular), and B-lymphocytes (humoral), is well-known. According to modern concepts, it is adaptive and can be only acquired. Adaptive (specific) immunity is common to higher (vertebrate) animals, it develops slowly (9 – 14 days or more), because it needs proliferation of a certain clone of lymphoid cells, gene activation and protein synthesis[1]. However, this time the body is protected due to innate mechanisms of nonspecific body resistance. These mechanisms include neural and humoral protective reactions, barrier mechanisms, nucleic acid reparation system, protein system of protection and reparation (chaperones), cytokines, innate (non-specific) immunity, etc.[5,6,7].

Innate immunity is common to virtually all living organisms (higher animals, invertebrates and plants). Indeed Mechnikov was an pioneer of the modern science of innate immunity, showing that certain leucocytes absorb and destroy pathogenic bacteria (phagocytosis)[9].

The beginning of the modern theory of innate immunity should be dated back to1996, when Toll-receptors in Drosophila melanogaster were shown to be essential for its antifungal defense[12]. It was the beginning of the doctrine of **pattern-recognition receptors (PRR)** and their role in the activation of innate immunity[10]. It is "discovery relating to innate immunity activation" for which Bruce **Beutler** and J.A.**Hoffmann** were awarded the Nobel Prize in Physiology or Medicine on October 3, 2011.

Innate immunity, as well as adaptive one, is cellular and humoral. The cellular is represented by the leukocytes, that produce antibacterial substances and perform phagocytic function (monocytes, neutrophils /in birds and several mammals –

heterophils/). It also includes basophils, eosinophils, natural killers (NK) and dendritic cells. Humoral immunity includes a system of complement, lysozyme, agglutinins, precipitins, perforins, proteins of acute phase and cytokine system (interferons, interleukins, tumor necrosis factor family, etc.)[1,7,8,9]. It is just cytokines that play a leading role in triggering defensive reactions like inflammation, acute phase response and fever[5,6,7]. Now, these reactions are considered the components of innate immunity.

At present, dendritic cells attract particular attention. Their discovery by **Steinman** was also noted by the Nobel Prize in 2011. Dendritic cells, which are of bone marrow origin, are divided into three subpopulations: myeloid, plasmocytoid, and recently discovered monocytoid-related one. They present antigens to T-lymphocytes and trigger the adaptive immunity, providing tolerance and preventing the development of autoimmune diseases[14,15,17]. However, dendritic cells also have Toll-like receptors and receptors for complement components, they produce a lot of cytokines and trigger immediate innate immunity. Therefore, they should be regarded a bridge between innate and adaptive immunity[15,17].

Soon after discovering of Toll-receptors in Drosophila, it has been found that similar receptors are also in mammals (human)[13]. They are available in all higher and lower animals, and even in plants[2,7]. Those receptors were called **Toll-like receptors (TLR).** Later, 13 members of their family were identified in mammals, and just at the beginning of this century it became evident that they are proteins, playing a key role in immune defense of the body[10].

Innate immunity is not strictly specific, and it distinguishes the groups of pathogenic factors using the patterns, encoded in the embryo cells. Examples of such **pathogen-associated molecular patterns (PAMP)** are a lipopolysaccharides of gram-negative bacteria, peptidoglycans of gram-positive microorganisms, modulin, flagelin, zymozan, two spiral viral RNA, DNA, rich in CpolyG-sequences, etc. These molecular patterns (structures) are not available in the host body, but they are common to certain groups of pathogens. Recognition of these patterns is performed by pattern-recognition receptors (PRR)[1,2,3,7]. In addition to PAMP, these receptors also recognize endogenous ligands, which are called the **DAMP (damage-associated molecular patterns or danger-associated molecular patterns**[)]. They send signals of danger, tissue damage and cell death[3,4,7,14].

Endogenous ligands arising at thermal, chemical and radiation-induced damage to the tissue, which are able of activating Toll-like receptors and other PRR include heat shock proteins (chaperones), non-histone proteins, uric acid crystals, surfactant protein A, fibrinogen, components of extracellular matrix: fibronectin and glycosaminoglycans (heparan sulfate, biglycan, hyaluronic acid)[4,7].

Currently, several classes of PRR are known, including: Toll-like receptors **(TLR**), NOD-like receptors (**NLR** – Nucleotide-binding oligomerization domain-like receptors), RIG-1-like receptors (**RLR**, Retinoic acid inducible gene I-like receptors), **C-type lectin** receptors, etc.[3,4,11]. Among them, the best understood TLR

are[4,11]. Other PRR can be divided into several groups: membrane proteins (scavenger- and C-type lectins), secreted molecules (components and acute phase proteins), cytosolic sensors and cytosolic receptors of viral nucleic acids[4].

Table 1.

Comparison of innate and adaptive immunity

Innate immunity	Adaptive immunity
Innate; exists before an exposure to pathogens.	Always acquired; it occurs after exposure to the relevant pathogen
Exists in higher animals and invertebrates, as well as plants	Inherent only in a higher (vertebrate) animals
Effective immediately, once maximum response	Contact time of antigen and maximum response is about 2 weeks
Reaction is non-specific - for groups (patterns) of pathogens or endogenous ligands	Reaction is specific – for one antigen
It has the cellular and humoral components	It has the cellular and humoral components
Key performers are leukocytes of myeloid-monocytic series	Implemented by lymphoid system, T- and B-lymphocytes
There is no immunological memory	Inherent immunological memory

It is now clearly shown that Toll-like and other PRR occupy the central position in protecting the host organism against bacterial and viral infections, start (activate) both innate and adaptive immunity. In addition, PRR play an important role in restoring damaged tissue and regeneration. They contribute to carcinogenesis[1,2,4,7,16]. Innate immunity is an early warning system of ingested pathogens, and it plays a primary role in organization of both non-specific defense reactions and induction of specific (adaptive) immunity[7,9,14,16]. However, PRR activation not always results in positive effects. Dysregulation of PRR signaling, their excessive activation, as well as their absence or injury, may cause the development of so-called "auto-inflammatory" diseases, including chronic inflammation, autoimmune diseases (autoimmune diabetes, systemic lupus erythematosus), immunodeficient diseases, atherosclerosis, etc.[1,3,7].

The contemporary investigations about innate and adaptive immunity, especially the discovery of pattern-recognition receptors and dendritic cells increase our abilities in prevention and therapy of infectious diseases and autoimmune disorders.

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Порівняльна характнеристика природженого і адаптивного імунітету.

Сукманський О.І.

В огляді коротко представлені порівняльні дані про природжений (вродженій) і адаптивний імунітет, а також про активацію першого патерн-розпізнавальними рецепторами.

Ключові слова: *природжений імунітет, адаптивний імунітет, паттерн-розпізнавальні рецептори, патоген-асоційовані і асоційовані з пошкодженням молекулярні патерни.*

Сравнительная характеристика врождённого и адаптивного иммунитета.

Сукманский О.И.

В обзоре кратко представлены сравнительные данные о врождённом и адаптивном иммунитете, а также об активации первого паттерн-распознающими рецепторами.

Ключевые слова: *врождённый иммунитет, адаптивный иммунитет, паттерн-распознающие рецепторы, патоген-ассоциированные и ассоциированные с повреждением молекулярные паттерны.*