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THE SIGNIFICANCE OF IMMUNOPATHOLOGY IN THE ORIGIN OF TUMOR CELLS AND THE MOLECULAR MECHANISMS OF OPPORTUNISTIC INFECTION CONTROL IN IMMUNODEFICIENCY

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Annotatsiya: Ushbu maqolada immunopatologiya tushunchasi, uning o‘sma (neoplastik) hujayralar kelibchiqishidagi o‘rni, shuningdek immun tanqislik holatlarida opportunistik infeksiyalarning rivojlanish vaboshqarilish mexanizmlari yoritilgan. Tadqiqot immun tizimining buzilishi natijasida yuzaga keladigan patologik jarayonlarning molekulyar asoslarini ochib beradi.

Kalit so‘zlari. Immunopatologiya, immunitet tizimi, autoimmun reaktsiyalar, immuntanqislik, o‘sma hujayralar, immun nazorat, T-limfotsitlar, NK hujayralar, PD-1/PD-L1 tizimi, MHCmolekulalari, Treg hujayralar, apoptoz.

Annotation. This article discusses the concept of immunopathology, its role in the development of neoplastic (tumor) cells, as well as the mechanisms of development and regulation of opportunistic infections in conditions of immunodeficiency. The study reveals the molecular basis of pathological processes arising as a result of immune system dysfunction.

Keywords. Immunopathology, immune system, autoimmune reactions, immunodeficiency, tumor cells, immune surveillance, T-lymphocytes, NK cells, PD-1/PD-L1 pathway, MHC molecules, Treg cells, apoptosis.

Аннотация. В данной статье рассматривается понятие иммунопатологии, её роль в возникновении неопластических (опухолевых) клеток, а также механизмы развития и регуляции оппортунистических инфекций при состояниях иммунодефицита. Исследование раскрывает молекулярные основы патологических процессов, возникающих вследствие нарушений в работе иммунной системы.

Ключевые слова. Иммунопатология, иммунная система, аутоиммунные реакции, иммунодефицит, опухолевые клетки, иммунный надзор, Т-лимфоциты, NK-клетки, система PD-1/PD-L1, молекулы MHC, Treg-клетки, апоптоз.

Introduction. Immunopathology is a field of science that studies diseases arising as a result of dysfunction of the immune system. It encompasses not only conditions associated with weakened immunity but also processes characterized by excessive immune activation. In modern

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medicine, immunopathological conditions are closely linked to tumors, autoimmune diseases, allergies, and immunodeficiency syndromes. The immune system is a complex biological mechanism that protects the body from external antigens. However, genetic, biochemical, or cellular-level imbalances in this system can lead to loss of control over tumor cells and activation of opportunistic infections.

1. Essence and Classification of Immunopathology

Immunopathology is a scientific discipline that studies diseases caused by disturbances in immune system function and analyzes pathological conditions associated with excessive, insufficient, or misdirected immune responses. In other words, immunopathological processes are conditions in which the immune system damages the body's own tissues instead of providing protection.

Immunopathological processes are divided into three main types:

1.1. Immunodeficiency States

In this condition, the immune system is unable to perform its protective functions adequately. As a result, the body becomes highly susceptible to bacterial, viral, fungal, and parasitic infections.

Immunodeficiencies are classified as:

Congenital (Primary) — caused by genetic defects that prevent proper development of immune cells or their components.
Examples: DiGeorge syndrome, Bruton's agammaglobulinemia.

Acquired (Secondary) — develop as a result of external factors.
The most well-known example is AIDS, associated with Human Immunodeficiency Virus (HIV) infection.

1.2. Autoimmune Reactions

In autoimmune conditions, the immune system recognizes its own healthy cells and tissues as "foreign" and produces antibodies against them. As a result, self-tissues are damaged and inflammatory processes develop.Examples include: Systemic lupus erythematosus (SLE), rheumatism, type 1 diabetes mellitus, multiple sclerosis, thyroiditis, and others.Genetic predisposition, hormonal changes, viral infections, and environmental factors play significant roles in the development of these conditions.

1.3. Allergic Reactions

Allergy is an exaggerated immune response to foreign substances (allergens). Allergens include dust, food products, medications, plant pollen, animal dander, and other substances.Allergic reactions are mediated by IgE antibodies and excessive release of mediators

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such as histamine.Clinical manifestations include nasal congestion, skin rashes, bronchial asthma, anaphylactic shock, and other inflammatory conditions.

General Mechanisms of Immunopathological Processes

- Disruption of antigen–antibody complexes and their accumulation in tissues, leading to inflammation
- Lymphocyte imbalance — altered ratio between T cells ($CD4^+$ and $CD8^+$)
- Dysregulated cytokine network — excessive production of cytokines such as IL-1, IL-6, and TNF-α, resulting in inflammation and tissue damage

Conclusion of Section 1

Immunopathological processes arise when immune balance is disrupted. Each represents a specific direction of immune dysfunction:

- Immunodeficiency — weak defense
- Autoimmunity — attack against self-tissues
- Allergy — excessive sensitivity

Therefore, studying immunopathology is crucial in modern medicine for understanding disease mechanisms and developing new therapeutic strategies.

2. Role of the Immune System in Tumor Cell Development

Every day, millions of cells divide in the human body, and genetic mutations occur in some of them. These mutations may allow cells to escape normal control mechanisms and acquire unlimited proliferative capacity.

In a healthy organism, this process is constantly monitored by the immune surveillance system, known as the **immunological surveillance theory**.

2.1. Essence of Immune Surveillance

Immune surveillance is the natural defense mechanism by which the immune system recognizes, eliminates, and prevents the development of tumor cells.

This process is mainly carried out by three types of cells:

- **Cytotoxic T lymphocytes ($CD8^+$ cells)** — recognize abnormal antigens on tumor cells and induce lysis via perforin and granzymes
- **Natural Killer (NK) cells** — eliminate cells lacking MHC class I expression through apoptosis

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- **Macrophages and dendritic cells** — engulf tumor antigens, present them to T lymphocytes, and secrete cytokines (IL-12, TNF-α, IFN-γ) to enhance antitumor immunity

2.2. Dynamic Balance Between the Immune System and Tumors (Immunoediting)

This process occurs in three stages:

Stage 1: Elimination

The immune system rapidly detects and destroys mutated cells. Interferons (IFN-α, IFN-γ) and cytotoxic lymphocytes play a major role.

Stage 2: Equilibrium

Some tumor cells survive immune attack and remain in a latent state for a long period, undergoing genetic changes that allow immune evasion.

Stage 3: Escape

Tumor cells completely evade immune control through:

- Reduced MHC class I expression
- Activation of inhibitory signals (PD-L1, CTLA-4)
- Secretion of immunosuppressive cytokines (IL-10, TGF-β)
- Increased regulatory T cells (Tregs)

2.3. Mechanisms of Escape from Apoptosis

Tumor cells avoid programmed cell death through:

- Inactivation of the p53 gene
- Overexpression of anti-apoptotic proteins (Bcl-2, Bcl-xL)
- Disruption of the Fas/FasL system

This enables uncontrolled proliferation, angiogenesis, and metastasis.

2.4. Immunotherapy — A Modern Approach

Current immunotherapeutic strategies include:

- **Monoclonal antibody therapy** (anti-PD-1, anti-PD-L1, anti-CTLA-4)
- **CAR-T cell therapy**
- **Cytokine therapy** (IFN-α, IL-2)

Conclusion of Section 2

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Although the immune system is the primary defense against tumor cells, tumors develop when immune surveillance weakens or is evaded. Therefore, molecular-level study of immunity is essential for tumor prevention and treatment.

3. Immunodeficiency and Opportunistic Infections

Immunodeficiency is a condition in which immune system components (T cells, B cells, phagocytes, or complement) fail to function adequately, resulting in weakened protection against infections.

As a result, the body becomes susceptible to microorganisms that are normally harmless — known as **opportunistic pathogens**.

3.1. Types of Immunodeficiency

a) Primary (Inherited) Immunodeficiencies

Caused by genetic mutations and usually manifest in childhood.

Examples:

- Bruton's agammaglobulinemia
- DiGeorge syndrome
- Severe combined immunodeficiency (SCID)

b) Secondary (Acquired) Immunodeficiencies

Caused by external factors such as:

- AIDS (HIV infection)
- Chemotherapy and radiation
- Chronic diseases (diabetes, liver or kidney failure)
- Malnutrition (protein and zinc deficiency)

3.2. Nature of Opportunistic Infections

Common opportunistic pathogens include:

Candida albicans — causes oral thrush, esophageal candidiasis, and sepsis
Pneumocystis jirovecii — causes severe pneumonia
Cytomegalovirus (CMV) — causes retinitis, encephalitis, and organ damage

3.3. Molecular Mechanisms of Opportunistic Infection Development

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- Decreased $CD4^+$ T cells → reduced IL-2 and IFN-γ
- Reduced macrophage activity → impaired phagocytosis
- B-cell dysfunction → decreased immunoglobulins
- Complement deficiency → impaired bacterial lysis

This creates a vicious cycle of immune suppression.

3.4. Treatment and Prevention

- Antiretroviral therapy (ART)
- Prophylactic antibiotics and antifungals
- Immunomodulators (interferons, gamma globulins)
- Nutritional support and vitamins (A, C, E, D)

4. Molecular Mechanisms of Opportunistic Infection Control

Key disruptions include:

- Cytokine signaling imbalance
- $CD4^+$ T-cell depletion
- NF-κB signaling pathway inhibition
- Excessive immune cell apoptosis

Molecular Therapeutic Strategies

- Recombinant interferons
- Cytokine agonists
- Immunomodulatory peptides
- NF-κB pathway activators

Conclusion

Immunopathology studies diseases resulting from immune system dysfunction, including immunodeficiency, autoimmunity, and allergic processes. Loss of immune surveillance leads to tumor development and activation of opportunistic infections. Immune system stability is the fundamental guarantee of organismal defense.

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