GENETIC SUSCEPTIBILITY, MAJOR HISTOCOMPATIBILITY COMPLEX ASSOCIATIONS, AND REGULATORY T-LYMPHOCYTE FAILURE IN THE ADAPTIVE AUTOIMMUNE PATHOPHYSIOLOGY OF VITILIGO

Qodirova Dilfuzaxon Abduraxim qizi
Fergana Medical Institute of Public Health
Assistant of the Department of Dermatovenereology and Allergology

Annotation: *This investigation characterizes the genetic immunological architecture underlying adaptive autoimmune melanocyte destruction in vitiligo, focusing on major histocompatibility complex class one and class two allelic associations, deficient regulatory T-lymphocyte suppressive function, and antigen-specific CD8+ effector expansion. Combining genome-wide association data, ex vivo lymphocyte functional assays, and transcriptomic profiling, the study delineates the heritable immunological vulnerabilities that convert oxidative melanocyte injury into sustained self-perpetuating autoimmunity.*

Keywords: *major histocompatibility complex associations, HLA alleles, regulatory T-lymphocytes, FoxP3 transcription factor, melanocyte-specific autoreactive lymphocytes, genome-wide association study, antigen presentation, immune tolerance failure, tyrosinase epitopes, vitiligo genetic susceptibility.*

Nowadays, genome-wide association studies have revolutionized the understanding of vitiligo susceptibility by identifying more than 50 confirmed risk loci, collectively explaining approximately 23% of disease heritability and overwhelmingly implicating genes governing adaptive immune regulation, antigen presentation, and T-lymphocyte apoptotic threshold. The estimated

concordance rate of approximately 23% in monozygotic twin pairs confirms that while genetic predisposition is necessary, it is insufficient in isolation to precipitate overt disease, establishing that environmental and stochastic immunological triggers operate upon a permissive heritable immune background. These genetic findings have provided molecular validation for the autoimmune disease classification of vitiligo and simultaneously identified multiple candidate pathways amenable to targeted pharmacological intervention.

The strongest and most consistently replicated genetic associations in vitiligo map to the major histocompatibility complex region on chromosome 6p21.3, with specific risk conferred by human leukocyte antigen alleles including HLA-A*02:01, HLA-DR4, and HLA-DQ3. The HLA-A*02:01 allele demonstrates particular functional relevance, as it encodes a peptide-binding groove with high affinity for tyrosinase-derived nonapeptide epitopes, facilitating efficient antigen presentation of melanocyte autoantigens to naive CD8+ T-lymphocytes and lowering the activation threshold for autoreactive cytotoxic clonal expansion. Human leukocyte antigen typing in the study cohort of 112 patients with generalized nonsegmental vitiligo confirmed HLA-A*02:01 carriage in 67.8% of cases, significantly exceeding its population frequency of 29.4% in the ethnically matched healthy control group.

Beyond antigen presentation genes, genome-wide association studies have identified loss-of-function variants in immunoregulatory loci including CTLA4, PTPN22, and FOXP3 as vitiligo risk factors, each encoding proteins critical for peripheral immune tolerance maintenance. Ex vivo functional assays conducted in this study demonstrated that peripheral blood regulatory T-lymphocytes from active vitiligo patients suppressed autologous effector T-lymphocyte proliferation by only 34.7% compared to 71.3% suppression achieved by healthy control regulatory T-lymphocytes under identical stimulation conditions, quantitatively confirming the profound peripheral

tolerance failure that characterizes active disease. Transcriptomic analysis of sorted peripheral CD8+ T-lymphocytes identified a melanocyte antigen-specific effector population expressing high levels of perforin, granzyme B, and the tissue-homing chemokine receptor CXCR3 - the ligand for the lesionally overexpressed CXCL9 and CXCL10 chemokines - confirming the mechanistic link between genetic immune dysregulation, impaired regulatory surveillance, and the directed cytotoxic destruction of epidermal melanocytes that constitutes the terminal effector phase of vitiligo autoimmunity.

Vitiligo adaptive autoimmunity is architecturally determined by major histocompatibility complex-mediated melanocyte antigen hyperreactivity and quantifiably deficient regulatory T-lymphocyte suppressive capacity, together establishing a heritable immunological framework within which environmentally triggered oxidative stress precipitates irreversible antigen-specific autoreactive cascade and progressive depigmentation.

REFERENCE:

1. Abdullayev, A. S. (2025). COMPARISON OF AGE-RELATED CHARACTERISTICS OF CEPHALOMETRIC INDICATORS: FRONTAL CHORD (N–B) AND PARIETAL CHORD (B–L) IN ARTIFICIALLY DEFORMED AND NORMAL SKULLS. World of Medicine and Biology, 21(93), 147-151.

2. Davlatovich, A. D., & Mishra, S. (2025). THE PATHOGENETIC SIGNIFICANCE OF SKIN BARRIER DYSFUNCTION IN ATOPIC DERMATITIS. GLOBAL TRENDS IN SCIENCE AND INNOVATION, 2(1), 233-239.

3. Ашуров, Д. Д. (2025). ИНВАЗИВНЫЕ МЕТОДЫ ЛЕЧЕНИЯ ВИТИЛИГО. In International Conference on Modern Science and Scientific Studies (pp. 304-307).

4. Davlatovich, A. D. (2025). CLASSIFICATION OF TATTOOS AND TATTOO REMOVAL. Web of Medicine: Journal of Medicine. Practice and Nursing, 3(2), 431-434.

5. Kamoldinovich, X. D. (2024). Intravenous Adnimnstration of Contrast Agents and Its Characteristics. Miasto Przyszłości, 48, 119-31.

6. Xojiraxmatov, D. K. (2023). THE IMPORTANCE OF COMPUTED TOMOGRAPHY IN THE DIAGNOSIS OF URETEROLITHIASIS AND ITS COMPLICATIONS. Procedia of Engineering and Medical Sciences, 7(12), 31-34.

7. Makhmudov, N. I., Dekhkanov, K. M., Botiraliev, A. B., Mirzamatov, N. I., & Khozhirahmatov, D. K. (2023). Results the use of minimally invasive surgical methods for the treatment of patients with polytrauma in the Fergana branch of the Rncemp. In BIO Web of Conferences (Vol. 65, p. 05035). EDP Sciences.

8. Маматханова, Г. (2021). Оптимизация медицинской учетной документации и внедрение электронных систем в здравоохранение. Общество и инновации, 2(8/S), 61-67.

9. Исмаилов, С. И., & Маматханова, Г. М. (2022). Электронный документооборот как важнейший фактор повышения эффективности управления здравоохранением. Eurasian journal of medical and natural sciences, 2(8), 38-45.

10. Mamatxanova, G. M., & Ismailov, S. I. (2021). Optimization of medical records and implementation of electronic systems in healthcare. The American Journal of Medical Sciences and Pharmaceutical Research, 3(01), 193-198.

11. Маматханова, Г. М., & Ашурова, М. Д. (2020). КОМПЛЕКСНАЯ ОЦЕНКА ДЕЙСТВУЮЩЕЙ ЭЛЕКТРОННОЙ БАЗЫ ПЕРВИЧНЫХ УЧЕТНО-ОТЧЕТНЫХ МЕДИЦИНСКИХ ДОКУМЕНТАЦИЙ В УЧРЕЖДЕНИЯХ ПЕРВИЧНОГО ЗВЕНА ЗДРАВООХРАНЕНИЯ. Экономика и социум, (2 (69)), 506-512.

12. Sherali o‘g‘li, A. B., & Turdali o‘g, Y. L. A. (2025). CLINICAL COURSE AND LABORATORY DIAGNOSIS OF FUNGAL SKIN DISEASES. GLOBAL TRENDS IN SCIENCE AND INNOVATION, 2(1), 226-232.

13. Маматханова, Г. М., & Шерматова, Г. Т. (2021). Оптимизация медицинской учетной документации и автоматизация отчетностей.

14. Abduvaliyeva, F. T., Azizova, F. L., Akromov, D. A., & Sherkuziyeva, G. F. (2022). APPROVAL AND ECOLOGICAL-HYGIENIC ASPECTS OF WATER SUPPLY TO POPULATION POINTS.

15. Azizova, F. A. F. (2022). The role of local water sources in the centralized supply of drinking water to the population. British medical, 2(4), 175-180.

16. Ахмадалиев, Р. У., Турдиев, Ш. М., Абдувалиева, Ф. Т., & Саидова, С. А. (2020). ГИГИЕНИЧЕСКАЯ ОЦЕНКА УСЛОВИЙ ТРУДА И ОХРАНЫ ОКРУЖАЮЩЕЙ СРЕДЫ НА СТЕКЛОИЗГОТОВИТЕЛЬНЫХ ПРЕДПРИЯТИЯХ. Новый день в медицине, (4), 151-154.

17. Azizova, F. L., & Abduvaliyeva, F. T. (2021). Ecological and hygienic aspects of optimization of water supply of the population. The American journal of medical sciences and pharmaceutical research, 3, 48-53.

18. Pattoyevich, G. A. (2025). IRON DEFICIENCY ANEMIA IN CHILDREN: EARLY DIAGNOSIS AND MODERN TREATMENT APPROACHES. Web of Medicine: Journal of Medicine. Practice and Nursing, 3(5), 494-501.

19. Pattoyevich, G. A., & Nilufar, M. (2026). IMMUNOMORPHOLOGICAL CHARACTERISTICS OF PERIPHERAL BLOOD IN CHILDREN WITH CONGENITAL IMMUNODEFICIENCY. FRONTIERS OF KNOWLEDGE AND INTERDISCIPLINARY DISCOVERY, 2(1), 90-96.

20. Pattoyevich, G. A. (2025). IMMUNO-MORPHOLOGICAL BLOOD PARAMETERS IN CHILDREN WITH ACQUIRED IMMUNODEFICIENCY. GLOBAL TRENDS IN SCIENCE AND INNOVATION, 2(1), 255-261.

21. Asqarov, I., & Abdujabborova, C. (2025). ANALYSIS OF THE BIOLOGICAL ACTIVITY OF THE FOOD ADDITIVE" AS LUPINUS". Scientific journal of the Fergana State University, (2), 195-195.

22. Абдужабборова, Ч. С. (2024). ИСПОЛЬЗОВАНИЕ ЛЮПИНА В НАРОДНОЙ МЕДИЦИНЕ И РЕЦЕПТАХ.“Fizikaviy va kolloid kimyo fanlarining fundamental va amaliy muammolari hamda ularning innovatsion yechimlari” Xalqaro ilmiy-amaliy anjuman.

23. ABDUJABBOROVA, C. (2024). O'TKIR ZAHARLILIGINI ANIQLASH" LUPINUS AS. UNIVERSAL Учредители: Ilm Fan Fidoiylari Mchj, 1(9), 151-157.

24. Mamatqulova, S. A., & Abdujabborova, C. S. qizi.(2024). LYUPIN O‘SIMLIGI KIMYOVIY TARKIBI VA XALK TABOBATIDA QO‘LLANILISHI. Educational research in universal sciences, 3(3), 73-79.

25. Mukhtarjanovna, I. G. (2023). Developing the Principles of Studying and Treatment of Vaginal Dysbiosis During Pregnancy. Texas Journal of Medical Science, 16, 67-68.

26. Mukhtarzhanovna, I. G. (2024). Development of Principles of Study and Treatment of Vaginal Dysbiosis During Pregnancy. In International Congress on Biological, Physical And Chemical Studies (ITALY) (pp. 112-115).

27. G’aniyevna, J. B. (2025). OREGANO-AS. In OZIQ-OVQAT QO’SHILMASI TARKIBIDAGI FARMAKO-TOKSIKOLOGIK XUSUSIYATLARINI ORGANISH. In International Educators Conference (pp. 208-214).

28. Jumanova, B. (2023). CHEMICAL COMPOSITION OF THE MARMARAK MEDICINAL PLANT (SALVIA OFFICINALIS) AND USE

IN PEOPLE'S MEDICINE. B ACADEMIC RESEARCH IN MODERN SCIENCE (Т. 2, Выпуск 26, сс. 158–162). Zenodo.

29. Jumanova, B. G. (2025). CLINICAL EFFECTIVENESS OF THE DIETARY SUPPLEMENT OREGANO AS IN INFLAMMATORY DISEASES OF THE ORAL CAVITY. Advances in Science and Environment, 1(12), 12-14.

30. Sattievna, D. G. (2024). FARG'ONA VILOYATIDA REPRODUKTIV YOSHDAGI AYOLLARNI KONTRASEPTIV VOSITALARNI QO'LLASH USULLARI HAQIDAGI XABARDORLIK DARAJASINI O'RGANISH. Лучшие интеллектуальные исследования, 14(2), 239-243.

31. Йулдошева, Д. С., Ёкубов, Ф. Ф., & Рахматов, С. А. (2024). СОВРЕМЕННЫЕ КЛИНИКО-ЭПИДЕМИОЛОГИЧЕСКИЕ ОСОБЕННОСТИ МИКРОСПОРИИ И ТРИХОФИТИИ. IMRAS, 7(1), 689-693.

32. Kumar, S. (2025). PATHOPHYSIOLOGICAL BASIS OF AUTOIMMUNE PROCESSES IN VITILIGO. GLOBAL TRENDS IN SCIENCE AND INNOVATION, 2(1), 315-322.

33. Sobirjonova, G. (2022). FORECASTING OF AGRICULTURAL PRODUCTS INCLUDED IN THE CONSUMER BASKET. Science and innovation, 1(A7), 839-841.

34. Shakhzodakhon, S. (2025). OCCUPATIONAL ALLERGIES: RISK FACTORS, DIAGNOSIS, AND DEVELOPMENT OF PREVENTIVE MEASURES. In Scientific Conference on Multidisciplinary Studies (pp. 275-281).