

Bölüm 9

İMMÜNOHİSTOLOJİ VE İMMÜNOPATOLOJİ

Sena YÜKSEL¹

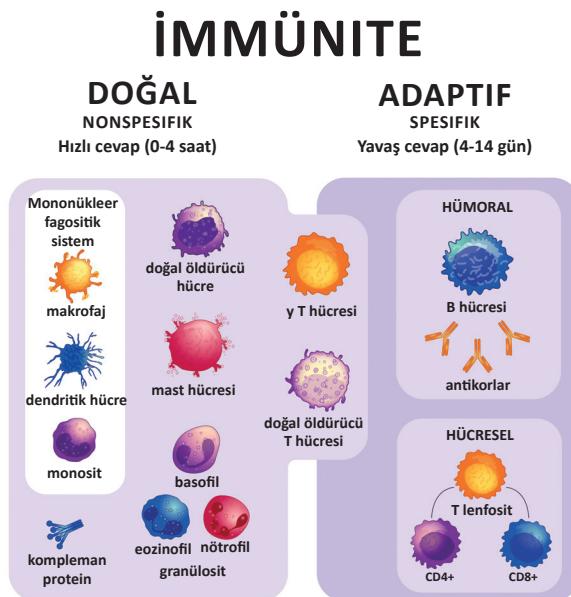
Mehmet Emin ÖNGER²

İMMÜN SİSTEM TANIMI

Bağışıklık sistemi, dış ortamda bulunan bakteriler, virusler, mantarlar ve parazitler dahil olmak üzere hastalığa yol açabilen ajanlardan ve diğer zararlı saldırılardan vücutu koruyan önemli bir savunma sistemidir. Bağışıklık sisteminden sorumlu hücreler ve proteinler, bağışıklık sistemini oluşturur ve yabancı organizmalara karşı düzenledikleri tepki, bağışıklık tepkisi olarak bilinir. Bu savunma sistemi, bağışıklık tepkisine göre iki genel işlevsel bölüme ayrılır; doğuştan gelen bağışıklık sistemi ve edinilmiş (spesifik veya adaptif) bağışıklık sistemi. Bu iki sistem, reaksiyon hızı, efektör hücre tipleri ve farklı patojenik organizma sınıflarının özgüllüğünü bakımından farklılık gösterir. Doğuştan gelen bağışıklık sistemi, potansiyel olarak zararlı ajana spesifik olmayan yanında bir yanıt verir ve yanıtını ezberleyemekten adaptif bağışıklık sistemi spesifik gecikmeli bir yanıt verir ve immünolojik hafızayı korur. Doğuştan gelen bağışıklık sistemi potansiyel olarak spesifik olmayan ancak bağışıklık sisteminin yanında savunmasını sağlayan nötrofiller, monositler, makrofajlar, kompleman, sitokinler ve akut faz proteinleri kapsar. Doğuştan gelen tepki hızlıdır, ancak bazen normal dokulara zarar verir. Adaptif bağışıklık sistemi, spesifik, gecikmeli bir yanıt verir. Bu yanıt, T lenfositler ve B lenfositler yoluyla antijene özgü reaksiyonlarından oluşur ve immünolojik hafızayı korur. Doğuştan gelen bağı-

¹ Ondokuz Mayıs Üniversitesi, Lisansüstü Eğitim Enstitüsü, Sinirbilimleri AD, Samsun.

² Doç. Dr., Ondokuz Mayıs Üniversitesi, Tıp Fakültesi, Histoloji ve Embriyoloji AD,
mehmetemin.onger@omu.edu.tr



Şekil 3: Bağışıklık sistemi hücreleri

Sekonder İmmun Yetmezlikler

Sekonder immün yetmezlikler, bağışıklık sistemi hücrelerini etkileyen genetik kusurların neden olduğu, immün hücre sayımlarında ve fonksiyonundaki kayıplarıdır. Sekonder immün yetersizlikler, altta yatan heterojen hastalıklar veya immün baskılıyıcı tedavinin bir sonucu olarak gelişir. Örneğin; enfeksiyöz ajanlar, ilaçlar, metabolik hastalıklar ve çevresel koşullar normal bir bağışıklık sistemini etkileyebilir. Bu bağışıklık eksiklikleri, komplikasyonları ve enfeksiyonların oluşması artan sıklığı ile kendini gösterir.

KAYNAKLAR

- Agarwal, S., Mayer, L. (2013). Diagnosis and treatment of gastrointestinal disorders in patients with primary immunodeficiency. *Clin Gastroenterol Hepatol.* 11(9):1050-63.
- Alsaleh, N.B., Brown, J.M. (2020). Engineered Nanomaterials and Type I Allergic Hypersensitivity Reactions. *Front Immunol.* 11:222.
- Arambula, A., Brown, J.R., Neff, L. (2021). Anatomy and physiology of the palatine tonsils, adenoids, and lingual tonsils. *World J Otorhinolaryngol Head Neck Surg.* 7(3):155-160.
- Ashorobi, D., Fernandez, R. (2022). Asplenia. In: StatPearls. Treasure Island (FL): StatPearls Publishing.
- Axisa, P.P., Hafler, D.A. (2016). Multiple sclerosis: genetics, biomarkers, treatments. *Curr Opin Neurol.* 29(3):345-53.

- Ballow, M., Sánchez-Ramón, S., Walter, J.E. (2022). Secondary Immune Deficiency and Primary Immune Deficiency Crossovers: Hematological Malignancies and Autoimmune Diseases. *Front Immunol.* 18;13:928062.
- Barcellini, W., Fattizzo, B. (2020). The Changing Landscape of Autoimmune Hemolytic Anemia. *Front Immunol* 11:946.
- Beales, I.L. (1994). An acquired-pseudo Bernard Soulier syndrome occurring with autoimmune chronic active hepatitis and anti-cardiolipin antibody. *Postgrad Med J.* 70(822):305-8.
- Binks, S., Vincent, A., Palace, J. (2016). Myasthenia gravis: a clinical-immunological update. *J Neurol.* 263(4):826-34.
- Bluestone, J.A., Herold, K., Eisenbarth, G. (2010). Genetics, pathogenesis and clinical interventions in type 1 diabetes. *Nature.* 464(7293):1293-300.
- Bowers, I., Shermetaro, C. (2022). Adenoiditis. In: StatPearls. Treasure Island (FL): StatPearls Publishing.
- Bruss, D.M., Ely, S. (2022). Anatomy, Head and Neck, Blood Thymus Barrier. In: StatPearls. Treasure Island (FL): StatPearls Publishing.
- Bujoreanu, I., Gupta, V. (2022). Anatomy, Lymph Nodes. In: StatPearls. Treasure Island (FL): StatPearls Publishing.
- Calder, P. (2013). Feeding the immune system. *Proceedings of the Nutrition Society,* 72(3), 299-309.
- Carrasco, A., Sjölander, I., Van, Acker, A., Dernstedt, A., Fehrm, J., Forsell, M., Friberg, D., Mjösberg, J., Rao, A. (2021). The Tonsil Lymphocyte Landscape in Pediatric Tonsil Hyperplasia and Obstructive Sleep Apnea. *Front Immunol.* 12:674080.
- Cavalcoli, F., Zilli, A., Conte, D., Massironi, S. (2017). Micronutrient deficiencies in patients with chronic atrophic autoimmune gastritis: A review. *World J Gastroenterol.* 23(4):563-572.
- Chang, H.D., Radbruch, A. (2021). Maintenance of quiescent immune memory in the bone marrow. *Eur. J. Immunol.*, 51: 1592-1601.
- Chapman, J., Goyal, A., Azevedo, A.M. (2022). Splenomegaly. In: StatPearls. Treasure Island (FL): StatPearls Publishing.
- Chinen, J., Shearer, W.T. (2010). Secondary immunodeficiencies, including HIV infection. *J Allergy Clin Immunol.* 125(2 Suppl 2):S195-203.
- Chung, W.S., Chung, S., Hsu, C.Y., Lin, C.L. (2021). Risk of Inflammatory Bowel Disease Following Appendectomy in Adulthood. *Front Med (Lausanne).* 8:661752.
- Corr, S.C., Gahan, C.C. Hill, C. (2008), M-cells: origin, morphology and role in mucosal immunity and microbial pathogenesis. *FEMS Immunology & Medical Microbiology,* 52: 2-12.
- Csaba, G. (2018). *Immunity and longevity. Acta Microbiologica et Immunologica Hungarica,* 1–17.
- DeVrieze, B.W., Hurley, J.A. (2022). Goodpasture Syndrome. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.
- Eibl, M.M., Wolf, H.M. (2015). Vaccination in patients with primary immune deficiency, secondary immune deficiency and autoimmunity with immune regulatory abnormalities. *Immunotherapy.* 7(12):1273-92.
- Elmore, S.A. (2006). Histopathology of the lymph nodes. *Toxicol Pathol.* 34(5):425-54.
- Flament, T., Bigot, A., Chaigne, B., Henique, H., Diot, E., Marchand-Adam, S. (2016). Pulmonary manifestations of Sjögren's syndrome. *Eur Respir Rev.* 25(140):110-23.
- Garg, N., Smith, T.W. (2015). An update on immunopathogenesis, diagnosis, and treatment of multiple sclerosis. *Brain Behav.* 5(9):e00362.
- Gernsheimer, T. (2009). Chronic Idiopathic Thrombocytopenic Purpura: Mechanisms of Pathogenesis, *The Oncologist,* 14(1);12–21.
- Gillespie, K.M. (2006). Type 1 diabetes: pathogenesis and prevention. *CMAJ.* 175(2):165-70.
- Gong, B., Wang, C., Meng, F., Wang, H., Song, B., Yang, Y., Shan, Z. (2021). Association Between Gut Microbiota and Autoimmune Thyroid Disease: A Systematic Review and Meta-Analysis. *Front Endocrinol (Lausanne).* 12:774362.

- Guan, Q. (2019). A Comprehensive Review and Update on the Pathogenesis of Inflammatory Bowel Disease. *J Immunol Res.* 2019:7247238.
- Hellmark, T., Segelmark, M. (2014). Diagnosis and classification of Goodpasture's disease (anti-tGBM), *Journal of Autoimmunity*, 108-112.
- Hemm, F., Fijak, M., Belikan, J., Kampschulte, M., El Khassawna, T., Pilatz, A., Heiss, C., Lips, K.S. (2021). Bone Status in a Mouse Model of Experimental Autoimmune-Orchitis. *Int J Mol Sci.* 22(15):7858.
- Hijazi, L.S., Zahra, F., Yarrarapu, S.N.S., et al. (2022). Functional Asplenism. In: StatPearls. Treasure Island (FL): StatPearls Publishing.
- Hill, A., Hill, Q.A. (2018). Autoimmune hemolytic anemia. *Hematology Am Soc Hematol Educ Program* 382-389.
- Hočević, A., Tomšić, M., Perdan Pirkmajer, K. (2021). Clinical Approach to Diagnosis and Therapy of Polyarteritis Nodosa. *Curr Rheumatol Rep.* 23(3):14.
- Hohenester, S., Oude-Elferink, R.P., Beuers, U. (2009). Primary biliary cirrhosis. *Semin Immunopathol.* 31(3):283-307.
- Illescas-Montes, R., Corona-Castro, C.C., Melguizo-Rodríguez, L., Ruiz, C., Costela-Ruiz, V.J. (2019). Infectious processes and systemic lupus erythematosus. *Immunology.* 158(3):153-160.
- Jarazo Dietrich, S., Fass, M.I., Jacobo, P.V., Sobarzo, C.M., Lustig, L., Theas, M.S. (2015). Inhibition of NOS-NO System Prevents Autoimmune Orchitis Development in Rats: Relevance of NO Released by Testicular Macrophages in Germ Cell Apoptosis and Testosterone Secretion. *PLoS One.* 10(6):e0128709.
- Jović, M., Avramović, V., Vlahović, P., Savić, V., Veličkov, A., Petrović, V. (2015). Ultrastructure of the human palatine tonsil and its functional significance. *Rom J Morphol Embryol.* 56(2):371-7.
- Kalfa, T.A. (2016). Warm antibody autoimmune hemolytic anemia. *Hematology Am Soc Hematol Educ Program.* 690-697.
- Kanegane, H., Hoshino, A., Okano, T., Yasumi, T., Wada, T., Takada, H., et al. (2018). Flow cytometry-based diagnosis of primary immunodeficiency diseases. *Allergology International.* 67(1):43-54.
- Killinger, B., Labrie, V. (2019). The Appendix in Parkinson's Disease: From Vestigial Remnant to Vital Organ? *J Parkinsons Dis.* 9(s2):S345-S358.
- Kim, D. (2017). The Role of Vitamin D in Thyroid Diseases. *Int J Mol Sci.* 18(9):1949.
- Klineova, S., Lublin, F.D. (2018). Clinical Course of Multiple Sclerosis. *Cold Spring Harb Perspect Med.* 8(9):a028928.
- Kobayashi, N., Takahashi, D., Takano, S., Kimura, S., Hase, K. (2019). The Roles of Peyer's Patches and Microfold Cells in the Gut Immune System: Relevance to Autoimmune Diseases. *Front Immunol.*
- Kraus, R.F., Gruber, M.A. (2021). Neutrophils-From Bone Marrow to First-Line Defense of the Innate Immune System. *Front Immunol.* 12:767175.
- Lee, H.J., Li, C.W., Hammerstad, S.S., Stefan, M., Tomer, Y. (2015). Immunogenetics of autoimmune thyroid diseases: A comprehensive review. *J Autoimmun.* 64:82-90.
- Lenz, H.J. (2007). Management and Preparedness for Infusion and Hypersensitivity Reactions. *The Oncologist.* 12(5):601–609.
- Levy, D.M., Kamphuis, S. (2012). Systemic lupus erythematosus in children and adolescents. *Pediatr Clin North Am.* 59(2):345-64.
- Lin, Y.J., Anzaghe, M., Schülke, S. (2020). Update on the Pathomechanism, Diagnosis, and Treatment Options for Rheumatoid Arthritis. *Cells.* 9(4):880.
- Lobo-Yeo, A., Mieli-Vergani, G., Mowat, A.P., Vergani, D. (1990). Soluble interleukin 2 receptors in autoimmune chronic active hepatitis. *Gut.* 31(6):690-3.
- Lucas, D. (2021). Structural organization of the bone marrow and its role in hematopoiesis. *Curr Opin Hematol.* 28(1):36-42.

- McComb, S., Thiriot, A., Akache, B., Krishnan, L., & Stark, F. (2019). *Introduction to the Immune System. Immunoproteomics*, 1–24.
- Minalyan, A., Benhammou, J.N., Artashesyan, A., Lewis, M.S., Pisegna, J.R. (2017). Autoimmune atrophic gastritis: current perspectives. *Clin Exp Gastroenterol.* 10:19-27.
- Mitroulis, I., Hajishengallis, G., Chavakis, T. (2021). Trained Immunity and Cardiometabolic Disease: The Role of Bone Marrow. *Arterioscler Thromb Vasc Biol.* 41(1):48-54.
- Müller, L., Di Benedetto, S., & Pawelec, G. (2019). *The Immune System and Its Dysregulation with Aging. Methods in Molecular Biology*, 21–43.
- Nguyen, D.L., Juran, B.D., Lazaridis, K.N. (2010). Primary biliary cirrhosis. *Best Pract Res Clin Gastroenterol.* 24(5):647-54.
- Null, M., Agarwal, M. (2022). Anatomy, Lymphatic System. In: StatPearls. Treasure Island (FL): StatPearls Publishing.
- Ortona, E., Pierdominici, M., Maselli, A., et al. (2016). Sex-based differences in autoimmune diseases. *Ann Ist Super Sanita.* 52(2): 205-212.
- Passali, M., Josefson, K., Frederiksen, J.L., Antvorskov, J.C. (2020). Current Evidence on the Efficacy of Gluten-Free Diets in Multiple Sclerosis, Psoriasis, Type 1 Diabetes and Autoimmune Thyroid Diseases. *Nutrients.* 12(8):2316.
- Puéchal, X. (2022). Polyarteritis Nodosus: State of the art. *Joint Bone Spine.* 89(4):105320.
- Radu, A.F., Bungau, S.G. (2011). Management of Rheumatoid Arthritis: An Overview. *Cells.* 10(11):2857.
- Rajan, T.V. (2003). The Gell-Coombs classification of hypersensitivity reactions: a re-interpretation. *Trends Immunol.* 24(7):376-9.
- Raje, N., Dinakar, C. (2015). Overview of Immunodeficiency Disorders. *Immunol Allergy Clin North Am.* 35(4):599-623.
- Rajesh, R., Shanmugam, M.P., Sagar, P. (2020). Idiopathic thrombocytopenic purpura and its fundus features in a patient with diabetes mellitus. *Indian J Ophthalmol.* 68(11):2587-2589.
- Reshetnyak, V.I. (2015). Primary biliary cirrhosis: Clinical and laboratory criteria for its diagnosis. *World J Gastroenterol.* 21(25):7683-708.
- Rodriguez-Castro, K.I., Franceschi M, Miraglia C, Russo M, Nouvenne A, Leandro G, Meschi T, De' Angelis, G,L, Di Mario, F. (2018). Autoimmune diseases in autoimmune atrophic gastritis. *Acta Biomed.* 89(8-S):100-103.
- Rosendahl, A-H, Schönborn, K, Krieg, T. (2022). Pathophysiology of systemic sclerosis (scleroderma). *Kaohsiung J Med Sci.* 38: 187– 195.
- Schirmer, J.H., Moosig, F. (2018). Update: Polyarteritis nodosa. *Z Rheumatol.* 77(5):397-408.
- Seyedian, S.S., Nokhostin, F., Malamir, M.D. (2019). A review of the diagnosis, prevention, and treatment methods of inflammatory bowel disease. *J Med Life.* 12(2):113-122.
- Shah, A.A., Wigley, F.M. (2013). My approach to the treatment of scleroderma. *Mayo Clin Proc.* 88(4):377-93.
- Sieb, J.P. (2014). Myasthenia gravis: an update for the clinician. *Clin Exp Immunol.* 175(3):408-18.
- Songu, M., Katılmış, H. (2012). Enfeksiyondan korunma ve immün sistem. Katip Çelebi Üniversitesi, Atatürk Eğitim ve Araştırma Hastanesi, Kulak Burun Boğaz Hastalıkları Kliniği, İzmir. 2(1):31-42.
- Stefanski, A.L., Tomiak, C., Pleyer, U., Dietrich, T., Burmester, G.R., Dörner, T. (2017). The Diagnosis and Treatment of Sjögren's Syndrome. *Dtsch Arztbl Int.* 114(20):354-361.
- Suresh, P.S. (2016). Bilateral disciform keratitis in Reiter's syndrome. *Indian J Ophthalmol.* 64(9):685-687.
- Thapa, P., Farber, D.L. (2019). The Role of the Thymus in the Immune Response. *Thorac Surg Clin.* 29(2):123-131.
- Tian, Y., Yang, H., Liu, N., Li, Y., Chen, J. (2021). Advances in Pathogenesis of Sjögren's Syndrome. *J Immunol Res.*
- Tomar, N., & De, R.K. (2014). A Brief Outline of the Immune System. *Immunoinformatics*, 3–12.

- Vaxman, I., Gertz, M. (2020). When to Suspect a Diagnosis of Amyloidosis
Acta Haematol. 143:304-31110.
- Wang, S., Breskovska, I., Gandhy, S., Punga, A.R., Guptill, J.T., Kaminski, H.J. (2018). Advances in autoimmune myasthenia gravis management. Expert Rev Neurother. 18(7):573-588.
- Wang, Z., Sun, Y., Yao, W., Ba, Q., Wang, H. (2021). Effects of Cadmium Exposure on the Immune System and Immunoregulation. Front. Immunol. 12:695484.
- Wasserman, A.M. (2011). Diagnosis and management of rheumatoid arthritis. Am Fam Physician. 84(11):1245-52.
- Wasserstein, A.G. (1997). Membranous glomerulonephritis. JF- Journal of the American Society of Nephrology. 8(4):664-674.
- Wright, M.F.A., Bush, A., Carr, S.B. (2018). Hypersensitivity reactions to intravenous antibiotics in cystic fibrosis. Paediatric Respiratory Reviews. 27:9-12.
- Xie, X., Wang, N., Xiang, J., He, H., Wang, X., Wang, Y. (2020). Renal cell carcinoma associated with idiopathic thrombocytopenic purpura. Int J Immunopathol Pharmacol.
- Yates, J.A., Stetz, L.C. (2006). Reiter's syndrome (reactive arthritis) and travelers' diarrhea. J Travel Med. 13(1):54-6.
- Yu, H., Nagafuchi, Y., Fujio, K. (2021). Clinical and Immunological Biomarkers for Systemic Lupus Erythematosus. Biomolecules. 11(7):928.
- Zhang, Y.Z., Li, Y.Y. (2014). Inflammatory bowel disease: pathogenesis. World J Gastroenterol. 20(1):91-9.