# Chapter 1

## AN OVERVIEW THE BLOOD HISTOLOGY AND CHRONIC MYELOID LEUKEMIA ASSOCIATED WITH DNA REPAIR GENE POLYMORPHISMS

### Pinar KOROGLU<sup>1</sup>, Nevra ALKANLI<sup>2</sup>

#### Introduction

Blood plays a key role in the fulfillment of many important functions in the body. Blood histology is a special area of histology where many biological parameters are physiologically modified. The disruption of the blood cells that make up the cellular part of the blood stems from problems regarding cells known as red blood cells, white blood cells and thrombocytes. These special blood cells are produced according to the needs of the body, and when the control mechanisms of the blood cells deteriorate, it is possible for the cells to grow to an extreme extent, and as a result blood diseases can occur. Knowing the blood histology is important for easier understanding of blood diseases. Hematology is a discipline that examining the blood diseases such as thrombocytopenia, anemia, lymphoma, multiple myeloma (Engert et al., 2016).

Leukemia from blood diseases is a disease characterized by neoplastic proliferation of various cell types such as granulocyte, monocyte, lymphocyte. Chronic myeloid leukemia (CML), a type of leukemia, is a myeloproliferative neoplasm and is characterized by the Philadelphia chromosome (Ph) (Pockharel, 2012; Jabbour & Kantarjian, 2012).

Common genetic polymorphisms in DNA repair genes that are thought to play an important role in the development of CML can affect protein function and DNA damage capacity. As a result, genetic instability and leukogenogenesis can occur. These polymorphisms, which reduce the kinetics of the DNA repair mechanism, are associated with cancer susceptibility, such as leukemia (Mohrenweiser, Wilson & Jones, 2003).

Identification of genetic polymorphisms that play an important role in the development of CML, one of the leukemia varieties, is important for our knowledgement of the mechanism of CML disease. Determining the relationships between genetic polymorphisms of DNA repair genes that are thought to play a role in disease mech-

<sup>&</sup>lt;sup>1</sup>Assist. Prof. Dr, Halic University, Faculty of Medicine, Department of Histology and Embryology, Istanbul, Turkey, pinarkoroglu@halic.edu.tr

<sup>&</sup>lt;sup>2</sup>Assist. Prof. Dr, Halic University, Faculty of Medicine, Department of Biophysic, Istanbul, Turkey, nevraalkanli@halic.edu.tr

#### Health Sciences Internal Sciences

with eosin. In addition to erythrocytes, leukocytes are visible which are subdivided into two groups; granulocytes and agranulocytes. Granulocytes are neutrophils, eosinophils and basophiles. Neutrophils have several lobulated nuclei and fine pink granules in their cytoplasm. Eosinophils can be identified with their cytoplasms that are full of distinct, large, eosinophilic (bright pink) granules. The nuclei of eosinophils typically is bilobed. The basophils are few in number. They contain nuclei which is not markedly lobulated and stained pale basophilic. Monocytes are the largest leukocytes. Their nuclei are usually horseshoe-shaped. Lymphocytes have few or no cytoplasmic granules and exhibit darkly stained round nuclei. Several tiny platelets are visible in the blood smear.

A blood cell disorder is the consequences of a problem with your red blood cells, white blood cells, or the smaller circulating cells called platelets, which are critical for clot formation. Leukemia, thrombocytopenia and anemia important blood diseases. Hematology is related with lymphoma, multiple myeloma, acute and chronic leukemia and similar disorders; bone marrow, lymphatic system and blood-related diseases. A large proportion of hematologic diseases have vital importance. Knowing blood tissue histology is very crucial for all hematologic diseases. In this chapter, general information about CML has been given from diseases that arise as a result of disorders that occurring in the cellular components of the blood, based on histology of blood tissue. An examination of genetic polymorphisms that play an important role in the development of CML blood disease will be crucial in order to have knowledge about the mechanisms that may lead to the disease and to use this information to develop new treatments for the disease.

#### References

Aburakawa, S. Kasai, K., Nakamura, T. Takami, H. (2017). UDP/P2Y6 receptor signaling regulates IgE-dependent degranulation in human basophils. *Allergology International*, *66*, 574–580.

Adewoyin, A.S. & Nwogoh, B. (2014) Peripheral blood film-a review. *Annals of Ibadan Postgraduate Medicine*, *12* (2), 71-79.

Altundag M.E. (2016). Kronik Myeloid Lösemi Hücrelerinde (K562) Apoptotik Süreç ve Reaktif Oksijen Türleri Arasındaki İlişkinin Araştırılması (Tez). Marmara Üniversitesi.

Annamaneni S. & et al. (2013). Association of XRCC1 gene polymorphisms with chronic myeloid leukemia in the population of Andhra Pradesh, India. *Hematology*, *18* (3), 163–168.

Awad, A. & et al. (2014). Natural killer cells induce eosinophil activation and apoptosis. *PLoS One*, 11, 9 (4):e94492. Doi: 10.1371/journal. pone.0094492. eCollection 2014.

Babiker HM, & Proytcheva M. (2014). Basophilic blast phase of chronic myelogenous leukemia. *Blood*, 15:124-2464.

Babitt, J.L. & Lin, H.Y. (2012). Mechanisms of anemia in CKD. Journals of the American Society of Nephrology, 23(10), 1631–1634.

Balderman, S. & Lichtman, M.A. (2011). A history of the discovery of random x chromosome inactivation in the human female and its significance. *Rambam Maimonides Medical Journal*, 2(3), e0058-0086. Doi:10.5041/RMMJ.10058.

Ba`nescu C. & et al. (2014). XRCC1 Arg194Trp and Arg399Gln polymorphisms are significantly associated with shorter survival in acute myeloid leukemia. *Leukemia and Lymphoma*, *55* (2), 365–370.

Ba`nescu C. & et al. (2014). Polymorphism of XRCC1, XRCC3, and XPD Genes and Risk of Chronic Myeloid Leukemia. *BioMed Research International*, 1-9. Doi: 10.1155/2014/213790.

Baron, M.H., Isern, J. & Fraser, S.T. (2012). The embryonic origins of erythropoiesis in mammals. *Blood*, *119* (21), 4828–4837.

Batar B. & et al. (2009). DNA repair gene XPD and XRCC1 polymorphisms and the risk of childhood acute lymphoblastic leukemia. *Leukemia Research*, *33* (6), 759–763.

Benhamou S., & Sarasin A., (2002). ERCC2/XPD gene polymorphisms and cancer risk. *Mutagenesis*, *17* (6), 463–469.

Braithwaite E., Wu X., & Wang Z. (1999). Repair of DNA lesions: mechanisms and relative repair efficiencies. *Mutation Research—Fundamental and Molecular Mechanisms of Mutagenesis*, 424 (1-2), 207–219.

Catana A. & et al. (2012). Genetic polymorphism of DNA repair gene ERCC2/XPD (Arg 156 Arg) (A22541C) and lung cancer risk in Northern Romania. *Revista Roma^na de Medicina de Laborator, 20* (2), 157–161.

Chan, Y.K. et al. (2010). Leukocyte nucleus segmentation and nucleus lobe counting. *Biomed Central Bioinformatics*, 11, 558-576.

Chasseriau J & et al. (2004). Characterization of the Different BCR-ABL Transcripts with a Single Multiplex RT-PCR. J Mol Diagn, 4: 343–347.

D'Andrea A. D. (2010). Targeting DNA repair pathways in AML. *Best Practice and Research: Clinical Haematology*, 23 (4), 469–473.

Deligezer U., Akisik E. E., & Dalay N. (2007). Lack of association of XRCC1 codon 399Gln polymorphism with chronic myeloge- nous leukemia. *Anticancer Research*, *27* (4), 2453–2456.

Diez-Silva, M. et al. (2010). Shape and biomechanical characteristics of human red blood cells in health and disease. *MRS Bull*, *35* (5), 382–388.

Dzierzak, E. & Philipsen, S. (2013). Erythropoiesis: development and differentiation. *Cold Spring Harb Perspectectives in Medicine*, *3*(4), 011601-011616. Doi: 10.1101/cshperspect. a011601.

Engert, A. & et al. (2006). EHA Roadmap for European Hematology Research The European Hematology Association Roadmap for European Hematology Research: a consensus document. *Haematologica*, *101*(2), 115-208. Doi: 10.3324/haematol.2015.136739.

Fogelson, A.L. & Neeves, K.B. (2015). Fluid mechanics of blood clot formation. *Annual Review of Fluid Mechanics*, 47, 377–403.

Foller, M., Huber S. M. & Lang, F. (2008). Erythrocyte programmed cell death. *IUBMB Life,60* (10), 661-668. Doi: 10.1002/iub.106.

Galanello, R. & Origa, R. (2010). Beta-thalassemia. Orphanet Journal of Rare Diseases, 5, 11. Doi: 0.1186/1750-1172-5-11.

García-Roa, M. & et al. (2017). Red blood cell storage time and transfusion: current practice, concerns and future perspectives. *Blood Transfusion*, *15*(3): 222–231. Doi: 10.2450/2017.0345-16.

Grundström, J. & et al. (2012). Human cord blood derived immature basophils show dual characteristics, expressing both basophil and eosinophil associated proteins. *PLoS One*, 7(10):e48308. Doi: 10.1371/ journal.pone.0048308-318.

Hung R. J. & et al. (2005). Genetic polymorphisms in the base excision repair pathway and cancer risk: a huge review. *The American Journal of Epidemiology*, *162* (10), 925–942.

Jabbour E. & Kantarjian H. (2012). Chronic myeloid leukemia: 2012 update on diagnosis, monitoring, and management. *The American Journal of Hematology*, 87 (11) 1037–1045.

Kosoff, R.E. & et al. (2015). Pak2 restrains endomitosis during megakaryopoiesis and alters cytoskeleton organization. *Blood*, *125*(19), 2995-3005. Doi: 10.1182/blood-2014-10-604504.

LaRosa, D.F & Orange, J.S. (2008). Lymphocytes. *Journal of Allergy and Clinical Immunology*, 121, 364-369.

Lindahl T. & Wood R. D. (1999). Quality control by DNA repair. Science, 286 (5446), 1897–1905.

Medvinsky, A. Rybtsov, S. & Taoudi, S. (2011). Embryonic origin of the adult hematopoietic system: advances and questions. *Development*, 138, 1017-1031 Doi:10.1242/dev.040998.

Mitra A. K. & et al. (2009). Statistically significant association of the single nucleotide polymorphism (SNP) rs13181 (ERCC2) with predisposition to squamous cell carcinomas of the head and neck (SCCHN) and breast cancer in the north Indian population. *Journal of Experimental and Clinical Cancer Research*, 28 (1), 104. Doi:10.1186/1756-9966-28-104.

Mohrenweiser H.W., Wilson D.M. &, Jones I.M. (2003). Challenges and complexities in estimating both the functional impact and the disease risk associated with the extensive genetic variation in human DNA repair genes. *Mutat Res*, 526:93–125.

Muller, W. A. (2013). Getting leukocytes to the site of inflammation. *Veterinary Pathology*, 50(1), 7–22.

Mutlu P. & et al. (2015). Identification of XRCC1 Arg399Gln and XRCC3 Thr241Met Polymorphisms in a Turkish Population and Their Association with the Risk of Chronic Lymphocytic Leukemia. *Indian J Hematol Blood Transfus*, *31*(3):332–338 Doi: 10.1007/s12288-014-0482-1.

Nahrendorf, M. & et al. (2007). The healing myocardium sequentially mobilizes two monocyte subsets with divergent and complementary functions. *Journal Experimental Medicine*, 204, 3037–3047.

Nicholson, L.B. (2016). The immune system. Essays Biochemical, 60 (3), 275–301.

Nikinmaa, M. (1997). Oxygen and carbon dioxide transport in vertebrate erythrocytes: an evolutionary change in the role of membrane transport. Journal of Experimental Biology, *200* (2), 369-380.

Pereira dos Santos J. & et al. (2016). Association of the XPD and XRCC3 gene polymorphisms with oral squamous cell carcinoma in a Northeastern Brazilian population: A pilot study. *Archives of Oral Biology*, 64:19–23. Doi: 10.1016/j.archoralbio.2015.12.004.

Pokharel M. (2012). Leukemia: A Review Article. IJARPB. 3:397-407.

Procopciuc L. M., & Osian G. (2014). Interaction between lifestyle factors and the XRCC1, XPD, and XRCC3 genetic variations modulates the risk for sporadic colorectal cancer. *Revista Roma*<sup>n</sup>*a*<sup>\*</sup> *de Medicina* <sup>\*</sup> *de Laborator*, *22* (1), 129–141.

Qinghai G. & et al. (2017). XRCC1 and XPD polymorphisms and their relation to the clinical course in hepatocarcinoma patients. *Oncology Letters*, 14:2783-2788, Doi: 10.3892/oI.2017.6522.

Repsold, L. & Joubert, A.M. (2018). Eryptosis: an erythrocyte's suicidal type of cell death. *BioMed Research International*, 9405617-9405627. Doi: 10.1155/2018/9405617. eCollection 2018.

Reinhart, R. & et al. (2018). BH3 mimetics efficiently induce apoptosis in mouse basophils and mast cells. *Cell Death Differentiation*, *25* (1), 204-216. Doi: 10.1038/cdd.2017.154. Epub 2017 Sep 29.

Rollinson S. & et al. (2007). RAD51 homologous recombination repair gene haplotypes and risk of acute myeloid leukaemia. *Leukemia Research*, *31* (2),169–174.

Ronen A. & Glickman B. W. (2001). Human DNA repair genes. *Environmental and Molecular Mutagenesis*, 37 (3), 241–283.

Saha, P. & Geissmann, F. (2011). Toward a functional characterization of blood monocytes, *Immunology Cell Biology*, 89, 2–4.

Sallmyr A., Fan J., & Rassool F. V. (2008). Genomic instability in myeloid malignancies: increased reactive oxygen species (ROS), DNA double strand breaks (DSBs) and error-prone repair. *Cancer Letters*, *270* (1), 1–9.

Sarkar, S. (2008). Artificial blood. Indian Journal of Critical Care Medicine, 12 (3), 140–144.

Selders, G.S. & et al. (2017). An overview of the role of neutrophils in innate immunity, inflammation and host-biomaterial integration. *Regenerative Biomaterial*, *4* (1), 55–68.

Tavian, M. & Peault, B. (2005) Embryonic development of the human hematopoietic system. *International Journal of Developmental Biology*, *49*, 243-250. Doi: 10.1387/ijdb.041957mt.

Wacleche, V.S. & et al. (2018). The Biology of monocytes and dendritic cells: contribution to HIV pathogenesis. *Viruses*, *10*(2). pii: E65. Doi: 10.3390/v10020065.

Yan Y. & et al. (2014). Association of XRCC3 Thr241Met polymorphisms and leukemia risk: evidence from a metaanalysis. *Leukemia and Lymphoma*, *55* (9), 2130-2134.