

Cancer Stem Cells as a Considerable Barrier in Anti-Cancer-Treatments

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Abstract

Today in mankind's modern society cancer is one of the heterogenous critical leading death causes in the world. Annually many victims of different types of cancer are being recorded throughout the world. Many researchers did many researches and experiments to find the causes and treatment for it. According to the reports it is estimated that more than 10 million deaths were recorded in 2020. One of the challenging studies in cancer research is to examine the role of cancer stem cells in this process and treatment. Cancer Stem Cells (CSCs) are a group of tumor cells that can possess tumor growth initiation and increase the bulk populations of non-tumorigenic cancer cell progeny through differentiation. Some of the particular characteristics give them the capability to be resistant to radio and chemotherapies.

This mini-review aims to investigate the recent researchers from 2019 to 2022 to get a better view of the function and specific options which can help to act as a barrier in the treatment process and examine good suggestions in order to get more success in the near future.

Keywords: Cancer stem cells; Barrier; Differentiation; Anti-cancer; Treatment.

Introduction

Cancer is a common and general term which points to a large group of disorders that can be effective in any part of the body. It consists of different types for instance breast cancer, lung cancer, pancreas, prostate, stomach, skin, etc [1]. Converting healthy cells to cancer cells needs a multi-stage group of

processes that help switch to the malignant tumor. Some helpful options for cancer stem cells include genetic instability, cell combining, their metabolic pathway, gene transition, and changes in the surrounding environment, which distinguish them from others [2]. Although clinical diagnosis and biological research has improved in recent years, according to global cancer statics,

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cancer frequency is different in various nations [3]. Every year, about 4,00,000 children develop cancer and more than 10 million victims are among adults. It is predicted that the number of victims will get to 29 million every year [4]. Many risk factors such as physical and chemical carcinogens, genetic background, tobacco use, unhealthy diet, and air pollution can be effective in increasing the probability of cancer occurrence in the population [5].

Cancer stem cells are capable of generating, differentiating, and DNA repairing in a faster way in comparison with other cells, the first identification was in myeloid leukemia. These options can turn the cancer stem cells into a big barrier and an acceptable response in the anti-cancer treatment cannot be achieved [6].

Despite of novel developments in medicine and biotechnology era, the results of experiments and studies are far from expectations. Many researchers tried to study the mechanisms of these types of cells to measure their sensitivity to various doses of radiation or medicines [7]. Estimating the frequency of tumor cells depends on the type of cells in solid tumors, number of CSCs is in the range of under 1% to more than 80% in lymphoblastic leukemia [8]. Many healthy cells may undergo some mutations and epigenetic transformations that help them to convert cancer cells [9]. By considering Wang's study which examined CSC's ligands it can be a reasonable model to describe the hierarchical manner in cancer studies. The differentiation can have two choices, first, it can be turned to tumor type by niche pathway. Second, it can turn to non-tumor cells [10]. One of the considerable points in

cancer cell studies is biological markers on the surface. CSCs do not have certain markers therefore their identification among healthy cells can be difficult and take a long time [11].

Some extrinsic and intrinsic reasons like the resource, character, markers and metabolic inflexibility might have a relation with their resistance [12]. Metastasis of these cells can improve the resistance and remain according to Lin, et al study CD133 can inhibit caspase 3 and 9 through heat shock 27 protein process [13].

Discussion

Through examining various studies and results could provide enough information for bolding the role of cancerous stem cells more than before. Considering some more studies can help getting better vision of this barrier. In 1964, Kleinsmith, et al primarily examined the linkage between stem cells and cancer. The results showed that there is a significant relationship between stem cells, cancer occurring, and spreading [14].

According to the Lagasse, et al study, genetic instability can be much more effective in cancer stem cell differentiation and proliferation [15]. Another study which was done by Lawrence, et al showed that in some situations gene fragments transferring can change the way of stem cells and turn them into cancer-type cells [16]. Cell fusion can have a positive role in metastasis and tumor movement to other parts of the body.

Environmental factors like alcohol drinking, smoking, miRNA, transcription factors, and immunological factors are other candidates for the risk of cancer occurrence [17]. CSCs have been proved to have

immunosuppressive effects on the T-cell type [18]. Genome-Wide Association Studies have revealed some surface antigens which can be a great development in distinguishing cancer cells and healthy types. One of the bold antigens in CSCs is CD133 which can be a key factor for distinguishing [19]. Several kinds of cancer have different antigens as a biomarker. Some of them have been pointed out in the following for instance CD34/CD38, and CD44/CD24, which decreases in blood after the tumor growth [20]. Lrg5 is examined as a suitable marker in colorectal cancer [21]. ROR1 as a receptor for Tyrosine kinase is another marker that can be identified in ovarian cancer [22]. $\alpha_2\beta_2$ integrin is another putative marker in prostate cancer. In Hepatocellular carcinoma, the expression of Toll-like receptor4 can be observed [23].

Hypoxia is another reason which improves cancer stem cell's resistance to treatment. Oxygen has potential role in cell respiratory metabolism and survival. HIF as an inducible factor act as a monitoring oxygen level in cells. It also can induce ROS, genotoxic effects and in following reduce transcriptional effects. HIF $_2\alpha$ is another factor which acts as a promoting growth in CSCs [24].

JAK/STAT signaling pathway plays a vital role in the transition of normal cells to cancer type. Many studies have shown the importance of STAT proteins distinctively helping to spread cancer cells [25]. In 2011, Peck's results revealed that dephosphorylation of STAT5 which is about the JAK/STAT pathway can be effective in breast cancer [26]. Another study in 2013 done by Mirit, et al showed on 562 patients the presence of STAT5 is related to prostate

cancer occurrence [27]. MEK/ERK pathway is responsible for the mitogenic activity and drug resistance. Jingyuan Li's observations illustrated that GTP γ S activation by MEK/ERK pathway can improve chemo resistance in CSCs [28]. Long non-coding RNAs as a new class of gene regulators are associated with proliferation, metastasis, and therapeutic resistance. Liu, et al revealed that their main functions have focused on being in signaling pathways, interacting with DNA and proteins, acting in gene transcription pathways to improve or inhibit some gene's transcription [29].

An accumulation of research throughout the world brings the consequence that combining all these results can be great prior pave in personalized medicine treatment and pharmacology industry in near future.

Conclusion

Several obstacles exist in the way of treatment and eliminating CSCs. Some novel achievements could improve the knowledge in this era. However, there are some ambiguities in the way of treatment. Therefore, further systematic clinical studies should be performed to get a better view of the character, functions, and resistance to chemo and radiotherapies. The lack of some inadequate schemes can be effective in spreading the knowledge and understanding of these types of cells. Improving Omics technology and NGS sequencing will be helpful in genome-editing, targeted medicine designing, earlier identifying and personalized treatments. Early detection can be useful in many cases and avoid raising the number of victims worldwide.

References

1. Arnold CR, Mangesius J, Skvortsova II, Ganswindt U. The Role of Cancer Stem Cells in Radiation Resistance. *Front Oncol.* 2020;10:164. [PubMed](#) | [CrossRef](#)
2. Yang L, Shi P, Zhao G, Xu J, Peng W, Zhang J, et al. Targeting Cancer Stem Cell Pathways for Cancer Therapy. *Signal Transduct Target Ther.* 2020;5(1):8. [PubMed](#) | [CrossRef](#)
3. Rycaj K, Tang DG. Cancer Stem Cells and Radioresistance. *Int J Radiat Biol.* 2014;90(8):615-21. [PubMed](#) | [CrossRef](#)
4. Jordan CT, Guzman ML, Noble M. Cancer Stem Cells. *N Engl J Med.* 2006;355(12):1253-61. [PubMed](#) | [CrossRef](#)
5. Huang J, Chan WC, Ngai CH, Lok V, Zhang L, Lucero-Prisno III DE, et al. Worldwide Burden, Risk Factors, and Temporal Trends of Ovarian Cancer: A Global Study. *Cancers (Basel).* 2022;14(9):2230. [PubMed](#) | [CrossRef](#)
6. Abad E, Graifer D, Lyakhovich A. DNA Damage Response and Resistance of Cancer Stem Cells. *Cancer Lett.* 2020;474:106-17. [PubMed](#) | [CrossRef](#)
7. Kumar R, Saha P. A Review on Artificial Intelligence and Machine Learning to Improve Cancer Management and Drug Discovery. *Int J Res Appl Sci Biotechnol.* 2022;9(3):149-56. [CrossRef](#)
8. He Y, Zhang L, Zhou R, Wang Y, Chen H. The Role of DNA Mismatch Repair in Immunotherapy of Human Cancer. *Int J Biol Sci.* 2022;18(7):2821. [PubMed](#) | [CrossRef](#)
9. Lee DJ, Hausler R, Le AN, Kelly G, Powers J, Ding J, et al. Association of Inherited Mutations in DNA Repair Genes with Localized Prostate Cancer. *Eur Urol.* 2022;81(6):559-67. [PubMed](#) | [CrossRef](#)
10. Yang CS, Wang X, Lu G, Picinich SC. Cancer Prevention by Tea: Animal Studies, Molecular Mechanisms and Human Relevance. *Nat Rev Cancer.* 2009;9(6):429-39. [PubMed](#) | [CrossRef](#)
11. Klonisch T, Wiechec E, Hombach-Klonisch S, Ande SR, Wesselborg S, Schulze-Osthoff K, et al. Cancer Stem Cell Markers in Common Cancers-Therapeutic Implications. *Trends Mol Med.* 2008;14(10):450-60. [PubMed](#) | [CrossRef](#)
12. Karsten U, Goletz S. What Makes Cancer Stem Cell Markers Different?. *Springerplus.* 2013;2(1):1-8. [PubMed](#) | [CrossRef](#)
13. Brooks SA, Lomax-Browne HJ, Carter TM, Kinch CE, Hall DM. Molecular Interactions in Cancer Cell Metastasis. *Acta Histochem.* 2010;112(1):3-25. [PubMed](#) | [CrossRef](#)
14. Kleinsmith LJ. Principles of Cancer Biology. Pearson Benjamin Cummings, San Francisco. 2006.
15. Francipane MG, Lagasse E. MTOR Pathway in Colorectal Cancer: An Update. *Oncotarget.* 2014;5(1):49. [PubMed](#) | [CrossRef](#)
16. Selvakumar P, Badgeley A, Murphy P, Anwar H, Sharma U, Lawrence K, et al. Flavonoids and Other Polyphenols Act as Epigenetic Modifiers in Breast Cancer. *Nutrients.* 2020;12(3):761. [PubMed](#) | [CrossRef](#)
17. Ercisli MF, Kahrizi D, Aziziaram Z. Environmental Factors Affecting the Risk of Breast Cancer and the Modulating Role of Vitamin D on this Malignancy. *Cent Asian J Environ Sci Tech Innov.* 2021;2(4):175-83. [CrossRef](#)
18. Milane LS. The Hallmarks of Cancer and Immunology. *Cancer Immunol Immunother.* 2022; 1-17. Academic Press. [CrossRef](#)
19. Liang B, Ding H, Huang L, Luo H, Zhu X. Gwas in Cancer: Progress and Challenges. *Mol Genet Genomics.* 2020;295:537-61. [PubMed](#) | [CrossRef](#)
20. Liou GY. CD133 as a Regulator of Cancer Metastasis Through the Cancer Stem Cells. *Int J Biochem Cell Biol.* 2019;106:1-7. [PubMed](#) | [CrossRef](#)
21. Daga S, Rosenberger A, Quehenberger F, Krisper N, Prietl B, Reinisch A, et al. High GPR56 Surface Expression Correlates with a Leukemic Stem Cell Gene Signature in CD34-Positive AML. *Cancer Med.* 2019;8(4):1771-8. [PubMed](#) | [CrossRef](#)
22. Zhao Y, Zhang D, Guo Y, Lu B, Zhao ZJ, Xu X, et al. Tyrosine Kinase ROR1 as a Target for Anti-Cancer Therapies. *Front Oncol.* 2021;11:680834. [PubMed](#) | [CrossRef](#)
23. Wallstabe L, Göttlich C, Nelke LC, Kühnemundt J, Schwarz T, Nerreter T, et al. ROR1-CAR T Cells are Effective Against Lung and Breast Cancer in Advanced Microphysiologic 3D Tumor Models. *JCI Insight.* 2019;4(18). [PubMed](#) | [CrossRef](#)

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24. Jing X, Yang F, Shao C, Wei K, Xie M, Shen H, et al. Role of Hypoxia in Cancer Therapy by Regulating the Tumor Microenvironment. *Mol Cancer*. 2019;18:1-5. [PubMed](#) | [CrossRef](#)
25. Owen KL, Brockwell NK, Parker BS. JAK-STAT Signaling: A Double-Edged Sword of Immune Regulation and Cancer Progression. *Cancers*. 2019;11(12):2002. [PubMed](#) | [CrossRef](#)
26. Queen MM, Ryan RE, Holzer RG, Keller-Peck CR, Jorcyk CL. Breast Cancer Cells Stimulate Neutrophils to Produce Oncostatin M: Potential Implications for Tumor Progression. *Cancer Res*. 2005;65(19):8896-904. [PubMed](#) | [CrossRef](#)
27. Fu H, Maunakea AK, Martin MM, Huang L, Zhang Y, Ryan M, et al. Methylation of Histone H3 on Lysine 79 Associates with a Group of Replication Origins and Helps Limit DNA Replication Once per Cell Cycle. *PLoS Genet*. 2013;9(7). [PubMed](#) | [CrossRef](#)
28. Yang S, Liu G. Targeting the Ras/Raf/MEK/ERK Pathway in Hepatocellular Carcinoma. *Oncol Lett*. 2017;13(3):1041-7. [PubMed](#) | [CrossRef](#)
29. Jiang MC, Ni JJ, Cui WY, Wang BY, Zhuo W. Emerging Roles of lncRNA in Cancer and Therapeutic Opportunities. *Am J Cancer Res*. 2019;9(7):1354. [PubMed](#)