The Continuous Relative Deficiency of Intracellular Potassium Is a Core Mechanism for the Occurrence and Metastasis of Tumor Cancer Cells

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Keywords: Potassium Ions, Relative Deficiency of Potassium Ions, Na+, K+-ATPase, Tumor Cancer Cells, Metastasis of Cancer Cells

Received: September 28, 2022  Accepted: November 7, 2022  Published: November 10, 2022

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ABSTRACT

The core mechanism for occurrence of tumor cancer cells is related to the continuous relative deficiency of potassium ions in the cells of organs and tissues, which results in embryonic like proliferation and differentiation in the affected cells. The purpose of the metastasis of cancer cells is to obtain and utilize the potassium resources in other organs in body. However, if the overall potassium storage in body is obviously insufficient, the metastatic cancer cells still fail to achieve the purpose of obtaining enough potassium and turn into normal cells, further proliferation and differentiation of cancer cells will continue, and finally will lead to functional decline in the organs and tissues affected or death. Therefore, the key means to prevent and treat tumors and cancers is to ensure the normal and balanced potassium ions in cells in various organs and tissues, so as to avoid the formation of tumors and cancer cells caused by obvious deficiency of potassium ions.

1. INTRODUCTION

In other recent papers, I have clarified the importance of the potassium/sodium (K+/Na+) ion system in realizing the functions of organs, tissues and tissue cells, as well as its important role in the natural non-specific immune mechanism [1], and I also analyzed the relationship between the relative deficiency of intracellular potassium and the functional changes and diseases in nervous and non-nervous systems [2, 3]. This article will discuss how the relative deficiency of intracellular potassium leads to the occurrence of tumor cancer cells and the mechanism for metastasis of cancer cells.

2. THE RELATIVE DEFICIENCY OF INTRACELLULAR POTASSIUM IONS IS RELATED TO CELL EXCESSIVE PROLIFERATION, TUMOR AND CARCINOGENESIS

Based on the discussion in the previous papers, I propose here that the core mechanism for the oc-
currence and formation of tumor cancer cell is caused by the continuous relative deficiency of potassium ions in organs and tissues.

There are many reasons for the relative deficiency of potassium ions, among which inadequate potassium obtained from diet may be the key one, which may be closely related to the reduction of potassium content in agricultural products and processed foods. The disordered or selected eating habits and inappropriate spread of so-called “healthy scientific knowledge” as well as the reduction of the absorption and utilization of potassium ions in the process of food digestion due to the functional changes in digestive system may also play a role. In addition, various endogenous and exogenous tumorigenic risk factors may accelerate the relative deficiency of intracellular potassium ions. The proliferating tumor cancer cells may compete to obtain potassium ions from extracellular fluid by increasing the number and activity of Na⁺, K⁺-ATPase on their cell membrane [4-14], and if such a process can supplement the deficiency of potassium, then the cells will stop proliferating and turn into normal state. However, if the potassium storage is insufficient overall in body, while the competitive process still cannot obtain enough potassium ions for the normal functions of cells, consequently, the cells will be accelerated to form cancer cells. In addition, some risk factors, such as the abnormal oxidative stress that can increase the production of reactive oxygen species (ROS) [15-18], may cause partial damage to the cell membrane, resulting in the weakening of the ability of cells to store potassium ions. Therefore, controlling the growth rate of tumor cancer cells and striving to transform them into normal cells is related to whether they can establish the same amount of intracellular potassium ions as the normal cells. However, such a transformation may be difficult in the aging process of organs and tissues. A series of physiological functions in body are reduced, leading to the inability to establish adequate storage of potassium ions in body, as a result, the insufficient potassium ions in organs and tissues will continue to present, and tumor cancer cells will occur irreversibly.

3. RELATIVE DEFICIENCY OF INTRACELLULAR POTASSIUM AND METASTASIS OF CANCER CELLS

The metastasis of cancer cells is an important factor that affects the function of the body and ultimately leads to the death of living body. There are different explanations for the mechanism of tumor cancer cell metastasis. Here, I propose that the purpose of tumor cancer cell metastasis is to obtain other non-in situ potassium ions, or it is a competitive cellular behavior to obtain potassium ions owned by other normal tissues. Fast-growing tumor cancer cells accompanied by the increased expression of Na⁺, K⁺-ATPase [19-33] lead to the huge consumption of potassium ions in situ tissues, while the potassium ions in blood circulation cannot support such a huge consumption, then it will lead to the death of fast-growing cancer cells if such a situation reaches a certain degree. The way to avoid the death of tumor cancer cells is to transfer through the blood and lymphatic system to meet the needs of tumor cancer cells for potassium ions. Tumor cancer cell metastasis usually tends to the organs and tissues, such as brain and lung, of which the potassium ion content is relatively higher. Some organs that also store relatively abundant potassium ions, such as heart and muscle tissue, are generally not conducive to tumor cancer cell metastasis because the cells in these organs and tissues have contractile function, which is not conducive to the stable growth of tumor cancer cells. The probability of tumor cancer cell metastasis is relatively low in some tissues, such as skin, which could contain a relatively less amount of potassium ions.

4. PREVENTION AND TREATMENT STRATEGIES FOR TUMORS AND CANCERS

Based on such discussions, the reason for tumor growth and carcinomatosis may be mainly due to the continuous relative deficiency of potassium in tissue cells, whereas other factors only strengthen the role. The core reason is the continuous shortage of the overall potassium ions in body. Therefore, to inhibit the growth and metastasis of tumor cancer cells, it is first necessary to meet the overall potassium needs in body and ensure the normal functions of various organs and tissues. Therefore, it is quite necessary to provide diary diet containing enough potassium ions, and then take appropriate measures to ensure that the digestive system can effectively absorb potassium ions, correct the persistent relative deficiency of po-
tassium in body, meet the potassium demand of tumor cancer cells that have occurred in the specific organs and tissues, and finally try to transform them into normal cells. Inhibiting of the activity of Na⁺, K⁺-ATPase may only inhibit the behavior of the tumor cancer cells with high expression of this enzyme for their huge consumption of potassium ions, and therefore, this therapeutic method may only achieve partial anti-cancer effects [19-33]. Similarly, the use of traditional medicine prescriptions can also partially correct the potassium deficiency in the body or improve the utilization efficiency of potassium ions. However, if the treatment is not at the early stage of the formation of tumor cancer cells, the therapeutic effect is limited, and may vary depending on the degree of individual potassium deficiency [34].

5. CONCLUSIONS AND SIGNIFICANCE

In this paper, it is proposed that the core mechanism for occurrence of tumors and cancer cells is caused by the continuous relative deficiency of potassium ions in the cells of specific organs and tissues, and the purpose of cancer cell metastasis is to obtain and utilize the potassium resources in other organs of body. However, if the overall potassium storage in body is obviously insufficient, and even the cancer cells after metastasis cannot achieve the purpose for obtaining enough potassium and turn into normal cells, then further ectopic proliferation of cancer cells will continue, and finally lead to the functional decline in key organs and tissues and the death of living body.

Therefore, the key means to prevent and treat tumors and cancers is to ensure the normal and balanced potassium storages in various organs and tissues, so as to avoid the relative deficiency of intracellular potassium in tissues and tissue cells and prevent normal cells from transforming into tumor cancer cells.

ACKNOWLEDGEMENTS

This work was supported by the innovation team fund of National Ethnic Affairs Commission (MZR20002) and the research funds of South-Central Minzu University (KTZ20039 and CZP 18003).

CONFLICTS OF INTEREST

The author declares no competing financial interests.

REFERENCES

1. Dai, J.P. (2022) Why Are There So Many Puzzles in Fighting against COVID-19 Pandemic? *Natural Science*, 14, 424-433. [https://doi.org/10.4236/ns.2022.1410036]
2. Dai, J.P. (2022) The Relative Deficiency of Potassium Ions in Nerve Cells Causes Abnormal Functions and Neurological and Mental Diseases. *Natural Science*, 14, 441-447. [https://doi.org/10.4236/ns.2022.1410038]
3. Dai, J.P. (2022) Relative Deficiency of Intracellular Potassium in Relation to the Functional Changes and Diseases in Non-Nervous System. *Natural Science*, 14, 497-502. [https://doi.org/10.4236/ns.2022.1411044]
4. Jansson, B. (1986) Geographic Cancer Risk and Intracellular Potassium/Sodium Ratios. *Cancer Detection and Prevention*, 9, 171-194.
5. Kunzelmann, K. (2005) Ion Channels and Cancer. *The Journal of Membrane Biology*, 205, 159-173. [https://doi.org/10.1007/s00232-005-0781-4]
6. Sandhiya, S. and Dkhar, S.A. (2009) Potassium Channels in Health, Disease & Development of Channel Modulators. *Indian Journal of Medical Research*, 129, 223-232.
7. Shen, Z., Yang, Q. and You, Q. (2009) Researches toward Potassium Channels on Tumor Progressions. *Current Topics in Medicinal Chemistry*, 9, 322-329. [https://doi.org/10.2174/156802609788317874]
8. Durlacher, C.T., Chow, K., Chen, X.W., He, Z.X., Zhang, X., Yang, T. and Zhou, S.F. (2015) Targeting Na⁺/K⁺-
Translocating Adenosine Triphosphatase in Cancer Treatment. *Clinical and Experimental Pharmacology and Physiology*, **42**, 427-443. https://doi.org/10.10111/1440-1681.12385

9. Cong, D., Zhu, W., Kuo, J.S., Hu, S. and Sun, D. (2015) Ion Transporters in Brain Tumors. *Current Medicinal Chemistry*, **22**, 1171-1181. https://doi.org/10.2174/0929867322666150114151946

10. Litan, A. and Langhans, S.A. (2015) Cancer as a Channelopathy: Ion Channels and Pumps in Tumor Development and Progression. *Frontiers in Cellular Neuroscience*, **9**, Article No. 86. https://doi.org/10.3389/fncel.2015.00086

11. Anderson, K.J., Cormier, R.T. and Scott, P.M. (2019) Role of Ion Channels in Gastrointestinal Cancer. *World Journal of Gastroenterology*, **25**, 5732-5772. https://doi.org/10.3748/wjg.v25.i38.5732

12. Patel, S.H., Edwards, M.J. and Ahmad, S.A. (2019) Intracellular Ion Channels in Pancreas Cancer. *Cellular Physiology and Biochemistry*, **53**, 44-51. https://doi.org/10.33594/000000193

13. Bejček, J., Spiwok, V., Kmoničková, E. and Rimpelová, S. (2021) Na+/K+-ATPase Revisited: On Its Mechanism of Action, Role in Cancer, and Activity Modulation. *Molecules*, **26**, Article No. 1905. https://doi.org/10.3390/molecules26071905

14. Themistocleous, S.C., Yiallouris, A., Tsioutis, C., Zaravinos, A., Johnson, E.O. and Patrikios, I. (2021) Clinical Significance of P-Class Pumps in Cancer. *Oncology Letters*, **22**, Article No. 658. https://doi.org/10.3892/ol.2021.12919

15. Blokhina, O., Virolainen, E. and Fagerstedt, K.V. (2003) Antioxidants, Oxidative Damage and Oxygen Deprivation Stress: A Review. *Annals of Botany*, **91**, 179-194. https://doi.org/10.1093/aob/mcf118

16. Noctor, C. (2005) Redox Homeostasis and Antioxidant Signaling: A Metabolic Interface between Stress Perception and Physiological Responses. **17**, 1866-1875. https://doi.org/10.1105/tpc.105.033589

17. Bayr, H. (2005) Reactive Oxygen Species. *Critical Care Medicine*, **33**, S498-S501. https://doi.org/10.1097/01.CCM.0000186787.64500.12

18. Linford, N.J., Schriner, S.E. and Rabinoivitch, P.S. (2006) Oxidative Damage and Aging: Spotlight on Mitochondria. *Cancer Research*, **66**, 2497-2499. https://doi.org/10.1158/0008-5472.CAN-05-3163

19. Weidemann, H. (2005) Na/K-ATPase, Endogenous Digitalis like Compounds and Cancer Development—A Hypothesis. *Frontiers in Bioscience*, **10**, 2165-2176. https://doi.org/10.2741/1688

20. Chen, J.Q., Contreras, R.G., Wang, R., Fernandez, S.V., Shoshani, L., Russo, I.H., Cereijido, M. and Russo, J. (2006) Sodium/Potassium ATPase (Na+, K+-ATPase) and Ouabain/Related Cardiac Glycosides: A New Paradigm for Development of Anti-Breast Cancer Drugs? *Breast Cancer Research and Treatment*, **96**, 1-15. https://doi.org/10.1007/s10549-005-9053-3

21. Mijatovic, T., Van Quaquebeke, E., Delest, B., Debeir, O., Darro, F. and Kiss, R. (2007) Cardiotonic Steroids on the Road to Anti-Cancer Therapy. *Biochimica et Biophysica Acta*, **1776**, 32-57. https://doi.org/10.1016/j.bbcan.2007.06.002

22. Yin, L.T., Fu, Y.J., Xu, Q.L., Yang, J., Liu, Z.L., Liang, A.H., Fan, X.J. and Xu, C.G. (2007) Potential Biochemical Therapy of Glioma Cancer. *Biochemical and Biophysical Research Communications*, **362**, 225-229. https://doi.org/10.1016/j.bbrc.2007.07.167

23. Sontheimer, H. (2008) An Unexpected Role for Ion Channels in Brain Tumor Metastasis. *Experimental Biology and Medicine (Maywood)*, **233**, 779-791. https://doi.org/10.3181/0711-MR-308

24. Newman, R.A., Yang, P., Pawlus, A.D. and Block, K.I. (2008) Cardiac Glycosides as Novel Cancer Therapeutic Agents. *Molecular Interventions*, **8**, 36-49. https://doi.org/10.1124/mi.8.1.8

25. Arcangeli, A. and Becchetti, A. (2010) New Trends in Cancer Therapy: Targeting Ion Channels and Transporters. *Pharmaceuticals (Basel)*, **3**, 1202-1224. https://doi.org/10.3390/ph3041202
26. Mijatovic, T., Dufrasne, F. and Kiss, R. (2012) Na+/K+-ATPase and Cancer. *Pharmaceutical Patent Analyst*, 1, 91-106. https://doi.org/10.4155/ppa.12.3

27. Wang, H.Y. and O’Doherty, G.A. (2012) Modulators of Na/K-ATPase: A Patent Review. *Expert Opinion on Therapeutic Patents*, 22, 587-605. https://doi.org/10.1517/13543776.2012.690033

28. Babula, P., Masarik, M., Adam, V., Provaznik, I. and Kizek, R. (2013) From Na+/K+-ATPase and Cardiac Glycosides to Cytotoxicity and Cancer Treatment. *Anti-Cancer Agents in Medicinal Chemistry*, 13, 1069-1087. https://doi.org/10.2174/18715206113139990304

29. Alevizopoulos, K., Calogeropoulou, T., Lang, F. and Stournaras, C. (2014) Na+/K+-ATPase Inhibitors in Cancer. *Current Drug Targets*, 15, 988-1000. https://doi.org/10.2174/1389450115666140908125025

30. Calderón-Montaño, J.M., Burgos-Morón, E., Orta, M.L., Maldonado-Navas, D., García-Domínguez, I. and López-Lázaro, M. (2014) Evaluating the Cancer Therapeutic Potential of Cardiac Glycosides. *BioMed Research International*, 2014, Article ID: 794930. https://doi.org/10.1155/2014/794930

31. Redmond, J., O’Rilley, D. and Buchanan, P. (2017) Role of Ion Channels in Natural Killer Cell Function towards Cancer. *Discovery Medicine*, 23, 353-360.

32. Felippe Gonçalves-de-Albuquerque, C., Ribeiro Silva, A., Ignácio da Silva, C., Caire Castro-Faria-Neto, H. and Burth, P. (2017) Na/K Pump and Beyond: Na/K-ATPase as a Modulator of Apoptosis and Autophagy. *Molecules*, 22, Article No. 578. https://doi.org/10.3390/molecules22040578

33. Silva, C.I.D., Gonçalves-de-Albuquerque, C.F., Moraes, B.P.T., Garcia, D.G. and Burth, P. (2021) Na/K-ATPase: Their Role in Cell Adhesion and Migration in Cancer. *Biochimie*, 185, 1-8. https://doi.org/10.1016/j.biochi.2021.03.002

34. Dai, J.P. (2022) The Core Mechanism of Traditional Medicine Is the Rational and Effective Use of Potassium Ions. *Natural Science*, 14, 483-491. https://doi.org/10.4236/ns.2022.1411042