

Commentary on “Crosstalk between DNA Damage Repair and Metabolic Regulation in Hematopoietic Stem Cells”

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About the Study

We recently shared our thoughts on a topic “Crosstalk between DNA Damage Repair (DDR) and metabolic regulation in Hematopoietic Stem Cells (HSC) [1]”. Research has increasingly focused on the crosstalk between cellular processes in recent years even considering mathematical modeling [2,3]. A growing body of literature indicates that the metabolic state of HSCs not only influences their ability to repair DNA but that DDR pathways, in turn, affect cellular metabolism [4-8]. This bidirectional relationship is particularly important for maintaining HSC homeostasis during periods of stress or aging and may have profound implications for both normal hematopoiesis and hematological diseases [9-12].

Among key aspects of interest in this area, “DDR and Metabolic Shifts” stands at the upfront. DDR doesn't just involve repairing DNA; it also interacts with various cellular processes, including metabolism, to ensure that the cell has the energy and resources to complete the repair process [13-16]. Such as, the activation of p53 or ATM/ATR pathways, intersecting with metabolic reprogramming, shifts between oxidative phosphorylation and glycolysis, etc. [8,17-20]. The metabolic changes can be a response to DNA damage and the regulation of metabolism plays a key role in DDR's outcomes. The integration of DDR and metabolism is a highly coordinated process. Cells must ensure that there is enough metabolic support to effectively repair damaged DNA, while also managing the consequences of oxidative stress and potential mitochondrial dysfunction. The connection between DDR and metabolism has significant implications for cancer and aging research. DDR and metabolic shifts are intricately connected. DNA damage leads to metabolic changes that support repair processes, but excessive damage or prolonged metabolic alterations can lead to cellular dysfunction or death. The interplay between DDR and metabolism is essential for maintaining cellular health and disruptions in these processes are implicated in various diseases, particularly cancer and aging. Understanding this relationship offers exciting potential for therapeutic interventions.

In addition, “Redox Balance and Stem Cell Fate” is worth emphasizing. It remains under investigated on the role of redox regulation in balancing DNA damage repair and metabolic function and how disruptions in redox homeostasis can impair HSC self-renewal or promote exhaustion [1]. Understanding the redox mechanisms governing stem cell fate can have important implications for stem cell-based therapies. Conversely, protecting stem cells from oxidative stress may enhance their regenerative potential, particularly in aging or disease contexts where oxidative damage compromises stem cell function [21-24]. Redox dysregulation in stem cells can lead to tumorigenesis. High Reactive Oxygen Species (ROS) levels, especially in the context of stem cell niches, have been associated with tumor initiation, metastasis and resistance to chemotherapy [25,26]. Balancing ROS levels in Cancer Stem Cells (CSCs) is an area of active research, with the goal of targeting CSCs for therapeutic interventions [27,28].

The convergence of DNA damage repair and metabolism reprogram in Hematopoietic Stem Cells is a rapidly evolving field with broad implications for regenerative medicine, cancer therapy and aging [1]. Understanding the molecular mechanisms driving this crosstalk could lead to novel therapeutic strategies aimed at rejuvenating stem cell function or correcting the metabolic defects seen in various hematopoietic diseases. By examining this dynamic interplay, we aim to uncover new insights into stem cell biology and provide a more holistic approach to therapeutic interventions in hematopoietic disorders.

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References

1. Xu, Jian, Peiwen Fei, Dennis W Simon and Michael J. Morowitz, et al. "Crosstalk between DNA Damage Repair and Metabolic Regulation in Hematopoietic Stem Cells." *Cells* 13(2024): 733.

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2. Konrath, Fabian, Alexander Loewer and Jana Wolf. "Resolving Crosstalk between Signaling Pathways using Mathematical Modeling and Time-Resolved Single Cell Data." *CMSN* (2023): 267-284.
3. Wang, Zhanwei, Dionyssios Katsaros, Junlong Wang and Nicholetta Biglio, et al. "Machine Learning-Based Cluster Analysis of Immune Cell Subtypes and Breast Cancer Survival." *Sci Rep* 13(2023): 18962.
4. Shao, Lijian, Yingying Wang, Jianhui Chang and Yi Luo, et al. "Hematopoietic Stem Cell Senescence and Cancer Therapy-Induced Long-Term Bone Marrow Injury." *Transl Cancer Res* 2(2013): 397.
5. Huang, Ruixue and Ping-Kun Zhou. "DNA Damage Repair: Historical Perspectives, Mechanistic Pathways and Clinical Translation for Targeted Cancer Therapy." *Signal Transduct Target Ther* 6(2021): 254.
6. Sobanski, Thais, Maddison Rose, Amila Surawewa and Kenneth O'Byrne, et al. "Cell Metabolism and DNA Repair Pathways: Implications for Cancer Therapy." *Front Cell Dev Biol* 9(2021): 633305.
7. Jackson, Benjamin T and Lydia WS Finley. "Metabolic Regulation of the Hallmarks of Stem Cell Biology." *Cell Stem Cell* 31(2024): 180.
8. Ou, Hui-Ling and Björn Schumacher. "DNA Damage Responses and P53 in the Aging Process." *Blood* 131(2018): 488-495.
9. Maldonado, Edio, Sebastián Morales-Pison, Fabiola Urbina and Aldo Solari. "Aging Hallmarks and the Role of Oxidative Stress." *Antioxidants* 12(2023): 651.
10. Jayabal, Panneerselvam, Chi Ma, Manoj Nepal and Yihang Shen, et al. "Involvement of FANCD2 in Energy Metabolism Via ATP5a." *Sci Rep* 7(2017): 4921.
11. Han, Bing, Hwan Ki Park, Travers Ching and Jayabal Panneerselvam, et al. "Human DBR1 Modulates the Recycling of snRNPs to Affect Alternative RNA Splicing and Contributes to the Suppression of Cancer Development." *Oncogene* 36(2017): 5382-5391.
12. Nepal, Manoj, Chi Ma, Guoxiang Xie and Wei Jia, et al. "Fanconi Anemia Complementation Group C Protein in Metabolic Disorders." *Aging* 10(2018): 1506.
13. Nepal, Manoj, Raymond Che, Jun Zhang and Chi Ma, et al. "Fanconi Anemia Signaling and Cancer." *Trends Cancer* 3(2017): 856.
14. Che, Raymond, Jun Zhang, Manoj Nepal and Bing Han, et al. "Multifaceted Fanconi Anemia Signaling." *Trends Genet* 34(2018): 183.
15. Zhan, Sudong, Jolene Siu, Zhanwei Wang and Herbert Yu, et al. "Focal Point of Fanconi Anemia Signaling." *Int J Mol Sci* 22(2021): 12976.
16. Groelly, Florian J, Matthew Fawkes, Rebecca A. Dagg and Andrew Blackford, et al. "Targeting DNA Damage Response Pathways in Cancer." *Nat Rev Cancer* 23(2023): 78-94.
17. Lacroix, Matthieu, Romain Riscal, Giuseppe Arena and Laetitia Karine Linares, et al. "Metabolic Functions of the Tumor Suppressor P53: Implications in Normal Physiology, Metabolic Disorders and Cancer." *Mol Metab* 33(2020): 2-22.
18. Burger, Kaspar, Ruth F. Ketley and Monika Gullerova. "Beyond the Trinity of ATM, ATR and DNA-PK: Multiple Kinases Shape the DNA Damage Response in Concert with RNA Metabolism." *Front Mol Biosci* 6(2019): 61.
19. Xie, Xiaochen, Ye Zhang, Zhuo Wang and Shanshan Wang, et al. "ATM at the Crossroads of Reactive Oxygen Species and Autophagy." *Int J Biol Sci* 17(2021): 3080.
20. Fei, Peiwen and Wafik S. El-Deiry. "P53 and Radiation Responses." *Oncogene* 22(2003): 5774-5783.
21. Li, Xiaoyu, Ou Jiang and Songlin Wang. "Molecular Mechanisms of Cellular Metabolic Homeostasis in Stem Cells." *Int J Oral Sci* 15(2023): 52.
22. Liang, Raymond and Saghi Ghaffari. "Stem Cells, Redox Signaling and Stem Cell Aging." *ARS* 20(2014): 1902-1916.
23. Dai, Xiaozhen, Xiaoqing Yan, Kupper A. Wintergerst and Lu Cai, et al. "Nrf2: Redox and Metabolic Regulator of Stem Cell State and Function." *Trends Mol Med* 26(2020): 185-200.
24. Maraldi, Tullia, Cristina Angeloni, Cecilia Prata and Silvana Hrelia. "NADPH Oxidases: Redox Regulators of Stem Cell Fate and Function." *Antioxidants* 10(2021): 973.
25. Tuy, Kaysaw, Lucas Rickenbacker and Anita B. Hjelmeland. "Reactive Oxygen Species Produced by Altered Tumor Metabolism Impacts Cancer Stem Cell Maintenance." *Redox Biol* 44(2021): 101953.
26. Liu, Wanning, Boda Wang, Mingzhen Zhou and Dan Liu, et al. "Redox Dysregulation in the Tumor Microenvironment Contributes to Cancer Metastasis." *ARS* 39(2023): 472-490.
27. Lendeckel, Uwe and Carmen Wolke. "Redox-Regulation in Cancer Stem Cells." *Biomedicines* 10(2022): 2413.
28. Chu, Xianjing, Wentao Tian, Jiaoyang Ning and Gang Xiao, et al. "Cancer Stem Cells: Advances in Knowledge and Implications for Cancer Therapy." *Signal Transduct Tar Ther* 9(2024): 170.

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