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

Peiwen Fei[1*], Wei Du[2], Jun Zhang[3] and Herbert Yu[1]

[1]*The University of Hawaii Cancer Center, University of Hawaii, Honolulu, USA*

[2]*UPMC Hillman Cancer Center, University of Pittsburgh, Pittsburgh, USA*

[3]*Department of Pathology and Laboratory Medicine, Mayo Clinic Arizona, Phoenix, USA*

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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***Address for Correspondence:** Peiwen Fei, The University of Hawaii Cancer Center, University of Hawaii, Honolulu, USA; E-mail: pfei@cc.hawaii.edu*

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