METABOLIC CHANGE IN HEMATOPOIETC STEM CELL UNDER STRESS

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Cellular metabolism is an area of recent intense research interest. However, the metabolic requirements and adaptations of stem cells and their niches remain largely unaddressed. We have analyzed hematopoietic stem cell (HSC) metabolism using metabolomics approaches. With step-wise differentiation of stem cells, the cell metabolism associated with each differentiation stage may be very different. We show that quiescent HSCs predominantly utilize glycolytic pathways under the control of hypoxia inducible factor (HIF) 1α, while proliferating HSCs use oxidative phosphorylation and purinergic metabolism to obtain the energy. It is well-known that HSCs are dormant in hypoxic areas and not rich in the mitochondria mass – a hallmark of oxidative phosphorylation for energy production. However, under the stress hematopoiesis, mitochondria biogenesis is enhanced through mTOR and PGC1α signal.

Here, we will show that "Ca-mitochondria activation –cell division" sequence at the time of HSC recovery. And we show the difference of mitochondrial quality in HSCs between the mitochondria autophagy-deficiency and newborn state. Finally, we will discuss whether thrombopoietin is able to prime the HSC fate through the mitochondrial activation or not.

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2. Nakamura-Ishizu A, Takubo K, Kobayashi H, Suzuki-Inoue, Suda T: CLEC-2 in megakaryocytes is critical for maintenance of hematopoietic stem cells in bone marrow. ***J Exp Med,*** 212: 2133-2146, 2015
3. Ito K et al. Self renewal of a purified Tie2+ hematopoietic stem cell population relies on mitochondrial clearance. ***Science,*** 354(6316):1156-1160, 2016

Suda‘s past work encompasses the study of the intrinsic and extrinsic regulation of HSCs, purification of potent HSCs, analyses of cell differentiation processes, identification of niche factor signalling in hematopoiesis, and the characterization of stem cell metabolism.

2014 – Present Senior Principal Investigator, Professor, CSI, NUS

2014 – Present Professor, IRCMS, Kumamoto University.

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