KEISUKE ITO, M.D., Ph.D.

Positions:
Associate Professor, Departments of Cell Biology and Medicine
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Research interests:

The central research goal of the Ito Lab is the expansion of our understanding of the regulatory pathways controlling the equilibrium of healthy and malignant hematopoietic stem cells. At the core of our work is the process of stem cell division, and the resulting balance between self-renewal or differentiation, which directly impacts tissue homeostasis. We are also devoting increased attention to targeting cellular metabolism as a therapeutic strategy, and have cut a path along the leading edge of research into the role of epigenetic-microRNA crosstalk, including physiologically relevant Ten-eleven translocation, in the pathogenesis of myelodysplastic syndrome. We believe our expertise in stem cell biology, hematology, and the bone marrow microenvironment, combined with our development of single-cell approaches and live imaging to tracking stem cell fate *in vivo* and leukocyte behavior in sickle cell disease animal models, will together facilitate a major contribution to the improvement of transplantation efficiency and the development of new therapies and treatments, and potentially even cures, for many forms of hematologic pathology.

Current grant funding:

R01DK098263 (Ito PI) (NIH/NIDDK)	04/01/13 – 03/31/23 The roles of lipid metabolism in the maintenance of HSCs
R01HL148852 (Ito PI, Dawlaty co-PI) (NIH/NHLBI)	07/01/19 – 06/30/23 The non-canonical function of Tet2 in HSCs and hematologic disorders
LLS Scholar (Ito PI) (Leukemia Lymphoma Society)	07/01/18 – 06/30/23 Targeting mitophagy of leukemia stem cells for therapy
R01DK115577 (Ito PI, Lin co-PI) (NIH/NIDDK)	09/15/17 – 06/30/22 Single cell approach to uncovering factors regulating HSC division symmetry in vivo
R01HL069438 (Kelly PI, Ito co-I) (NIH/NHLBI)	09/25/21 – 08/31/25 Adhesion mechanisms mediating sickle cell vasoocclusion

Recent publications (selected):

1. Morganti C, Ito K, Yanase C, Verma A, TeruyaFeldstein J, Ito K. *NPM1* ablation induces HSC aging and inflammation to develop myelodysplastic syndrome exacerbated by *p53* loss. ***EMBO Rep***. in press.
2. Ma L *et al.*, Tet-mediated DNA demethylation regulates specification of hematopoietic stem and progenitor cells during mammalian embryogenesis. ***Sci Advances***. in press.
3. Schönberger K*, Obier N* *et al.*, Multilayer omics analysis reveals a non-classical retinoic acid signaling axis that regulates hematopoietic stem cell identity. ***Cell Stem Cell***. Cell Stem Cell. 2022 Jan 6;29(1):131-148.
4. Morganti C *et al.*, Mitochondrial contributions to HSC aging. ***Int J Mol Sci***. 2021 Oct 15;22(20):11117.
5. Wu HC *et al.*, Actinomycin D targets NPM1c-primed mitochondria to restore PML-driven senescence in AML therapy. ***Cancer Discovery***. 2021 Jul 23. doi: 10.1158/2159-8290.CD-21-0177.
6. Nakamura-Ishizu A *et al.*, HSC metabolism during development and aging. ***Dev Cell***. 2020 Jul;54(2):239-255.
7. Ito K*, Lee J* *et al.*, Non-catalytic roles of Tet2 are essential to regulate hematopoietic stem and progenitor cell homeostasis. ***Cell Rep***. 2019 Sep 3;28:2480-2490.
8. Weiss CN *et al.*, Ito K, microRNA-22 promotes megakaryocyte differentiation through repression of its target, GFI1. ***Blood Adv***. 2019 Jan 8;3:33-46.
9. Bonora M *et al.*, Mitochondrial volume expansion during HSC commitment. ***Exp Hematol***. 2018;68:30-37.
10. Ito K *et al.*, Self-renewal of a purified Tie2^{+} hematopoietic stem cell population relies on mitochondrial clearance. ***Science***. 2016 Dec;354:1156-1160.
11. Ito K*, Suda T*, Metabolic requirements for the maintenance of self-renewing stem cells. ***Nat Rev Mol Cell Biol*** 2014 Apr;15:243-256.
12. Song SJ*, Ito K* *et al.*, The oncogenic microRNA miR-22 targets the TET2 tumor suppressor to promote hematopoietic stem cell self-renewal and transformation. ***Cell Stem Cell*** 2013 Jul 3;13:87-101.
13. Ito K*, Carracedo A* *et al.*, A PML-PPAR-delta pathway for fatty acid oxidation regulates hematopoietic stem cell maintenance. ***Nat Med*** 2012 Sep;18:1350-1358.
14. Ito K *et al.*, PML targeting eradicates quiescent leukaemia-initiating cells. ***Nature*** 2008 June;453:1072-1078.
15. Ito K*, Hirao A* et al., Regulation of oxidative stress by ATM is required for self-renewal of haematopoietic stem cells. ***Nature*** Oct 21;431:997-1002.