Maria Maryanovich Ph.D.

Positions:
Assistant Professor, Department of Cell biology
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Research interests:

Life-long production of blood depends on the ability of hematopoietic stem cells (HSCs) to self-renew, differentiate, and form all blood cell lineages. HSCs rely upon a tight interaction with their microenvironment in the bone marrow (also termed the "niche") to preserve quiescence and maintain normal blood output. These interactions are based upon membrane-bound, locally secreted, and/or long-range signals produced by a complex network of blood vessels, sympathetic nerve fibers, mesenchymal stem cells (MSCs), stromal cells, and hematopoietic cells. Aging of the hematopoietic system is associated with an age-dependent decline in HSC function leading to myeloid cell expansion and a reduction in lymphoid output that contribute to the development of myeloid malignancies. Many advances have been made toward deciphering intrinsic mechanisms that control HSC aging. However, the dependence of HSC dysfunction on the aging microenvironment remains underexplored.

Our interest is to understand mechanisms that control niche aging and contribute to the remodeling of niches that support myeloid malignancy and leukemic stem cells (LSCs). We use rigorous genetic models that target different niche constituents combined with innovative 3D imaging technology to detect endogenous HSC distribution in their native microenvironment. These approaches will provide novel insights into the molecular mechanisms underlying age-dependent stem cell dysfunction and identify factors that can be targeted to develop novel therapies to rejuvenate stem cells niches.

Recent publications (selected):

1. Pinho S, Wei Q, Maryanovich M, Zhang D, Pierce H, Nakahara F, Di Staulo A, Bartholdy B, Xu J, Borger D, Verma A and Frenette PS. VCAM1 confers innate immune tolerance on haematopoietic and leukaemic stem cells. **Nature Cell Biology** (*In Press*)

2. Nakahara F, Borger DK, Wei Q, Pinho S, Maryanovich M, Zahalka AH, Suzuki M, Cruz CD, Wang Z, Xu C, Boulais PE, Ma'ayan A, Greally JM, Frenette PS. *Engineering a haematopoietic stem cell niche by revitalizing mesenchymal stromal cells*. **Nature Cell Biology**. 2019 May;21(5):560-567

3. Maryanovich M, Zahalka AH, Pierce H, Pinho S, Nakahara F, Asada N, Wei Q, Wang X, Ciero P, Xu J, Leftin A, Frenette PS. *Adrenergic nerve degeneration in bone marrow drives aging of the hematopoietic stem cell niche*. Nature Medicine. 2018 May 7; 24:782–791

4. Maryanovich M, Takeishi S, Frenette PS. *Neural Regulation of Bone and Bone Marrow*. **Cold Spring Harb Perspect Med**. 2018 Mar 2. pii: a031344

5. Zahalka AH, Arnal-Estapé A, Maryanovich M, Nakahara F, Cruz CD, Frenette PS. *Adrenergic nerves activate an angio-metabolic switch in prostate cancer.* **Science**. 2017 Oct 20; 358(6361):321-326

6. Maryanovich M, Zaltsman Y, Ruggiero A, Goldman A, Shachnai L, Zaidman SL, Porat Z, Golan K, Lapidot T, Gross A. *A MTCH2 pathway repressing mitochondria metabolism regulates haematopoietic stem cell fate.* **Nature Communications**. 2015 Jul 29; 6:7901

7. Hanoun M*, Maryanovich M*, Arnal-Estapé A*, Frenette PS. *Neural Regulation of hematopoiesis, inflammation and Cancer*. **Neuron**. 2015 Apr 22; 86(2):360-73. Review. (*Co-first author)

8. Maryanovich M, Oberkovitz G, Niv H, Vorobiyov L, Zaltsman Y, Brenner O, Lapidot T, Jung S, Gross A. *The ATM-BID Pathway regulates quiescence and survival of haematopoietic stem cells*. **Nature Cell Biology**. 2012 Mar 25; 14(5):535-41