Postdoc, student, and technician positions at Harvard Medical School

Immediate postdoc, student or technician positions are available. Our laboratory focuses on the novel interface between the stem cell biology and immunology, termed "**stem-immunology**". A manuscript from our group has been most recently accepted in ***Nature*** **(Accepted in press; 2024 November**; https://doi.org/10.21203/rs.3.rs-2469338/v1).

Despite the growing application of tumor immunotherapy and stem cell transplantation, the interplay between stem cells and the immune system has remained unclear. It remains unclear how the immune system controls stem cells. It is largely unclear how the immune response against stem cells, either normal or malignant, is controlled.

Toward such questions in the new "stem-immunology", Dr. Fujisaki's group tests whether the specialized microenvironment for stem cells, termed the stem cell niche, serves as an immunological sanctuary for stem cells. This would theoretically shield normal/malignant/transplanted stem cells from immune attack, as well as from cellular stress reactions. It was demonstrated in the 1950s that testis and placenta serve as immune privileged sites, where transplanted allogeneic (allo-) or xenogeneic grafts might persist long term, even in the absence of immune suppression. While tissue-committed stem cell niches have been recently identified within various tissues, the niche itself has not been evaluated in the immunological context. Little is unknown whether somatic stem cell niches are broadly immune privileged.

We have recently demonstrated that the hematopoietic stem cell (HSC) niche within the bone marrow accommodates a unique regulatory T cell population that renders the niche immune privileged (*Cell Stem Cell* 22, 445-453, 2018; *Nature* 474(7350), 216-9, 2011).

Our most recent manuscript in Nature (2024 November, Accepted in Press) has further identified highly immune privileged, highly primitive HSCs, amongst other HSCs; shielded by highly immunoprotective niches, amongst distinct BM niche sites. We demonstrated that high-level nitric oxide (NO)-generating HSCs are refractory to immune attack; and exhibit unique "sleeping beauty-like late-rising" but robust and long-term blood reconstitution. Such highly immune-privileged, highly primitive NO^{Hi} HSCs localize at distinctive endosteum capillaries at the metaphysis, as characterized by high levels of immune-checkpoint molecules CD200, primary cilia, and molecular/phenotypic features of vascular sprouting. These specialized capillaries control the regenerative functions of NO^{Hi} HSCs via innovative ciliary protein IFT20/CD200/eNOS/autophagy axis. The capillaries further maintain the pool sizes of niche Tregs, boosting immune privilege of NO^{Hi} HSCs. Of note, less immune-privileged, less potent NO^{Low} HSCs co-localize at previously-described niche constituents, sinusoids or Type H vessels. These observations demonstrate the novel hierarchical structures within HSCs and distinct BM niches, that dictate both the regenerative function and immune tolerance.

We are now extending this innovative project in multi-directions in: stem cell/niche regulation; self-tolerance; Treg biology; stem cells in different peripheral organs; and cancer.

Multiple experimental approaches, including transgenic animal models, human samples, RNA/TCR sequencing, spatial transcriptomics, and intravital two-photon microscopy, are used. Successful candidates of postdoctoral fellows will have a Ph.D. and/or M.D. degree. Candidates are preferred to (but do not need to) possess expertise in one of the following fields: stem cell biology; immunology; cancer biology; RNA/DNA sequencing; T cell receptor sequencing; cell reprogramming; and computational biology. We are looking for candidates who are interested in

participating in our ambitious multidisciplinary research. To apply for this position, please send your CV with names/contact info of 3 references to Dr. Joji Fujisaki (jfujisak@bidmc.harvard.edu). Feel free emailing to ask any questions.

Dr. Fujisaki is a former Associate Professor at Columbia University in NY. Dr. Fujisaki has been most recently recruited as Associate Professor, Deputy Director at Center for Inflammation Research within Beth Israel Deaconess Medical Center, Harvard Medical School. Dr. Fujisaki's laboratory is located within the Center for Life Science Building in the Longwood Medical Area.

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