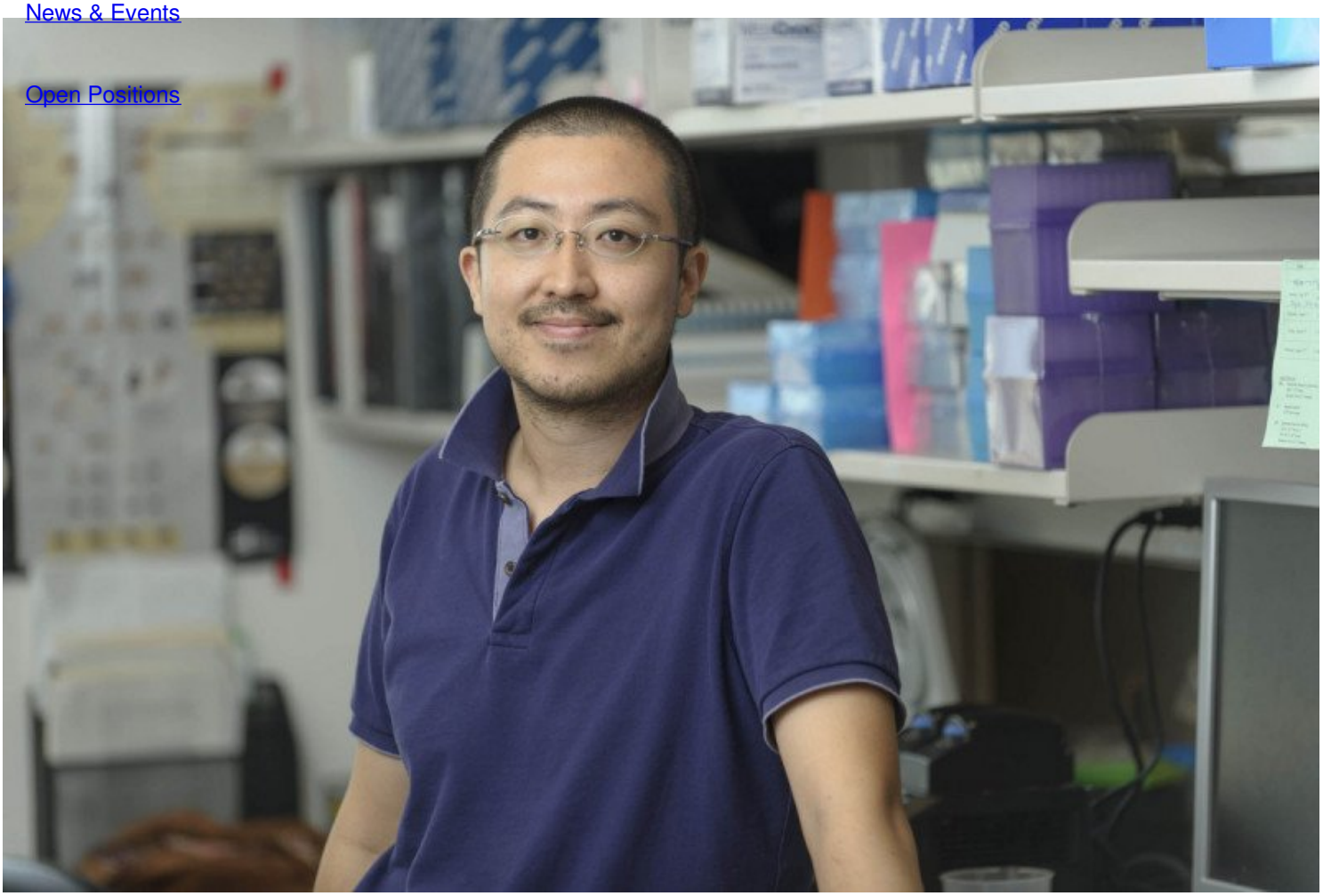
Memorial Sloan Kettering Cancer Center

Yusuke Shono, MD, PhD

Visiting Investigator



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Education

Hokkaido University Graduate School of Medicine, Sapporo, Japan; Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) has become widely applied for hematological (and more recently even for non-hematological) disorders. However, allo-HSCT is a “two-edeged” swords; this treatment has preferable strong graft-versus-tumor effects (GVT) to cure diseases while at the same time this causes graft-versus-host disease (GVHD) that could lead to the adverse prognoses of treated patients. As a hematologist I observed many of the complications including GVHD after allo-HSCT, and also as a researcher I elucidated the effects of GVHD on hematopoiesis/hematopoietic niche, I keep on pursuing my research in this field of transplantation immunology trying to reveal the detailed mechanisms of GVHD and GVT. After joining in the lab since April 2011, I have been focusing attention on a network hub controlling immunity, inflammation, and cancer - especially a transcriptional factor c-Rel that controls T-cell activation and proliferation contributing to pathophysiology of GVHD/GVT. We have small molecule c-Rel inhibitor compounds in our hands and by utilizing these compounds *in vivo* and *in vitro*, we observed effective suppression of c-Rel resulting in improved GVHD while preserving GVT activity. Intestinal damages are also important to initiate/sustain GVHD, so my projects also include models using knock-out mice of specific genes relevant to intestinal immune homeostasis. In addition, I am also involved in the project focusing on mucosal immunology and examine how it can impact on intestinal GVHD, including the microbial flora and dietary factors. The ultimate goal is to develop promising methods to improve clinical outcomes of allo-HSCT.

Honors and Awards

Fellowship Award from the Uehara Memorial Foundation (2011-2013)

ASH Abstract Achievement Award (2012)

ASH Abstract Achievement Award (2013)

ASBMT Best Abstract Award (2013)

ASBMT Best Abstract Award (2014)

ASH Abstract Achievement Award (2014)

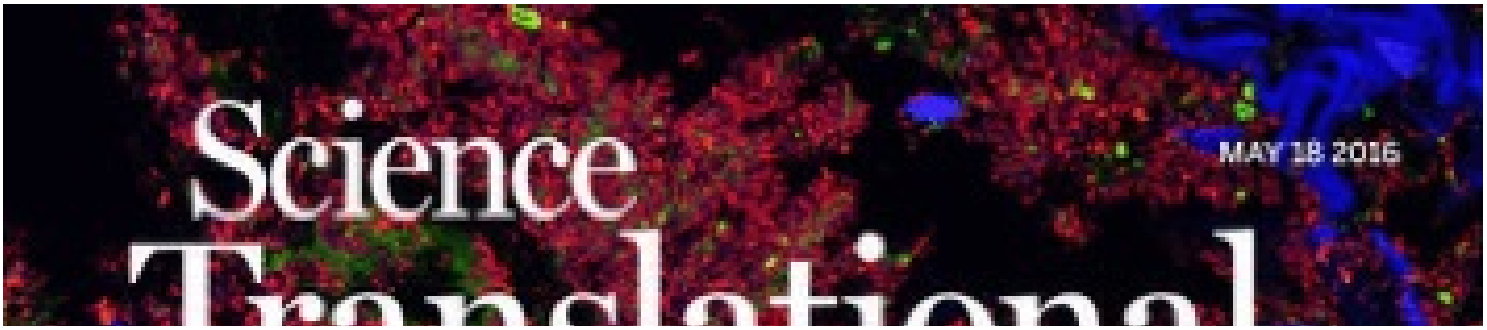
ASBMT Best Abstract Award (2015)

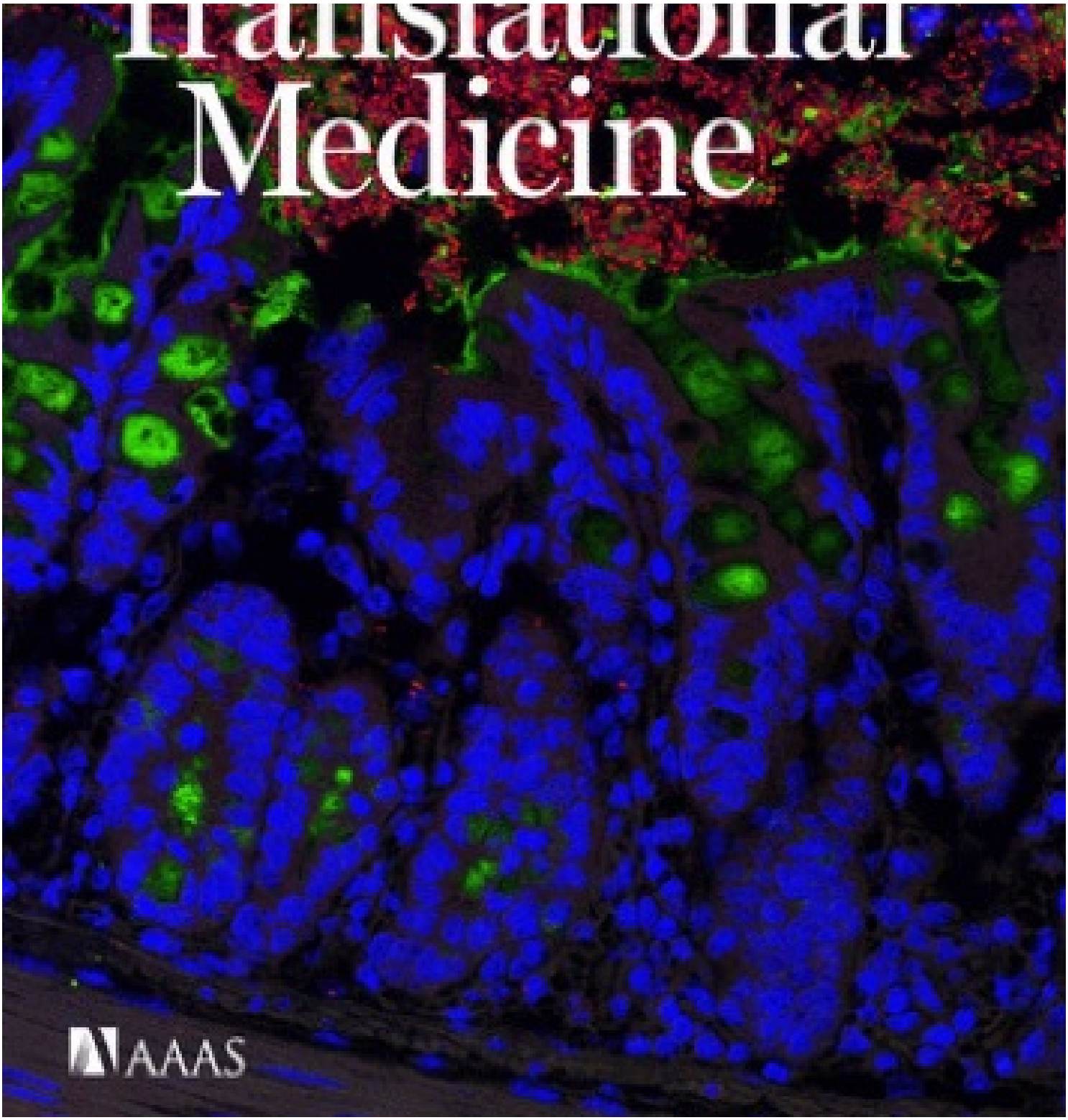
Ongoing Research Support

Lymphoma Research Foundation, Post-Doctoral Fellowship (2013-2015)

ASBMT New Investigator Award (2015-2017)

Research Highlight





Patients receiving an allogeneic hematopoietic stem cell transplant often develop neutropenic fever, which is treated with antibiotics. Such antibiotic treatment also may inadvertently wipe out beneficial intestinal bacteria that reduce gut inflammation. Transplant patients treated with certain broad-spectrum antibiotics show an increase in graft-versus-host disease in the colon (Shono *et al.*). Analysis of a mouse model revealed that this was due to loss of beneficial gut bacteria and overgrowth of bacterial strains that consumed the protective mucus layer of the colon rendering it more susceptible to inflammation and injury.

Publications

Shono Y, Docampo MD, Peled JU, Perobelli SM, Velardi E, Tsai JJ, Slingerland AE, Smith OM, Young LF, Gupta J, Lieberman SR, Jay HV, Ahr KF, Porosnicu Rodriguez KA, Xu K, Calarfiore M, Poeck H, Caballero S, Devlin SM, Rapaport F, Dudakov JA, Hanash AM, Gyurkocza B, Murphy GF, Gomes CG, Liu C, Moss EL, Falconer SB, Bhatt AS, Taur Y, Pamer EG, van den Brink MR*, Jenq RR*. Increased GVHD-related mortality with broad-spectrum antibiotic use after allogeneic hematopoietic stem cell transplantation in mice and human patients. *Sci Transl Med*, 2016, *In press.* *shared last authorship

Commentary in *Science* (http://goo.gl/HE9sBA)

Featured in Medical Daily (http://goo.gl/kvDZia)

Featured in EurekAlert!(AAAS) (http://goo.gl/wNAt8v)

Featured in TheScientist (http://goo.gl/DJO683)

Shono Y, Tuckett AZ, Liou HC, Doubrovina E, Derenzini E, Ouk S, Tsai JJ, Smith OM, Levy ER, Kreines FM, Ziegler CGK, Scallion MI, Doubrovin M, Heller G, Younes A, O'Reilly RJ, van den Brink MR*, Zakrzewski JL*. Characterization of a c-Rel inhibitor that mediates anticancer properties in hematologic malignancies by blocking NF-kB-controlled oxidative stress responses. *Cancer Res*, 2016, 76:377-389. *shared last authorship

Hubbard-Lucey VM*, Shono Y*, Maurer K, West ML, Singer NV, Ziegler CG, Lezcano C, Motta AC, Schmid K, Levi SM, Murphy GF, Liu C, Winkler JD, Amaravadi RK, Rogler G, Dickinson AM, Holler E, van den Brink MR**, Cadwell K**. Autophagy gene Atg16L1 prevents lethal T cell alloreactivity mediated by dendritic cells. *Immunity* 2014, 41:579-91. *shared first authorship, **shared last authorship

Shono Y, Tuckett A, Ouk S, Liou H, Altan-Bonnet G, Tsai J, Oyler J, Smith M, West M, Singer N, Doubrovina E, Pankov D, Undhad C, Murphy G, Lezcano C, Liu C, O'Reilly R, van den Brink MR*, Zakrzewski J*. A small molecule c-Rel inhibitor reduces alloactivation of T-cells without compromising anti-tumor activity. *Cancer Dsicov* 2014, 4:578-591. *shared last authorship

Shono Y*, Shiratori S*, Kosugi-Kanaya M, Ueha S, Sugita J, Shigematsu A, Kondo T, Hashimoto D, Fujimoto K, Endo T, Nishio M, Hashino S, Matsuno Y, Matsushima K, Tanaka J, Imamura M, Teshima T. Bone Marrow graft-versus-host disease: evidence of its clinical impact on disrupted hematopoiesis after allogeneic hematopoietic stem cell transplantation *Biol Blood Marrow Transplant* 2014, 20:495-500. *shared first authorship

Shono Y, Kosugi-Kanaya M, Shiratori S, Sugita J, Fujimoto K, Kondo T, Nishio M, Tanaka J, Imamura M. Donor cell leukemia after umbilical cord blood transplantation: recurrent or de novo? The importance of diagnosis for therapeutic decision making. *Int J Hematol* 2011, 93:563-565.

Shono Y, Ueha S, Wang Y, Abe J, Kurachi M, Matsuno Y, Sugiyama T, Nagasawa T, Imamura M, Matsushima K. Bone marrow graft-versus-host disease: early destruction of hematopoietic niche after MHC-mismatched hematopoietic stem cell transplantation. *Blood* 2010, 115:5401-5411. (Commentary in *Blood* 2010, 115:5284-5285.)

Social Media

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ResearchGate_Yusuke SHONO

My Projects

Mechanisms Regulating Graft-versus-Host Disease