

## **1. CURRICULUM VITAE**

### **Hitoshi Takizawa**



#### **Personal Information:**

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Family name: Takizawa

Forenames: Hitoshi

Academic title: Ph.D.

Position and Work address:

Professor and Vice Director  
International Research Center for Medical Sciences, Kumamoto University  
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#### **Education:**

- 2003 April - 2007 Mar. Department of Immunology, Institute of Medical Science, Graduate School of Medical Science, The University of Tokyo, Tokyo, Japan  
Awarded the degree of PhD in Medical Science  
Advisor: Prof. Dr. Kiyoshi Takatsu
- 2001 April - 2003 Mar. Department of Immunology, Institute of Medical Science, Graduate School of Medical Science, The University of Tokyo, Tokyo, Japan  
Awarded the degree of Master in Medical Science  
Advisor: Prof. Dr. Kiyoshi Takatsu
- 1997 April - 2001 Mar. Department of Bioscience, Tokyo Institute of Technology, Tokyo, Japan  
Awarded the degree of BSc in Bioscience  
Advisor: Prof. Dr. Yuji Saito

#### **Research training:**

- 2009 Sept. - 2012 Jan. Postdoctoral Research Fellow  
Division of Experimental Hematology, University Hospital Zürich, Switzerland  
Advisor: Prof. Dr. med. Markus G. Manz
- 2007 April - 2009 Aug. Postdoctoral Research Fellow  
Hematopoiesis Laboratory, Institute for Research in Biomedicine, Switzerland  
Advisor: Dr. med. Markus G. Manz

#### **Academic appointments:**

- 2017 Jan. - Professor and Vice Director  
International Research Center for Medical Sciences, Kumamoto University, Japan
- 2015 Jan. - 2016 Dec. Associate Professor  
International Research Center for Medical Sciences, Kumamoto University, Japan
- 2015 Jan. - 2015 Dec. Visiting Scientist  
Division of Experimental Hematology, University Hospital Zürich, Switzerland
- 2012 Feb. - 2014 Dec. Junior group Leader  
Division of Experimental Hematology, University Hospital Zürich, Switzerland
- 2009 April - 2011 Mar. Research Fellowship for Research Abroad, Japanese Science for the Promotion of Science
- 2007 April - 2008 Mar. Research Fellowship, Japanese Science for the Promotion of Science
- 2006 April - 2007 Mar. Research Fellowship for Young Scientist, Japanese Science for the Promotion of Science

## 2: List of accomplishments

# and \* indicate co-first and corresponding author, respectively.

1. Sezaki M<sup>#</sup>, Hayashi Y<sup>#</sup>, Wang Y, Johansson A, Umemoto T, **Takizawa H**, Immuno-modulation of hematopoietic stem and progenitor cells in inflammation, *Front Immunol.*, *in press*
2. Nasser H<sup>#</sup>, Adhikary P<sup>#</sup>, Abdel-Daim A<sup>#</sup>, Noyori O, Kariya R, Okada S, Ma W, Baba M, **Takizawa H**, Yamane M, Niwa H, Suzu S\*. Establishment of bone marrow-derived M-CSF receptor-dependent self-renewing macrophages., *Cell Death Discov.* 2020 Jul 23;6:63. doi: 10.1038/s41420-020-00300-3. eCollection 2020.
3. Morishima T\*, **Takizawa H\***. Genetic fingerprint defines hematopoietic stem cell pool size and function. *Haematologica*, 2020 Mar;105(3):526-528. doi: 10.3324/haematol.2019.241299. No abstract available. PMID: 32115410
4. Mende N, Bastos H, Santoro A, Sham K, Mahbubani KT, Curd A, **Takizawa H**, Wilson NK, Gottgens B, Saeb-Parsy K, Laurenti E\*. Quantitative and molecular differences distinguish adult human medullary and extramedullary haematopoietic stem and progenitor cell landscapes, *bioRxiv* February 20, 2020
5. Hayashi Y, **Takizawa H**. Innate immune signal-mediated hematopoietic regulation and alteration *Rinsho Ketsueki.*, 2020; 61 (6) :651-656
6. Suzuki D, Yoshikawa N, Stirblyte I, Akasaka M, Nakamura S, Manz MG, Hotta A, **Takizawa H**, Eto K\*, Sugimoto N\*. iPSC-derived platelets depleted 1 of HLA class-I are inert to anti-HLA class-I and NK cell immunity, *Stem Cell Reports.*, 2020 Jan 14;14(1):49-59. doi: 10.1016/j.stemcr.2019.11.011. Epub 2019 Dec 26.
7. Fukushima T, Tanaka Y, Hamey FK, Chang CH, Oki T, Umemoto T, Asada S, Hayashi Y, Fujino T, Yonezawa T, Takeda R, Kawabata KC, Fukuyama T, Goyama S, **Takizawa H**, Ishihama Y, Honda H, Göttgens B, and Kitamura T\*. Discrimination of dormant and active hematopoietic stem cells by G0 marker reveals dormancy regulation by cytoplasmic calcium, *Cell Rep.*, 2019 Dec 17;29(12):4144-4158
8. Hayashi Y, Goyama S, Liu X, Tamura M, Asada S, Tanaka Y, Fukuyama T, Wunderlich M, O'Brien E, Mizukawa B, Yamazaki S, Matsumoto A, Yamasaki S, Shibata T, Matsuda K, Sashida G, **Takizawa H**, Kitamura T\*. Antitumor immunity augments the therapeutic effects of p53 activation on acute myeloid leukemia. *Nat Commun.* 2019 Oct 25;10(1):4869
9. Bourguine PE, Fritsch K, Pigeot S, **Takizawa H**, Kunz L, Kokkaliaris KD, Coutu DL, Manz MG\*, Martin I\*, Schroeder T\*. Fate distribution and regulatory role of human mesenchymal stromal cells in engineered hematopoietic bone organs. *iScience.* 2019 Sep 27;19:504-513
10. Yokomizo T\*, Watanabe N, Umemoto T, Matsuo J, Harai R, Kihara Y, Nakamura E, Tada N, Sato T, Takaku T, Shimono A, **Takizawa H**, Nakagata N, Mori S, Kurokawa M, Tenen DG, Osato M, Suda T\*, Komatsu N. Hlf marks the developmental pathway for hematopoietic stem cells but not for erythroid-myeloid progenitors, *J Exp Med.*, 2019 Jul 1;216(7):1599-1614
11. Hayashi Y<sup>#</sup>, Sezaki M<sup>#</sup>, **Takizawa H\***, Development of the Hematopoietic System: Role of Inflammatory Factors, *Wiley Interdiscip Rev Dev Biol.*, 2019 Jul;8(4): e341
12. Nakamura-Ishizu A, Umemoto T, Matsumura T, Stumpf PS, Takihara Y, **Takizawa H**, O'Neil A, Abdul Majeed AB, MacArthur BD, and Suda T\*. Thrombopoietin metabolically primes hematopoietic stem cells to megakaryocyte lineage differentiation, *Cell Rep.*, 2018 Nov 13;25(7):1772-1785
13. **Takizawa H\***, Hayashi Y. Inflammation and early hematopoiesis. *Rinsho Ketsueki.*, 2018;59(10):1955-1961
14. Fritsch K, Pigeot S, Bourguine PE, Feng X, Schroeder T, Martin I, Manz MG, **Takizawa H\***, Engineered humanized bone organs maintain human hematopoiesis in vivo, *Exp Hematol.*, 2018 May;61:45-51
15. **Takizawa H\***, Fritsch K, Kovtonyuk LV, Saito Y, Yakkala C, Jacobs K, Ahuja AK, Lopes M, Hausmann A, Hardt WD, Gomariz Á, Nombela-Arrieta C and Manz MG. Pathogen-induced TLR4-TRIF innate immune signaling in hematopoietic stem cells promotes proliferation but reduces competitive fitness. *Cell Stem Cell.*, 2017 Aug 3;21(2):225-240
16. **Takizawa H\*** and Manz MG. Impact of inflammation on early hematopoiesis and the microenvironment. *Int. J. Hematol.*, 2017 Jul;106(1):27-33
17. Kovtonyuk LV, Fritsch K, Feng X, Manz MG, **Takizawa H\***. Inflamm-Aging of Hematopoiesis, Hematopoietic Stem Cells and the Bone Marrow Microenvironment. *Front Immunol.*, 2016, Nov 14;7:502
18. Rauch PJ, Ellegast JM, Widmer CC, Fritsch K, Goede JS, Valk PJ, Löwenberg B, **Takizawa H**, Manz MG. MPL expression on AML blasts predicts peripheral blood neutropenia and thrombocytopenia. *Blood.*, 2016 Nov 3;128(18):2253-2257
19. **Takizawa H**. Hematopoietic stem cell response to inflammation. *Rinsho Ketsueki.*, 2016 Aug;57(8):1059-1065
20. Kovtonyuk LV, Manz MG, **Takizawa H\***. Enhanced thrombopoietin but not G-CSF receptor stimulation induces self-renewing hematopoietic stem cell divisions in vivo. *Blood.*, 2016 Jun 23;127(25):3175-3179
21. Ziegler P, Boettcher S, **Takizawa H**, Manz MG, Brümmendorf TH. LPS-stimulated human bone marrow stroma cells support myeloid cell development and progenitor cell maintenance. *Ann Hematol.*, 2016 Jan;95(2):173-178
22. Berres ML, Lim KP, Peters T, Price J, **Takizawa H**, Salmon H, Idoyaga J, Ruzo A, Lupo PJ, Hicks MJ, Shih A, Simko SJ, Abhyankar H, Chakraborty R, Leboeuf M, Beltrão M, Lira SA, Heym KM, Clausen BE, Bigley V, Collin M, Manz MG, McClain K, Merad M, Allen CE. *BRAF-V600E* expression in precursor versus differentiated dendritic cells defines clinically distinct LCH risk groups. *J Exp Med.*, 2015 Feb 9;212(2):281
23. Kovtonyuk LV, **Takizawa H\***. Mouse genetic background and human hematopoietic stem cells biology; tips for humanization. *Humanized Mice for HIV Research, Springer.*, 2015

24. Nakamura-Ishizu A, **Takizawa H**, Suda T. The analysis, roles and regulation of quiescence in hematopoietic stem cells. *Development.*, 2014 Dec;141(24):4656-4666
25. Lundberg P<sup>#</sup>, **Takizawa H**<sup>#</sup>, Kubovcakova L<sup>#</sup>, Guo G, Hao-Shen H, Dirnhofer S, Orkin SH, Manz MG, Skoda RC. Myeloproliferative neoplasms can be initiated from a single hematopoietic stem cell expressing JAK2-V617F. *J Exp Med.*, 2014 Oct 20;211(11):2213-2230
26. Strassberger V, Gutbrodt KL, Krall N, Roesli C, **Takizawa H**, Manz MG, Fugmann T, Neri D. A comprehensive surface proteome analysis of myeloid leukemia cell lines for therapeutic antibody development. *J Proteomics.*, 2014 Mar 17;99 :138-151
27. Wueest S, Mueller R, Blüher M, Item F, Chin AS, Wiedemann MS, **Takizawa H**, Kovtonyuk L, Chervonsky AV, Schoenle EJ, Manz MG, Konrad D. Fas (CD95) expression in myeloid cells promotes obesity-induced muscle insulin resistance. *EMBO Mol Med.*, 2014 Jan ;6(1):43-56
28. Scotti C<sup>#</sup>, Piccinini E<sup>#</sup>, **Takizawa H**<sup>#</sup>, Todorov A, Bourguine P, Papadimitropoulos A, Barbero A, Manz MG, Martin I. Engineering of a functional bone organ through endochondral ossification. *Proc Natl Acad Sci U S A.*, 2013, Mar 5;110(10):3997-4002
29. Rongvaux A, **Takizawa H**, Strowig T, Willinger T, Eynon EE, Flavell RA, Manz MG. Human Hemato-Lymphoid System Mice: Current Use and Future Potential for Medicine. *Annu Rev Immunol.*, 2013;31:635-674
30. **Takizawa H**<sup>\*</sup>, Manz MG. In vivo divisional tracking of hematopoietic stem cells. *Ann N Y Acad Sci.*, 2012 Aug;1266(1):40-46
31. Boettcher S, Ziegler P, Schmid MA, **Takizawa H**, van Rooijen N, Kopf M, Heikenwalder M, Manz MG. Cutting edge: LPS-induced emergency myelopoiesis depends on TLR4-expressing nonhematopoietic cells. *J Immunol.*, 2012 Jun 15;188(12):5824-5828
32. **Takizawa H**, Boettcher S, Manz MG. Demand-adapted regulation of early hematopoiesis in infection and inflammation. *Blood.*, 2012 Mar 29;119(13):2991-3002
33. **Takizawa H**, Schanz U, Manz MG. Ex vivo expansion of hematopoietic stem cells: mission accomplished? *Swiss Med Wkly.*, 2011 Dec 29;141:w13316
34. Schmid MA, **Takizawa H**, Baumjohann DR, Saito Y, Manz MG. Bone marrow dendritic cell progenitors in mice sense pathogens via Toll-like receptors and subsequently migrate to inflamed lymph nodes. *Blood.*, 2011 Nov 3;118(18):4829-4840
35. Strowig T, Rongvaux A, Rathinam C, **Takizawa H**, Borsotti C, Philbrick W, Eynon EE, Manz MG, Flavell RA. Transgenic expression of human signal regulatory protein alpha in Rag2<sup>-/-</sup>gammac<sup>-/-</sup> mice improves engraftment of human hematopoietic cells in humanized mice. *Proc Natl Acad Sci U S A.*, 2011 Aug 9;108(32):13218-13223
36. **Takizawa H**, Manz MG. Dynamic regulation of hematopoietic stem cell cycling. *Cell Cycle.*, 2011 Jul 15;10(14):2246-2247
37. **Takizawa H**<sup>#</sup>, Regoes RR<sup>#</sup>, Boddupalli CS, Bonhoeffer S, Manz MG. Dynamic variation in cycling of hematopoietic stem cells in steady state and inflammation. *J Exp Med.*, 2011 Feb; 14;208(2):273-284
38. Rongvaux A, Willinger T, **Takizawa H**, Rathinam C, Auerbach W, Murphy AJ, Valenzuela DM, Yancopoulos GD, Eynon EE, Stevens S, Manz MG, Flavell RA. Human thrombopoietin knockin mice efficiently support human hematopoiesis in vivo. *Proc Natl Acad Sci U S A.*, 2011 Feb 8;108(6):2378-2383
39. Willinger T, Rongvaux A, **Takizawa H**, Yancopoulos GD, Valenzuela DM, Murphy AJ, Auerbach W, Eynon EE, Stevens S, Manz MG, Flavell RA. Human IL-3/GM-CSF knock-in mice support human alveolar macrophage development and human immune responses in the lung. *Proc Natl Acad Sci U S A.*, 2011 Feb 8; 108(6):2390-2395
40. **Takizawa H**<sup>#</sup>, Nishimura S<sup>#</sup>, Nishikii H, Takayama N, Oda A, Kakinuma S, Morita Y, Yamazaki S, Tamura N, Goto S, Sawaguchi A, Manabe I, Takatsu Ki, Nakauchi H, Takaki S, Eto K. Lnk/Sh2b3 regulates integrin αIIbβ3 outside in signaling in platelets leading to stabilization of developing thrombus in vivo. *J Clin Invest.*, 2010 Jan;120(1):179-190
41. Legrand N, Ploss A, Balling R, Becker PD, Borsotti C, Brezillon N, Debarry J, de Jong Y, Deng H, Di Santo JP, Eisenbarth S, Eynon E, Flavell RA, Guzman CA, Huntington ND, Kremsdorf D, Manns MP, Manz MG, Mention JJ, Ott M, Rathinam C, Rice CM, Rongvaux A, Stevens S, Spits H, Strick-Marchand H, **Takizawa H**, van Lent AU, Wang C, Weijer K, Willinger T, Ziegler P. Humanized mice for modeling human infectious disease: challenges, progress, and outlook. *Cell Host Microbe.*, 2009 Jul 23;6(1):5-9
42. **Takizawa H**, Eto K, Yoshikawa A, Nakauchi H, Takatsu K, Takaki S. Growth and maturation of megakaryocytes is regulated by Lnk/Sh2b3 adaptor protein through crosstalk between cytokine- and integrin-mediated signals. *Exp Hematol.*, 2008 Jul; 36(7): 897-906
43. **Takizawa H**, Manz MG. Macrophage tolerance: CD47-SIRP-alpha-mediated signals matter. *Nat Immunol.*, 2007 Dec; 8(12): 1287-1289
44. **Takizawa H**, Kubo-Akashi C, Nobuhisa I, Kwon SM, Iseki M, Taga T, Takatsu K, Takaki S. Enhanced engraftment of hematopoietic stem/progenitor cells by the transient inhibition of an adaptor protein, Lnk. *Blood.*, 2006 Apr 1; 107(7): 2968-2975
45. Kubo-Akashi C, Iseki M, Kwon SM, **Takizawa H**, Takatsu K, Takaki S. Roles of a conserved family of adaptor proteins, Lnk, SH2-B, and APS, for mast cell development, growth, and functions: APS-deficiency causes augmented degranulation and reduced actin assembly. *Biochem Biophys Res Commun.*, 2004 Mar 5; 312(2): 356-362

### **3 : Honors and Awards**

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2020 Healthy Longevity Grand Challenge Catalysis Award (The United States National Academy of Science)  
2019 AMED Interstellar Initiative  
2018 JSPS Japanese-German Frontiers of Science Symposium  
2013 Bruno Speck Award, Basel Stem Cell Network 2013  
2013 Basic Science Award, 39th Annual meeting of the European Group For Blood and Marrow Transplantation  
2011 Travel Award, International Society for Stem Cell Research  
2010 Travel Award, American Society for Hematology  
2009 - 2011 Research Fellowship for Research Abroad, Japanese Science for the Promotion of Science  
2009 Young Investigator Award, 2nd International Workshop on Humanized Mice  
2007 - 2008 Research Fellowship, Japanese Science for the Promotion of Science  
2006 - 2007 Research Fellowship for Young Scientist, Japanese Science for the Promotion of Science  
2005 Fritz Melcher's travel award, Annual meeting of Japanese Society for Immunology  
2004 Young Investigator Award, 13th Molecular Immunology Forum Tokyo

#### **Professional organizations and societies:**

International Society for Experimental Hematology (ISEH): New Investigator Committee Member (2018-2020), Scientific Committee (since 2020-)  
Japanese Society for Hematology (JSH): Board member (since 2019), Scientific program committee (2019-)  
Japanese Society for Immunology (JSI), The Molecular Biology Society of Japan, and American society for hematology (ASH): Regular membership

#### **Ad hoc Journal Editorial Referee:**

Nature Communications, Scientific Reports, Biochemical and Biophysical Research Communications, Haematologica, Blood, Journal of the Royal Society Interface, Cell proliferation, Swiss Medical Weekly, Experimental Cell Research, Annals of the New York Academy of Sciences, Experimental Hematology, Stem Cells International, Journal of Experimental Medicine, Stem Cells, Frontiers in Immunology, Aging Cell, Cell Report, Frontiers in Immunology, Frontiers in Cell Development Biology, Blood Advances, Journal of Immunology

#### **International committee for Research Grant:**

Japanese Society for Promotion of Science (Japan), Competitive Research Grants (CRG) program (Saudi Arabia), Swiss National Science Foundation (Switzerland), Czech Science Foundation (Czech), Biotechnology and Biological Sciences Research Council (UK)

#### **Commitment in Scientific Community:**

1. Meeting organizing committee for Japanese Society of Hematology since 2019
2. Meeting organizing committee for stem cell research symposium since 2019
3. New investigator committee for international society for experimental hematology since 2018

#### **Symposium or meeting organization:**

1. The 6<sup>th</sup> International Workshop for Humanized Mice, October, 2021, Kyoto, Japan
2. Meeting of Leukemic and Hematopoietic Stem Cells in Kumamoto, Feb 14, 2020, Kumamoto, Japan
3. Program committee for Japanese Society of Hematology 2019, Tokyo, Japan
4. JSPS-INSERM "IMPLICATIONS OF SENESENCE IN AGE RELATED DISORDERS: TOWARDS HEALTHY AGING" JSPS bilateral seminar, Sept 5-6 2019, Paris, France
5. New investigator committee for international society for experimental hematology (2018-)
6. Co-chair for the session "Hematopoiesis and Immune Environment" in Japanese Society for Immunology (with Dr Takashi Nagasawa), Dec 12-14<sup>th</sup> 2017, Sendai, Japan