

# CURRICULUM VITAE

Norifumi Takeda, M.D., Ph.D.



**BORN:** July 6, 1973 in Ehime, Japan

**PRESENT POSITION:** Senior Lecturer

Department of Cardiovascular Medicine

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**EDUCATION:** University of Tokyo, Japan:

Ph.D., 2006 in Cardiovascular Medicine

“Effect of Synthetic Retinoid Am80 on Atherogenic Model.”

- Supervisor: Ryozo Nagai

M.D., 1998

University of Pennsylvania:

Postdoctoral training with Prof. Jonathan A. Epstein,

Cell and Developmental Biology, 2010-2013

## PROFESSIONAL AND SOCIETY MEMBERSHIPS:

Fellowship: 2008 The Japanese Circulation Society.

2007 The Japanese Society of Internal Medicine.

Membership:

International Society for Heart Research.

The Japanese College of Cardiology.

The Japanese Heart Failure Society.

Japanese Society for Adult Congenital Heart Disease.

The Society of Cardiovascular Endocrinology and Metabolism.

The Japanese Society of Inflammation and Regeneration.

The Japanese Vascular Biology and Medicine Organization.

International Society for Heart Research.

The Japanese College of Cardiology

**AWARDS:**

- (1) Medical Research Encouragement Prize of The Japanese medical Association. 2017/11/1 (Tokyo, Japan)
- (2) Jokichi Takamine Young Investigator Award. 2017/12/8-10 (Osaka, Japan)
- (3) Medical Award of Tokyo University Medical Association. 2010/4/26 (Tokyo, Japan)
- (4) Young Investigator Award, in the 74<sup>th</sup> Annual Scientific Meeting of the Japanese Circulation Society. 2010/3/5-7 (Kyoto, Japan)
- (5) Young Investigator Award, in the 26<sup>th</sup> Annual Meeting of the International Society for Heart Research Japanese Section (ISHR). 2009/12/4-5 (Sapporo, Japan)
- (6) Finalist, Louis N. And Arnold M. Katz Basic Science Research Prize For Young Investigators, in America Heart Association (AHA), Scientific Sessions 2009. 2009/11/14-18. (Orland, Florida)
- (7) Young Investigator Award, in the 13<sup>th</sup> Scientific Session of the Society of Cardiovascular Endocrinology and Metabolism (CVEM). 2009/10/23-4 (Omiya, Japan)
- (8) Research Incentive Award, in the 19<sup>th</sup> Tokyo Hypertension Conference. 2009/9/5 (Tokyo, Japan)

**EMPLOYMENT:**

- Senior Lecturer. From September 2016 to present  
Department of Cardiovascular Medicine,  
The University of Tokyo Hospital, Japan
- Assistant Professor. April 2013 to August 2016  
Department of Cardiovascular Medicine,  
The University of Tokyo Hospital, Japan
- Visiting Scholar. May 2010 to March 2013  
Cell and Developmental Biology (Jonathan A. Epstein Lab.),  
University of Pennsylvania, U.S.A.
- Assistant Professor. July 2007 to March 2010  
Department of Cardiovascular Medicine,  
The University of Tokyo Hospital, Japan
- Fellow in Cardiovascular Medicine. 2006-2007  
The University of Tokyo Hospital, Japan
- Research Fellow (DC1). 2003-2006  
The Japan Society for the Promotion of Science (JSPS)  
Tokyo University Graduate School of Medicine, Japan, 2002-2006  
Residency, Cardiovascular Center Sakakibara Hospital, Japan, 2000-2002.  
Internship, Kanto Central Hospital, Japan, 1999-2000.  
Internship, The University of Tokyo Hospital, Japan, 1998-1999.

## PUBLICATIONS:

1. **Takeda N#**, Inuzuka R, Maemura S, Morita H, Nawata K, Fujita D, Taniguchi Y, Yamauchi H, Yagi H, Kato Masayoshi, Nishimura H, Hirata Y, Ikeda Y, Kumagai H, Amiya E, Hara H, Fujiwara T, Akazawa H, Suzuki J, Imai Y, Nagai R, Takamoto S, Hirata Y, Ono Minoru, Komuro I. Impact of pathogenic *FBNI* variant types on the progression of aortic disease in patients with Marfan syndrome. *Circulation: Genomic and Precision Medicine*, 2018 inpress. (#Corresponding Author)
2. **Takeda N\*#**, Fujiwara T\*, Hara H, Morita H, Kishihara J, Inuzuka R, Yagi H, Maemura S, Toko H, Harada M, Ikeda Y, Kumagai H, Nomura S, Takimoto E, Akazawa H, Ako J, Komuro I. Distinct variants affecting differential splicing of *TGFBR1* exon5 cause either Loeys-Dietz syndrome or multiple self-healing squamous epithelioma. *European Journal of Human Genetics*, 2018 inpress (\*equally first authors) (#Corresponding Author)
3. Hara H, **Takeda N#**, Komuro I. Pathophysiology and therapeutic potential of cardiac fibrosis. *Inflammation and Regeneration* 37:13,2017. (#Corresponding Author).
4. **Takeda N\***, Sayama S\*, Iriyama T, Inuzuka R, Maemura S, Fujita D, Yamauchi H, Nawata K, Bougaki M, Hyodo H, Shitara R, Nakayama T, Komatsu A, Nagamatsu T, Osuga Y, Fujii T. Authors' reply Re: Peripartum type B aortic dissection in patients with Marfan syndrome who underwent aortic root replacement. *BJOG: An International Journal of Obstetrics & Gynaecology*, 2018;125:502-503. (\*equally first authors)
5. Oshima Y, Hara H, **Takeda N#**, Hasumi E, Kuroda Y, Tanguchi G, Inuzuka R, Nawata K, Morita H, Komuro I. A novel mutation of *NFIX* causes Sotos-like syndrome (Malan syndrome) complicated with thoracic aortic aneurysm and dissection. *Hum Genome Var* 4:17022, 2017 (#Corresponding Author).
6. **Takeda N\***, Sayama S\*, Iriyama T, Inuzuka R, Maemura S, Fujita D, Yamauchi H, Nawata K, Bougaki M, Hyodo H, Shitara R, Nakayama T, Komatsu A, Nagamatsu T, Osuga Y, Fujii T. Peripartum type B aortic dissection in patients with Marfan syndrome who underwent aortic root replacement. *BJOG: An International Journal of Obstetrics & Gynaecology* 2018;125:487-493. (\*equally first authors)
7. **Takeda N\*#**, Hara H, Morita H, Hatano M, Amiya E, Maki H, Minatsuki S, Taki M, Shiraishi Y, Fujiwara T, Maemura S, Komuro I. Three novel *BMPR2* mutations associated with advanced pulmonary arterial hypertension. *Hum Genome Var.* 4:17010, 2017 (\*equally first authors) (#Corresponding Author).
8. Kamo T, Akazawa H, Suda W, Saga-Kamo A, Shimizu Y, Yagi H, Liu Q, Nomura S, Naito AT, **Takeda N**, Harada M, Toko H, Kumagai H, Ikeda Y, Takimoto E, Suzuki JI, Honda K, Morita H, Hattori M, Komuro I. Dysbiosis and compositional alterations with aging in the gut microbiota of patients with heart failure. *PLoS One* 12(3):e0174099, 2017.
9. Harada M, **Takeda N**, Toko H. Prostaglandin E2 signaling as a target of anti-cardiac fibrosis in heart failure treatment. *Int Heart J.* 58;3-4, 2017.
10. Amiya E, Morita H, Hatano M, Nitta D, Hosoya Y, Maki H, Motozawa Y, Sato N, Ishiura H, Numakura S, Shintani Y, Kinugawa K, **Takeda N**, Shimizu J, Tsuji S, Komuro I. Fukutin gene mutations that cause left ventricular noncompaction. *Int J Cardiol.* 222:727-9, 2016.
11. **Takeda N#**, Yagi H, Hara H, Fujiwara T, Fujita D, Nawata K, Inuzuka R, Taniguchi Y, Harada M, Toko H, Akazawa H, Komuro I. Pathophysiology and management of cardiovascular manifestations in Marfan and Loeys-Dietz syndrome. *Int Heart J.* 57:271-7, 2016 (#Corresponding Author)
12. Suzuki JI, Imai Y, Aoki M, Fujita D, **Takeda N**, Aoyama N, Wakayama K, Ikeda Y, Kumagai H, Akazawa H, Izumi Y, Isobe M, Komuro I, Hirata Y. Periodontitis may deteriorate sinus of Valsalva dilatation in Marfan syndrome patients. *Int Heart J.* 57:456-60,2016
13. Li D, **Takeda N**, Jain R, Manderfield LJ, Liu F, Li L, Anderson SA, Epstein JA. Hopx distinguishes hippocampal from lateral ventricle neural stem cells. *Stem Cell Res* 15:522-529, 2015
14. **Takeda N#**, Morita H, Fujita D, Inuzuka R, Taniguchi Y, Nawata K, Komuro I. A deleterious *MYH11* mutation causing familial thoracic aortic dissection. *Hum Genome Var.* 2:15028, 2015 (#Corresponding Author)
15. **Takeda N\*#**, Fujita D\*, Morita H, Kato M, Nishimura H, Inuzuka R, Taniguchi Y, Nawata K, Hyodo H, Imai Y, Hirata Y, Komuro I. A novel mutation of *TGFBR2* causing Loeys-Dietz syndrome complicated with pregnancy-related fatal cervical arterial dissections. *Int J Cardiol* 201:288-290, 2015 (\*equally first authors) (#Corresponding Author)
16. **Takeda N\***, Imai Y\*, Morita H\*, Miya F, Hyodo H, Fujita D, Tajima T, Tsunoda T, Nagai R,

- Kubo M, Komuor I. A deletion mutation in myosin heavy chain 11 causing familial thoracic aortic dissection in two Japanese pedigrees. *Int J Cardiol* 195:290-292, 2015 (\*equally first authors)
17. Kumagai H, Ikeda Y, Motozawa Y, Fujishiro M, Okamura T, Fujio K, Okazaki H, Nomura S, **Takeda N**, Harada M, Toko H, Takimoto E, Akazawa H, Morita H, Suzuki J, Yamazaki T, Yamamoto K, Komuro I, Yanagisawa. Quantitative measurement of GPCR endocytosis via pulse-chase covalent labeling. *PLoS One* 10:e0129394, 2015
  18. **Takeda N**, Morita H, Fujita D, Inuzuka R, Taniguchi Y, Imai Y, Hirata Y, Komuro I. Congenital contractual arachnodactyly complicated with aortic dilatation and dissection: Case Report and review of literature. *Am J Med Genet A* 167:2382-2387, 2015
  19. Ikeda Y, Kumagai H, Okazaki H, Fujishiro M, Motozawa Y, Nomura S, **Takeda N**, Toko H, Takimoto E, Akazawa H, Morita H, Suzuki J, Yamazaki T, Komuro I, Yanagisawa M. Monitoring β-arrestin recruitment via β-lactamase enzyme fragment complementation: purification of peptide E as a low-affinity ligand for mammalian bombesin receptors. *PLoS One* 10:e0127445, 2015
  20. Jain R, Barkauskas C.E, **Takeda N**, Bowie E.J, Aghajanian H, Wang Q, Padmanabhan A, Manderfield L.J, Gupta M, Li D, Li L, Trivedi C.M, Hoan L.M, Epstein J.A. Plasticity of Hopx(+) type I alveolar cells to regenerate type II cells in the lung. *Nat Commun* 6:6727, 2015
  21. Yagi H, Hatano M, **Takeda N#**, Harada S, Suzuki Y, Taniguchi Y, Shintani Y, Morita H, Kanamori N, Aoyama T, Watanabe M, Manabe I, Akazawa H, Kinugawa K, Komuro I. A case of congenital contractual arachnodactyly without *FBN1* or *FBN2* gene mutation, complicated with dilated cardiomyopathy. *Intern Med* 54:1237-1241, 2015. (#Corresponding Author)
  22. Fujita D, **Takeda N#**, Imai Y, Inuzuka R, Komuro I, Hirata Y. Pathophysiology and Japanese clinical characteristics in Marfan syndrome. *Pediatr Int* 56:484-91, 2014 (#Corresponding Author)
  23. **Takeda N#**, Jain R, Li Deqiang, Li L, Lu MM, Epstein JA. Lgr5 identifies progenitor cells capable of taste bud regeneration after injury. *PLoS One* 8(6):e66314, 2013 (#Corresponding Author)
  24. **Takeda N**, Jain R, LeBoeuf MR, Padmanabhan A, Wnag Q, Li L, Lu MM, Millar SE, Epstein JA. Hopx expression defines a subset of multipotent hair follicle stem cells and a progenitor population primed to give rise to K6<sup>+</sup> niche cells. *Development* 140:1655-1664, 2013
  25. Ogawa N, Imai Y, Nishimura H, Kato M, **Takeda N**, Nawata K, Taketani T, Morota T, Takamoto S, Nagai R, Hirata Y. Circulating transforming growth factor beta-1 level in Japanese patients with Marfan syndrome. *Int Heart J* 54:23-26, 2013
  26. Sakamoto A, Nagai R, Saito K, Imai Y, Takahashi M, Hosoya Y, **Takeda N**, Hirano K, Koike K, Enomoto Y, Kume H, Homma Y, Maeda D, Yamada H, Fukayama M, Hirata Y, Ishizaka N. Idiopathic retroperitoneal fibrosis, inflammatory aortic aneurysm, and inflammatory pericarditis - Retrospective analysis of 11 case histories. *J Cardiol* 59:139-146, 2012
  27. **Takeda N**, Jain R, Leboeuf MR, Wang Q, Lu MM, Epstein JA. Interconversion between intestinal stem cell populations in distinct niches. *Science* 334:1420-1424, 2011
  28. Ogawa M, Imai Y, Takahashi Y, Nawata K, Hara K, Nishimura H, Kato M, **Takeda N**, Kohro T, Morita H, Taketani T, Yamazaki T, Goto J, Tsuji S, Takamoto S, Nagai R, Hirata Y. Evaluating Japanese patients with the Marfan syndrome using high-throughput microarray-based mutational analysis of Fibrillin-1 gene. *Am J Cardiol* 108:1801-1807, 2011
  29. McConnell BB, Kim SS, Yu K, Ghaleb AM, **Takeda N**, Manabe I, Nusrat A, Nagai R, Yang VW. Kruppel-like factor 5 is important for maintenance of crypt architecture and barrier function in mouse intestine. *Gastroenterology* 141:1302-1313, 2011
  30. **Takeda N**, Manabe I. Cellular interplay between cardiomyocytes and non-myocytes in cardiac remodeling. *Int J Inflam*. 2011:535241, 2011
  31. Takahashi M, Shimizu T, Inajima T, Hosoya Y, **Takeda N**, Ishizaka N, Yamashita H, Hirata Y, Nagai R. A case of localized IgG4-related thoracic periarteritis and recurrent nerve palse. *Am J Med Sci*. 341:166-9, 2011
  32. Iwata H, Manabe I, Fujiu K, Yamamoto T, **Takeda N**, Eguchi K, Furuya A, Kuro-O M, Sata M, Nagai R. Bone marrow-derived cells contribute to vascular inflammation but do not differentiate into smooth muscle cell lineages. *Circulation* 122:2048-57, 2010
  33. **Takeda N**, Manabe I, Uchino Y, Eguchi K, Matsumoto S, Nishimura S, Shindo T, Sano M, Otsu K, Snider P, Conway SJ, Nagai R. Cardiac fibroblasts are essential for the adaptive response of the murine heart to pressure overload. *J Clin Invest* 120:254-265, 2010
  34. **Takeda N#**, Seko Y, Oriuchi Y, Nagai R. Gamma-delta T-cell-mediated dilated cardiomyopathy. *Int J Cardiol* 125:130-132, 2008 (#Corresponding Author)
  35. Shinoda Y, Ogata N, Higashikawa A, Manabe I, Shindo T, Yamada T, Kugimiya F, Ikeda T,

- Kawamura N, Kawasaki Y, Tsushima K, **Takeda N**, Nagai R, Hoshi K, Nakamura K, Chung UI, Kawaguchi H. Kruppel-like factor 5 causes cartilage degradation through transactivation of matrix metalloproteinase 9. *J Biol Chem* 283:24682-24689,2008
36. Kato H, Ishida J, Nagano K, Sugaya T, **Takeda N**, Sugiyama F, Yagami KI, Fujita T, Nangaku M, Fukamizu A. Deterioration of atherosclerosis in mice lacking angiotensin II type 1A receptor in bone marrow-derived cells. *Lab Invest* 88:731-739,2008
37. Kada N, Suzuki T, Aizawa K, Matsumura T, Ishibashi N, Suzuki N, **Takeda N**, Munemasa Y, Sawaki D, Ishikawa T, Nagai R. Acyclic retinoid inhibits neointima formation through retinoic acid receptor beta-induced apoptosis. *Arterioscler Thromb Vasc Biol* 27:1535-1541,2007
38. **Takeda N#**, Nakajima J, Yamada N, Hiroi Y, Hirata Y, Nagai R. Rupture of bronchogenic cyst in the pericardium with high carbohydrate antigen 19-9 production. *Respiratory Medicine Extra* 3:76-78,2007 (#Corresponding Author)
39. Shimizu T, **Takeda N#**, Takahashi M, Imai Y, Ishizaka N, Hirata Y, Nagai R. Subarachnoid Hemorrhage from Mycotic Aneurysms. *Intern Med* 45:1189-1190,2006 (#Corresponding Author)
40. **Takeda N**, Manabe I, Iwata H, Iimuro S, Kagechika H, Shudo K, Nagai R. Synthetic retinoid Am80 reduces scavenger receptor expression and atherosclerosis in mice by inhibiting IL-6. *Arterioscler Thromb Vasc Biol* 26:1177-1183,2006
41. **Takeda N#**, Takahashi T, Seko Y, Maemura K, Nakasone H, Sakamoto K, Hirata Y, Nagai R. Takayasu myocarditis mediated by cytotoxic T lymphocytes. *Intern Med* 44:256-260,2005 (#Corresponding Author)
42. **Takeda N#**, Ohtaki E, Kitahara K, Nagayama M, Nagasaki M. Pulmonary thromboembolism in a patient with an anomalous right coronary artery as a cause of unusual biventricular myocardial infarction. *Circ J* 68:883-886,2004 (#Corresponding Author)
43. Iimuro S, Shindo T, Moriyama N, Amaki T, Niu P, **Takeda N**, Iwata H, Zhang Y, Ebihara A, Nagai R. Angiogenic effects of adrenomedullin in ischemia and tumor growth. *Circ Res* 95:415-423,2004
44. Niu P, Shindo T, Iwata H, Iimuro S, **Takeda N**, Zhang Y, Ebihara A, Suematsu Y, Kangawa K, Hirata Y, Nagai R. Protective effects of endogenous adrenomedullin on cardiac hypertrophy, fibrosis, and renal damage. *Circulation* 109:1789-1794,2004
45. Niu P, Shindo T, Iwata H, Ebihara A, Suematsu Y, Zhang Y, **Takeda N**, Iimuro S, Hirata Y, Nagai R. Accelerated cardiac hypertrophy and renal damage induced by angiotensin II in adrenomedullin knockout mice. *Hypertens Res* 26:731-736,2003
46. **Takeda N**, Ohtaki E, Kasegawa H, Tobaru T, Nagayama M, Misu K, Asano R, Kitahara K, Umemura J, Sumiyoshi T, Hosoda S. Infective Endocarditis Associated With Quadricuspid Aortic Valve: A Case Report. *Jpn Heart J* 44:441-445,2003
47. **Takeda N**, Ohtaki E, Misu K, Asano R, Tobaru T, Nagayama M, Kitahara K, Umemura J, Sumiyoshi T, Hosoda S. Normalization of left ventricular parameters following carvedilol treatment in a case of unclassified cardiomyopathy with longstanding refractory status. *Intern Med* 41:1147-1152,2002
48. **Takeda N#**, Kitahara K, Sumiyoshi T. Chronic Advanced Pulmonary Hypertension. *Intern Med* 41:675,2002 (#Corresponding Author)
49. **Takeda N**, Ihn H, Teramoto S. Markedly increased levels of IL-6 and CA125 in pleural fluid of an elderly person with overlap syndrome of systemic sclerosis and systemic lupus erythematosus. *Age Ageing*. 30:17,2001
50. Machida U, Kami M, Kanda Y, Takeuchi K, Akahane M, Yamaguchi I, Kakiuchi C, **Takeda N**, Tanaka Y, Chiba S, Honda H, Hirai H. Aspergillus tracheobronchitis after allogeneic bone marrow transplantation. *Bone Marrow Transplant* 24:1145-1149,1999
51. **Takeda N**, Shibuya M, Maru Y. The BCR-ABL oncogene potentially interacts with the xeroderma pigmentosum group B protein. *Proc Natl Acad Sci USA* 96:203-207,1999