

## CURRICULUM VITAE

Ichiro SAKUMA, M.D., Ph.D.

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Date of Birth: September 10, 1954

Gender: Male

Place of Birth: Sapporo, Japan

Citizenship: Japan

### Education and Degrees:

1973                    Graduated from Sapporo Minami High School, Sapporo, Japan  
1979                    M.D., Graduated from Hokkaido University School of Medicine,  
                             Sapporo, Japan  
                             Sum Cum Laude (Ranked 1st in class 120)  
                             Physician's License in Japan  
1983                    Ph.D., Graduated from Hokkaido University Graduate School of  
                             Medicine, Sapporo, Japan  
                             Thesis: Application of Multi-slice ECG-gated X-ray Computed

## Tomography for the Assessment of Cardiac Functions

### Board Certifications:

1985	Board Certification in Sports Medicine in Japan
1990	Board Certification in Internal Medicine in Japan
1990	Board Certification in Cardiology in Japan
1995	Board Certification in Clinical Pharmacology in Japan
1997	Board Certification in Industrial Physician in Japan
1999	Board Certification in Japanese College of Cardiology (FJCC)
2000	Board Certification in Clinical Pharmacology Instructor in Japan
2001	Board Certification in The Japan Sexual Function Society in Japan
2008	Board Certification in The Japan Society for Menopause and Women's Health
2008	Board Certification in The Japan Mibyo System Association
2010	Board Certification in The Japan Society of Ningen Dock
2012	Board Certification in The Japan Society for Tobacco Control
2013	Board Certification in The Japan Physicians Association
2014	Board Certification in The Japanese Society of Clinical Nutrition
2015	Board Certification in The Japan Atherosclerosis Society Instructor
2016	Board Certification in Specialist in Dementia Support

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### Research & Professional Experience:

1979-1980	Resident in Department of Cardiovascular Medicine Hokkaido University Hospital
1980-1981	Resident in Division of Internal Medicine & Cardiology Tonan Hospital, Sapporo, Japan
1981-1983	Resident in Department of Cardiovascular Medicine Hokkaido University Hospital, Sapporo, Japan
1983-1985	Staff Doctor Division of Preventive Medicine & Internal Medicine Sapporo Teishin Hospital, Sapporo, Japan
1985-1986	Staff Doctor Department of Cardiovascular Medicine Hokkaido University Hospital, Sapporo, Japan

1986-1988      Research Fellow  
Department of Pharmacology  
Cornell University Medical College, New York, USA

1988-1993      Staff Doctor  
Department of Cardiovascular Medicine  
Hokkaido University Hospital, Sapporo, Japan

1993-1999      Assistant Professor  
Department of Cardiovascular Medicine  
Hokkaido University School of Medicine, Sapporo, Japan

1999-2000      Assistant Professor (Lecturer)  
Department of Cardiovascular Medicine  
Hokkaido University School of Medicine, Sapporo, Japan

2000-2007      Assistant Professor (Lecturer)  
Department of Cardiovascular Medicine  
Hokkaido University Hospital  
Hokkaido University Graduate School of Medicine, Sapporo, Japan

2007-            Director  
Caress Sapporo Hokko Memorial Clinic

2016-            Visiting Professor  
Life Science University of Hokkaido

Professional Organizations:

American Heart Association (since 1995)

International Society of Heart Research (since 1993)

International Society of Sexual Medicine (Since 2016)

Japanese:

Japanese Heart Association (since 1979)

Japanese College of Cardiology (since 1980, JFCC since 1999)

Japanese Society of Internal Medicine (since 1982)

Japanese Society of Vasoactive Substances (since 1988)

Japanese Society of Angiology (since 1988)

Japanese Society of Clinical Pharmacology (since 1989, council member since 1999)

Japanese Society of Medical Engineering (since 1989)

Japanese Society of Circulatory Regulation (since 1993, council member since 1999)  
 Japanese Society of Vascular Cellular Biology (since 1997, council member since 1997)  
 Japanese Society of Vascular Endocrinology and Metabolism (since 1997)  
 Japanese Society of Blood Substitutes (since 1997, council member since 1999)  
 Japanese Society of Gerontology (since 1997)  
 Japanese Society of Physical Strength (since 1985,)  
 The Japan Society for Menopause and Women`s Health (since 1998)  
 Japanese Society of Heart Failure (since 1998, council member 2001-2007)  
 Japanese Society of Sexual Function (since 2000, council member 2001-)  
 Japanese Society of Clinical Sports Medicine (since 2000)  
 The Japan Mibyou System Society (since 2001, council member 2001-)  
 The Japan Atherosclerosis Society (since 2002)  
 The Japan Diabetic Society (since 2007)  
 Japanese Psychogeriatric Society (since 2008)  
 The Japan Society for Dementia Research (since 2008)  
 The Japan Society of Ningen Dock (since 2008)  
 The Japan Society for Tobacco Control (since 2008)  
 The Japanese Association of gender specific Medicine (since 2008, director 2010-)  
 The Japanese Society of Clinical Nutrition (since 2008, council member 2013-)  
 Japan Society of Metabolism and Clinical Nutrition (since 2010)

Award:

1990	Research Grant Award of Japanese Adult Vascular Disease Research Foundation for a Study "EDRF and Hypertension"
1991	Research Grant Award of Hokkaido Heart Association for a Study "Contribution of EDRF to Development of Hypertension"
1991	Uehara Memorial Life Science Foundation Research Award for a Study "Relationship Between EDRF and Development of Hypertension"
1993	Takakuwa Memorial Scholarship Foundation Research Award for a Study "Development of a New Model of Coronary Microvascular Damage by Inhibition of EDRF"
1993	Research Grant Award of Japan Heart Foundation for a Study "Development of a New Model of Coronary Microvascular Damage of Rat and Its Application for Treatment of Patients"

- 1994                    Research Grant Award of Yokoyama Clinical Pharmacology Research Grant Foundation for a Study "Effects of Hormone Replacement Therapy to Prevent Progression of Ischemic Heart Disease in Postmenopausal Female Patients"
- 1994                    Research Grant Award of Japanese Clinical Pharmacology Research Foundation for a Study "Effects of Hormone Replacement Therapy to Prevent Progression of Ischemic Heart Disease in Elderly Female Patients"
- 2017                    The best activity award of The Japanese Society of Clinical Nutrition

Invited Talk (Lectures in International Meetings only):

1. Ichiro Sakuma: Role for NO in regulation of sympathetic nerve system. Invited Lecture of Kobe International Symposium on NO in Cardiovascular Disease (10/1996, Kobe, Japan)
2. Ichiro Sakuma: Role of NO in microcirculation. Invited lecture in Sapporo International Symposium "Recent Advances in Nitric Oxide Research" (9/1997, Sapporo, Japan)
3. Ichiro Sakuma: Role of Hormone Replacement Therapy in Japanese Women. Symposium in 1st Congress of the Asian Pacific Society of Atherosclerosis and Vascular Diseases (9/1998, Suita, Japan)
4. Ichiro Sakuma: Attenuation of Cardiovascular Risk Factors by ACE Inhibition. Symposium in 2nd Congress of the Asian Pacific Society of Atherosclerosis and Vascular Diseases (2/1/2000, ChiangMai, Thailand)
5. Ichiro Sakuma: Lipids, Menopause and Coronary Heart Disease in Japanese Women. Symposium in 2nd Congress of the Asian Pacific Society of Atherosclerosis and Vascular Diseases (2/2/2000, ChiangMai, Thailand)
6. Ichiro Sakuma: Effects of Various Estrogen Regimens on Coagulation/Fibrinolysis. Gachon Cardiovascular Symposium and Live Demonstration 2000 (6/17/2000, Inchon, Korea)
7. Ichiro Sakuma: HRT and coagulation/fibrinolysis. 1st Scientific Meeting of the Asia-Pacific Menopause Federation (5/28/2001, Seoul, Korea)
8. Ichiro Sakuma: The role of hormone replacement therapy in preventing cardiovascular diseases in post-menopausal women. The 5th International

- Conference on Preventive Cardiology (5/30/2001, Osaka, Japan)
9. Ichiro Sakuma: S-Nitrosylated polyethylene glycol-conjugated hemoglobin derivative as a candidate material for oxygen therapeutics. International Symposium on Polymer Therapeutics (7/14/2001, Nara, Japan)
  10. Ichiro Sakuma: HORMONE REPLACEMENT THERAPY (HRT) FOR CARDIOVASCULAR PREVENTION IN WOMEN. Symposium in 3rd Congress of the Asian Pacific Society of Atherosclerosis and Vascular Diseases (2/20/2002, Cebu, Philippines)
  11. Ichiro Sakuma: Effects of Diabetes and Estrogen on Angiogenesis of the Heart. 23th Spring Scientific Conference of the Korean Society of Lipidology and Atherosclerosis (3/9/2003, Seoul, Korea)
  12. Ichiro Sakuma: The role of angiotensin II receptor antagonist and calcium channel antagonist on diabetic microangiopathy in the rat heart. Gachon Endovascular Live Demonstration 2002 (9/13/2002, Incheon, Korea)
  13. Ichiro Sakuma: Gender Influences on the Role of EDHF in Vasodilation. EDHF: Looking Beyond Nitric Oxide and Prostacyclin. The American Heart Association Scientific Sessions 2003 (11/9/2003, Orlando, U.S.A.)
  14. Ichiro Sakuma, Akira Kitabatake: s-Nitroso-Hemoglobin and Autoregulation of Capillary Blood Flow. The 1st Meeting of Cardiovascular Physiome (12/7/2003, Okayama, Japan)
  15. Ichiro Sakuma, Atsushi Sato, David D. Gutterman, Akira Kitabatake: Interaction of NO and EDHF in human microvessels. The 3<sup>rd</sup> International Conference on the Biology, Chemistry, and Therapeutic Applications of Nitric Oxide. (5/24/2004, Nara, Japan)

Editorial board:

Frontiers in Cardiovascular Medicine

Reviewer:

American Journal of Physiology-Heart and Circulatory Physiology

Atherosclerosis

Basic & Clinical Pharmacology & Toxicology

Behavioral and Brain Functions  
Biochemical Pharmacology  
Circulation Journal  
Geriatrics and Gerontology International  
International Heart Journal  
International Journal of Cardiology  
International Journal of Endocrinology  
Journal of Atherosclerosis and Thrombosis  
Journal: Diabetes Research and Clinical Practice  
Journal of Pharmacology and Experimental Therapeutics  
Livestock Science  
Molecular Pharmacology  
Naunyn-Schmiedeberg's Archives of Pharmacology  
Pharmacology & Therapeutics

#### Bibliography:

In recent 5 years

Review papers

1. Kyoung Im Cho, Ichiro Sakuma, Il Suk Sohn, Sang-Ho Jo, Kwang Kon Koh: Inflammatory and metabolic mechanisms underlying the calcific aortic valve disease. *Atherosclerosis* 277: 60-65, 2018
2. Ichiro Sakuma, Katsunori Ikewaki: Should measures of HDL function be added to the LDL-C target level based guidelines for prevention of atherosclerotic disease? *Circ J* 82(5): 1251-1252, 2018
3. Kyoung Im Cho, Ichiro Sakuma, Il Suk Sohn, Toshio Hayashi, Kazunori Shimada, Kwang Kon Koh: Best Treatment Strategies with Statins to Maximize the CardioMetabolic Benefits. *Circ J* 82(4): 937-943, 2018
4. Ichiro Sakuma, Toshihisa Anzai: What Should Be Generalized Diagnostic Markers for Peripartum Cardiomyopathy? *Circ J* 81(11): 1578-1579, 2017
5. Kwang Kon Koh, Ichiro Sakuma, Kazunori Shimada, Toshio Hayashi, Michael J Quon: Combining Potent Statin Therapy with Other Drugs to Optimize Simultaneous Cardiovascular and Metabolic Benefits while Minimizing Adverse Events. *Korean Circ*

J 47(4): 432-439, 2017

6. Kwang Kon Koh, Seung Hwan Han, Ichiro Sakuma, Dong Zhao: Calming down chaos regarding redefining blood pressure targets-the importance of statin-based therapy. *Int J Cardiol* 221: 572–574, 2016
7. Seung Hwan Han, Stephen J Nicholls, Ichiro Sakuma, Dong Zhao, Kwang Kon Koh: Hypertriglyceridemia and Cardiovascular Diseases: Revisited. *Korean Circ J* 46(2): 135-144, 2016
8. Pyung Chun Oh, Ichiro Sakuma, Toshio Hayashi, Kwang Kon Koh: Angiotensin converting enzyme inhibitors remain the first treatment of choice. *Korean J Intern Med* 31: 237-241, 2016
9. Kwang Kon Koh, Pyung Chun Oh, Ichiro Sakuma: Reply to comment on: Effects of ezetimibe/simvastatin combination on metabolic parameters by Prof. Moses S Elisaf. *Int J Cardiol* 202: 154–155, 2016
10. Koh KK, Sakuma I, Hayashi T, Kim SH, Chung WJ: Renin-angiotensin system inhibitor and statins combination therapeutics - what have we learnt? *Expert Opin Pharmacother* 16(7): 949-953, 2015
11. Lim S, Oh PC, Sakuma I, Koh KK: How to Balance Cardioresnometabolic Benefits and Risks of Statins. *Atherosclerosis*: 235: 644-648, 2014.
12. Lim S, Sakuma I, Quon M, Koh KK: Differential Metabolic Actions of Specific Statins: Clinical and Therapeutic Considerations. *Antioxid Redox Signal* 20(8):1286-1299, 2014
13. Hae-Young Lee, Ichiro Sakuma, Sang-Hyun Ihm, Choong-Won Goh, Kwang Kon Koh: Statins and Renin-Angiotensin System Inhibitor Combination Treatment to Prevent Cardiovascular Disease. *Circ J* 78: 281-287, 2014.
14. Lim S, Sakuma I, Quon MJ, Koh KK: Potentially Important Considerations in Choosing Specific Statin Treatments to Reduce Overall Morbidity and Mortality. *Int J Cardiol* 167(9): 1696-1702, 2013
15. Lim S, Park YM, Sakuma I, Koh KK: How to control residual cardiovascular risk despite statin treatment: Focusing on HDL-cholesterol. *Int J Cardiol* 166(1): 8-14, 2013.

#### Original papers

1. Koretsune Y, Etoh T, Katsuda Y, Suetsugu T, Kumeda K, Sakuma I, Eshima K, Shibuya M, Ando SI, Yokota N, Goto S, Pieper KS, Allu J, Kakkar AK; GARFIELD-AF Investigators: Risk Profile and 1-Year Outcome of Newly

Diagnosed Atrial Fibrillation in Japan - Insights From GARFIELD-AF. *Circ J* 2018 Dec 4. doi: 10.1253/circj.CJ-18-0655. [Epub ahead of print]

2. Isao Taguchi, Satoshi Iimuro, Hiroshi Iwata, Hiroaki Takashima, Mitsuru Abe, Eisuke Amiya, Takanori Ogawa, Yukio Ozaki, Ichiro Sakuma, Yoshihisa Nakagawa, Kiyoshi Hibi, Takafumi Hiro, Yoshihiro Fukumoto, Seiji Hokimoto, Katsumi Miyauchi, Tsutomu Yamazaki, Hiroshi Ito, Yutaka Otsuji, Kazuo Kimura, Jun Takahashi, Atsushi Hirayama, Hiroyoshi Yokoi, Kazuo Kitagawa, Takao Urabe, Yasushi Okada, Yasuo Terayama, Kazunori Toyoda, Takehiko Nagao, Masayasu Matsumoto, Yasuo Ohashi, Tetsuji Kaneko, Retsu Fujita, Hiroshi Ohtsu, Hisao Ogawa, MD, Hiroyuki Daida, Hiroaki Shimokawa, Yasushi Saito, Takeshi Kimura, Teruo Inoue, Masunori Matsuzaki, Ryoza Nagai: High-dose versus Low-dose Pitavastatin in Japanese Patients with Stable Coronary Artery Disease 5 (REAL-CAD): a randomized superiority trial. *Circulation* 137(19): 1997-2009, 2018
3. Miyauchi K, Kimura T, Shimokawa H, Daida H, Iimuro S, Iwata H, Ozaki Y, Sakuma I, Nakagawa Y, Hibi K, Hiro T, Fukumoto Y, Hokimoto S, Ohashi Y, Ohtsu H, Saito Y, Matsuzaki M, Nagai R: REAL-CAD Trial Investigators: Rationale and Design of Randomized Evaluation of Aggressive or Moderate Lipid Lowering Therapy with Pitavastatin in Coronary Artery Disease (REAL-CAD) Trial. *Int Heart J* 59(2): 315-320, 2018
4. Shimokawa H, Yamashita T, Uchiyama S, Kitazono T, Shimizu W, Ikeda T, Kamouchi M, Kaikita K, Fukuda K, Origasa H, Sakuma I, Saku K, Okumura Y, Nakamura Y, Morimoto H, Matsumoto N, Tsuchida A, Ako J, Sugishita N, Shimizu S, Atarashi H, Inoue H: The EXPAND study: Efficacy and safety of rivaroxaban in Japanese patients with non-valvular atrial fibrillation. *Int J Cardiol* 258: 126-132, 2018
5. Takanori Ikeda, Hirotugu Atarashi, Hiroshi Inoue, Shinichiro Uchiyama, Takanari Kitazono, Takeshi Yamashita, Wataru Shimizu, Masahiro Kamouchi, Koichi Kaikita, Koji Fukuda, Hideki Origasa, Ichiro Sakuma, Keiji Saku, Yasuo Okumura, Yuichiro Nakamura, Hideo Morimoto, Naoki Matsumoto, Akihito Tsuchida, Junya Ako, Nobuyoshi Sugishita, Shogo Shimizu, Hiroaki Shimokawa: Study Design and Baseline Characteristics of the EXPAND Study: Evaluation of Effectiveness and Safety of Xa Inhibitor, Rivaroxaban for the Prevention of Stroke and Systemic Embolism in a Nationwide Cohort of Japanese Patients Diagnosed as Non-Valvular Atrial Fibrillation. *Tohoku J Exp Med* 240: 259-268, 2015.

6. Koh KK, Oh PC, Sakuma I, Lee Y, Han SH, Shin EK: Rosuvastatin dose-dependently improves flow-mediated dilation, but reduces adiponectin levels and insulin sensitivity in hypercholesteremic patients. *Int J Cardiol.* 223: 488-493, 2016
7. Koh KK, Oh PC, Sakuma I, Lee Y, Han SH, Shin EK: Vascular and metabolic effects of omega-3 fatty acids combined with fenofibrate in patients with hypertriglyceridemia. *Int J Cardiol* 221: 342-346, 2016
8. Koh KK, Oh PC, Sakuma I, Kim EY, Lee Y, Hayashi T, Han SH, Park YM, Shin EK: Vascular and metabolic effects of ezetimibe combined with simvastatin in patients with hypercholesterolemia. *Int J Cardiol* 199: 126-131. 2015.
9. Toshio Hayashi, Kiyoshi Kubota, Seinosuke Kawashima, Hirohito Sone, Hiroshi Watanabe, Takashi Ohru, Koutaro Yokote, Minoru Takemoto, Atsushi Araki, Mitsuhiro Noda, Hiroshi Noto, Ichiro Sakuma, Masao Yoshizumi, Koichiro Ina, Hideki Nomura, on behalf of Japan CDM group: Efficacy of HMG-CoA reductase inhibitors in the prevention of cerebrovascular attack in 1016 patients older than 75 years among 4014 type 2 diabetic individuals. *Int J Cardiol.* 177: 860–866, 2014
10. Oh PC, Koh KK, Sakuma I, Lim S, Lee Y, Lee S, Lee K, Han SH, Shin EK: Omega-3 fatty acid therapy dose-dependently and significantly decreased triglycerides and improved flow-mediated dilation, however, did not significantly improve insulin sensitivity in patients with hypertriglyceridemia. *Int J Cardiol* 176: 696-702, 2014
11. Daida H, Nohara R, Hata M, Kaku K, Kawamori R, Kishimoto J, Kurabayashi M, Masuda I, Sakuma I, Yamazaki T, Yokoi H, Yoshida M: Can Intensive Lipid-Lowering Therapy Improve the Carotid Intima-Media Thickness in Japanese Subjects Under Primary Prevention for Cardiovascular Disease?: The JART and JART Extension Subanalysis. *J Atheroscler Thromb* 21(7): 739-754, 2014
12. Yokoi H, Nohara R, Daida H, Hata M, Kaku K, Kawamori R, Kishimoto J, Kurabayashi M, Masuda I, Sakuma I, Yamazaki T, Yoshida M: Change in carotid intima-media thickness in a high-risk group of patients by intensive lipid-lowering therapy with rosuvastatin. *Int Heart J* 55(2): 146-152, 2014
13. Koh KK, Lim S, Choi H, Lee Y, Han SH, Lee K, Oh PC, Sakuma I, Shin EK, Quon MJ.: Combination Pravastatin and Valsartan Treatment have Additive Beneficial Effects to Simultaneously Improve Both Metabolic and Cardiovascular Phenotypes beyond that of Monotherapy with Either Drug In Patients with Primary Hypercholesterolemia. *Diabetes* 62(10): 3547-3552, 2013.

14. Koh KK, Quon MJ, Sakuma I, Han SH, Choi H, Lee K, Shin EK: Differential metabolic effects of rosuvastatin and pravastatin in hypercholesterolemic patients. *Int J Cardiol* 166(6): 509-515, 2013.
15. Nohara R, Daida H, Hata M, Kaku K, Kawamori R, Kishimoto J, Kurabayashi M, Masuda I, Sakuma I, Yamazaki T, Yokoi H, Yoshida M, for the Justification for Atherosclerosis Regression Treatment (JART) Investigators: Effect of Long-Term Intensive Lipid-Lowering Therapy With Rosuvastatin on Progression of Carotid Intima-Media Thickness -Justification for Atherosclerosis Regression Treatment (JART) Extension Study-. *Circ J* 77(6): 1526-1533, 2013.
16. Yamazaki T, Nohara R, Daida H, Hata M, Kaku K, Kawamori R, Kishimoto J, Kurabayashi M, Masuda I, Sakuma I, Yokoi H, Yoshida M; Justification for Atherosclerosis Regression Treatment (JART) Investigators.: Intensive lipid-lowering therapy for slowing progression as well as inducing regression of atherosclerosis in Japanese patients. *Int Heart J* 54(1): 33-39, 2013

#### Important review papers

1. Ichiro Sakuma and Akira Kitabatake: Menopause and Cardiovascular Diseases in Women. *Internal Medicine* 43(2): 151-154, 2004
2. Kwang Kon Koh, Ichiro Sakuma: Should Progestins Be Blamed for the Failure of Hormone Replacement Therapy to Reduce Cardiovascular Events in Randomized Controlled Trials? *Arterioscler Thromb Vasc Biol* 24: 1-9, 2004.
3. Han SH, Sakuma I, Shin EK, Koh KK: Antiatherosclerotic and anti-insulin resistance effects of adiponectin: basic and clinical studies. *Prog Cardiovasc Dis* 52(2): 126-140, 2009.
4. Koh KK, Sakuma I, Quon MJ: Differential metabolic effects of distinct statins. *Atherosclerosis* 215(1):1-8, 2011
5. Ichiro Sakuma: What Type of Statin and What Level of Low-Density Lipoprotein Cholesterol Should Be Appropriate for Secondary Prevention for Japanese Patients With Coronary Artery Disease? *Circ J* 76(6): 1324-1325, 2012
6. Koh KK, Lim S, Sakuma I, Quon MJ. Caveats to aggressive lowering of lipids by specific statins. *Int J Cardiol* 154(1): 97-101, 2012.

#### Important original papers

1. Ichiro Sakuma, Dennis Stuehr, Steven S. Gross, Carl Nathan and Roberto Levi: Identification of arginine as a precursor of endothelium-derived relaxing factor. *Proc Natl Acad Sci USA* 85: 8664-8667, 1988
2. Dennis Stuehr, Steven S. Gross, Ichiro Sakuma, Roberto Levi and Carl F. Nathan: Activated murine macrophages secrete a metabolite of arginine with the bioactivity of endothelium-derived relaxing factor and the chemical reactivity of nitric oxide. *J Exp Med* 169: 1011-1020, 1989
3. Ichiro Sakuma, Yasuhiro Akaishi, Mitsuhiro Fukao, Yasuhiro Makita, Masaaki Makita, Takeshi Kobayashi, Kazuhiko Matsuno, Tamotsu Miyazaki and Hisakazu Yasuda: Dipyridamole potentiates the anti-aggregating effect of endothelium-derived relaxing factor. *Thromb Res* 60(S12): 87-90, 1990
4. Mitsuru Munakata, Yoshitaka Masaki, Ichiro Sakuma, Hideaki Ukita, Yoshinori Ohtsuka, Yukihiro Homma and Yoshikazu Kawakami: Pharmacological differentiation of epithelium-derived relaxing factor from nitric oxide. *J Appl Physiol* 69: 665-670, 1990
5. Michihisa Tohda, Ichiro Sakuma and Yoshiyuki Nomura: The slow cyclic GMP increase caused by serotonin in NG108-15 cells is not inhibited by antagonists of known serotonin receptors: possible existence of a new receptor subtype coupled with membrane-bound guanylate cyclase. *J Neurochem* 57: 714-717, 1991
6. Ichiro Sakuma, Hiroko Togashi, Mitsuhiro Yoshioka, Hideya Saito, Miwa Yanagida, Mamoru Tamura, Takeshi Kobayashi, Hisakazu Yasuda, Steven S. Gross and Roberto Levi: N G-methyl-L-arginine, an inhibitor of L-arginine-derived nitric oxide synthesis, stimulates renal sympathetic nerve activity in vivo: a role for nitric oxide in the central regulation of sympathetic tone? *Circ Res* 70: 607-611, 1992
7. Hiroko Togashi, Ichiro Sakuma, Mitsuhiro Yoshioka, Akira Kitabatake, Hisakazu Yasuda, Hideya Saito, Steven S. Gross and Roberto Levi: A CNS action of nitric oxide in blood pressure regulation. *J Pharmacol Exp Ther* 262: 343-347, 1992
8. Takehiro Yamashita, Haruaki Nakaya, Noritsugu Tohse, Masumi Kusaka, Hiroko Uemura, Ichiro Sakuma, Hisakazu Yasuda, Morio Kanno and Akira Kitabatake: Depressed responsiveness to angiotensin II in ventricular myocytes of hypertrophic cardiomyopathic Syrian hamster. *J Mol Cell Cardiol* 26: 1429-1438, 1994
9. Mitsuhiro Fukao, Yuichi Hattori, Morio Kanno, Ichiro Sakuma and Akira Kitabatake: Thapsigargin- and cyclopiazonic acid-induced endothelium-dependent hyperpolarization in rat mesenteric artery. *Br J Pharmacol* 115: 987-992, 1995
10. Mitsuhiro Fukao, Yuichi Hattori, Morio Kanno, Ichiro Sakuma and Akira Kitabatake: Evidence for selective inhibition by lysophosphatidylcholine of

acetylcholine-induced endothelium-dependent hyperpolarization and relaxation in rat mesenteric artery. *Br J Pharmacol* 116: 1541-1544, 1995

11. Mitsuhiro Fukao, Yuichi Hattori, Morio Kanno, Ichiro Sakuma and Akira Kitabatake: Evidence against a role of cytochrome P450-derived arachidonic acid metabolites in endothelium-dependent hyperpolarization by acetylcholine in rat mesenteric artery. *Br J Pharmacol* 120: 439-446, 1997

12. Mitsuhiro Fukao, Yuichi Hattori, Morio Kanno, Ichiro Sakuma and Akira Kitabatake: Sources of Ca<sup>2+</sup> in relation to generation of acetylcholine-induced endothelium-dependent hyperpolarization. *Br J Pharmacol* 120: 1328-1334, 1997

13. Mitsuhiro Fukao, Yuichi Hattori, Morio Kanno, Ichiro Sakuma and Akira Kitabatake: Alterations in endothelium-dependent hyperpolarization and relaxation in mesenteric arteries from streptozotocin-induced diabetic rats. *Br J Pharmacol* 121: 1383-1391, 1997

14. Hiroshi Tomioka, Yuichi Hattori, Mitsuhiro Fukao, Watanabe H, Yasuhiro Akaishi, Atsushi Sato, Kim TQ, Ichiro Sakuma, Akira Kitabatake, Morio Kanno: Role of endothelial Ni<sup>2+</sup>-sensitive Ca<sup>2+</sup> entry pathway in regulation of EDHF in porcine coronary artery. *Am J Physiol* 280(2): H730-H737, 2001

15. Zaman AK, Fujii S, Sawa H, Goto D, Ishimori N, Watano K, Kaneko T, Furumoto T, Sugawara T, Sakuma I, Kitabatake A, Sobel BE: Angiotensin-converting enzyme inhibition attenuates hypofibrinolysis and reduces cardiac perivascular fibrosis in genetically obese diabetic mice. *Circulation* 103(25): 3123-3128, 2001

16. Ichiro Sakuma, Ming-Yue Liu, Atsushi Sato, Toshio Hayashi, Akihisa Iguchi, Akira Kitabatake, Yuichi Hattori. Endothelium-dependent hyperpolarization and relaxation in mesenteric arteries of middle-aged rats: influence of oestrogen. *Br J Pharmacol* 135(1): 48-54, 2002

17. Matsuzaki M, Hiramori K, Imaizumi T, Kitabatake A, Hishida H, Nomura M, Fujii T, Sakuma I, Fukami K, Honda T, Ogawa H, Yamagishi M: Intravascular ultrasound evaluation of coronary plaque regression by low density lipoprotein-apheresis in familial hypercholesterolemia. The Low Density Lipoprotein-Apheresis Coronary Morphology and Reserve Trial (LACMART). *J Am Coll Cardiol* 40(2): 220-227, 2002

18. Jesmin S, Hattori Y, Sakuma I, Liu MY, Mowa CN, Kitabatake A: Estrogen deprivation and replacement modulate cerebral capillary density with vascular expression of angiogenic molecules in middle-aged female rats. *J Cereb Blood Flow Metab.* 23(2): 181-189, 2003

19. Sasayama S, Ishii N, Ishikura F, Kamijima G, Ogawa S, Kanmatsuse K, Kimoto Y,

Sakuma I, Nonogi H, Matsumori A, Yamamoto Y: Men's Health Study. *Circ J* 67(8): 656-659, 2003

20. Jesmin S, Sakuma I, Hattori Y, Kitabatake A: Role of Angiotensin II in Altered Expression of Molecules Responsible for Coronary Matrix Remodeling in Insulin-Resistant Diabetic Rats. *Arterioscler Thromb Vasc Biol* 23(11): 2021-2026, 2003

21. S Jesmin, I Sakuma, A Salah-eldin, K Nonomura, Y Hattori and A kitabatake: Diminished penile expression of vascular endothelial growth factor and its receptors at the insulin-resistant stage of a Type II diabetic rat model: a possible cause for erectile dysfunction in diabetes. *J Mol Endocrinol* 31(3): 401-418, 2003

22. Sato A, Sakuma I, Gutterman DD: Mechanism of dilation to reactive oxygen species in human coronary arterioles. *Am J Physiol Heart Circ Physiol* 285(6): H2345-H2354, 2003

23. Matsuda N, Jesmin S, Takahashi Y, Hatta E, Kobayashi M, Matsuyama K, Kawakami N, Sakuma I, Gando S, Fukui H, Hattori Y, Levi R: Histamine H1- and H2-Receptor Gene and Protein Levels Are Differentially Expressed in the Hearts of Rodents and Humans. *J Pharmacol Exp Ther* 309(2):786-795, 2004

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