

Curriculum Vitae

Shin-ichi Kamachi , Ph.D.

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Senior Consultant

BCG-Japan

Chuo-ku, Tokyo

EXPERTISE

Strong scientific background, plan development of bio-product, prepare application dossier of biological medicinal products and diagnostics, negotiate with Japanese authorities.

EDUCATION

Ph.D. University of Kyushu (1980)

D.S. Pharmaceutical Sciences, University of Kyushu (1977)

M.S. Pharmaceutical Sciences, University of Kyushu (1974)

EXPERIENCE

BCG-Japan *Senior Consultant*

Chuo-ku, Tokyo (2008 - present)

ZXY Consulting Co., *Consultant*

(Oct. 2004 – Jan. 2008)

Chugai Pharma, *Senior Leader, CMC Planning & Coordination Development*

(Apr. 2001 – Sep. 2004)

Chugai Pharma., *Principal Researcher, Production Technical Division*

(Oct. 1999 – Mar. 2001)

(Biosensor Laboratories Co., Ltd., *Managing Director, concurrently* (Jul. 1999 – Jun. 2001)

Chugai Pharma, *Principal Researcher, Application Research Division*

(Jul. 1996 – Sep. 1999)

Chugai Pharma, *Principal Researcher, Pharmacokinetics Division*

(Apr. 1995 – Jun. 1996)

Chugai Pharma, *Director, Analytic Technical Division*

(Oct. 1994 – Mar. 1995)

Chugai Pharma, *Principal Researcher, Analytic Technical Division*

(Dec. 1992 – Sep. 1994)

Shin-ichi Kamachi, Ph.D.

Chugai Pharma, *Senior Researcher, Analytic Technical Division*.
(Dec. 1991 – Nov. 1992)

Chugai Pharma, *Assistant Director, Diagnostic Division*
(Dec. 1988 – Nov. 1991)
(Biosensor Laboratories Co., Ltd., Senior Researcher, concurrently Mar. 1988 – Jul. 1988)

Chugai Pharma, *Senior Researcher, Diagnostic Division*
(Dec. 1985 – Nov. 1988)
(Jichi Medical School (Tochigi-pre.), Visiting Scientist, concurrently Dec. 1983 – May 1990)

Chugai Pharma, *Researcher, Biochemical and Diagnostic Division*.
(Apr. 1977 – Nov. 1985)

HONORS AND AWARDS

- Received two awards for distinguished activities from Chugai Pharma. (1989 and 1993).

QUALIFICATIONS

- The license of work environment analyst (1987)
- The license of diagnostic technical expert (1976)
- The license of radiant rays handling manager (1975)
- Pharmacist (1972)

ACHIEVEMENTS

Prostate Specific Antigen: γ -Seminoprotein (γ -Sm)

- Discovered that the prostate specific antigen (γ -Sm) is useful as the tumor marker of prostate cancer.
- Developed EIA for γ -Sm in serum, gave the clinical studies, submitted application dossier as biological medicinal product, and get approval.
- γ -Sm is specified at the diagnosis textbook as the tumor marker of prostate cancer, and γ -Sm is popular widely in clinic at present.
- γ -Sm was discovered as the first tumor marker in Japan, and a monoclonal antibody was used as the first product in Japan.

Erythropoietin (EPO)

- Developed high sensitive RIA for EPO in serum, measured the samples of the clinical studies, and performed the bio-equivalent studies.
- I developed EIA of EPO and impurities for specifications of EPO in the drug substance and drug product.
- Developed the assay of antibodies in serum from patients administrated with EPO.
- Prepared the application dossier for Japanese authorities.
- Carried out compatibility studies of EPO injection and other injectable preparations.
- I investigated non-clinical research for a new clinical application of EPO.

Granulocyte Colony Stimulating Factor (G-CSF)

- Developed high sensitive EIA for G-CSF in serum, measured the samples of the clinical studies, and performed the bio-equivalent studies.
- Developed EIA of G-CSF and impurities for specifications of EPO in the drug substance and drug product.
- Developed the assay of antibodies in serum from patients administrated with G-CSF.
- Prepared the application dossier for Japanese and EU authorities.
- Prepared the application dossier for the amendment of manufacturing and specifications.
- Developed the G-CSF receptor assay by FACS for a clinical application of G-CSF.
- Investigated the properties of natural G-CSF, the stabilities of G-CSF in serum, the production of G-CSF by stromal cells, pharmacokinetics studies of G-CSF in hematological disorders, serum levels in a patient with neutropenia.

Vitamin D Derivatives

- Developed a new convenient assay for vitamin D metabolites using fluorescence-labeling reagent.
- Developed RIA for the determination of 22-oxacalcitriol in rat and human plasma, measured the samples of the clinical studies.
- Prepared the application dossier for Japanese authorities.
- Investigated the metabolic activation of vitamin D.

Nicorandil

- Investigated the interrelationship of cardiovascular effects, plasma and tissue of nicorandil, and vascular cGMP formation.
- Investigated non-clinical research for a new clinical application of Nicorandil.

Tocilizumab (Humanized anti-IL-6 receptor antibody, MRA)

- Promoted and planed CMC development of MRA.
- Planed the CMC strategy of MRA for tripartite applications.
- Prepared the application dossier for Japan according to CTD.
- Negotiated with Japanese authorities for CMC issues.

PROFESSIONAL FIELD OF RESEARCH

Analytical studies

- Assay for drugs levels in serum
- Assay for Anti-drug antibody levels in serum
- Biosensor

Biochemical studies

- Research of tumor marker
- Research of receptor
- Research of mechanism and effect

Pharmacokinetics studies

- Bio-equivalent studies

- Pharmacokinetics

Protein engineering

- Molecular design of peptide

MANAGEMENT

- Establishment of two R&D companies with Japanese authorities.
- Managing director of Biosensor Laboratories Co. Ltd.
- MBA training in Chugai Pharma. and University of California, Berkeley.
- Senior Researcher in Chugai Pharma.
- Assistant Director of Diagnostic Division in Chugai Pharma.
- Principal Researcher in Chugai Pharma.
- Director of Technical Division in Chugai Pharma.
- Senior Leader of CMC Planning & Coordination Development, Chugai Pharma.

PUBLICATIONS

- 1) Imazeki, S.Kamachi: Drug Interaction of EPO and Ace, Clinical Kidney Dialysis, 17, 1277(2001).
- 2) S.Kamachi, K.Sugimoto, T.Yamasaki, N.Hirose, H.Ide and Y.Ohyama : Metabolic activation of 1α -hydroxyvitamin D₃ in human liver microsomes, Xenobiotica, 31, 701(2001).
- 3) S.Kamachi, K.Usuda, M.Saito: Tissue Distribution of (¹⁴C)Thamazole in Rat, Current Therapy, 18(4), 216(2000).
- 4) Kawase, F.Ichikawa, N.Koike, S.Kamachi, W.E.Stump, Y.Nishii and N.Kubodera :Synthesis and Pharmacokinetics of 1α -Hydroxyvitamin D₃ Tritiated at 22 and 23 Position Showing High Specific Radioactivity, Chem.Pharm.Bull, 48, 215(2000).
- 5) K.Kashimura, K.Yoden, M.Ueda, N.Nagai, S.Yamamoto, E.Hoshino, S.Kamachi, T.Matsuno: Compatibility Test of Ulerlmin Suspension, Pharm.Regul.Sci., 30, 8(1999).
- 6) K.Sakai, M.Akima, S.Kamachi, M.Moriyasu, S.Kitajima : Interrelationship of cardiovascular effects, plasma levels of nicorandil, and vascular cGMP formation in conscious rats, J. Pharm. Pharmacol., 50, 661(1998).
- 7) K.Sakai, M.Moriyasu, S.Kitajima, M.Akima, S.Kamachi and M.Tanikawa : Vascular levels and cGMP-increasing effects of nicorandil administered orally to rats, J. Cardiovasc. Pharmacol., 31, 595(1998).
- 8) T.Nakamura, C.Akiyoshi, H.Taki, S.Kamachi, K.Zaitso: Compatibility of Recombinant Human Erythropoietin (rHuEPO) Injection with Other Injectable Preparations, Pharm.Regul.Sci., 29, 203(1998).
- 9) K.Watari, K.Ozawa, S.Takahashi, A.Tojo, K.Tani, S.Kamachi, S.Asano : Pharmacokinetic studies of intravenous glycosylated recombinant human granulocyte colony-stimulating

factor in various hematological disorder: inverse correlation between the half-life and bone marrowmyeloid cell pool, Intern. J. Hematol., 66, 57(1997).

- 10) Kobayashi, K. Shimada, H. Taki, Y. Sakamoto and S. Kamachi : Radioimmunoassay Method for the Determination of 22-Oxacalcitriol, a Novel Analog of $1\alpha,25$ -Dihydroxyvitamin D₃ Having Valuable Clinical Potency, in Rat and Human Plasma, Bio. Pharm. Bull., 18, 382(1995).
- 11) Aoyagi, K. Arasawa, A. Matsuyuki, S. Kamachi, M. Fukushima, N. Osawa Chemiluminescence sandwich enzyme immunoassay for determination of human granulocyte colony stimulating factor(G-CSF), J. Biolumin. Chemilumin., 10, 345(1995).
- 12) K. Watari, K. Ozawa, K. Tajika, A. Tojo, K. Tani, S. Kamachi, et al. : Production of Human Granulocyte Colony Stimulating Factor by Various Kinds of Stromal Cells In Vitro Detected by Enzyme Immunoassay and In Situ Hybridization, Stem Cells, 12, 416(1994).
- 13) M. Ono, M. Oh-eda, S. Kamachi, M. Kato, Y. Endo and N. Ochi : Structure of G-CSF : significance of the sugar chain, J. Nutritional Science & Vitaminology, Spec No, 337(1992).
- 14) M. Kishita, H. Motojima, K. Oheda, T. Kojima, S. Kamachi, M. Fukushima: Stability of Granulocyte Colony-stimulating Factor (G-CSF) in Serum, Clinical Report, 26, 221(1992).
- 15) S. Kamachi, H. Motojima, K. Oheda, T. Kojima, E. Matsuda, K. Yamamoto: properties of Natural Granulocyte Colony-stimulating Factor (G-CSF), Clinical Report, 25, 4061(1991).
- 16) M. Shimizu, S. Kamachi, Y. Nishii and S. Yamada : Synthesis of Reagent for Fluorescence-Labeling of Vitamin D and Its Use in Assay Vitamin D Metabolites, Anal. Biochem., 194, 77(1991).
- 17) M. Misago, M. Kikuchi, J. Tsukada, T. Hanamura, S. Kamachi, S. Eto : Serum levels of G-CSF, M-CSF and GM-CSF in a patient with cyclic neutropenia, Europ. J. Haematol., 46, 312(1991).
- 18) M. Yamazaki, M. Aogaki, S. Kamachi, M. Fukushima: Immunological Comparison of Recombinant human G-CSF and Natural G-CSF, Jap. Pharmacol. Therap., 18, 75(1990).
- 19) S. Kamachi, K. Matsubara, T. Kobayashi, H. Motojima, M. Shimane, K. Mizuno, M. Fukushima: Preparation and Characteristics of Anti-recombinant human G-CSF Antibody, Jap. Pharmacol. Therap., 18, 51(1990).
- 20) K. Matsubara, T. Yoshimura, S. Kamachi, M. Fukushima, M. Hino and H. Morii : Radioimmunoassay for erythropoietin using anti-recombinant erythropoietin antibody with high affinity, Clin. Chim. Acta, 185, 177(1989).
- 21) K. Watari, S. Asano, N. Shirafuji, H. Kodo, K. Ozawa, F. Takaku and S. Kamachi : Serum Granulocyte-Stimulating Factor Levels in Healthy Volunteers and Patients with Various Disorders as Estimated by Enzyme Immunoassay, Blood, 73, 117(1989).

- 22) H.Motojima, T.Kobayashi, M.Shimane, S.Kamachi and M.Fukushima : Quantitative enzyme immunoassay for granulocyte colony stimulating factor (G-CSF), *J. Immunol. Methods*, 118, 187(1989).
- 23) S.Kamachi, T.Ishibashi: Determination of γ -Sm, *Jap.J.Clin.Pathol.*, 34, 65(1986).
- 24) S.Ishikawa, K.Tozuka, S.Ishiyama, K.Goto, S.Ohba, Y.Yonese, S.Kamachi, I.Sakurabayashi, T.Kawai: The significance of serum gamma-seminoprotein in prostatic cancer, *Acta Urol. Jap.*, 31, 961(1985).
- 25) S.Kamachi: γ -Seminoprotein (γ -Sm), *Medical Technology*, 13, (1985).
- 26) T.Okabe, S.Noda, K.Eto, K.Sagawa, M.Yokoyama, S.Kamachi: Clinical evaluation of prostate specific antigens (gamma-seminoprotein), *Jap.J.Urol.*, 76, 165(1985).
- 27) K.Tsuda, H.Iki, S.Kamachi, M.Hara: Demonstration of seminal stains by enzyme labeled anti- γ -Seminoprotein antibody, *Jap.J.Leg.Med.*, 39, 30(1985).
- 28) S.Kamachi, T.Yoshimura, T.Kobayashi, N.Yoshimura, K.Kumaki, K.Wakabayashi, et.al.: Studies on Determination of γ -Seminoprotein (γ -Sm) in Sera by Enzymeimmunoassy-1, *Rinsho Kensa*, 29, 87(1985).
- 29) S.Kamachi, T.Yoshimura, T.Kobayashi, N.Yoshimura, K.Kumaki, K.Wakabayashi, et.al.: Studies on Determination of γ -Seminoprotein (γ -Sm) in Sera by Enzymeimmunoassy-1, *Rinsho Kensa*, 28, 1755(1984).
- 30) S.Kamachi, I.Sakurabayashi, T.Kawai: Studies on prostate specific antigen, gamma-seminoprotein as a tumor marker of prostate cancer, *Jap.J.Clin.Pathol.*, 32, 781 (1984).
- 31) S.Kamachi, K.Wakabayashi, K.Zaitzu, Y.Ohkura: New chromogenic substrate for the esterase : acetate and butyrate of phenolic naphthylazo compounds with sulfonic acid group, *Chem.Pharm.Bull.*, 31, 172(1983).
- 32) S.Kamachi, K.Wakabayashi, M.Yamaguchi, Y.Ohkura: Spectrophotometric assay for lipase in serum using a chromogenic substrate, Orange I laurate, *Chem.Pharm. Bull.*, 31, 2732(1993).
- 33) S.Kamachi, K.Wakabayashi, M.Yamaguchi and Y.Ohkura: Orange-I Laurate, A New Chromogenic Substrate for the Assay of Lipase in Blood, *Analytica Clinica Acta* 148, 255(1983).