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Education

2005-2007　Ph.D. in Pharmaceutical Science: Toyama University Institute of Natural Medicine Research Center for Ethnomedicine, Division of Biofunctional Evaluation
Thesis:　"Preparation, Characterization and Anti-oxidative Effects of Oligomeric Proanthocayanidin-L-Cysteine Complexes"

1987-1989　MSc.: Kyoto University Graduate School of Engineering Department of Polymer Chemistry

1983-1987　Kyoto University Faculty of Engineering: Undergraduate School of Industrial Chemistry, Department of Polymer Chemistry

1980-1983　Hokkaido Sapporo Kita High School

Work Experience

1989-Present　Amino Up Chemical Co., ltd.

September, 2012-Present　President/COO

2011-2012　Senior Executive Director

2006-2011　Executive Director, Research and Development Division

1989-2006　Researcher, Research and Development Division

- Engaged in natural products chemistry;
  Purification, identification and quantification of compounds.
  Analysis of the structure-activity relation
  Developing the process from experimental scale to industrial scale.

1989-1998 Asahi Glass Co., LTD:

Central Research Lab., Biochemical Group

- Engaged in synthetic organic chemistry:

  Synthesis of fluorine-containing prostaglandin, fluorine-containing nucleic acid, phospholipids derivative, and modified enzymes.

- Experienced drug development along with introducing GCP and GMP

- Conducted pre-clinical trials and compositional analysis.

Publications

(1) Lipase modification by various synthetic polymers for use in chloroform

Y. Ito, H. Fujii, Y. Imanishi

Department of Polymer Chemistry, Kyoto University

Biotech. Lett., **14,** 1149-1152 (1992)

(2) Enzymatic hybridization with synthetic polymers for use in organic media

Y. Ito, H. Fujii, Y. Imanishi

Department of Polymer Chemistry, Kyoto University

Macromol. Chem. Rapid Commun., **13**, 315-319 (1992)

(3) Catalytic peptide synthesis by trypsin modified with polystyrene in chloroform

Y. Ito, H. Fujii, Y. Imanishi

Department of Polymer Chemistry, Kyoto University

Biotechnol Prog., **9** (2), 128-130 (1993)

(4) Lecithinization of IL-6 enhances its thrombopoietic activity in mice

R. Igarashi, Y. Tsutsumi, H. Fujii, S. Tsunoda, A. Ochiai, M. Takenaga, Y. Morizawa, T. Mayumi, Y. Mizushima

Division of Drug Delivery Systems, St. Marianna University

J. Pharm. Pharmacol., **49** (1), 113-118 (1997)

(5) Effect of oral treatment of *Perilla frutescens* and its constituents on type-I allergy in mice

T. Makino, A. Furuta, H. Fujii, T. Nakagawa, H. Wakushima, K. Saito, Y. Kano

Department of Kampo Medicinal Sciences, Hokkaido College of Pharmacy

Biol. Pharm. Bull., **24** (10), 1206-1209 (2001)

(6) Isoflavone aglycon produced by culture of soybean extracts with basidiomycetes and its anti-angiogenic activity

T. Miura, L. Yuan, B. Sun, H. Fujii, M. Yoshida,K. Wakame, K. Kosuna

Department of Biochemistry, Amino Up Chemical Co., Ltd.

Biosci. Biotechnol. Biochem., **66** (12), 2626-2631 (2002)

(7) Inhibition of human breast cancer growth by GCP (genistein combined polysaccharide) in xenogeneic athymic mice: involvement of genistein biotransformation by β-glucuronidase from tumor tissues
L. Yuan, C. Wagatsuma, M. Yoshida, T. Miura, T. Mukoda, H. Fujii, B. Sun, J. H. Kim, Y. J. Surh
Department of Biochemistry, Amino Up Chemical Co Ltd.
Mutat. Res., 523-524: 55-62 (2003)

(8) Anti-allergic effect of *Perilla frutescens* and its active constituents
T. Makino, Y. Furuta, H. Wakushima, H. Fujii, K. Saito, Y. Kano
Department of Kampo Medicinal Sciences, Hokkaido College of Pharmacy
Phytother. Res., **17** (3), 240-243 (2003)

(9) Active hexose correlated compound enhances tumor surveillance through regulating both innate and adaptive immune responses.
Y. Gao, D. Zhang, B. Sun, H. Fujii, K. Kosuna, Z. Yin
Department of Medicine, Yale School of Medicine
Cancer Immunol Immunother., **55** (10), 1258-1266 (2005)

(10) Active hexose correlated compound enhances tumor surveillance through regulating both innate and adaptive immune responses.
Y. Gao, D. Zhang, B. Sun, H. Fujii, K. Kosuna, Z. Yin
Department of Medicine, Yale School of Medicine
Cancer Immunol Immunother., **55** (10), 1258-1266 (2005)

(11) Comparative efficacy of oligonol, catechin and (-)-epigallocatechin 3-O-gallate in modulating the potassium bromate-induced renal toxicity in rats
H. Nishioka, H. Fujii, B. Sun, OI. Aruoma
SourceAmino Up Chemical Co. Ltd.
Toxicology, **226** (2-3), 181-187 (2006)

(12) Low molecular proanthocyanidin dietary biofactor Oligonol: Its modulation of oxidative stress, bioefficacy, neuroprotection, food application and chemoprevention potentials
OI. Aruoma, B. Sun, H. Fujii, VS. Neergheen, T. Bahorun, KS. Kang, MK. Sung
Faculty of Health and Social Care, London South Bank University
Biofactors, **27** (1-4), 245-265 (2006)

(13) Protective effect of grape seed polyphenols against high glucose-induced oxidative stress
H. Fujii, T. Yokozawa, YA. Kim, C. Tohda, G. Nonaka
Institute of Natural Medicine, University of Toyama
Biosci. Biotechnol. Biochem., **70** (9), 2104-2111 (2006)

(14)

(15) Nutritional Food Active Hexose Correlated Compound (AHCC) Enhances Resistance against Bird Flu
H. Fujii, H. Nishioka, K. Wakame, B. Sun
Amino Up Chemical Co Ltd.
Jpn. J. Complement. Altern. Med., **4** (1), 37-40 (2007)

(16) The influence of active hexose correlated compound (AHCC) on cisplatin-evoked chemotherapeutic and side effects in tumor-bearing mice.
A. Hirose, E. Sato, H. Fujii, B. Sun, H. Nishioka, OI. Aruoma
Amino Up Chemical Co Ltd.
Toxicol. Appl. Pharmacol., **222** (2), 152-158 (2007)

(17) A Phase I study of the safety of the nutritional supplement, active hexose correlated compound, AHCC, in healthy volunteers
EL. Spierings, H. Fujii, B. Sun, T. Walshe
Medvadis Research Corporation, Wellesley Hills
J. Nutr. Sci. Vitaminol., **53** (6), 536-539 (2007)

(18) Evaluation of the safety and toxicity of the oligomerized polyphenol Oligonol
H. Fujii, B. Sun, H. Nishioka, A. Hirose, OI. Aruoma
Amino Up Chemical Co Ltd.
Food Chem. Toxicol., **45** (3), 378-387 (2007)

(19) Preparation, characterization, and antioxidative effects of oligomeric proanthocyanidin-L-cysteine complexes
H. Fujii, T. Nakagawa, H. Nishioka, E. Sato, A. Hirose, Y. Ueno, B. Sun, T. Yokozawa, G. Nonaka
Amino Up Chemical Co Ltd.
J. Agric. Food Chem., **55** (4), 1525-1531 (2007)

(20) Modulation of infection-induced inflammation and locomotive deficit and longevity in senescence-accelerated mice-prone (SAMP8) model by the oligomerized polyphenol Oligonol
K. Tomobe, H. Fujii, B. Sun, H. Nishioka, OI. Aruoma
Amino Up Chemical Co Ltd.
Biomed. Pharmacother., **61** (7), 427-434 (2007)

(21) Platelet Reactivity in Male Smokers Following the Acute Consumption of a Flavanol-Rich Grapeseed Extract
JA. Polagruto, HB. Gross, F. Kamangar, K. Kosuna, B. Sun, H. Fujii, CL. Keen, RM. Hackman
Department of Family and Consumer Science, Sacramento City College
J. Med. Food., **10** (4), 725-730 (2007)

(22) Active hexose correlated compound activates immune function to decrease bacterial load in a murine model of intramuscular infection.
H. Aviles, P. O'Donnell, J. Orshal, H. Fujii, B. Sun, G. Sonnenfeld
Department of Biological Sciences, Binghamton University, State University of New York
Am. J. Surg., **195** (4), 537-545 (2008)

(23) Evaluation of active hexose correlated compound hepatic metabolism and potential for drug interactions with chemotherapy agents.
CM. Mach, H. Fujii, K. Wakame, J. Smith
Division of Pharmacy, The University of Texas M.D. Anderson Cancer Center
J. Soc. Integr. Oncol., **6** (3), 105-109 (2008)

(24) Flavanols: digestion, absorption and bioactivity
R. Hackman, J. Polagruto, QY. Zhu, B. Sun, H. Fujii, C. Keen
Department of Nutrition, University of California
Phytochemistry Reviews, **7**, 195-208 (2008)

(25) Oligonol inhibits UVB-induced COX-2 expression in HR-1 hairless mouse skin--AP-1 and C/EBP as potential upstream targets
JK. Kundu, EJ. Chang, H. Fujii, B. Sun, YJ. Surh
College of Pharmacy, Seoul National University
Photochem. Photobiol., **84** (2), 399-406 (2008)

(26) Antioxidative effects of a new lychee fruit-derived polyphenol mixture, oligonol, converted into a low-molecular form in adipocytes
T. Sakurai, H. Nishioka, H. Fujii, N. Nakano, T. Kizaki, Z. Radak, T. Izawa, S. Haga, H. Ohno
Department of Molecular Predictive Medicine and Sport Science, Kyorin University
Biosci. Biotechnol. Biochem., **72** (2), 463-476 (2008)

(27) The Supplementation of Oligonol, the New Lychee Fruit-derived Polyphenol Converting into a Low-molecular Form, Has a Positive Effect on Fatigue during Regular Track-and-field Training in Young Athletes
H. Ohno,T. Sakurai,T. Hisajima, S. Abe, T. Kizaki, J. Ogasawara, Y. Ishibashi, K. Imaizumi, T. Takemasa, S. Haga, K. Kitadate, H. Nishioka, H. Fujii
Department of Molecular Predictive Medicine and Sport Science, Kyorin University
Adv. Exer. Sports Physiol., **13** (4), 93-99 (2008)

(28) Acute, subchronic and genotoxicity studies conducted with Oligonol, an oligomerized polyphenol formulated from lychee and green tea extracts
H. Fujii, H. Nishioka, K. Wakame, BA. Magnuson, A. Roberts
Amino Up Chemical Co., Ltd.
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(29) Oral administration of active hexose correlated compound enhances host resistance to West Nile encephalitis in mice.
S. Wang, T. Welte, H. Fang, GJ. Chang, WK. Born, RL. O'Brien, B. Sun, H. Fujii, K. Kosuna, T. Wang
Department of Microbiology, Immunology and Pathology, Colorado State University
J Nutr., **139** (3), 598-602 (2009)

(30) The effect of active hexose correlated compound in modulating cytosine arabinoside-induced hair loss, and 6-mercaptopurine- and methotrexate-induced liver injury in rodents.
B. Sun, K. Wakame, E. Sato, H. Nishioka, OI. Aruoma, H. Fujii
Amino Up Chemical Co Ltd.
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K. Shigama, A. Nakaya, K. Wakame, H. Nishioka, H. Fujii
Amino Up Chemical Co Ltd.
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(32) Inhibitory effects of oligonol on phorbol ester-induced tumor promotion and COX-2 expression in mouse skin: NF-kappaB and C/EBP as potential targets
JK. Kundu, DM. Hwang, JC. Lee, EJ. Chang, YK. Shin, H. Fujii, B. Sun, YJ. Surh
College of Pharmacy, Seoul National University
Cancer Lett., **273** (1), 86-97 (2009)

(33) Oligonol, a lychee fruit-derived low molecular weight polyphenol formulation, inhibits UVB-induced cyclooxygenase-2 expression, and induces NAD(P)H:quinone oxidoreductase-1 expression in hairless mouse skin
JK. Kundu, KS. Choi, H. Fujii, B. Sun, YJ. Surh
College of Pharmacy, Seoul National University
Journal of Functional Foods, **1** (1), 98-108 (2009)

(34) Oligonol, a new lychee fruit-derived low-molecular form of polyphenol, enhances lipolysis in primary rat adipocytes through activation of the ERK1/2 pathway.
J. Ogasawara, K. Kitadate, H. Nishioka, H. Fujii, T. Sakurai, T. Kizaki, T. Izawa, H. Ishida, H. Ohno
Department of Molecular Predictive Medicine and Sport Science, Kyorin University
Phytother. Res., **23** (11), 1626-1633 (2009)

(35) Amelioration of abdominal obesity by low-molecular-weight polyphenol (Oligonol) from lychee

J. Nishihira, M. Sato-Ueshima, K. Kitadate, K. Wakame, H. Fujii
Department of Medical Management and Informatics, Hokkaido Information University
Journal of Functional Foods, **1** (4), 341-348 (2009)

(36) Review of Cancer Therapy with AHCC(R) and GCP(R); The Long-Term Follow-Up over 12 Years for Stage IV (M1) Cancer of the Lung and the Breast
R. Ishizuka, H. Fujii, T. Miura, Y. Fukuchi, K. Tajima
Tajima Clinic
Inter. J. Integr. Med., **2** (1), 98-111 (2010)

(37) Effects of active hexose correlated compound on frequency of $CD4^+$ and $CD8^+$ T cells producing interferon-γ and/or tumor necrosis factor–α in healthy adults
Z. Yin, H. Fujii, T. Walshe
Department of Internal Medicine, Yale School of Medicine
Human Immunol., **71**, 1187-1190 (2010)

(38) Oligomerized grape seed polyphenols attenuate inflammatory changes due to antioxidative properties in coculture of adipocytes and macrophages
T. Sakurai, K. Kitadate, H. Nishioka, H. Fujii, T. Kizaki, Y. Kondoh, T. Izawa, H. Ishida, Z. Radák, H. Ohno
SourceDepartment of Molecular Predictive Medicine and Sport Science, Kyorin University
J. Nutr. Biochem., **21** (1), 47-54 (2010)

(39) Beneficial effect of the oligomerized polyphenol oligonol on high glucose-induced changes in eNOS phosphorylation and dephosphorylation in endothelial cells
XH. Zhang, H. Yokoo, H. Nishioka, H. Fujii, N. Matsuda, T. Hayashi, Y. Hattori
Department of Molecular and Medical Pharmacology, Graduate School of Medicine and Pharmaceutical Sciences, University of Toyama
Br. J. Pharmacol., **159** (4), 928-938 (2010)

(40) Bioactivity of a flavanol-rich lychee fruit extract in adipocytes and its effects on oxidant defense and indices of metabolic syndrome in animal models
S. Kalgaonkar, H. Nishioka, HB. Gross, H. Fujii, CL. Keen, RM. Hackman
Department of Nutrition, University of California
Phytother. Res., **24** (8), 1223-1228 (2010)

(41) Hypolipidaemic and antioxidative effects of oligonol, a low-molecular-weight polyphenol derived from lychee fruit, on renal damage in type 2 diabetic mice
JS. Noh, HY Kim, CH. Park, H. Fujii, T. Yokozawa
Institute of Natural Medicine, University of Toyama
Br. J. Nutr., **104** (8), 1120-1128 (2010)

(42) Oligonol, an oligomerized lychee fruit-derived polyphenol, activates the Ras/ Raf-1/ **MEK1/2 cascade independent of the IL-6 signaling pathway in rat primary adipocytes**
J. Ogasawara, K. Kitadate, H. Nishioka, H. Fujii, T. Sakurai, T. Kizaki, T. Izawa, H. Ishida, M. Tanno, H. Ohno
Department of Molecular Predictive Medicine and Sport Science, Kyorin University
Biochem. Biophys. Res. Commun., **402** (3), 554-559 (2010)

(43) **Comparison of the Effect of Oligonol, A New Lychee Fruit-derived Low Molecular Form of Polyphenol, and Epigallocatechin-3-gallate on Lipolysis in Rat Primary Adipocytes**
J. Ogasawara, K. Kitadate, H. Nishioka, H. Fujii, T. Sakurai, T. Kizaki, T. Izawa, H. Ishida, H. Ohno
Department of Molecular Predictive Medicine and Sport Science, Kyorin University
Phytother. Res., **25** (3), 467-471 (2010)

(44) **Genotoxicity and subchronic toxicity evaluation of Active Hexose Correlated Compound (AHCC).**
H. Fujii, N. Nishioka, R. Simon, R. Kaur, B. Lynch, A. Roberts
Amino Up Chemical Co Ltd.
Regul Toxicol Pharmacol., **59** (2), 237-250 (2011)

(45) **Evaluation of active hexose correlated compound (AHCC) in combination with pegylated liposomal doxorubicin for treatment of ovarian cancer**
R. Hunter, H. Fujii, K. Wakame, A. Gaikwad, JK. Wolf, JA. Smith
Division of Pharmacy, The University of Texas M.D. Anderson Cancer Center
Inter. J. Appl. Res., **4** (3), 6-14 (2011)

(46) **Active Hexose Correlated Compound promotes T helper (Th) 17 and 1 cell responses via inducing IL-1b production from monocytes in humans**
W. Lee, N. Lee, H. Fujii, I. Kang
Department of Internal Medicine, Yale University School of Medicine
Cellular Immunol., **275**, 19-23 (2012)

(47) **Personalized cancer therapy for stage IV non-small cell lung cancer: Combined use of active hexose correlated compound and genistein concentrated polysaccharide**
R. Ishizuka, H. Fujii, T. Miura, Y. Fukuchi, K. Tajima
Tajima Clinic
Personalized Med. Univ., **1**, 39-44 (2012)

(48) **Active Hexose Correlated Compound (AHCC) Alleviates Gemcitabine-Induced Hematological Toxicity in Non-Tumor-Bearing Mice**
D. Nakamoto, K. Shigama, H. Nishioka, H. Fujii
Amino Up Chemical Co Ltd.
Inter. J. Clin. Med., **3**, 361-367 (2012)

(49) Oligonol-induced Degradation of Perilipin 1 is Regulated through Lysosomal Degradation Machinery

J. Ogasawara, K. Kitadate, H. Nishioka, H. Fujii, T. Sakurai, T. Kizaki, T. Izawa, H. Ishida, H. Ohno
Department of Molecular Predictive Medicine and Sport Science, Kyorin University
Natur. Product Commun., **7** (9), 1193-1196 (2012)

(50) Safety of oligonol, a highly bioavailable lychee-derived polyphenolic antioxidant, on liver, kidney and heart function in rats.

M. Thirunavukkarasu, L. Zhan, K. Wakame, H. Fujii, H. Moriyama, M. Bagchi
Department of Surgery, Molecular Cardiology and Angiogenesis Laboratory, University of Connecticut Health Center
Toxicol. Mech. Methods, **22** (7), 555-559 (2012)