

## Symposium

# “Basics & Clinical practice of Plasmalogens” - Efficacy on Alzheimer’s Disease -

As seen in situations in U.S.A. and Japan, and the joint statement issued at G8 Dementia Summit, it is obvious that Alzheimer’s disease (AD) has become an urgent and important issue in the world. The preceding research in U.S.A. reported that plasmalogens (Pls: One of phospholipids) in the brain and blood were decreased in AD patients, which might deserve attention for prevention and treatment of AD.

The Institute of Hemorheological Function of Foods, also started a joint research in 2003, and succeeded in mass extraction and purification of Pls for the first time in the world. This enabled us to investigate the effect of Pls on animals and humans. We have found evidences indicating a beneficial effect of Pls on AD patients.

This symposium aims at publishing our research progress, expanding the study network for advancement of further research, and proceeding to practical use of Pls in the nearest future. We believe that this symposium will be a big step for new preventive and therapeutic strategies against AD.

### 1. Symposium 13:00 – 16:00

- Opening Speech 13:00 – 13:10
- Guest Speech 13:10 – 13:20
- Keynote Speech 13:20 – 13:50 (30 min.)

#### “History of Pls R&D: Our achievements and their Values”

Takehiko Fujino (M.D. & Ph.D., Emeritus Professor of Kyushu University)

- Presentations 14:00 – 16:00 (120 min.)

#### “Pls Basics and Oral Administration of Purified Pls on rats”

Shiro Mawatari (M.D. & Ph.D., Director of the Institute of Hemorheological Function of Foods)

#### “Importance of Pls in Nervous System”

Toshihiko Katafuchi (M.D. & Ph.D., Associate Professor, Department of Integrative Physiology, Graduate School of Medical Sciences, Kyushu University)

#### “Dynamics of Pls in the blood of AD patients and Cognitive Function Improvement Effects of Pls supplement – Single-blinded Clinical Trial -

Yoshio Tsuboi (M.D. & Ph.D., Professor of Department of Neurology, Fukuoka University School of Medicine)

Shinji OMa (M.D. & Ph.D., Associate Professor of Department of Neurology, Fukuoka University School of Medicine)

**Discussion** Takehiko Fujino, General Coordinator

### 2. Press Conference 16:10 – 16:40

### 3. Social Gathering 17:00 – 18:30 (Fee: 1,000 JPY)

**Date & Time: Tue, Feb. 4, 2014** Open at 12:30

\*Reservation required. Please fax the registration form on the reverse side of this leaflet.

**Venue: Centennial Hall Kyushu University School of Medicine (Hall 1 & 2)**

**3-1-1 Maidashi, Higashi-ku, Fukuoka, Japan TEL: +81-92-642-6257**

**150 seats available for the first applicants**

**Admission Fee: 3,000 JPY for General, Free for Members**

Organizer: Plasmalogens Research Society, 6-18-6F Tenya-machi, Hakata-ku, Fukuoka, 812-0025, JAPAN TEL: +81-92-273-2411

## ■ Our Discoveries around Plasmalogens

[Journal of Neuroinflammation 2012, 9:197](#) Masataka Ifuku, Toshihiko Katafuchi, Shiro Mawatari, Mami Noda, Kiyotaka Miake, Masaaki Sugiyama and Takehiko Fujino: Anti-inflammatory/anti-amyloidogenic effects of plasmalogens in lipopolysaccharide-induced neuroinflammation in adult mice

<<Abstract>> **Results:** Intraperitoneal (i.p.) injections of LPS (250 µg/kg) for seven days resulted in increases in the number of Iba-1-positive microglia and glial fibrillary acidic protein (GFAP)-positive astrocytes in the prefrontal cortex (PFC) and hippocampus accompanied by the enhanced expression of IL-1β and TNF-α mRNAs. In addition, β-amyloid (Aβ3-16)-positive neurons appeared in the PFC and hippocampus of LPS-injected animals. The co-administration of Pls (i.p., 20 mg/kg) after daily LPS injections significantly attenuated both the activation of glial cells and the accumulation of Aβ proteins. Finally, the amount of Pls in the PFC and hippocampus decreased following the LPS injections and this reduction was suppressed by co-treatment with Pls. **Conclusions:** These findings suggest that Pls have anti-neuroinflammatory and anti-amyloidogenic effects, thereby indicating the preventive or therapeutic application of Pls against AD.

[Lipids in Health and Disease 2012, 11:161](#) Shiro Mawatari, Toshihiko Katafuchi, Kiyotaka Miake and Takehiko Fujino: Dietary plasmalogen increases erythrocyte membrane plasmalogen in rats

<<Abstract>> **Results:** The PlsEtn diet given to Zucker diabetic fatty (ZDF) rats for 4 weeks caused decreases of plasma cholesterol and plasma phospholipid as compared to control diet. The other routine laboratory tests of plasma including triacylglycerol, glucose, liver and renal functions, albumin, and body weight were not different. Relative compositions of erythrocyte PlsEtn and phosphatidylethanolamine (PE) increased, and that of phosphatidylcholine (PC) decreased in PlsEtn diet group. The PlsEtn diet given to normal rats for 9 weeks again caused decrease of plasma cholesterol and phospholipid, and it induced increase of relative composition of PlsEtn of the erythrocyte membrane. The other routine laboratory tests of plasma and body weight were not different. **Conclusions:** Dietary PlsEtn increases relative composition of PlsEtn of erythrocyte membranes in normal and ZDF rats, and it causes decreases of plasma cholesterol and plasma phospholipids. Dietary PlsEtn for 9 weeks seemingly causes no adverse effect to health of normal rats.

[Dement Geriatr Cogn Disord Extra 2012\(2\),298-303](#) Shinji Oma, Shiro Mawatari, Kazuyuki Saito, Chikako Wakana, Yoshio Tsuboi, Tatsuo Yamada, Takehiko Fujino. : Changes in Phospholipid Composition of Erythrocyte Membrane in Alzheimer's Disease

<<Abstract>> **Results:** The ratios of pl-PE, phosphatidylethanolamine (PE) and phosphatidylserine (PS) to sphingomyelin were low as compared to those of the age-matched controls. **Conclusion:** These changes in erythrocyte phospholipids may reflect changes induced by oxidative stress, indicating the presence of high oxidative stress in the peripheral blood of AD patients.

[PLoS ONE 2013, 8: e83508. doi:10.1371/journal.pone.0083508](#) Md Shamim Hossain, Masataka Ifuku, Sachiko Take, Jun Kawamura, Kiyotaka Miake, Toshihiko Katafuchi: Plasmalogens rescue neuronal cell death through an activation of AKT and ERK survival signaling

<<Abstract>> In the present study, we have found that plasmalogens (Pls), which are glycerophospholipids containing vinyl ether linkage at sn-1 position, can protect the neuronal cell death upon serum deprivation. Interestingly, caspase-9, but not caspase-8 and caspase-12, was cleaved upon the serum starvation in Neuro-2A cells. Pls treatments effectively reduced the activation of caspase-9. Furthermore, cellular signaling experiments showed that Pls enhanced phosphorylation of the phosphoinositide 3-kinase (PI3K)-dependent serine/threoninespecific protein kinase AKT and extracellular-signal-regulated kinases ERK1/2. PI3K/AKT inhibitor LY294002 and MAPK/ERK kinase (MEK) inhibitor U0126 treatments study clearly indicated that Pls-mediated cell survival was dependent on the activation of these kinases. In addition, Pls also inhibited primary mouse hippocampal neuronal cell death induced by nutrient deprivation, which was associated with the inhibition of caspase-9 and caspase-3 cleavages. The present findings suggest that Pls have an anti-apoptotic action in the brain. Further studies on precise mechanisms of Pls-mediated protection against cell death may lead us to establish a novel therapeutic approach to cure neurodegenerative disorders.

[Analytical Biochemistry 370 \(2007\) 54-59](#) Shiro Mawatari, Yumika Okuma, Takehiko Fujino: Separation of intact plasmalogens and all other phospholipids by a single run of high-performance liquid chromatography

<<Abstract>> Plasmalogens are a unique subclass of glycerophospholipids characterized by the presence of a vinyl ether bond at the sn-1 position of the glycerol backbone, and they are found in high concentration in cellular membranes of many mammalian tissues. However, separation of plasmalogens as intact phospholipids has not been reported. This article describes a high-performance liquid chromatographic method that can separate intact ethanolamine plasmalogens (pl-PEs) and choline plasmalogens (pl-PCs) as well as all other phospholipid classes usually found in mammalian tissues by a single chromatographic run. The separation was obtained using an HPLC diol column and a gradient of a hexane/isopropanol/water system containing 1% acetic acid and 0.08% triethylamine. The HPLC method allowed a clear separation of plasmalogens from their diacyl analogues. The HPLC method, as applied to the study of peroxidation in human erythrocytes by a hydroperoxide, demonstrated that pl-PEs were targeted twice as much as their diacyl analogues.

## Symposium & Press Conference "Basics & Clinical practice of Plasmalogens" Registration form

Company		# of people	
Name			
Address			
TEL/FAX			
E-Mail			
Attendance at Social gathering Fee: 1,000 JPY	<b>Yes</b> (# of people:    ) / <b>No</b> ※Please make sure to circle the applicable one.		

Application Deadline: Tuesday January 28, 2014

**Secretariat of Plasmalogens Research Society: FAX +81-92-283-685**