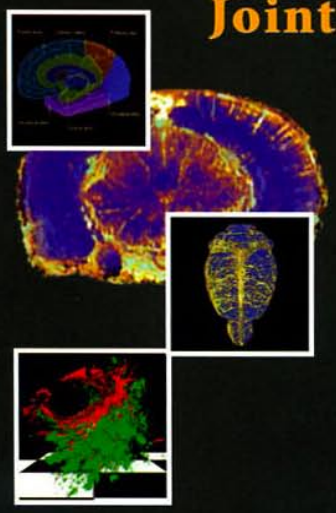
The 22nd Biennial Meeting of the ISN/APSN
Joint Meeting Taiwan Satellite Conference



NOVEL STRATEGIES FOR INTERVENTION IN NEURODEGENERATIVE DISEASES

Program Book

Date: August 30 - September 2 (Sunday-Wednesday), 2009

Place: B1C Auditorium, Institute of Biomedical Sciences,
ACADEMIA SINICA, TAIPEI, TAIWAN

International Society for Neurochemistry

Asian-Pacific Society for Neurochemistry

Program at a glance

Sunday (Aug 30)	Monday (Aug 31)	Tuesday (Sept 1)	Wednesday (Sept 2)
	8:00 - 17:00 Registration	8:30 - 17:00 Registration	8:30 - 17:00 Registration
	8:30 - 8:45 Opening ceremony Gibson Wood Andrew HJ. Wang (Vice President of Academia Sinica) Ing-Kang Ho (Vice President of NHRI) Chok-Yung Chai (Director of Foundation of Biomedical Sciences) Yuan-Tsong Chen (Director of IBMS) 8:45 - 9:00 A tribute to Dr. Lloyd A. Horrocks (1932 - 2007) Grace Sun		
	9:00 - 9:45 Chair: Grace Y. Sun Plenary Speaker **Nicolas G. Bazan**	9:00 - 9:45 Chair: Chun Y. Hsu Plenary Speaker **Pak H. Chan**	9:00 - 9:45 Chair: Andrew HJ. Wang Plenary Speaker **Stuart A. Lipton**
		Session 4 Stroke Chair: Albert Sun & SZ. Lin 9:45 - 10:15 Yau-Huei Wei *National Yang Ming University* 10:15 - 10:30 Teng-Nan Lin *Academia Sinica*	**Session 7 PD** Chair: De-Maw Chuang & FC. Liu 9:45 - 10:15 Jau-Shyong Hong *National Institute of Environmental Health Science* 10:15 - 10:30 Lung-Sen Kao *National Yang Ming University*
	9:45 - 10:15 Break (Photo session)	10:30 - 10:45 Break	9:45 - 10:15 Break
	Session 1 AD-Mitochondria Chair: Gibson Wood & JG Chung 10:15 - 10:45 Gary Gibson *Cornell University* 10:45 - 11:15 Walter Muller *University Frankfurt* 11:15 - 11:45 Xiongwei Zu *Case Western University* 11:45 - 12:00 Frank Lu *National Cheng-Kung University* 12:00 - 12:15 Yi-Hsuan Lee *Taipei Medical University*	**Session 4 Stroke (continued)** 10:45 - 11:15 De-Maw Chuang *NIH/National Institutes of Mental Health* 11:15 - 11:45 Xiao Ming Xu *University of Indiana* 11:45 - 12:15 Albert Sun *University of Missouri* 12:15 - 12:30 Alessandro Prinetti *University of Milan*	**Session 7 PD (continued)** 10:45 - 11:15 Zezong Gu *University of Missouri* 11:55 - 11:45 Jang-Yen Wu *Florida Atlantic University* 11:45 - 12:15 Albert Yu *Peking University* 12:15 - 12:30 Ben Tu *Academia Sinica*
	12:15 - 13:00 Lunch Poster Presentations	12:15 - 13:15 Lunch Poster Presentations	12:30 - 13:15 Lunch Poster Presentations
	Session 2 AD-Ox-Inflam Chairs: Eric Klann & Julie Chan 13:00 - 13:30 Guy Brown *Cambridge University* 13:30 - 14:00 Eric Klann *New York University* 14:00 - 14:30 Lih-Fen Lue *Sun Health Research Institute* 14:30 - 15:00 Xianlin Han *Washington University*	**Session 5 Visual Degeneration** Chairs: Joe Hollyfield & CT. Chien 13:15 - 13:45 Haydee Bazan *Louisiana State University* 13:45 - 14:15 Robert Anderson *University of Oklahoma* 14:15 - 14:45 Joe Hollyfield *Cleveland Clinic and Foundation* 14:45 - 15:00 Yi-Shuian Huang *Academia Sinica*	**Session 8 Other Neuro-Diseases and Therapy** Chairs: Michael Collins & BW. Soog 13:15 - 13:45 Anne Eckert *University of Basel* 13:45 - 14:15 Michael Collins *Loyola University* 14:15 - 14:45 Shi Du Yan *Columbia University* 14:45 - 15:00 Yijuang Chern *Academia Sinica*
	15:00 - 15:15 break	15:00 - 15:15 break	15:00 - 15:15 break
	Session 3 AD-Lipids and their Enzymes Chairs: Franco Goracci & IH, Tsai 15:15 - 15:45 Akhlaq Farooqui *Ohio State University* 15:45 - 16:15 Grace Sun *University of Missouri* 16:15 - 16:45 Franco Goracci *University of Perugia* 16:45 - 17:15 Gunter Eckert *University of Frankfurt*	**Session 6 Receptor-Signal Pathways** Chairs: Gary Weisman & Eminy Lee 15:15 - 15:45 Joanna Strosznajder *Polish Academy of Sciences* 15:45 - 16:15 Gary Weisman *University of Missouri* 16:15 - 16:45 James Lee *University of Missouri* 16:45 - 17:15 Wei-Yi Ong *National University of Singapore* 17:15 - 17:30 Jameel Dennis *Virginia Commonwealth University* 17:30 - 17:45 Synthia Sun *National Yang Ming University*	**Session 8 Other Neuro-Diseases and Therapy (continued)** Chair: Terry BJ. Kuo 15:15 - 15:45 Gibson Wood *University of Minnesota* 15:45 - 16:15 Sally Frautschy *University of California, Los Angeles* 16:15 - 16:30 Li-Kai Tsai *National Taiwan University Hospital* 16:30 - 17:00 (Poster Competition Awards) Gibson Wood 17:00 - 17:30 **Session 9 Closing Remarks and Future Directions** Moderators: Grace Sun and Gibson Wood Panel dicussants: Nicolas Bazan, Pak Chan, Stuart Lipton and Greg Cole
17:00 - 19:00 Registration & Reception	18:00 - Welcome dinner, Activity Center banquet room	Free night	19:00 - Farewell dinner San Want Hotel

Outline of Program

Sunday (Aug 30)

17:00 - 19:00 Registration & Reception

Monday (Aug 31)

08:00 - 17:00 Registration

08:30 - 08:45 Opening ceremony
Dr. Gibson Wood
Dr. Andrew HJ. Wang (Vice President of Academia Sinica)
Dr. Ing-Kang Ho (Vice President of NHRI)
Dr. Chok-Yung Chai (Director of Foundation of Biomedical Sciences)
Dr. Yuan-Tsong Chen (Director of IBMS, Academia Sinica)

08:45 - 09:00 A tribute to Dr. Lloyd A. Horrocks (1932-2007) Grace Sun

09:00 - 09:45 Chair: Grace Y. Sun
Plenary Speaker 1
Omega-3 essential fatty acids modulates initiation and progression of neurodegenerative diseases
Dr. Nicolas G. Bazan
Professor and Director of the Neuroscience Center of Excellence, LSU Health Sciences Center, New Orleans, LA, USA

09:45 - 10:15 **Break (photo session)**

Session 1 AD - Mitochondria
Chairs: Gibson Wood & Jing-Gung Chung (China Medical University)

10:15 - 10:45 Diminished metabolism and/or oxidative stress in neurodegenerative diseases, a double-edged sword?
Dr. Gary E. Gibson
Professor of Weill Medical College of Cornell University, Burke Medical Research Institute, White Plains, NY, USA

11:15 - 11:45 Neuroprotective and regenerative strategies for the repair of spinal cord injury
Dr. Xiao-Ming Xu
Professor and Scientific Director of Spinal Cord and Brain Injury Research Group, Indiana University School of Medicine, Indianapolis, IN, USA

11:45 - 12:15 Neuroprotective effects fo resveratrol: implication for stroke damage
Dr. Albert Y. Sun
Professor of Department of Medical Pharmacology and Physiology, Univ. Missouri, Columbia, MO, USA

12:15 - 12:30 Deregulated sphingolipid mechanism in neurodegenerative disorders: lessons from acidic sphingomyelinase knockout mice, an animal model for Neimann-Pick disease type A
Dr. Alessandro Prinetti
Professor of Biochemistry, Department of Medical Chemistry, Biochemistry and Biotechnology, School of Medicine, University of Milan, Milan, Italy

12:30 - 13:15 Lunch (Poster)

Session 5 Visual Degeneration
Chair: Joe Hollyfield & Cheng-Ting Chien (IMB, Academia Sinica)

13:15 - 13:45 Neurotrophins and DHA induce nerve regeneration
Dr. Haydee E.P. Bazan
Professor of Ophthalmology, and Biochemistry and Molecular Biology and Neuroscience, LSU Health Sciences Center, New Orleans, LA, USA

13:45 - 14:15 Neuroprotection of the retina through light activation of the insulin receptor
Dr. Robert E. Anderson
Professor of Ophthalmology and Cell Biology, The University of Oklahoma Health Sciences Center, Oklahoma City, OK USA

Nicolas G. Bazan

Professor and Director

**Neuroscience Center of Excellence,
LSU Health Sciences Center,
New Orleans, LA, USA**

Research Interests:

Synaptic signaling in neuronal plasticity and neuroprotection; oxidative stress and neuronal retinal cell survival

Selected Publications:

1. Mukherjee PK, Marcheselli VL, Barreiro S, Hu J, Bok D, **Bazan NG**. Neurotrophins enhance retinal pigment epithelial cell survival through neuroprotectin D1 signaling. Proc. Natl. Acad. Sci. USA. 104 (2007) 13152-13157.
2. Mukherjee PK, Marcheselli VL, de Rivero Vaccari JC, Gordon WC, Jackson FE, **Bazan NG**. Photoreceptor outer segment phagocytosis attenuates oxidative stress-induced apoptosis with concomitant neuroprotection D1 synthesis. Proc. Natl. Acad. Sci. USA 104 (2007) 13158-13163.
3. **Bazan NG**. Cell survival matters: docosahexaenoic acid signaling, neuroprotection and photoreceptors. Trends Neurosci. 29 (2006) 263-271.
4. Cole-Edwards KK, Musto AE, **Bazan NG**. JNK activation responses induced by hippocampal kindling are mediated by reactive astrocytes. J. Neurosci. (2006) 8295-8304.
5. Lukiw WJ, Cui JG, Marcheselli VL, Bodker M, Botkjaer A, Gotlinger K, Serhan CN, **Bazan NG**. A role for docosahexaenoic acid-derived neuroprotection D1 in neural cell survival and Alzheimer disease. J Clin Invest. 115 (2005) 2774-2783.
6. Mukherjee PK, Marcheselli VL, Serhan CN, **Bazan NG**. Neuroprotectin D1: a docosahexaenoic acid-derived docosatriene protects human retinal pigment epithelial cells from oxidative stress. Proc. Natl. Acad. Sci. USA 101 (2004) 8491-8496.
7. Rodriguez de Turco EB, Tang W, Tophan MK, Sakane F, Marcheselli VL, Chen C, Taketomi A, Prescott SM, **Bazan NG**. Diacylglycerol kinase ε regulates seizure susceptibility and long-term potentiation through arachidonoyl-inositol lipid signaling. Proc. Natl. Acad. Sci. 98 (2001) 4740-4745.

Omega-3 essential fatty acids modulate initiation and progression of neurodegenerative diseases

Nicolas G. Bazan

Neuroscience Center of Excellence, Louisiana State University Health Sciences Center, School of Medicine, New Orleans, Louisiana, USA

The significance of the selective enrichment in omega-3 essential fatty acids (docosahexaenoyl - DHA-chains of membrane phospholipids, 22C and 6 double bonds) in the nervous system (e.g. photoreceptors, synaptic membranes) has remained, until recently, incompletely understood. While studying mechanisms of cell survival in neurodegenerations, we discovered a docosanoid synthesized from DHA by a 15-lipoxygenase, which we dubbed neuroprotectin D1 (NPD1, 10*R*, 17*S*-dihydroxy-docosa-4*Z*, 7*Z*, 11*E*, 13*E*, 15*E*, 19*Z* hexaenoic acid). This mediator is a docosanoid because it is derived from a 22C precursor (DHA), unlike eicosanoids, which are derived from the 20 C arachidonic acid family member of essential fatty acids not enriched in the nervous system. We found that NPD1 is promptly made in response to oxidative stress and brain ischemia-reperfusion, and in the presence of neurotrophins. NPD1 is neuroprotective in experimental brain damage, oxidative-stress retinal pigment epithelial (RPE) cells, and in human brain cells exposed to amyloid-β peptide. Thus we envision NPD1 as a protective sentinel, one of the very first defenses activated when cell homeostasis is threatened by neurodegenerations. We provide here recent experimental examples that highlight the specificity and potency of NPD1 spanning beneficial bioactivity during initiation and early progression of neurodegenerations: 1) Photoreceptors renew membrane disks containing the phototransduction apparatus and DHA intermittently via shedding of their tips and phagocytosis by retinal pigment epithelial (RPE) cells. At the same time, new membrane disks are made at the base of the outer segments; their length remains constant and cell integrity is maintained remarkably unchanged throughout many decades. This outcome occurs in spite of the fact that the photoreceptors are in an oxidative stress-prone environment (light, high O_2 consumption, high polyunsaturated fatty acid fluxes, etc.) We show that phagocytosis of photoreceptor disks promotes via NPD1 synthesis specific refractoriness to oxidative stress-induced apoptosis in RPE cells, which in turn fosters homeostatic photoreceptor cell integrity. Disruptions of the sentinel role of NPD1 in photoreceptor renewal may participate in macular degeneration and other retinal degenerations leading to blindness. 2) In brain ischemia-reperfusion, DHA is released and used for NPD1 synthesis, thus eliciting neuroprotection. Anti-apoptotic BCL-2 family of proteins are negatively regulated, as is the arrival of leukocytes due to neurovascular unit breakdown. 3) We found that NPD1 is drastically reduced in CA1 areas from Alzheimer's patients. Thus we have explored the significance of NPD1 in cellular models that recapitulate part of the Alzheimer's pathology. Human neurons and astrocytes challenged by amyloid-β or by overexpressing APPsw (double Swedish mutation) show that NPD1 down-regulates amyloidogenic processing of amyloid-β precursor protein, switches off pro-inflammatory gene expression (TNF-α, COX-2 and B-94-TNF-α inducible pro-inflammatory element), and promotes neural cell survival. The apoptotic cascade involves mutiple checkpoints. NPD1 regulation targets upstream events of apoptosis as well as neuroinflammatory signaling, in turn promoting homeostatic regulation of cell integrity. (Supported by NIH: NINDS R01 NS046741, NEI R01 EY005121 and NCRR P20 RR016816, and by the National Foundation Fighting Blindness).

Haydee E.P. Bazan

Professor

Ophthalmology, and Biochemistry and Molecular Biology and Neuroscience, LSU Health Sciences Center, New Orleans, LA, USA

Research Interests:

1.) Lipids Involved in Signal Transduction Mechanisms in the Eye
2.) Cell signal transduction events during corneal wound healing, particularly how specific growth factors that are released during injury activate kinase to communicate their signals from the cell membrane to the nuclei.

Selected Publications:

1. Kakazu A, Sharma G, **Bazan HE**. Association of protein tyrosine phosphatases (PTPs)-1B with c-Met receptor and modulation of corneal epithelial wound healing. Invest Ophthalmol Vis Sci. 2008 Jul;49(7):2927-35.
2. He J, **Bazan HE**. Epidermal growth factor synergism with TGF-beta1 via PI-3 kinase activity in corneal keratocyte differentiation. Invest Opthalmol Vis Sci. 2008 Jul;49(7):2936-45.
3. Esquenazi S, He J, Li N, Bazan NG, Esquenazi I, **Bazan HE**. Comparative *in vivo* high-resolution confocal microscopy of corneal epithelium, sub-basal nerves and stromal cells in mice with and without dry eye after photorefractive keratectomy. Clin Experiment Ophthalmol. 3007 Aug;35(6):545-9.
4. Sharma GD, Kakazu A, **Bazan HE**. Protein kinase C alpha and epsilon differentially modulate hepatocyte growth factor-induced epithelial proliferation and migration. Exp Eye Res. 2007 Aug;85(2):289-97. Epub 2007 May 26.
5. Taheri F, **Bazan HE**. Platelet-activating factor overturns the transcriptional repressor disposition of Sp1 in the expression of MMP-9 in human corneal epithelial cells. Invest Opthalmol Vis Sci. 2007 May;48(5):1931-41.
6. He J, **Bazan HE**. Synergistic effect of platelet-activating factor and tumor necrosis factor-alpha on corneal myofibroblast apoptosis. Invest Ophthalmol Vis Sci. 2006 Mar;47(3):883-01.
7. **Bazan HE**, Tao Y, Bazan NG. Platelet-activating factor induces collagenase expression in corneal epithelial cells. Proc Natl Acad Sci U S A. 1993 Sep15;90(18):8678-82.

Neurotrophins and DHA induce nerve regeneration

Haydee E.P. Bazan

Department of Ophthalmology and Neuroscience Center of Excellence, Louisiana State University Health Sciences Center, School of Medicine, New Orleans, Louisiana, USA

The cornea has the highest nerve density and the highest sensitivity among tissues. Damage of the nerves after trauma, surgery or infection leads to neurotrophic keratitis, a condition characterized by decreased blink reflex and reduction of tear flow that, in turn, produces dry eye and consequently damage to the corneal epithelium. In severe cases, damage could lead to corneal ulceration.

Docosahexaenoic acid (DHA) is the precursor of neuroprotectin D1 (NPD1), a newly-discovered lipid mediator that protects retinal pigment epithelial (RPE) cells and neural cells from oxidative stress. Synthesis of NPD1 in RPE cells is stimulated by several mechanisms *(Bazan NG, Adv Exp Med Biol, 2008)*.

We have found that treatment with nerve growth factor (NGF) or pigment epithelial-derived growth factor (PEDF) in conjunction with DHA enhances nerve regeneration of corneal nerves damaged post surgery. At 2 and 4 weeks post surgery, there was a 2.5 increase in corneal nerve area, and further increase was seen after 8 weeks. Epithelial cell proliferation also was increased after treatment. Neurotrophins or DHA alone do not have the same effect. NPD1 synthesis was four times higher in the PEDF+DHA-treated group compared to control.

This data demonstrates a new mechanism by which neurotrophin-mediated NPD1 synthesis is involved in nerve regeneration. This signaling mechanism may be targeted in neurotrophic keratitis as well as in other diseases where nerve repair is needed. (Supported by NIH-RO1 EY19465).

Depakine
Sodium Valproate/Valproic Acid

DEPAKINE

帝拔癲 (sodium valproate)

適應症：癲癇之大發作、小發作、混合型及顳葉癲癇；躁病
劑　量：孩童：30 mg/kg/day
青少年及成人：20~30 mg/kg/day

衛署藥輸字第 022008 號
本藥須由醫師處方使用

成份
每錠含　Sodium Valproate .....333 mg
Valproic Acid .....145 mg
主成分相當於Sodium Valproate 500mg為有刻痕的錠劑(Scored Tablet)。

適應症
癲癇之大發作、小發作、混合型及顳葉癲癇；躁病。

說明
癲癇
成人及兒童：可以單藥治療或與其他抗癲癇藥物併用治療下列癲癇：
- 全面性癲癇發作：陣攣性癲癇發作、強直性癲癇發作、大發作、小發作、肌陣攣性或失張性癲癇發作、Lennox-Gastaut症候群。
- 局部性癲癇發作：局部性癲癇發作或局部性癲癇發作後繼發全面性癲癇發作。

躁病

用法用量
本藥須由醫師處方使用

癲癇
劑量
基於劑量之考量，本藥適用於成人及體重17公斤以上之兒童。
本藥不適用於六歲以下的孩童(考慮吞食錠劑可能引起窒息的危險)。
每日平均劑量為20 ~ 30mg/kg。
用法
口服使用。每日劑量分一到二次服用，建議與餐點同時服用。
對於控制良好的癲癇病人，建議一天服藥一次。
吞服本藥時不可壓碎或咬碎錠劑。
開始使用sodium valproate治療
- 若以持續性藥效錠取代sodium valproate的一般錠劑時，以目前對本藥之了解，建議維持原先使用之日劑量。
- 若病人已服用的其他抗癲癇藥物治療時，應以漸進方式逐漸加入sodium valproate，在二星期內增加至最適當的劑量，若有需要，原先的抗癲癇藥物可在病情控制下慢慢減量。
- 沒有服用其它抗癲癇藥物的病人，每隔2到3天逐次增加sodium valproate的劑量，約在一星期內可達到最適當的治療劑量。

躁病
建議以日劑量600 mg開始給藥，再以日劑量200 mg，每三天為間隔，逐步增加劑量至病情被控制為止。一般劑量範圍為1000 mg/day到2000 mg/day(即20~30mg/kg)，若在此劑量範圍內仍未能控制病情，可增加劑量至最高2500 mg/day。Bowden之臨床研究顯示，血漿濃度超過45 μg/mL時有較佳之療效(此血中濃度可改善燥症評估表超過20%。
Bowden 亦觀察到當血漿濃度超過125 μg/mL時，有較多藥物不良反應發生。在此劑量範圍內，其劑量和濃度之相關性並不清楚。

禁忌
- 對valproate sodium或本藥其他成份過敏者。
- 急性肝炎患者。
- 慢性肝炎患者。
- 有嚴重肝炎家史者，特別是藥物引起的肝炎。
- 肝性咯紫質沉著症(hepatic porphyria)。
- 和mefloquine合併使用。
- 一般而言，本藥不建議與lamotrigine併用。

警語
開始使用抗癲癇藥物治療，在極罕見的情況下，病人可能會增加癲癇發作的頻率或產生新的癲癇發作形態，和原有的癲癇發作形態完全不同。關於valproate，上述情況的發生通常會牽涉到其他併用藥物的改變或藥動學的交互作用、毒性或過量。

不良反應
- 有極少數胰臟炎的病例被報告，須儘早停止治療，嚴重者可能造成死亡。
- 偶而有肝功能正常的高氨血症的病例被報告，特別容易發生在使用多種抗癲癇藥物治療的病人，應不至於導致停藥。高氨血症引起神經方面症狀亦曾被報告過，此神經方面的症狀可能逐漸惡化到昏迷，此時應做進一步檢查。
- 催畸性
- 在剛開始治療時，有些病人可能會有消化方面的症狀(噁心、胃痛)，但通常不需停藥，幾天後就會消失。暫時性以及與劑量有關的不良反應：掉頭髮、輕微顫抖和昏昏欲睡

使用前詳閱說明書警語及注意事項

sanofi aventis
Because health matters

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使用前詳閱說明書警語及注意事項

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衛署藥輸字第022008號
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