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# Bristol-Myers Squibb Company

Worldwide Medicines Group

One Squibb Drive ♦ P.O. Box 191 ♦ New Brunswick, New Jersey 08903-0191

732-519-2000

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April 12, 2000

Elizabeth Ullrich  
US Nuclear Regulatory Commission Region I  
475 Allendale Road  
King of Prussia, PA 19406-1415

**RE: RADIOACTIVE MATERIAL LICENSE #29-008139-02**

Dear Ms. Ullrich:

This notice is to inform the Commission of changes in the membership of our Radiation Safety Committee. H. Bartlett, B. Gavin, and D. Johnson have left the committee. R. Pooler and T. Lin have joined the committee. Their résumés are attached. The current committee membership is now:

- S. Voigt, Chair
- J. Frankowski
- T. Lin
- G. Matsueda
- R. Pooler
- K. Rinehart
- C. Taday
- M. Vala
- C. Woodard
- F. Yost

If you require any additional information, please do not hesitate to contact me at (732) 519-2987.

Sincerely,

Michael J. Vala, CHP  
Radiation Safety Officer

MJV:bl

Attachments (2)

MJV\NRC2000.DOC

Information in this record was deleted in  
accordance with the Freedom of Information Act.  
Exemptions 6  
FOIA/PA 201-0063

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Bristol-Myers Squibb Company

# Talk Inside First

Name: Pooler, J. Richard	Joined BMS: 1996
Title: Senior Staff Attorney	Current Position Since: 1996
Division/Department: Pharm Legal/Tech Ops Phone Number: 315-432-2774 Fax Number: 315-432-2279	Description of Current Duties (brief): Assist Division Counsel in advising Tech Ops Management and Worldwide Manufacturing / Development Facilities; Environmental, Health, and Safety specialization.

## Prior Position with Company & Description (if applicable):

Division/Location	Title/Description of Duties	Period

## Experience Prior to Joining BMS

Firm / Company	Title/Description of Duties	Period
Weston; The Darien Group; BBL	Environmental, health, and safety management and compliance consulting; merger/acquisition support.	1988 - 1996
New York City Department of Environmental Protection	Enforcement Counsel (Industrial Pretreatment and Emergency Response)	1984 - 1986
ConEdison; New York Power Authority	Operational, compliance, and management systems auditing.	1982 - 1984; 1986 - 1988
Norwich-Eaton Pharmaceuticals	Assistant Regulatory Counsel (EPA, FDA, FTC)	1980 - 1982

## Education

	Institution	Degree	Major
Law School	Syracuse University College of Law	J.D.	
College	Rensselaer Polytechnic Institute	B.S.	Environmental Engineering
Other			

## Significant and Substantial Experience in the following areas:

Comfortable giving advice/acting as a resource in the following areas: (i.e., - those you would feel comfortable advising/discussing with others). *Some examples are set forth below, but please feel free to describe your own expertise.*

**\*\* Please describe in detail.**



Experience in	Describe your own expertise
<p>Contracts: (Software Licenses/CRADA/Construction/Supply/Distribution), Environmental: Litigation and Regulatory, Other:</p>	<p>Health and Safety</p>

**Other Comments:**

Note: Membership in Practice Group or if an in-house coordinator.



Tai-An Lin

**Business address:**

Bristol-Myers Squibb, PRI  
P.O. Box 4000, Princeton, NJ 08543  
Tel: (609)252-5272/Fax: (609)252-6058  
Email: JLint@bms.com

**Home address:**

[REDACTED]  
[REDACTED]  
[REDACTED]

**PROFESSIONAL APPOINTMENTS AND RESEARCH EXPERIENCES:**

**Senior Research Investigator I** (May 1999 – present), Immunology and Inflammation Drug Discovery, Bristol-Myers Squibb, Pharmaceutical Research Institute, Princeton, NJ

**Research Investigator II** (September 1997 - April 1999), Immunology and Inflammation Drug Discovery, Bristol-Myers Squibb, Pharmaceutical Research Institute, Princeton, NJ

**Research Investigator II** (April 1996 - August 1997), Immunological Diseases, Bristol-Myers Squibb, Pharmaceutical Research Institute, Seattle, WA.

- Cloned, expressed, and purified human Lck and the catalytic domain of Lck.
- Optimized Lck filter-based assay and performed initial SAR with chemists for the Lck screening hits.
- Completed enzyme kinetic studies for the imidazoquinoxoline, benzothiazole and thiazole chemotypes of the Lck inhibitors.
- Started the development of JAK3 screening assay using baculovirus-expressed mouse JAK3.
- Cloned, expressed, and purified the tyrosine kinases ZAP-70 and Syk. Initiated cloning, expression and purification of SLP-76.
- Developed the ZAP-70 screening assays and transferred the HTS assay to the Lead Discovery Group.
- Developed the Syk filter-based assay for the compound selectivity measurement.
- Screened the kinase library (~4000 compounds) from the Oncology Drug Discovery for the ZAP-70 inhibitory activity and identified more than 20 hits. Worked with research associates to screen the kinase library (~9000 compounds) from the Combinatorial Drug Discovery for the ZAP-70 inhibitory activity.
- Completed the selective studies for the tyrosine kinase inhibitors of indole chemotype. Worked together with research associates to characterize the *in vitro* and cellular activities of six ZAP-70 inhibitors published by the Celltech Therapeutic Inc.
- Finished cloning and expression of the full length mammalian Target of Rapamycin (mTOR, 289 kDa protein).
- Cloned, expressed and purified four substrate proteins for mTOR.
- Initiated the development of a HTS assay to search for the mTOR inhibitors.

**Postdoctoral Research Fellow** (1993-1996), Department of Molecular Biology and Pharmacology, Washington University School of Medicine, St. Louis, MO. Supervisor: Dr. John C. Lawrence, Jr.

Designed and conducted experiments to elucidate cellular signal transduction mechanisms linked to insulin and growth factor receptors. Primarily focused on the relationship between the kinase cascades and protein synthesis, glycogen synthesis and glucose transport. Cloned mouse cDNAs for two novel regulatory proteins of translation initiation. Experienced in current technology of molecular biology and biochemistry, such as molecular cloning, recombinant protein production, protein purification, FPLC, ELISA, immunoprecipitation, Northern, Western Blotting and so forth. Responsibility included directing and teaching technicians (BS/MS level) to undertake research program.

**EDUCATION:**

**Ph. D.** (b)(6) Department of Biochemistry, University of Missouri School of Medicine, Columbia, Missouri. Dissertation title: Metabolism of inositol phosphates in cerebral ischemia. Advisor: Dr. Grace Y. Sun.



Research emphasized on the signal transduction pathways linked to the G protein-coupled receptors and the enzymes that are related to the second messenger metabolism in stroke and Alzheimer diseases. In-depth knowledge of second messenger biochemistry, phospholipid metabolism and receptor binding studies. Hands-on experiences in several analytical techniques including HPLC, GC, HPTLC, radioreceptor binding assays and  $[Ca^{2+}]_i$  measurement. Familiar with several animal models and cell culture systems.

BS (b)(6) Department of Food Science, Tunghai University, Taichung, Taiwan, ROC.

Graduated with the highest distinction.

#### PERSONAL DATA:

Tai-An Lin was born [REDACTED] in [REDACTED]. He immigrated to US in [REDACTED] and became naturalized US citizen in [REDACTED]. He is married to [REDACTED] and has [REDACTED].

#### PUBLICATIONS:

##### Peer-reviewed Journals:

Tai-An Lin, T-N. Lin, Y.Y. He, C.Y. Hsu and G.Y. Sun (1992) Effects of focal cerebral ischemia on inositol 1,4,5-trisphosphate 3-kinase and 5-phosphatase activities in rat cortex. *Biochem. Biophys. Res. Commun.* 184, 871-877.

Tai-An Lin, Kevin D. Lustig, Michael G. Sportiello, Gary A. Weisman and Grace Y. Sun (1993) Signal transduction pathways coupled to a  $P_{2U}$  purinergic receptor in Neuroblastoma X Glioma (NG108-15) cells. *J. Neurochem.* 60, 1115-1125.

L-Y. Chau, Tai-An Lin, W-T. Chang, C-W. Chen, M-J. Shue, Y-S. Hsu, C-Y. Hu, W-H. Tsai and G. Y. Sun. (1993) Endothelin-mediated calcium response and inositol 1,4,5-trisphosphate release in Neuroblastoma-Glioma hybrid cells (NG108-15): Cross talk with ATP and bradykinin. *J. Neurochem.* 60, 454-460.

Tai-An Lin, Jian-Ping Zhang and Grace Y. Sun (1993) Metabolism of inositol 1,4,5-trisphosphate in mouse brain due to decapitation ischemic insult: Effects of acute lithium administration and temporal relationship to diacylglycerols, free fatty acids and energy metabolites. *Brain Res.* 606, 200-206.

Tai-An Lin, Meena Navidi, William James, Teng-Nan Lin and Grace Y. Sun (1993) Effects of acute ethanol administration on poly-phosphoinositide turnover and levels of inositol 1,4,5-trisphosphate in mouse cerebrum and cerebellum. *Alcohol. Clin. Exp. Res.* 17, 401-405.

Tai-An Lin, Jian-Ping Zhang and Grace Y. Sun (1993) The cholinergic receptor-linked phosphoinositide metabolism in mouse cerebrum and cerebellum in vivo. *Brain Res.* 622, 169-176.

Tai-An Lin and John C. Lawrence, Jr. (1994) Activation of ribosomal protein S6 kinases does not increase glycogen synthesis or glucose transport in rat adipocytes. *J. Biol. Chem.* 269, 21255-21261.

Timothy A. J. Haystead, Clare M. M. Haystead, Chaobin Hu, Tai-An Lin and John C. Lawrence, Jr. (1994) Phosphorylation of PHAS-I by mitogen-activated protein (MAP) kinase. Identification of a site phosphorylated by MAP kinase in vitro and in response to insulin in rat adipocytes. *J. Biol. Chem.* 269, 23185-23191.

Tai-An Lin, Xianming Kong, Timothy A. J. Haystead, Arnim Pause, Graham Belsham, Nahum Sonenberg, John C. Lawrence Jr. (1994) PHAS-I as a link between mitogen-activated protein kinase and translation initiation. *Science* 266, 653-656.



Arnim Pause, Graham J. Belsham, Anne-Claude Gingras, Olivier Donze, Tai-An Lin, John C. Lawrence Jr and Nahum Sonenberg (1994) Insulin-dependent stimulation of protein synthesis by phosphorylation of a regulator of 5'-cap function. *Nature* 371, 762-767.

H.-M. Huang, Tai-An Lin, G. Y. Sun and G. E. Gibson (1995) Increased inositol 1,4,5-trisphosphate accumulation correlates with an up-regulation of bradykinin receptors in Alzheimer's disease. *J. Neurochem.* 64, 761-766.

L. M. Graves, E. E. Bornfeldt, G. M. Argast, E. G. Krebs, X. Kong, Tai-An Lin and J. C. Lawrence, Jr. (1995) cAMP- and rapamycin-sensitive regulation of the association of eIF-4E and the translation regulator PHAS-I in aortic smooth muscle cells. *Proc. Natl. Acad. Sci* 92, 7222-7226.

G. Y. Sun, J.-P. Zhang, Tai-An Lin, T.-N. Lin, Y. Y. He and C. Y. Hsu (1995) Inositol triphosphate, polyphosphoinositide turnover, and high-energy metabolites in focal cerebral ischemia and reperfusion. *Stroke* 26, 1893 - 1990.

Tai-An Lin, Xianming Kong, Alan R. Saltiel, Perry J. Blakeshear, and John C. Lawrence, Jr. (1995) Control of PHAS-I by insulin in 3T3-L1 adipocytes: synthesis, degradation, and phosphorylation by a rapamycin-sensitive and MAP kinase-independent pathway. *J. Biol. Chem.* 270 18531-18538

Tai-An Lin and J. C. Lawrence, Jr. (1996) Control of the translational regulator PHAS-I and PHAS-II by Insulin and cAMP in 3T3-L1 adipocytes. *J. Biol. Chem.* 271, 30199-30204.

Tai-An Lin and J. C. Lawrence, Jr. (1997) Control of PHAS-I phosphorylation in 3T3-L1 adipocytes: effects of inhibiting protein phosphatases and the p70S6K signaling pathway. *Diabetologia* 1997, 40 Suppl 2: S18-S24.

Guang Xu, Connie A. Marshall, Tai-An Lin, Guim Kwon, Raghava B. Munivenkatappa, Jeanette R. Hill, John C. Lawrence, Jr., and Michael L. McDaniel (1998) Insulin Mediates Glucose-stimulated Phosphorylation of PHAS-I by Pancreatic Beta Cells. An Insulin-receptor Mechanism for Autoregulation of Protein Synthesis by Translation. *J. Biol. Chem.* 273: 4485-4491.

Guang Xu, Guim Kwon, Connie A. Marshall, Tai-An Lin, John C. Lawrence, Jr., and Michael L. McDaniel (1998) Branched-chain amino acids are essential in the regulation of PHAS-I and p70 S6 kinase by Pancreatic  $\beta$ -cells. A possible role in protein translation and mitogenic signaling. *J. Biol. Chem.* 273: 28178-28184.

#### Book Chapters and Reviews:

G. Y. Sun, Tai-An Lin, P. Wixom, R. T. Zoeller, T.-N. Lin, Y. Y. He, and C. Y. Hsu (1993) Effects of focal cerebral ischemia on expression and activity of inositol 1,4,5-trisphosphate 3-kinase in rat cortex. In "Marker of Neuronal Injury and Degeneration". New York Academy of Science. Vol. 679, pp 382-387, New York, New York.

J. C. Lawrence, Tai-An Lin, X. Kong, T. A. J. Haystead, and C. Hu (1995) PHAS-I, a new player in insulin signal transduction in "Diabetes 1994" (BaBa, S. and Kaneko, T. eds) pp622-629, Elsevier Science, Amsterdam.

J.C. Lawrence, Jr., P. Fadden, T.A. Haystead, and T.A. Lin (1997) PHAS proteins as mediators of the actions of insulin, growth factors and cAMP on protein synthesis and cell proliferation. *Adv. Enzyme Regul.* 37, 239-267.

#### ABSTRACTS AND PRESENTATIONS:

#### Internal presentations at Bristol-Myers Squibb:



Presented ZAP-70 early phase program at the Immunology and Inflammation Drug Discovery annual review (1998).

Presented research results regularly to the autoimmunity and transplantation departmental meetings in Seattle and the signal transduction group meetings in Lawrenceville.

Presented results at the Lck working group meetings (1996-1997).

Selected external abstracts and presentations:

T-A Lin, K.D. Lustig, M.G. Sportiello, G.Y. Sun and G.A. Weisman (1989) ATP induces polyphosphoinositide breakdown and an increase in cytoplasmic, free calcium levels in neuroblastoma X glioma hybrid cells. 19th annual meeting of Society for Neuroscience. Oct. 29 - Nov. 3, 1989, Phoenix, Arizona.

G.Y. Sun, T-A Lin, K.D. Lustig, M.G. Sportiello, and G.A. Weisman. (1989) P<sub>2</sub>-purinergic receptor responses in NG108-15 cells. International symposium on neurotransmission and signal transduction. Taipei, Taiwan, Republic of China, October 16-18, 1989.

Meena Navidi, Tai-An Lin, Julia Raye, Albert Y. Sun and Grace Y. Sun. Relationship between lipid changes in serum and liver microsomes of Sinclair (S-1) miniature swine after voluntary alcohol consumption. 1989 RSA scientific conference.

T-A Lin, G.A. Weisman and G.Y. Sun (1990) P<sub>2</sub> purinergic and bradykinin receptor-induced calcium response and inositol phosphate release in NG108-15 cells. 20th annual meeting of Society for Neuroscience. Oct. 28 - Nov. 2, 1990, St. Louis, Missouri.

Tai-An Lin and G.Y. Sun (1991) Effect of chronic ethanol administration on inositol trisphosphates in mouse brain. 1991 Research Society of Alcoholism Meeting, Marco Island, Florida, July 8-13, 1991.

T-A Lin, J-P Zhang and G.Y. Sun (1991) Lithium effects on decapitation-induced releases of inositol phosphates, diacyl-glycerols and free fatty acids in mouse cerebrum. 21st annual meeting of Society for Neuroscience. Nov. 10 - 15, 1991, New Orleans, Louisiana.

G.Y. Sun, T-A Lin, Y-Y. He, and C.Y. Hsu. (1991) Effects of rat focal cerebral ischemia on levels of Ins(1,4,5)P<sub>3</sub>. 21st annual meeting of Society for Neuroscience. Nov. 10 - 15, 1991, New Orleans, Louisiana.

T-A Lin, P. Wixom, Z-P Zhang, T-N Lin, Y-Y. Hsu, Zoeller and G.Y. Sun (1992) Effects of focal cerebral ischemia on Ins(1,4,5)P<sub>3</sub> 3-kinase. 23rd annual meeting of American society for Neurochemistry. Mar. 15 - 20, 1992, Houston, TX.

Huang H.-M., Lin T.-A., Sun G.Y. and Gibson G.E. (1992) Enhanced bradykinin-induced inositol (1,4,5) trisphosphate formation in Alzheimer's disease fibroblasts. 23rd annual meeting of American society for Neurochemistry. Mar. 15 - 20, 1992, Houston, TX.

Grace Y. Sun, Tai-An Lin and Jian-ping Zhang (1992) Ethanol effects on poly-phosphoinositide turnover: Evidence for tolerance development. ISBRA Satellite Meeting. June 29 - July 1, 1992, Lund, Sweden.

T.-A. Lin, J.P. Zhang and G. Y. Sun (1992) Chronic ethanol administration results in tolerance development in poly-PI turnover in mouse brain. 22nd annual meeting of Society for Neuroscience. Oct. 25 - 30, 1992. Anaheim, California.



G.Y. Sun, P. Wixom, T.A. Lin, T.N. Lin, R.T. Zoeller and C.Y. Hsu (1992) Decrease in Ins(1,4,5)P<sub>3</sub> 3-kinase mRNA expression in focal cerebral ischemia. 22nd annual meeting of Society for Neuroscience. Oct. 25 - 30, 1992. Anaheim, California.

Tai-An Lin and Grace Y. Sun (1993) Receptor-mediated IP<sub>3</sub> production is enhanced in calcium-induced delayed cell death. 23rd annual meeting of Society for Neuroscience. Nov. 7-12, Washington, D.C.

G.Y. Sun, T.-A. Lin, J. Wu, Z.Y. Hu and G.A. Weisman (1993) IL-1 $\beta$  enhances ATP receptor response in cultured astrocytes cell line. 23rd annual meeting of Society for Neuroscience. Nov. 7-12, Washington, D.C.

T.-A. Lin, M. M. Fang, and J. C. Lawrence, Jr. (1994) Activation of ribosomal S6 protein kinases dose not increase glycogen synthase activity in rat fat cells. ASBMB meeting 1994. May 17-22, Washington, D. C.

#### REFERENCES AND SUPERVISORS:

Dr. Grace Y. Sun, M121 Medical Sciences Building, Biochemistry Department, University of Missouri School of Medicine, Columbia, MO 65212. Tel: (573) 882-5377/Fax: (573) 884-4597.

Dr. John C. Lawrence Jr., Department of Pharmacology, University of Virginia School of Medicine, Charlottesville, Virginia 22903. Tel: (804)924-1584./Fax: (804)982-2635

Dr. Gary Schieven, Immunology and Inflammatory Drug Discovery, Bristol-Myers Squibb, PRI. P.O. Box 4000, Princeton, NJ 08543-4000. Tel: (609)252-6135/Fax: (609)252-6058

Dr. Steve B. Kanner, Immunology and Inflammatory Drug Discovery, Bristol-Myers Squibb, PRI. P.O. Box 4000, Princeton, NJ 08543-4000. Tel: (609)252-6322/Fax: (609)252-6058



BETWEEN:

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: (FOR LFMS USE)
: INFORMATION FROM LTS
: -----
:
: Program Code: 03211
: Status Code: 0
: Fee Category: 3A
: Exp. Date: 20080930
: Fee Comments: -----
: Decom Fin Assur Req'd: Y
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## A. REGION

Applicant/Licensee: E. R. SQUIBB & SONS, INC:  
Received Date: 20000418  
Docket No: 3005222  
Control No.: 128015  
License No.: 29-00139-02  
Action Type: Amendment

Amount: \_\_\_\_\_  
Check No.: \_\_\_\_\_

Signed R. J. Brown  
Date 4/19/00

1. Fee Category and Amount: \_\_\_\_\_

Amendment \_\_\_\_\_  
Renewal \_\_\_\_\_  
License \_\_\_\_\_

Signed \_\_\_\_\_  
Date \_\_\_\_\_



This is to acknowledge the receipt of your letter/application dated

4-12-00, and to inform you that the initial processing which includes an administrative review has been performed.

☒ *Amend* *29-00139-02*  
There were no administrative omissions. Your application was assigned to a technical reviewer. Please note that the technical review may identify additional omissions or require additional information.

☐ Please provide to this office within 30 days of your receipt of this card

A copy of your action has been forwarded to our License Fee & Accounts Receivable Branch, who will contact you separately if there is a fee issue involved.

Your action has been assigned Mail Control Number **128015**  
When calling to inquire about this action, please refer to this control number.  
You may call us on (610) 337-5398, or 337-5260.

NRC FORM 532 (R0)  
(6-98)

Sincerely,  
Licensing Assistance Team Leader