

## Asst Professor Martin J LEAR

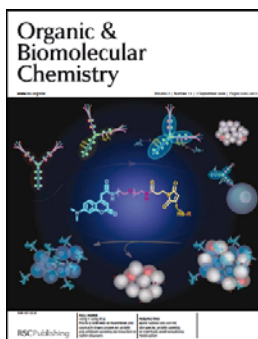
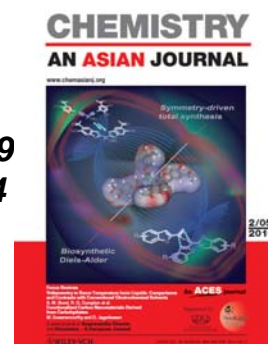


### Background

- PhD, Univ of Glasgow, UK, 1995
- Postdoc, Parke-Davis (UK), 1996
- Postdoc, CNRS (France)/Japan, 1997-1999
- Asst Prof, Tohoku Univ, Japan, 2000-2004

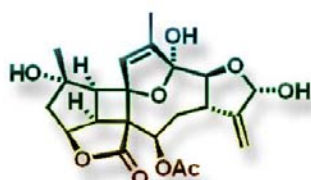
### Research Interests:

- Total and analogue synthesis of natural products with high biological relevance

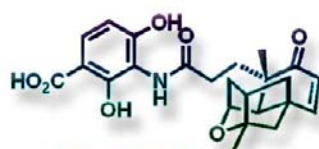


### Selected Publications:

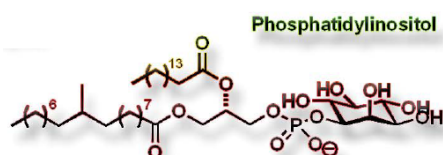
- **Total synthesis confirms laetiobin as a formal Diels-Alder adduct**, O. Simon, B. Reux, JJ La Clair, MJ Lear\*, *Chem. Asian J.* 2010, 5, 342-251. (Cover-page feature).
- **Total synthesis of a fully lipidated form of phosphatidylmyo-inositol dimannoside (PIM-2) of Mycobacterium tuberculosis**, A Ali, MR Wenk, MJ Lear\*, *Tetrahedron Lett.* 2009, 50, 5664-5666.
- **Stereocontrolled entry to the tricyclo[3.3.0]joxoheptane core of bielschowskysin by a [2+2] cycloaddition of an allene-butenolide**, R Miao, SG Gramani, MJ Lear\*, *Tetrahedron Lett.* 2009, 50, 1731-1733.
- **Practical synthesis of maleimides and coumarin-linked probes for protein and antibody labelling via reduction of native disulfides**, HY Song, MH Ngai, ZY Song, PA MacAry, J Hopley, MJ Lear\*, *Org. Biomol. Chem.* 2009, 7, 3400-3406. (Inside cover-page; Top-10 article in Aug. 2009).
- **Identification of the binding of sceptrin to MreB via a bidirectional affinity protocol**, AD Rodriguez\*, MJ Lear\*, JJ La Clair\*, *J. Am. Chem. Soc.* 2008, 130, 7256-7258.



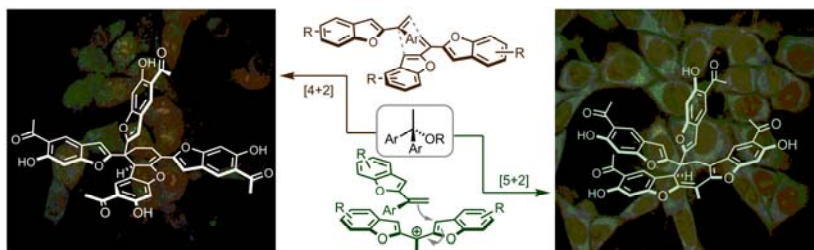
Bielschowskysin



Platensimycin



Phosphatidylinositol





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Asst. Prof., Tohoku Univ., 2000; Postdoc., Parke-Davis & CNRS, 1997; Ph.D., Univ. of Glasgow, 1995; B.Sc. (Hons), Univ. of Glasgow, 1991

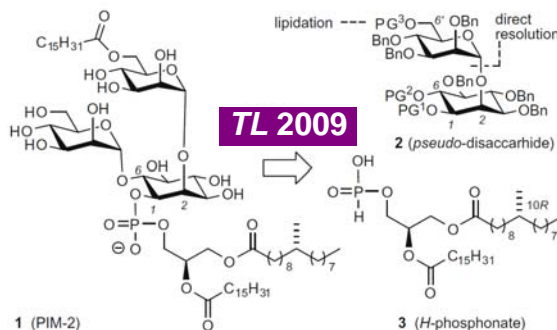
[http://www.chemistry.nus.edu.sg/ourpeople/academic\\_staff/lear.htm](http://www.chemistry.nus.edu.sg/ourpeople/academic_staff/lear.htm)

Email: [chmlmj@nus.edu.sg](mailto:chmlmj@nus.edu.sg)

### RESEARCH INTERESTS

Total & analogue synthesis of natural products & glycolipids of high biological relevance & structural complexity.

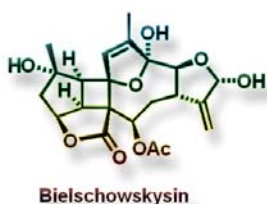
- Total synthesis of antimalarial (e.g. bielschowskysin) and antibiotic (e.g. platensimycin) leads
- Development of transannulation and desymmetrisation strategies to natural product carbon frameworks
- Discovery of biological targets of natural products and biologics through chemical biology approaches



### RECENT HIGHLIGHTS

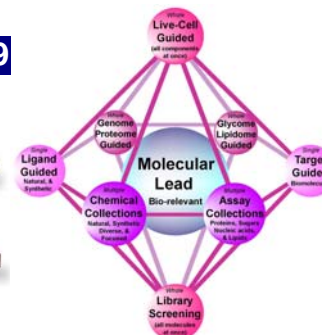
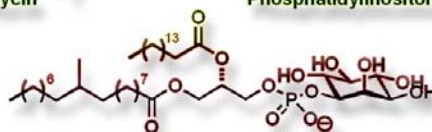
Total and Analogue Synthesis of Antimalarials and Antibiotics including Lipodomics

#### in progress ...



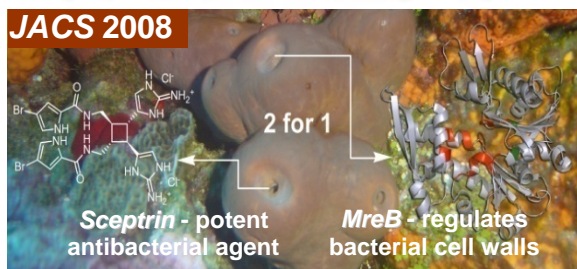
#### Biotech. J. 2009

#### Phosphatidylinositol



Lear-group at <http://staff.science.nus.edu.sg/~chmlmj/>

#### JACS 2008



#### OBC 2009



### PREMIUM PUBLICATIONS

- Practical synthesis of maleimides and coumarin-linked probes for protein and antibody labelling via reduction of native disulfides, HY Song, MH Ngai, ZY Song, PA MacAry, J Hobley, MJ Lear\*, *Org. Biomol. Chem.* **2009**, 7, 3400-3406. (Featured article with inside cover-page).
- Total synthesis of a fully lipidated form of phosphatidyl-myo-inositol dimannoside (PIM-2) of *Mycobacterium tuberculosis*, A Ali, MR Wenk, MJ Lear\*, *Tetrahedron Lett.* **2009**, 50, 5664-5666.
- A mild method for the protection of alcohols using a *para*-methoxybenzylthio tetrazole (PMB-ST) under dual acid-base activation, SR Kotturi, JS Tan and MJ Lear\*, *Tetrahedron Lett.* **2009**, 50, 5267-5269.
- Stereocontrolled entry to the tricyclo[3.3.0]oxoheptane core of bielschowskysin by a [2+2] cycloaddition of an allene-butenolide, R Miao, SG Gramani, MJ Lear\*, *Tetrahedron Lett.* **2009**, 50, 1731-1733.
- Singapore R&D and Globetrotting, MJ Lear\*, B Salmons, WH Gunzburg, JA Dangerfield\*, *Biotech. J.* **2009**, 4 (2), 179-185 (*Biotech Highlight, dedicated to 80th Anniversary of NUS Science in Singapore*).
- Identification of the binding of sceptrin to MreB via a bidirectional affinity protocol, AD Rodriguez\*, MJ Lear\*, JJ La Clair\*, *J. Am. Chem. Soc.* **2008**, 130, 7256-7258.

**NGS APPLICANT: MARTIN J. LEAR**

ASSISTANT PROFESSOR AND CORE MEMBER

Department of Chemistry and Medicinal Chemistry Programme  
Life Sciences Institute (LSI), Faculty of Science, Block S5-03-01, 3 Science Drive-3  
National University of Singapore (NUS), Singapore 117543  
E-mail: chmlmj@nus.edu.sg Phone: +65 6516 3998

**Education (University of Glasgow, Scotland, UK)**

1991-1994 PhD - *Synthesis & Biological Evaluation of Anticancer Agents* – Prof. D. J. Robins  
1987-1991 BSc - *Honours (Special) in Chemistry with Computer Applications* – 1<sup>st</sup> Class

**Positions & Employment**

1994-1995 Industrial post-doctoral researcher (Parke-Davis, Cambridge, UK)  
*Design & synthesis of non-peptidic mimetics & potential neuropeptide antagonists*  
1996-1997 Synthélabo-funded post-doctoral researcher (ICSN-CNRS, Gif-sur-Yvette, France)  
*Asymmetric synthesis of novel N-heterocycles with Profs J. Royer & H.-P. Husson*  
1997-1999 JSPS post-doctoral fellow (Tohoku University, Sendai, Japan)  
*Synthetic studies of the kedarcidin chromophore with Prof. M. Hirama*  
1999-2000 CREST post-doctoral fellow (Tohoku University, Sendai, Japan)  
*Towards the total synthesis of the kedarcidin chromophore with Prof. M. Hirama*  
2000-2004 Assistant professor with Masahiro Hirama (Tohoku University, COE, Sendai, Japan)  
2005-date Assistant professor (National University of Singapore, Singapore)

**Honours**

1991-1994 Prestigious Ph.D. Scholarship, Senate of the University of Glasgow, Scotland, UK  
1995 CChem, Chartered Chemist awarded by the Royal Society of Chemistry  
1995-1996 Fellow of Wolfson College, Cambridge University, UK  
1997-1999 JSPS Post-doctoral Research Fellow, Tohoku University, Japan  
1999-2000 CREST Post-doctoral Research Fellow, Tohoku University, Japan – highest level  
2004 Best presentation (organic synthesis) with Yasuhito Koyama, CSJ Annual meeting  
Jul. 2005 Session Leader, Gordon Research Conference on Natural Products (GRC), USA  
Mar 2008 UK-SIN Collaborative Travel Grant with Benjamin Davis, Oxford Univ, UK.

**Grants Awarded**

1. Lipidomics, novel tools and applications (NRF-G-CRP 2007-04: S\$9,974k total; ca. S\$500k over 5- yrs until Jan.2013 **as co-PI**)
2. Synthesis and biology of future anti-malarials derived from bielschowskysin (AcRF-MoE Tier-II, T206B1112: R-143-000-324-112; S\$630k over 3-yrs until Sep.2009 **as PI**)
3. Towards a Single Molecule to Image, Identify, Fixate, and Validate Biological Targets and Binding Events (SBIC-BMRC RP INN-006/2006: \$50k over 2-yrs until Mar.2009 **as PI**)
4. Silicon and Microwave-based Flourination of Biomolecules (ARF-NUS: R-143-000-304-112; S\$97k over 3-yrs until Aug.2009 **as PI**)
5. Cysteine-based Tailoring of Radiopharmaceuticals and Probes (SBIC-BMRC collaborative-005/2005: R-143-000-285-305; S\$685k total; ca. S\$110k over 3-yrs until Jan.2009 **as co-PI**)

**Invited Lectures and Conference Organization (under NUS affiliation)**

Jul. 2004, Invited talk, Gordon Research Conference on Natural Products (GRC), USA  
Jul. 2005, Session Leader, Gordon Research Conference on Natural Products (GRC), USA  
Dec. 2005, Organic Session Chair, Singapore International Chemical Conference-4 (SICC-4), NUS  
May 2006, MedChem Practical Workshop for Teachers, NUS  
May 2007, Exploiting the Bio-relevance of Natural products in Pharmaceutical Endeavours, THAILAND  
Jul 2007, UK-SINGAPORE Symposium on Drug Discovery in the 21<sup>st</sup> Century, SINGAPORE  
Jul 2007, GEM4-ICMAT: Bioimaging of Cancer, SINGAPORE  
Mar 2008, Hungarian-Singaporean Workshop on Drug Discovery and Biomaterials, HUNGARY  
Feb 2008, UK-SINGAPORE Contemporary Organic Synthesis, Methods and Techniques, SINGAPORE

**NUS-Chemistry Collaborators**

Yao-Qin Shao, Chemistry/Biology Department, Faculty of Science – **Chemical biology**  
Tanja Weil, Chemistry/MedChem Department, Faculty of Science – **Drug delivery and optimisation**  
Yin-Thai Chan, Chemistry Department and IMRE, Faculty of Science – **Microchip technology**

### **NUS-faculty Collaborators**

Paul A. McAry, Microbiology Department, Faculty of Medicine – **Antiviral biology**  
Mark B. Taylor, Microbiology Department, Faculty of Medicine – **Antibiotic biology**  
Kevin Tan, Microbiology Department, Faculty of Medicine – **Antimalarial biology**  
Markus R. Wenk, Biochemistry Department, Faculty of Medicine – **Anti-TB (glycolipid) biology**  
OLS-group associations – **Medicinal Chemistry, Cancer, and Immunology Programs**

### **External Collaborators (outside NUS-affiliation)**

Thomas Dick, Novartis (NITD) – **Malaria and TB biology.**  
Mark S. Butler, MerLion Pharmaceutical, Singapore – **Natural product chemistry**  
James J. La Clair, Xenobe research Institute (XRI), San Diego, USA – **Chemical biology**  
Abimael Rodriguez, University of Puerto Rico (UPR), Puerto Rico – **Natural product chemistry**  
Shih Chang Wang, National University Hospital (NUH), Singapore – **Clinical diagnostic radiology**  
Edwin Yeow, Nanyang Technological University (NTU), Singapore – **Optical analysis**  
Yang Yiyan, Institute of Bioengineering and Nanotechnology (IBN) A\*Star, Singapore – **Drug delivery**  
Jonathan Hobley, Institute of Materials Research & Engineering (IMRE) A\*Star, Singapore – **Bioimaging**

### **--CURRENT TRAINEES--**

#### **PhD Candidates (since Jan'06) – all under NRF-CRP and AcRF-Tier-2**

- (1,2) Kotturi Rajaiah Santosh Kumar/Kunal Hemant Mahajan (*Synthesis of Antimalarial Probes*)
- (3) Shibaji Kumar Ghosh (*Synthesis & Medicinal Development of Antimalarial Agents*)
- (4) Ngai Mun Hong (*Fluorescent Labeling: Probe Design and Bioconjugation*)
- (5,6) Ravi Kumar Sriramula/Sandip Pasari (*Synthesis of Immunogenic Glycolipids against TB*)
- (7) Govindan Subramanian (*Total Synthesis of Bielschowskysin, an Antimalarial Lead*)
- (8) Eey Tze Chiang, Stanley (*Total Synthesis of Platensimycin, a Potent Antibiotic*)
- (9) Simon Oliver (*Discovery, Total Synthesis & Biological Studies of Laetirobin*)

#### **NUS Honours Student (AY2009/10)**

- (1) Xu Wang (*Synthesis and Probe Development of Legumain Inhibitors*) with Kevin Tan@Microbiology

### **---ALUMNI---**

#### **NUS Post-Doctoral Researchers**

- (1) Asif Ali (*Synthesis of Immunogenic Glycolipids*) – NRF-CRP & Novartis (NITD)
- (2) Song Hongyan (*Synthesis of Fluorescent Biological Probes*) – SBIC-A\*STAR-CCO-IMRE
- (3,4) Ru Miao & Farhanullah (*Synthesis of Bielschowskysin*) – AcRF-Tier-2-MoE

#### **Graduate Member (AY2006/07)**

- (1) Hoang Truong Giang (Departmental TA trained in group and promoted to go for a PhD in the US at the University of Minnesota)

#### **NUS Honours Students (AY2008/09)**

- (1) Tan Song Wei Benjamin (*Transannulation Strategies to Bielschowskysin*) – at Oxford under AGS
- (2) Jason Tan Jia Sheng (*Transannulation Strategies to Platensimycin*) – at NIE under MoE

#### **NUS Honours Students (AY2007/08)**

- (1) Li Yihua (*Synthesis of Benzophenone Oxygen Sensors*) with Dr. Hobley @ IMRE
- (2) Li Jiexun (*Functionalisation & Immobilisation Studies onto Silica Surfaces*) with Dr. Hobley@IMRE
- (3) Lee Yingqi (*Synthetic Studies to Precisely Functionalize Silicon Surfaces*) with Dr. Hobley@IMRE
- (4) Teo Hwee (*Synthesis of Photoswitchable Spiropyran Sensors*) with Dr. Hobley @ IMRE
- (5) Lee Tian Xin (*Synthetic Studies of a Fragment of Sieboldine A*)
- (6) Yang Guorong Eugene (*Towards a Rapid Synthesis of Tamiflu and Analogues*)
- (7) Huang Xinhui (*Synthesis of the Cyclohexenone Fragment of Platensimycin*)
- (8) Ng Theng Eng Stella (*Synthesis of Inositol-based Effectors & Inhibitors of Biological Processes*)
- (9) Liew Peiqin (*Synthesis of Inositol-based Effectors and Inhibitors*) with Dr. Wenk @ CeLS
- (10) Neo Yining (*Synthesis of Labeled Glutamic and Adepic Semialdehydes*) with Dr. Jenner @ CeLS
- (11) Teow Yi Wei (*Synthesis of Labeled Dityrosine and 2-Oxohystidine*) with Dr. Jenner @ CeLS
- (12) Khor Dingyue (Effect of Peptide Composition on Gene Transfection Efficiency) with Dr. Yan @ IBN

#### **NUS UROPS Students (AY2007/08)**

- (1) Low Joo Leng (*Synthesis of Biologically useful Inositols*)
- (2) Tan Song Wei Benjamin (*Synthesis of Platensimycin Aromatic Fragment*)
- (3) Jason Tan Jia Sheng (*Development of New Protective Group Reagents and Protocols*)

**NUS Honours Students (AY2006/07)**

- (1) Cho Bokun (*Synthetic Study of the Anti-malarial Lead, Bielschowskysin*)
- (2) Yamada Kimi (*Synthesis and Linking of Bird-flu Inhibitors*)
- (3) Tan Wei Ling Diana (*Synthetic Studies in Protective Group Chemistry*)
- (4) Toh Qiao Yan (*Rapidly Fluorination of Tagged Biomolecules*) – **at Cambridge under AGS**
- (5) Mai Minh Tien (*Synthesis of Metal Chelating Tags for Radiopharmaceutical Imaging*)

**NUS UROPS Student (AY2006/07)**

- (1) Tan Zhi Kuang (*Synthetic Studies in Protective Group Chemistry*)

**NUS Honours Students (AY2005/06)**

- (1) Eey Tze Chiang, Stanley (*Synthesis Towards a  $\gamma$ -Butenolide Fragment of Bielschowskysin*)
- (2) Lim Yew Heng (*Synthesis Towards a Tartrate-Derived Fragment of Bielschowskysin*)
- (3) Ang Yee Swan (*Methodology towards Mild Protective Group Reagents*)

**Patents Pending:**

1. **M J LEAR\*** and **K S W Tan\***, "Synthesis & Use of Fluorophore-tagged Antimalarials", US Provisional Application No. 61 221,304 (ILO ref. 09132N - US PRV) - 20 July **2009** .
2. **M J LEAR\*** and J J La Clair\*, "Laetiporina Scaffold & Methods for the Use Thereof", US Provisional Application No. 61 247,979 (ILO ref. 09157N - US PRV) - 2 October **2009**.

**Papers, Book Chapters & Presentations:**

*See attached print-out from NUS database.*