出國報告（出國類別：其他）

生質料源之高值化應用
-多元醇醱酵技術研究
參加第二屆國際今昔綠色化學研究系統研討會出國報告

服務機關：台灣中油股份有限公司綠能科技研究所

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派赴國家：美國

出國期間：104年9月13日至18日

報告日期：104年11月18日

摘要

永續性的生質能源，為延續地球永存不可或缺的條件，也是國內外能源公司重視的研發目標。台灣中油公司綠能科技研究所設立的宗旨之一，為帶動公司進行石化產業高值化，因此生質能源技術發展與工業化應用，為本公司綠能科技研究所研發重點。而在本公司生質高值化研究主題中，生質多元醇更是具龐大商業化潛力的化學品標的，因此列為生物科技組發展重點之一。然而，國內業界針對生質多元醇之研究，與國外相較之下稍顯薄弱，亦需要更多產官學研各界交流平台。為瞭解國際間生質能源的最新發展技術及研發趨勢，因此參加美國奧蘭多第二屆國際今昔綠色化學研究系統研討會 (2nd International Conference on Past and Present Research Systems of Green Chemistry, ICPPRSGC_2015)，並投稿發表兩篇國際會議論文。本報告將研討會內容分為主要主題演講 (Keynote Forum)、專題演講 (Special Session)、論文海報發表 (Poster Presentation) 等三部分進行整理及分析、並簡述會議中關於全球生質能市場及相關產業的發展近況，最後提出心得與建議。

目次

1　目的

由於人類長期依賴石化能源，燃燒散逸的二氧化碳氣體，不斷加速溫室效應，造成全球氣候變遷逐年劇烈，風災、水災、海嘯、旱災、暴風雪等極端氣候強度與頻率比以往更高，我們在追求經濟發展同時，犧牲的不僅是自己也是下一代的居住環境。再生能源具有永續性，雖不能立竿見影改變氣候，卻是正確而值得長期發展的方向，而非因應化石燃料存量下降而曇花一現的茶餘話題。

近一年以來，由於產油國與美國金權鬥爭，油價受刻意操作而下跌，中油公司因而虧損三百多億，便宜的油價使人們暫時忘卻能源不足的危機，然而人們越放肆地使用能源，也就更難滿足無上限擴大的能源需求，未來能源枯竭的日子就更近。有鑑於此，此時更應把握時機全力發展再生能源，未雨綢繆。如今約5%原油用於化學產業，95%用於燃料與能源，但兩者產生的盈餘相同，也顯示生質化學品的經濟規模遠大於生質能源。世界經濟論壇 (WEF) 預估至 2020 年全球生物精煉產業含生質燃料、生質精煉及生質化學品市場規模可達 2,300 億美元，其中可帶動農業產值 1,040 億美元，為價值鏈中最高者，其中生質料源以高值化生質化學品的應用最具發展潛力。

除了二氧化碳減量之訴求外，由於美國頁岩氣開採技術成熟及產量逐年提高，天然氣、乙烷價格有下修的趨勢，驅使石化業者紛紛擴建乙烷裂煉廠，提高以廉價的天然氣或頁岩氣作為石化生產原料的比例，而逐步淘汰以石油腦為進料之傳統裂煉廠。然而，以天然氣或頁岩氣為進料，僅能產出C2與C3系列的石化原料，預計此類產品及衍生物將出現供過於求的情況，反觀僅能由石油腦提煉出的 C4 及芳香烴等石化原料，將因傳統裂煉廠的式微，產量下降，而且在天然氣價格與原油價格逐漸脫鉤的情況下，C4及芳香烴系列產品將會出現短缺，價格也將水漲船高。由於上述趨勢，生質化學品 (特別是C4以上的原料) 發展儼然已成為各國發展的重點，不僅僅是考量取代石化燃料以達環保減碳，更進一步將是補足化學原料上的缺口。

生質化學品發展的歷史雖短不長，但在全球廠商的致力研究及政府的鼓勵下，開發出的產品日新月異。由於台灣綠能相關研究起步較晚，尤其是生質化學品原料方面研究未能與世界接軌，亦缺乏適當產官學研交流平台，為瞭解國際間生質能源的最新

發展技術及工業化趨勢，因此參加第二屆國際今昔綠色化學研究系統研討會 (2nd International Conference on Past and Present Research Systems of Green Chemistry, ICPPRSGC 2015)，並投稿發表兩篇國際會議論文，藉由研討會中各項再生能源研究分享，蒐集國際間生質能源的最新發展技術、實施經驗及未來趨勢，有助於提升本公司研發能量與新創事業開發之可行性評估。

2　過程

出國行程與時間安排如表一。

表一、出國行程表。

日期	起訖地點	工　作　紀　要
104/9/13	台灣桃園 ~美國佛羅里達州奧蘭多	啟程(台北-桃園國際機場-美國奧蘭多機場)
104/9/14	美國佛羅里達州奧蘭多	參加研討會議程
104/9/15	美國佛羅里達州奧蘭多	參加研討會議程
104/9/16	美國佛羅里達州奧蘭多	參加研討會議程
104/9/17	美國佛羅里達州奧蘭多 ~台灣桃園	返程(美國奧蘭多機場-台灣桃園國際機場)
104/9/18	美國佛羅里達州奧蘭多 ~台灣桃園	返程(美國奧蘭多機場-台灣桃園國際機場)

3　研討會內容整理

3.1　研討會簡介與發表論文內容

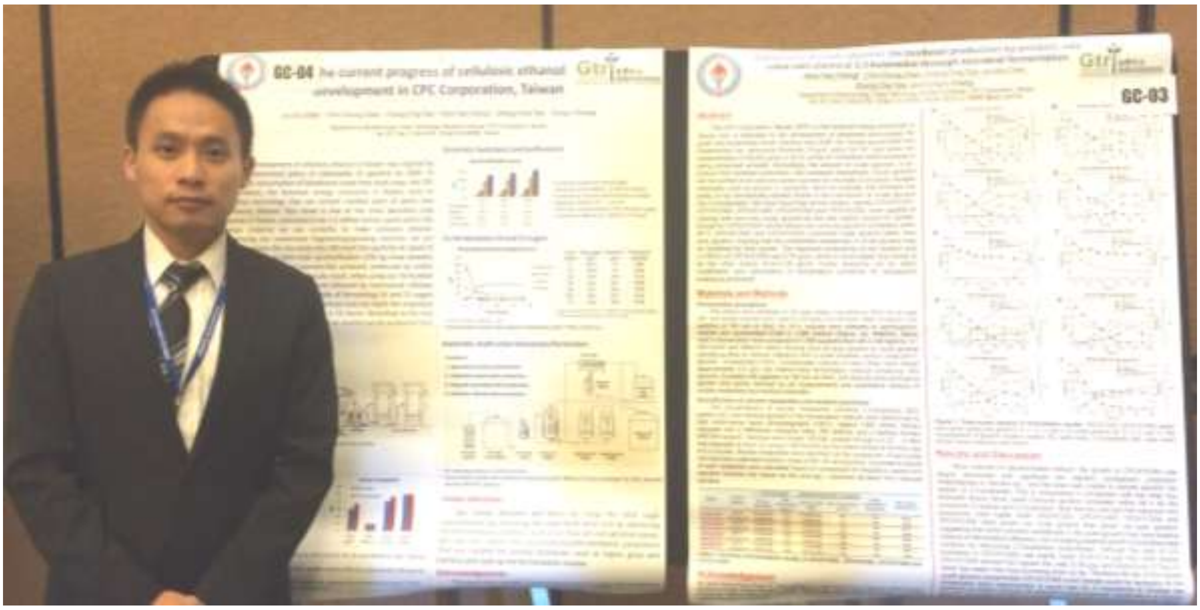
第二屆國際今昔綠色化學研究系統研討會 (2nd International Conference on Past and Present Research Systems of Green Chemistry, ICPPRSGC 2015, 以下簡稱綠色化學研討會) 由 OMICS International 集團主辦，日期為 2015 年 9 月 14-16 日，於美國奧蘭多國際機場凱悅酒店 (Hyatt Regency Orlando International Airport) 舉行。本次綠色化學研討會參加對象包括學術界 (大學及研究機構) 及綠色化學相關協會組織等，共有 13 個不同研究主題及 68 場演講，主題圍繞「增進綠色化學全球化深度發展」(見圖一)。

除演講外，論文壁報發表更提供研討會高度自由的討論空間。本次研討會也聚集了各界優秀的演講者，彼此交流並與聽眾互動，提供最新知識外，也引入新穎的研究主題，豐富了綠色化學相關研究視野。

本次研討會主辦單位 OMICS International 除邀請綠色化學之父 John C. Warner 博士 (現為美國 Warner Babcock Institute for Green Chemistry 研究所所長) 擔任演講嘉賓，亦邀請 John Littleton 博士 (University of Kentucky, USA)、Lothar Brecker 博士 (University of Vienna, Austria)、Mahdi M Abu-Omar 博士 (Purdue University, USA) 及 Craig L Hill 博士 (Emory University, USA) 等知名學者共同主持主題演講並分享研究成果。

本次研討會中，由本人代表本組發表論文「The current progress of cellulosic ethanol development in CPC Corporation, Taiwan」(#GC-04，本組陳瑞惠博士為主要作者) 及「Conversion of crude glycerol, the biodiesel production by-product, into value-add chemical 2,3-butanediol through microbial fermentation」(#GC-03，本人為主要作者) (圖二)。其中纖維素酒精的論文獲得評審好評，並獲頒論文獎第二名 (圖三)。

圖一、第二屆國際今昔綠色化學研究系統研討會 (2nd International Conference on Past and Present Research Systems of Green Chemistry, ICPPRSGC 2015)。舉辦地點為美國奧蘭多國際機場凱悅酒店 (Hyatt Regency Orlando International Airport)。



圖二、第二屆國際今昔綠色化學研究系統研討會論文發表。論文「The current progress of cellulosic ethanol development in CPC Corporation, Taiwan」(左，GC-04，本組陳瑞惠博士為主要作者) 及 「Conversion of crude glycerol, the biodiesel production by-product, into value-add chemical 2,3-butanediol through microbial fermentation」(右，GC-03，本人為主要作者)。

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Best Poster Award

(2nd Position)

Awarded to Jui-Hui Chen
Green Technology Research Institute, Taiwan

for presenting the poster entitled:
The current progress of cellulosic ethanol development in CPC Corporation, Taiwan

at the "2nd International Conference on
Past and Present Research Systems of Green Chemistry"
held on September 14-16, 2015 in Orlando, USA

The award has been attributed in recognition of research paper quality, novelty and significance.

John C Warner
John C Warner
Warner Babcock Institute for Green Chemistry, USA

圖三、第二屆國際今昔綠色化學研究系統研討會論文獲獎獎狀。發表論文獲本次研討會論文競賽第二名：(GC-04)「The current progress of cellulosic ethanol development in CPC Corporation, Taiwan」(本組陳瑞惠博士為主要作者)。

3.2 主要主題演講

3.2.1 綠色化學：成長契機與競爭優勢 (Green chemistry: An opportunity for growth and competitive advantage)

演講者：John C. Warner, Ph.D.

機構名稱：Warner Babcock Institute for Green Chemistry, USA

演講摘要：

Warner 博士在成立 Warner Babcock Institute for Green Chemistry (WBI) 之前已有相當多年學術界經驗 (1997-2007, 麻薩諸塞大學洛厄爾分校(University of Massachusetts Lowell)) 且獲獎無數，由於研究成果卓越更於 2014 年獲美國工業化學學會頒發象徵業界最高榮譽之柏金獎章 (Perkin Medal，鉑金獎章是紀念世界第一個人工苯胺染料苯胺紫發現五十週年，因此第一屆的獎章就授予發現者威廉‧珀金)。Warner 博士體認現今社會往往較關注「發現」及「定義」問題，而較少著重「解決」問題 (…Our society pays more attention to discovery/identifying a problem, rather than solving a problem.)，因此設立 WBI，搭起學術界/研究機構與產業界/公司/財團法人單位間的橋樑。

WBI 內部績效並非以國際期刊發表篇數來認定 (2011~2013 共 3 篇，http://www.warnerbabcock.com/about-us/journal-publications/)，而是鼓勵申請專利，因此自 1991 年成立以來已有超過 50 件專利 (至 2014 年共 54 件，http://www.warnerbabcock.com/about-us/patents/)，可說是完全以應用或產品導向進行研發，以如此精簡的研發團隊 (不到 40 位科學家) 而言，可以說是產量驚人。

綠色化學的觀念，涵蓋產品開發至產品使用結束、分解回收等，我們身邊接觸的每一項事物，從早晨使用的牙膏、客廳傢俱至幾乎人人俱備的行動電話，都來自無數化學原料；因應不同需求，我們利用化學修飾得到各種功能：藉由材質化學表面處理，使地毯變得不易沾染汙垢、藉由不同成分及比例調配，使乳液變得滑順等。然而，功能性之外若考慮健康、對環境影響等

因素，不少產品由於化學物質標示不全或誤導，往往使人低估潛在危險：如塑膠玩具中含有鄰苯二甲基酯類 (Phthalates，塑化劑)、水壺中含有酚甲烷 (Bisphenol A，雙酚 A)，近來造成大眾廣泛擔憂及對於日常使用化學品的恐懼。至於為何有潛在危險的化學物質，會進入日常生活用品，可能原因之一是研發、創造、生產這些化學原料及產品的眾多化學家、化工學家、材料科學家並未受到綠色化學薰陶。雖然難以置信，但對於大部分化工原料及其產品，研究者未受過毒性測試、環境分解性、生物潛在累積性及致病性的訓練，因此，許多使生活過更便利的產品，不一定使得生活過得更安全。

如何確保產品不僅帶來生活上的便利，更能夠增加環境的永續性，或至少對環境影響降低至合理範圍？科學家及工程師必須具備足夠知識，來選擇並使用更符合綠色化學的原料。綠色化學的 12 項原則提供研發及製造產品時，對於化學原料選擇的大方向：

- POLLUTION PREVENTION：It is better to prevent waste than to treat and clean up waste after it is formed.
- ATOM ECONOMY：Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.
- LESS HAZARDOUS SYNTHESIS：Whenever practicable, synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and the environment.
- DESIGN SAFER CHEMICALS：Chemical products should be designed to preserve efficacy of the function while reducing toxicity.
- SAFER SOLVENTS AND AUXILIARIES：The use of auxiliary substances (solvents, separations agents, etc.) should be made unnecessary whenever possible and, when used, innocuous.
- DESIGN FOR ENERGY EFFICIENCY：Energy requirements should be recognized for their environmental and economic impacts and should be

minimized. Synthetic methods should be conducted to ambient temperature and pressure.

- USE OF RENEWABLE FEEDSTOCKS：A raw material or feedstock should be renewable rather than depleting whenever technically and economically practical.
- REDUCE DERIVATIVES：Unnecessary derivatization (blocking group, protection/deprotection, temporary modification of physical/chemical processes) should be avoided whenever possible.
- CATALYSIS：Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.
- DESIGN FOR DEGRADATION：Chemical products should be designed so that at the end of their function they do not persist in the environment and instead breakdown into innocuous degradation products.
- REAL-TIME ANALYSIS FOR POLLUTION PREVENTION：Analytical methodologies need to be further developed to allow for real-time in-process monitoring and control prior to the formation of hazardous substances.
- INHERENTLY SAFER CHEMISTRY FOR ACCIDENT PREVENTION：Substance and the form of a substance used in a chemical process should be chosen so as to minimize the potential for chemical accidents, including releases, explosions and fires.

Warner 博士謙虛的表示，他只是很幸運在最適當的時機寫下綠色化學這本教科書，但從演講中提到的 WBI 數項研究成果，可以見證綠色化學如何將理論與研究轉化為實際產品及應用：

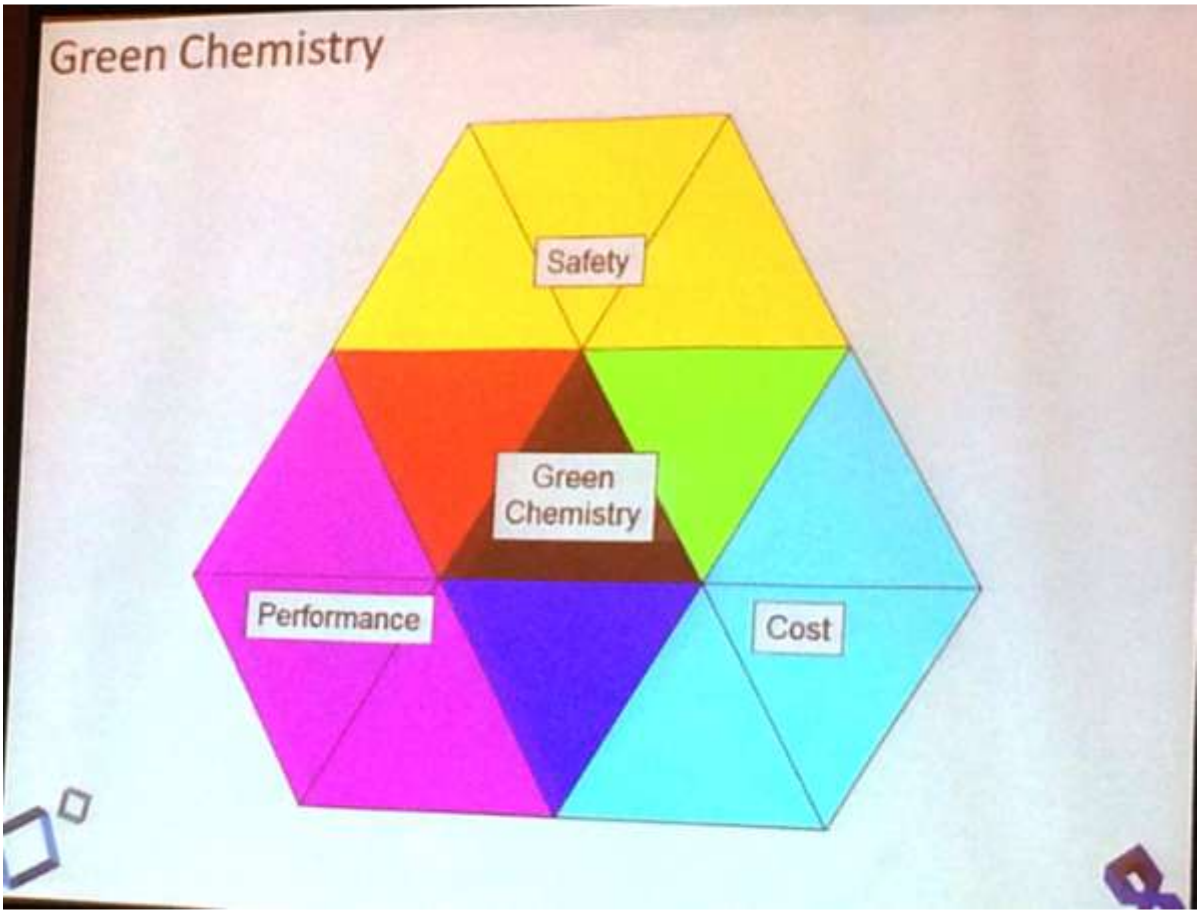
以往鋪平路面使用的柏油跟綠色化學很難聯想在一起，此外但 WBI 發現一種來自植物新的化合物 Delta-S^{TM}，用於柏油再生時可提高舊柏油使用率，除減低鋪設路面的費用外，更可降低汙染。通常並非雨水、雪或低溫造成博油快速老化而是氧化作用：空氣中的氧氣與柏油路成份作用，使路面變乾、

脆化、產生裂痕甚至碎裂。Delta-S^{TM} 可逆化這個過程，使柏油成份軟化，舊柏油回收使用比例可由原先~25%提升為~50%，大幅降低原料費用 (舊柏油幾乎不須成本)，鋪設溫度更從 380℉ 降為 180 ℉ (~193℃ 降為~82℃)，使得較少高溫油氣溢出造成汙染及浪費。其他公司生產可重覆利用舊柏油的產品，通常含有高毒性化合物例如 hydrolene，此石油抽提物具造成癌症、胎兒先天缺陷、器官傷害等潛在風險，相較之下 Delta-S^{TM} 無毒性，也使得操作上更安全。

自古以來，無論男女皆使用含有礦物及植物萃取成分染髮，但在過去 100 年以來，化工方法的發展，使這個習俗對健康造成傷害。The Nature of Hair, LLC (dba Hairprint) 公司與 WBI 合作推出染髮劑產品 Hairprint®，可在 90 分鐘內將白髮染回原本顏色。這個產品的靈感，來自於觀察蟑螂等昆蟲在成蟲蛻變時，可於極短時間將原本白色的外殼變成深棕色，之後顏色不會變淡且表面具有金屬光澤。Hairprint®本身不含色素，可取代市面上許多含鉛的染髮劑，其原理很簡單：頭髮的顏色與特殊色素分子排列方式有關，白髮或者髮色減淡是因為隨年紀增加排列方式逐漸改變；藉由模擬昆蟲「重整」色素分子排列順序的過程，可以讓髮色回復為原本的色澤與亮度。由於這個方式不使用含有色素或含鉛成份的藥劑，可以減低染髮時金屬成分殘留頭皮造成的潛在毒害。

Warner 博士除了簡介 WBI、介紹數項該機構重要研究成果外，更點出教育下一代的重要性，由 WBI 研究者創立的「beyondbenign」機構，致力於推動綠色化學教育，包括 K-12 (美國基礎教育，約為我國幼稚園至高中) 師資養成、網路學習、短期課程訓練、社區關懷計畫、大學生成員計畫等；針對大學以上，也包含職業發展及培訓、綠色化學相關工具及化學家毒物學訓練等。

整體而言，Warner 博士的綠色化學理念兼具深度與廣度，連結了學界、業界，成功將研發成果商業化，或改進目前汙染較高之製程，此外更注重未來人才的培育及在職人員培訓，為全世界樹立良好的楷模，也非常值得我們借鏡。以下將報告內容重要投影片列出：



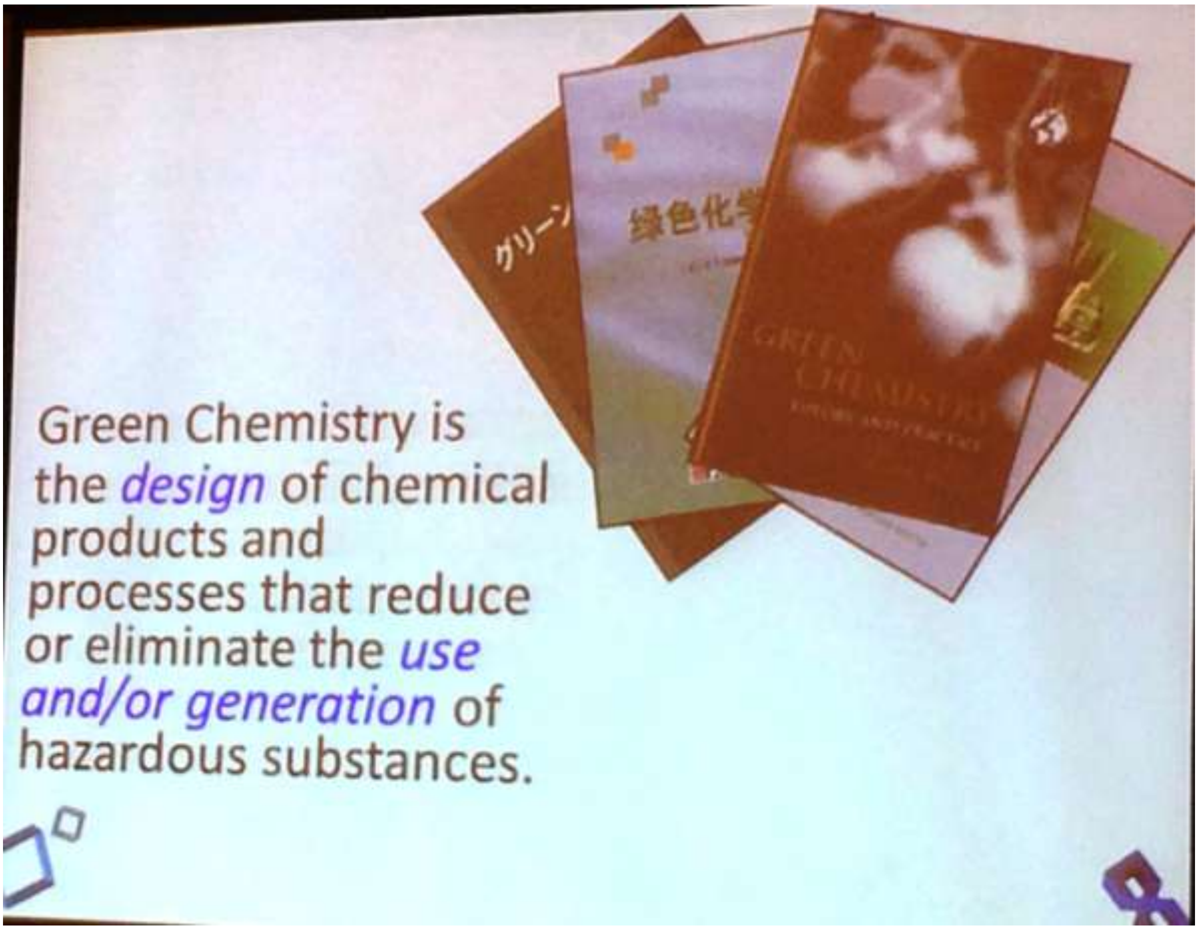
Green Chemistry

Safety

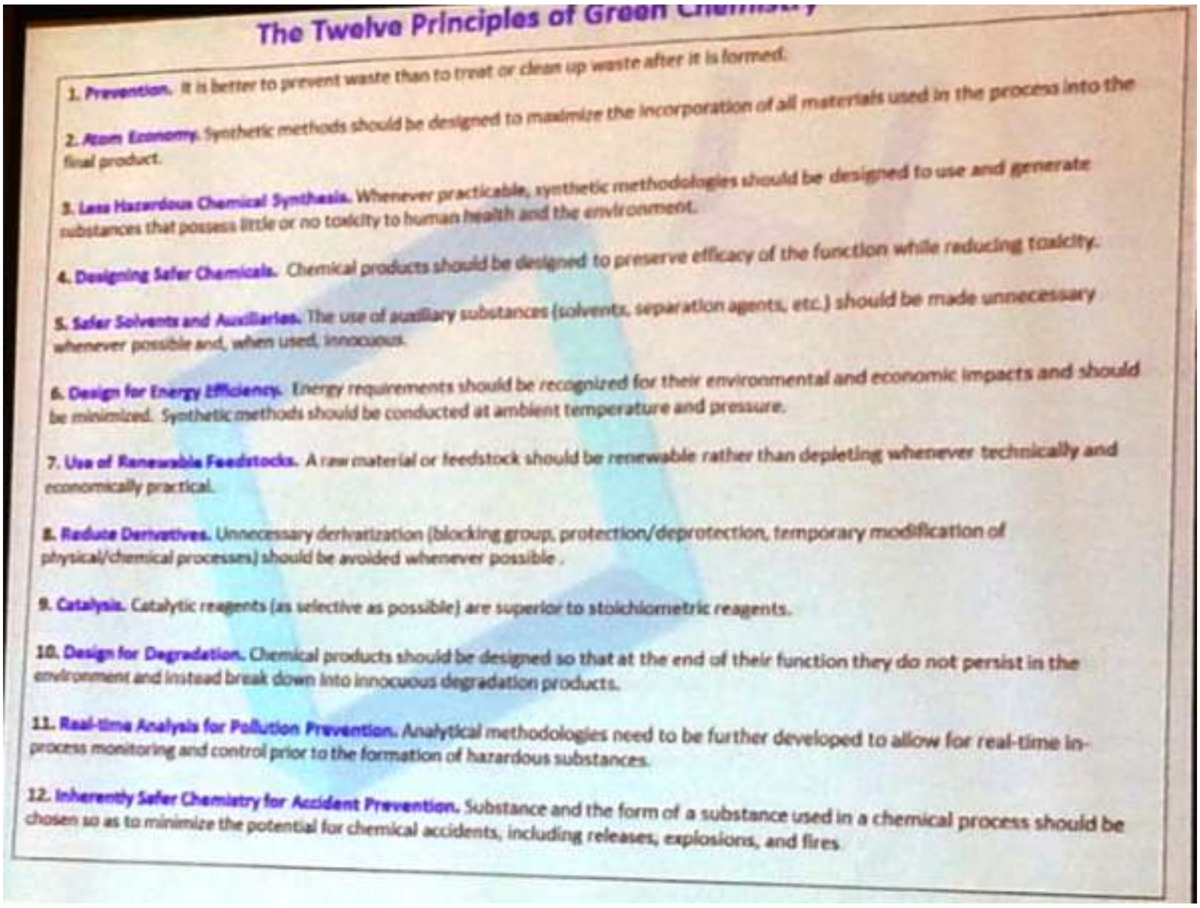
Green Chemistry

Performance

Cost



Green Chemistry is the *design* of chemical products and processes that reduce or eliminate the *use and/or generation* of hazardous substances.



The Twelve Principles of Green Chemistry

1. Prevention. It is better to prevent waste than to treat or clean up waste after it is formed.

2. Atom Economy. Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.

3. Less Hazardous Chemical Synthesis. Whenever practicable, synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and the environment.

4. Designing Safer Chemicals. Chemical products should be designed to preserve efficacy of the function while reducing toxicity.

5. Safer Solvents and Auxiliaries. The use of auxiliary substances (solvents, separation agents, etc.) should be made unnecessary whenever possible and, when used, innocuous.

6. Design for Energy Efficiency. Energy requirements should be recognized for their environmental and economic impacts and should be minimized. Synthetic methods should be conducted at ambient temperature and pressure.

7. Use of Renewable Feedstocks. A raw material or feedstock should be renewable rather than depleting whenever technically and economically practical.

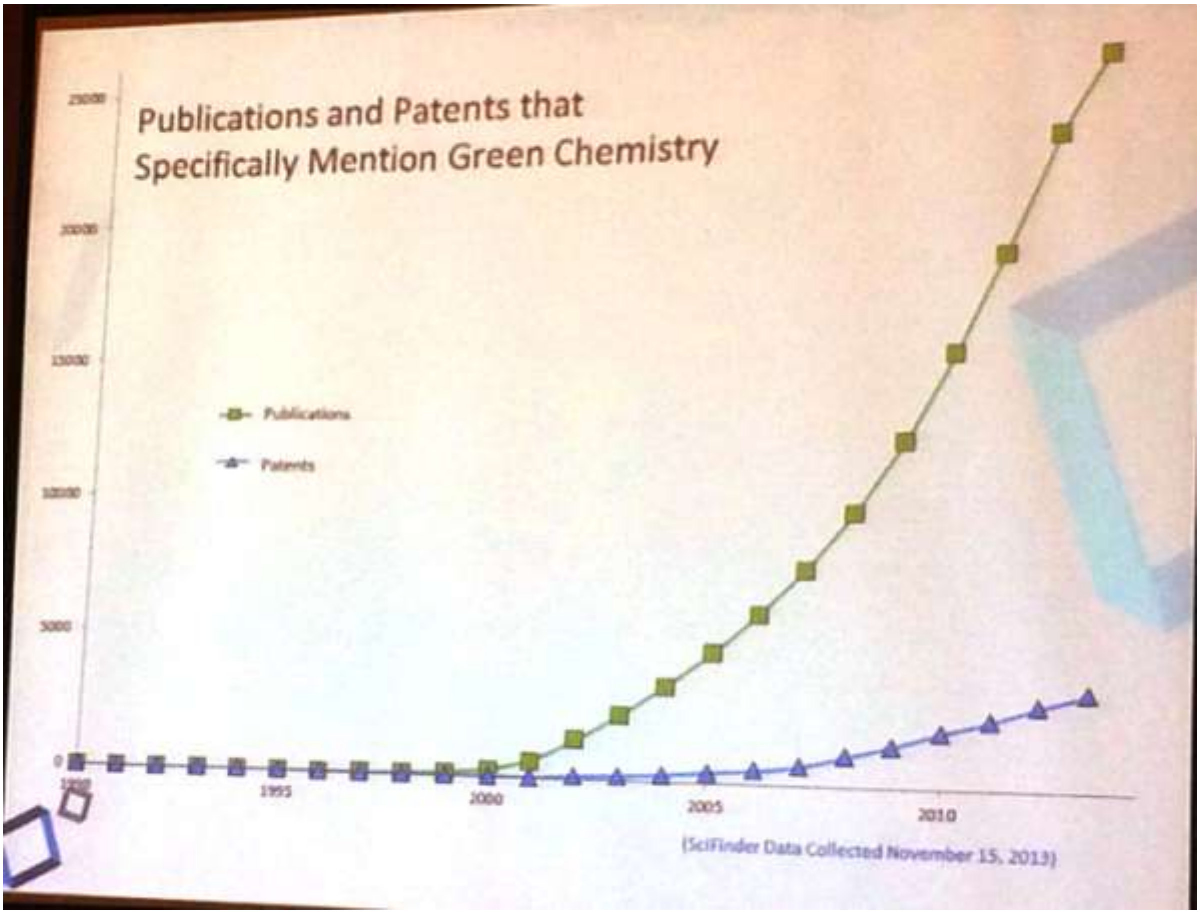
8. Reduce Derivatives. Unnecessary derivatization (blocking group, protection/deprotection, temporary modification of physical/chemical processes) should be avoided whenever possible .

9. Catalysis. Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.

10. Design for Degradation. Chemical products should be designed so that at the end of their function they do not persist in the environment and instead break down into innocuous degradation products.

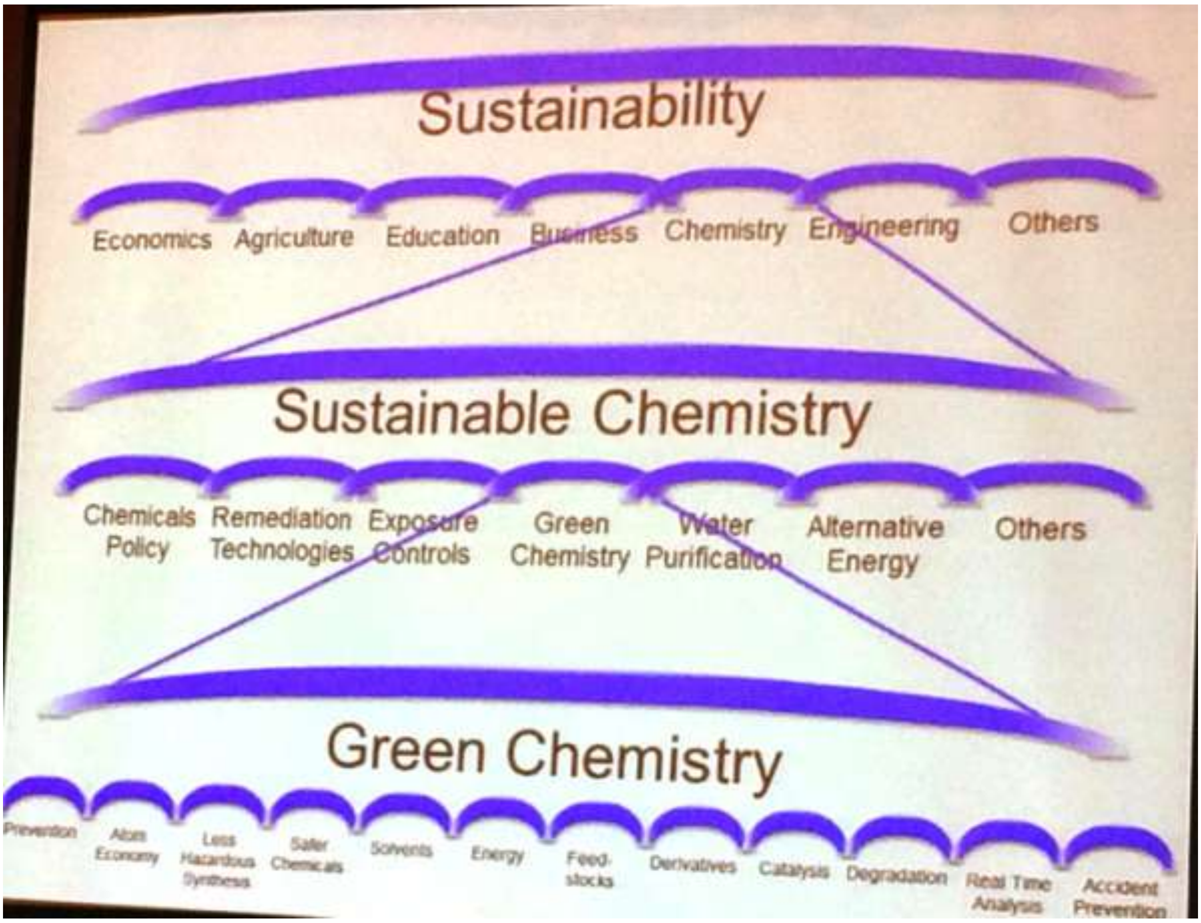
11. Real-time Analysis for Pollution Prevention. Analytical methodologies need to be further developed to allow for real-time in-process monitoring and control prior to the formation of hazardous substances.

12. Inherently Safer Chemistry for Accident Prevention. Substance and the form of a substance used in a chemical process should be chosen so as to minimize the potential for chemical accidents, including releases, explosions, and fires



Publications and Patents that Specifically Mention Green Chemistry

(SciFinder Data Collected November 15, 2013)



Sustainability

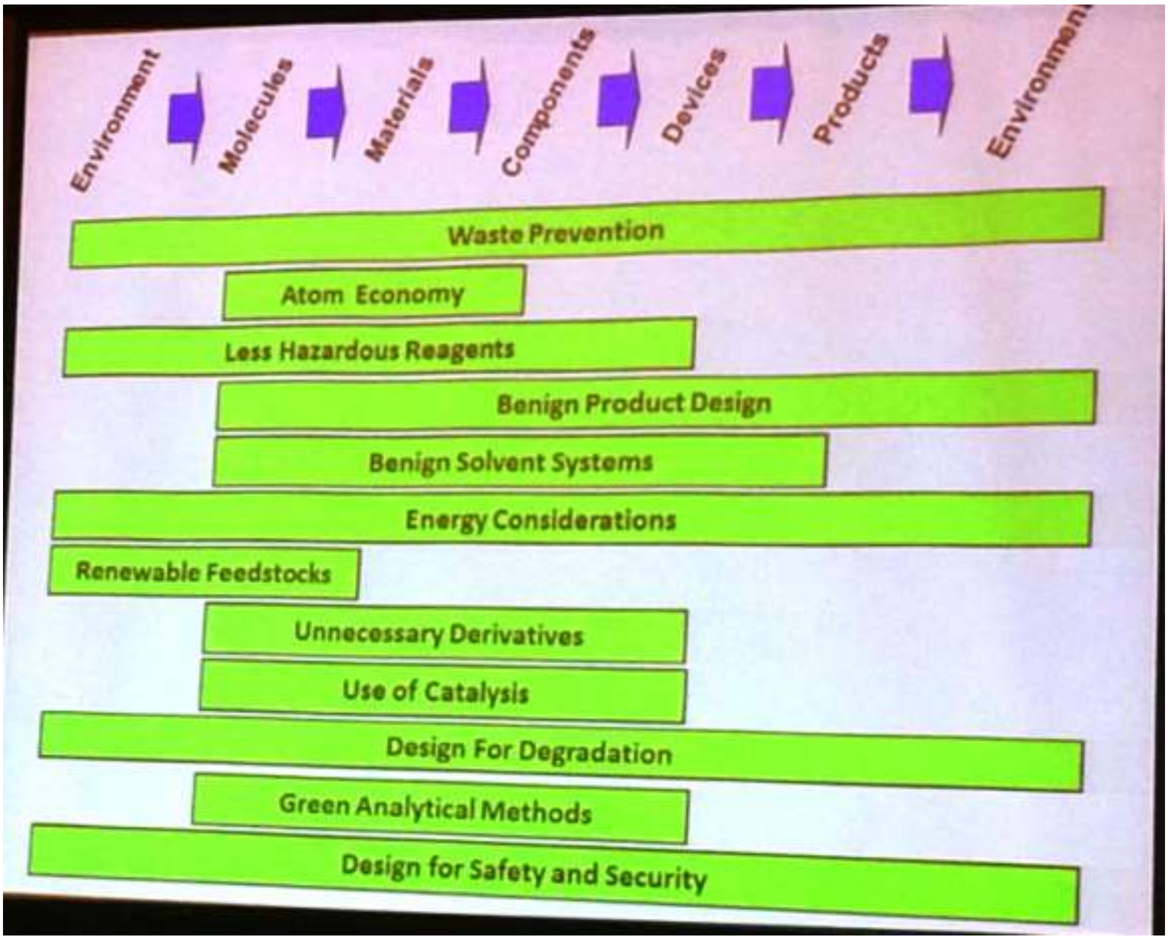
Economics
Agriculture
Education
Business
Chemistry
Engineering
Others

Sustainable Chemistry

Chemicals Policy
Remediation Technologies
Exposure Controls
Green Chemistry
Water Purification
Alternative Energy
Others

Green Chemistry

Prevention
Atom Economy
Less Hazardous Synthesis
Safer Chemicals
Solvents
Energy
Feed-stocks
Derivatives
Catalysis
Degradation
Real Time Analysis
Accident Prevention



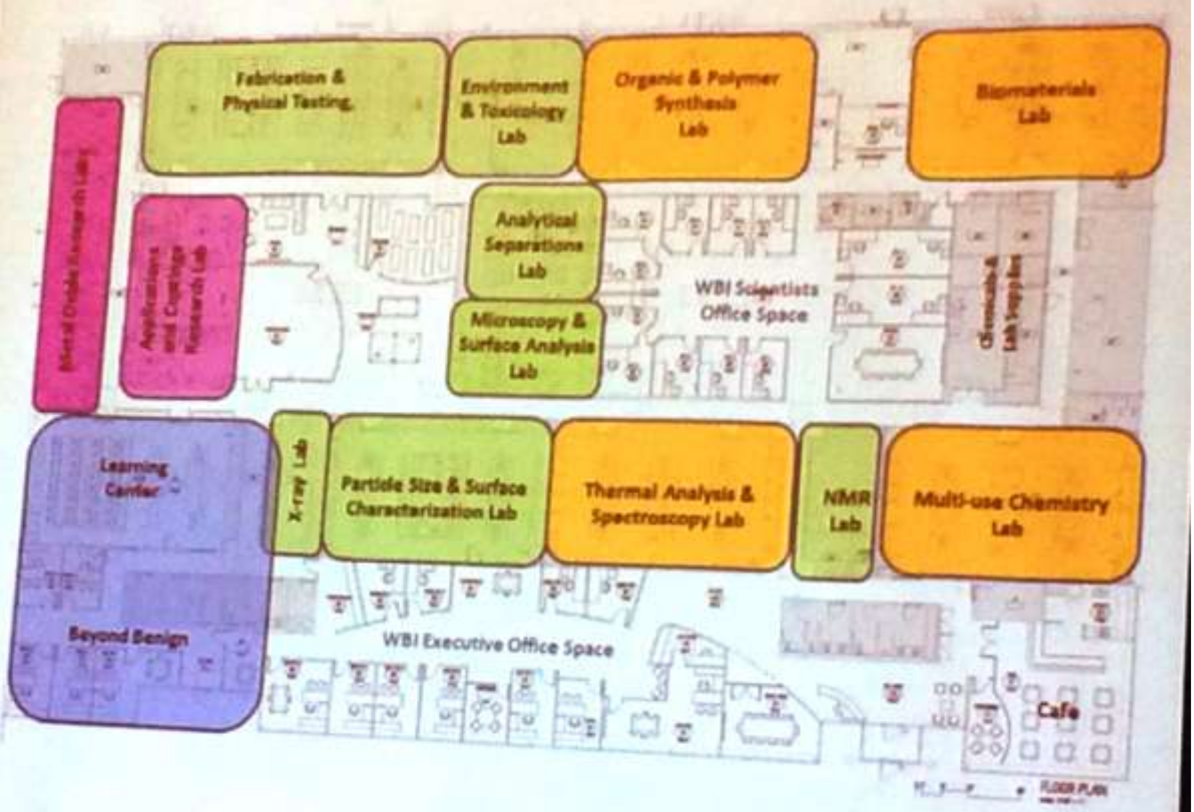
Environment
Molecules
Materials
Components
Devices
Products
Environmen

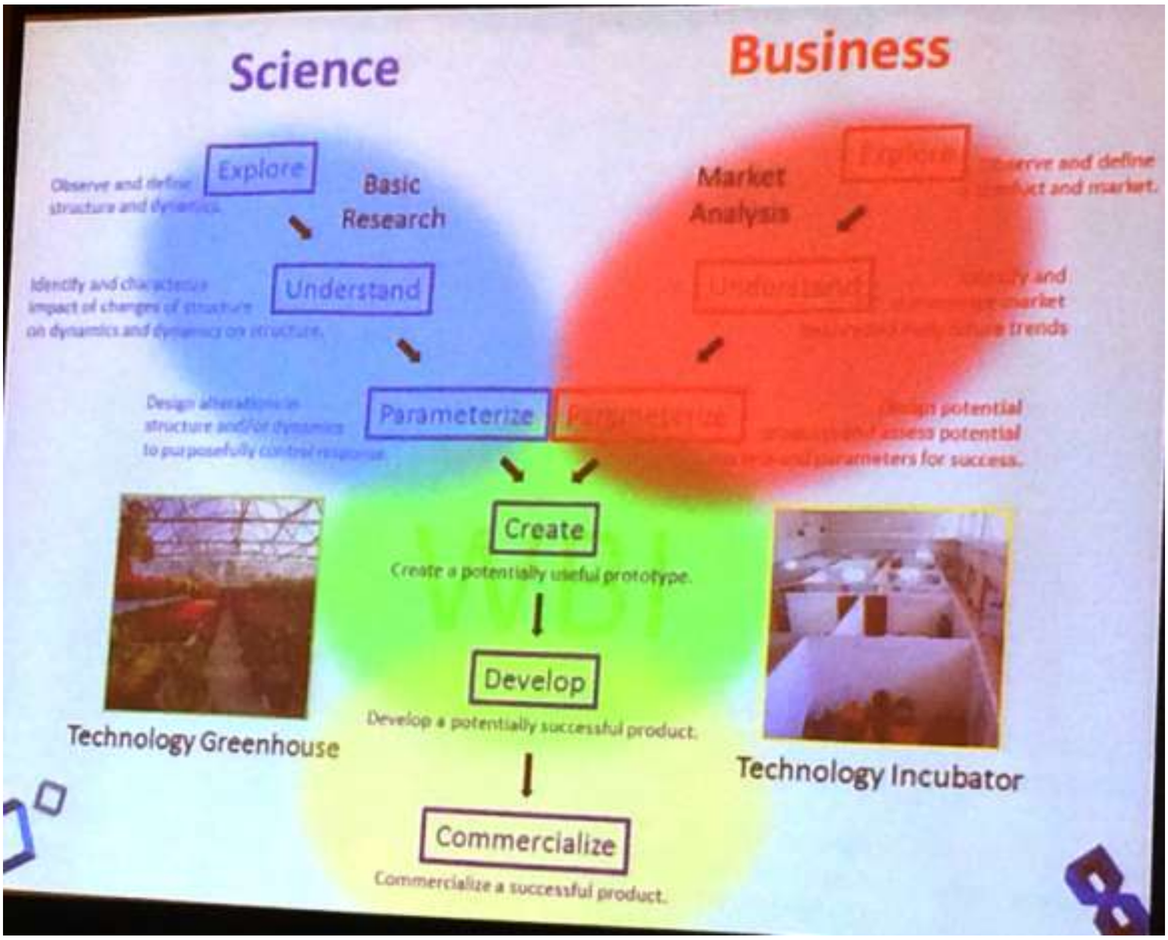
Waste Prevention
Atom Economy
Less Hazardous Reagents
Benign Product Design
Benign Solvent Systems
Energy Considerations
Renewable Feedstocks
Unnecessary Derivatives
Use of Catalysis
Design For Degradation
Green Analytical Methods
Design for Safety and Security

Chart 1.1 ***Green Chemical Market by Region, World Markets: 2011-2020***

(Source: Pike Research)

PikeResearch
Cleantech Market Intelligence





Science

Business

Explore

Observe and define structure and dynamics.

Basic Research

Understand

Identify and characterize impact of changes of structure on dynamics and dynamics on structure.

Parameterize

Design alterations in structure and/or dynamics to purposefully control response.

Market Analysis

Explore

Observe and define product and market.

Understand

Identify and [illegible] market [illegible] future trends

Parameterize

Design potential [illegible] assess potential [illegible] parameters for success.

Create

Create a potentially useful prototype.

WBI

Develop

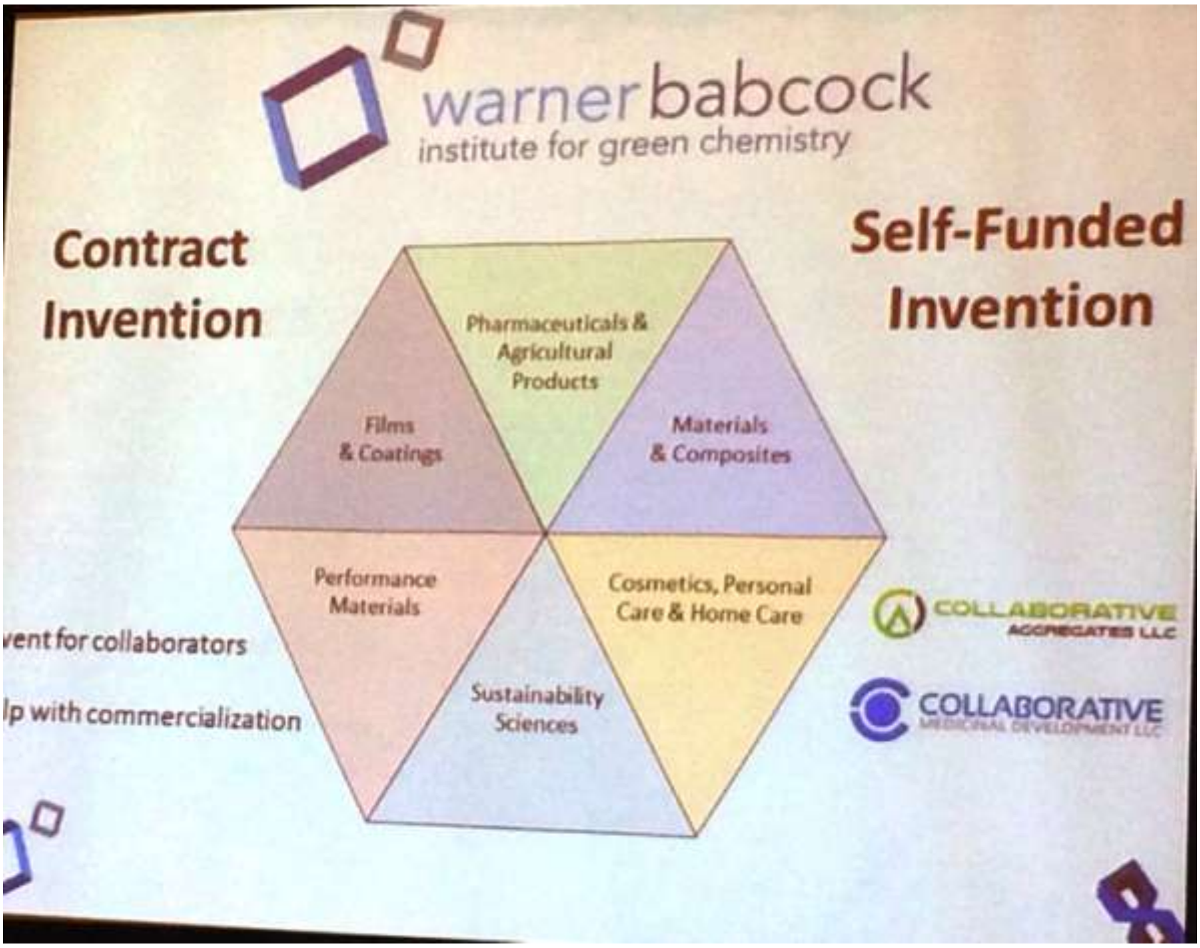
Develop a potentially successful product.

Commercialize

Commercialize a successful product.

Technology Greenhouse

Technology Incubator



warnerbabcock
institute for green chemistry

Contract Invention

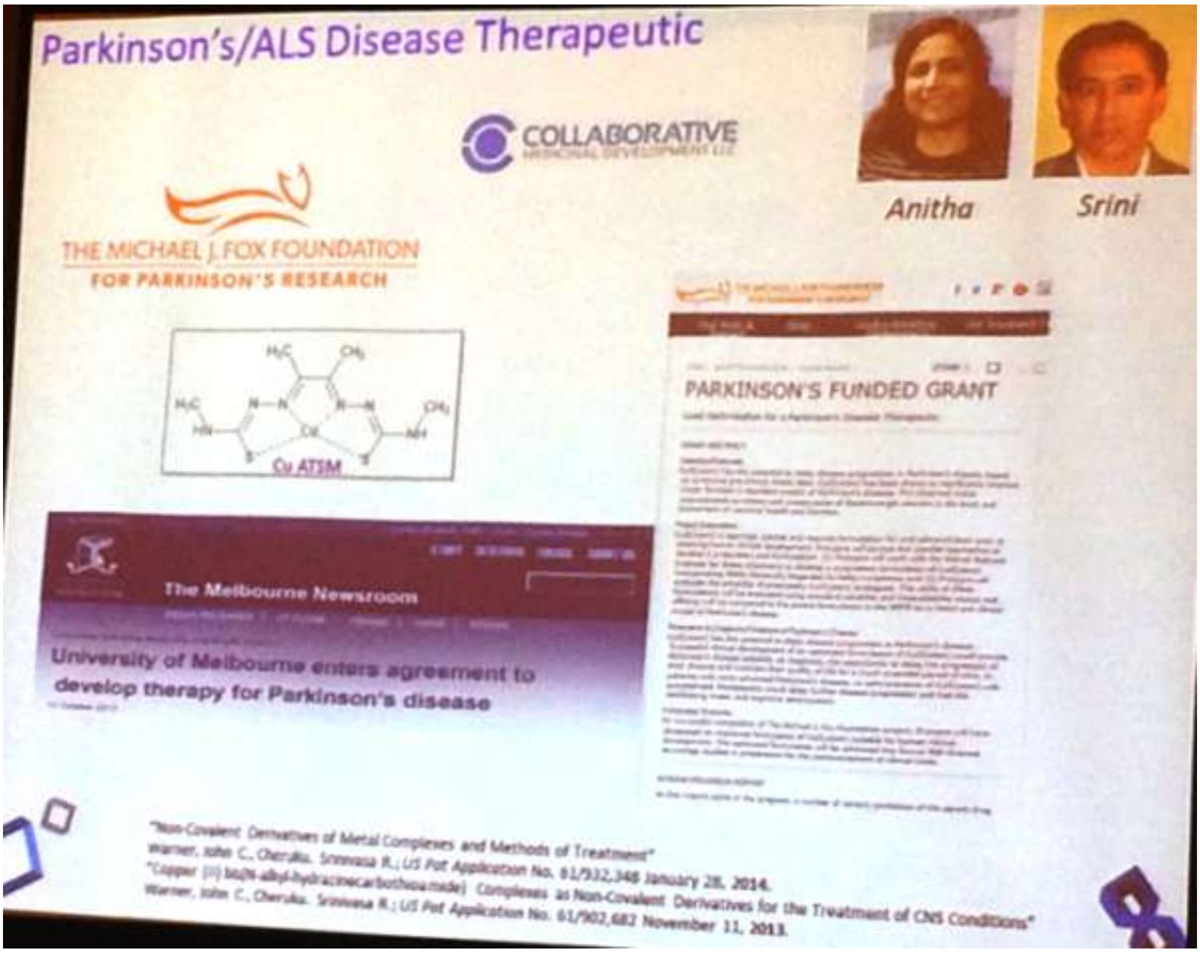
Self-Funded Invention

vent for collaborators

lp with commercialization

COLLABORATIVE AGGREGATES LLC

COLLABORATIVE MEDICINAL DEVELOPMENT LLC



Parkinson's/ALS Disease Therapeutic

COLLABORATIVE MEDICINAL DEVELOPMENT LLC

Anitha *Srini*

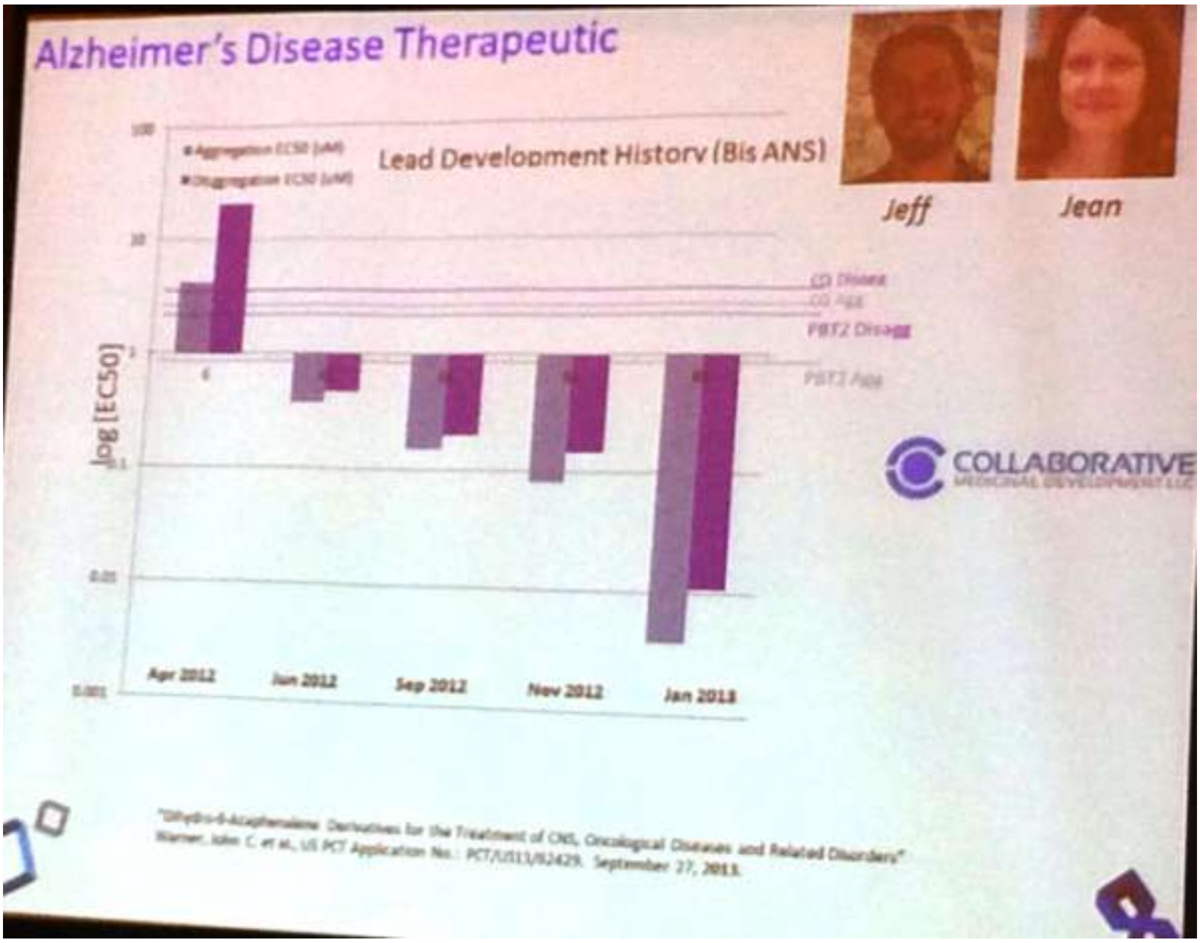
THE MICHAEL J. FOX FOUNDATION
FOR PARKINSON'S RESEARCH

The Melbourne Newsroom

University of Melbourne enters agreement to develop therapy for Parkinson's disease

PARKINSON'S FUNDED GRANT

"Non-Covalent Derivatives of Metal Complexes and Methods of Treatment"
Warner, John C., Cheruku, Srinivasa R.; US Pat Application No. 61/932,348 January 28, 2014.
"Copper (II) bis(N-alkyl-hydrazinecarbothioamide) Complexes as Non-Covalent Derivatives for the Treatment of CNS Conditions"
Warner, John C., Cheruku, Srinivasa R.; US Pat Application No. 61/902,682 November 11, 2013.



Alzheimer's Disease Therapeutic

"Dihydro-6-Azaphenalene Derivatives for the Treatment of CNS, Oncological Diseases and Related Disorders" Warner, John C. et al., US PCT Application No.: PCT/US13/62429. September 27, 2013.

Construction Materials: Asphalt Paving

> 50% Recycled Material < 20°F

Delta-S

"Asphalt Binder Additive Compositions and Related Materials" Warner, John C., Muollo, Laura R.; Walker, Rowan L., Bianchini, J. R. PCT Int. Appl. WO 2015070180. May 14, 2015.
"Composition to Rejuvenate Asphalt" Warner, John C., Muollo, Laura R., Walker, Rowan L. US Pat Application No. 61/902,706, November 11, 2013.

Construction Materials: Asphalt Paving

> 50% Recycled Material < 20°F

"Asphalt Binder Additive Compositions and Related Materials" Warner, John C., Muollo, Laura R.; Walker, Rowan L., Bianchini, J. R. PCT Int. Appl. WO 2015070180. May 14, 2015.
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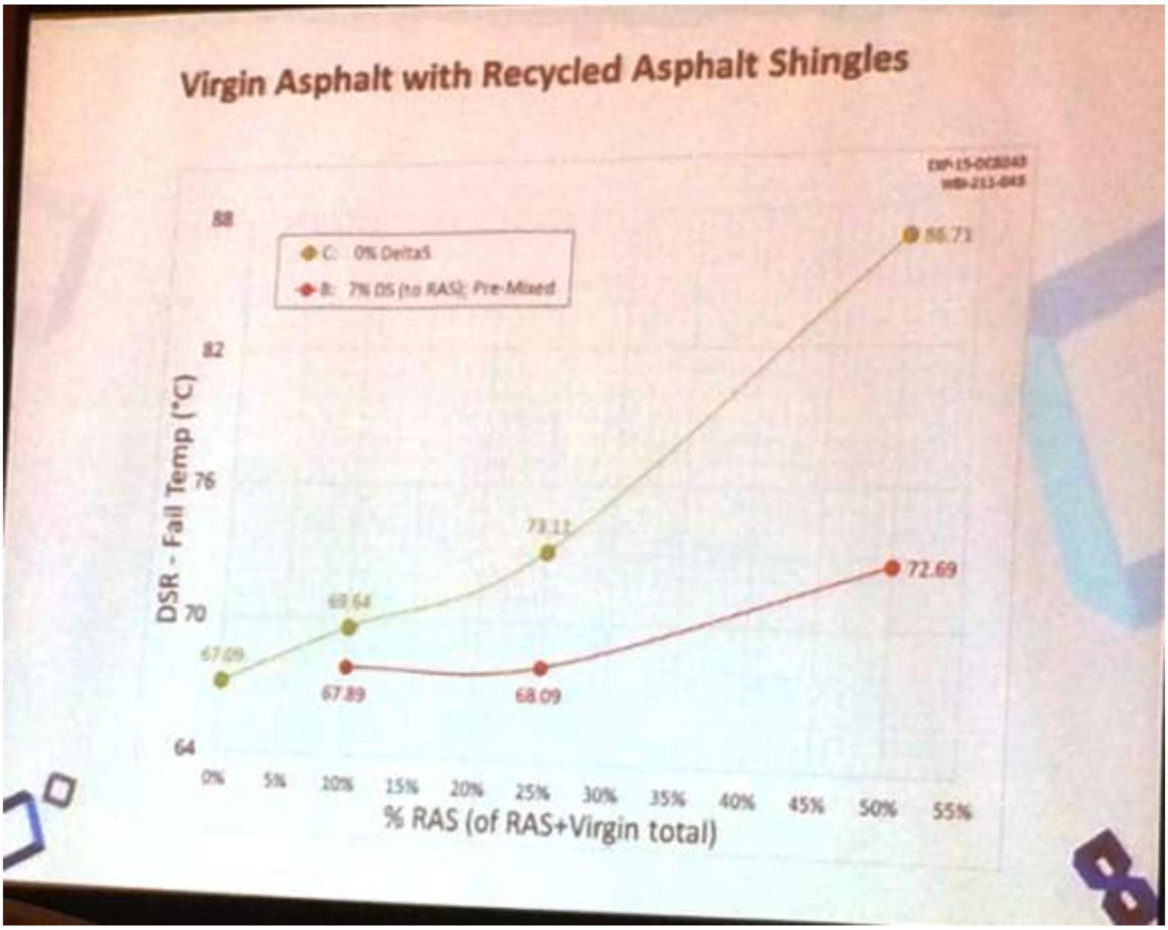
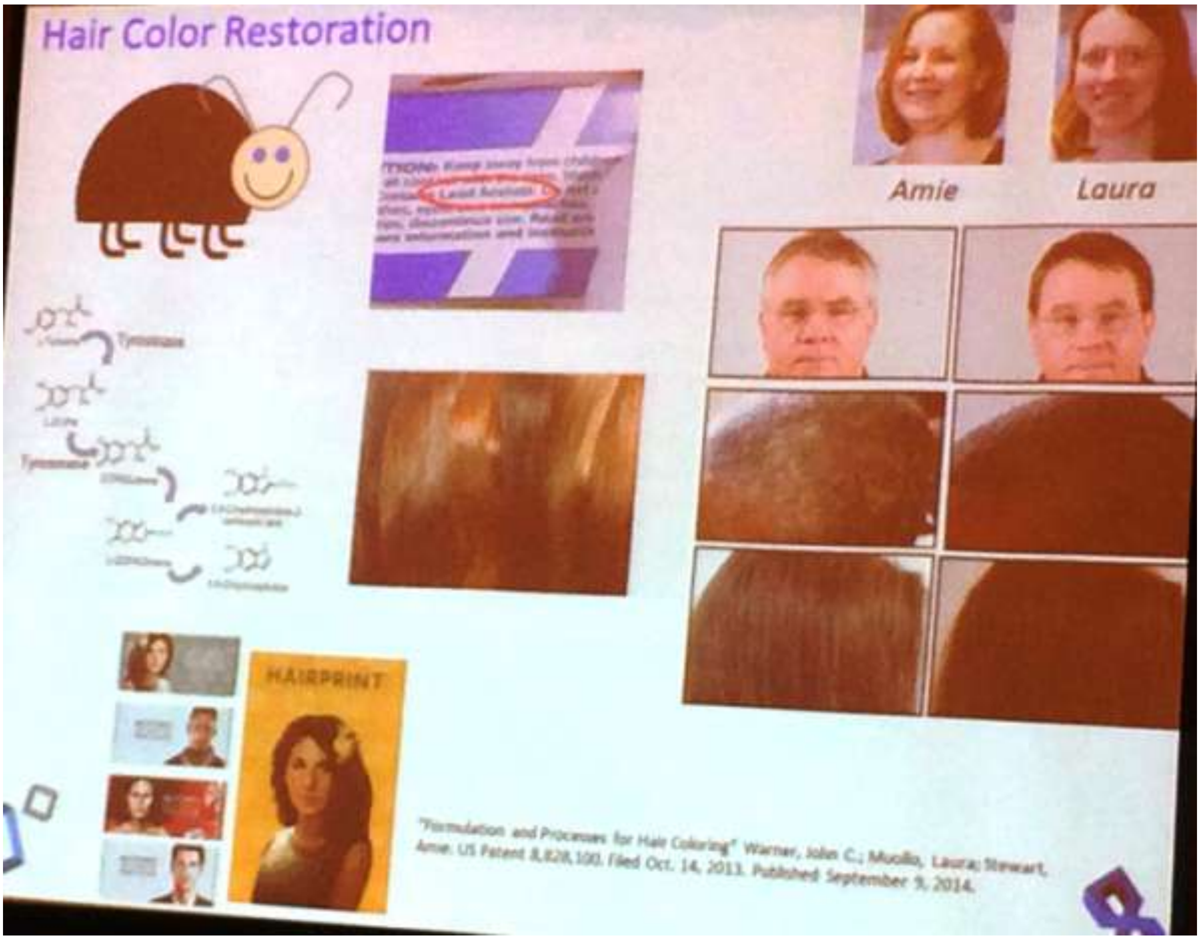
US Pat Application No. 61/902,706, November 11, 2013.



Virgin Asphalt with Recycled Asphalt Shingles



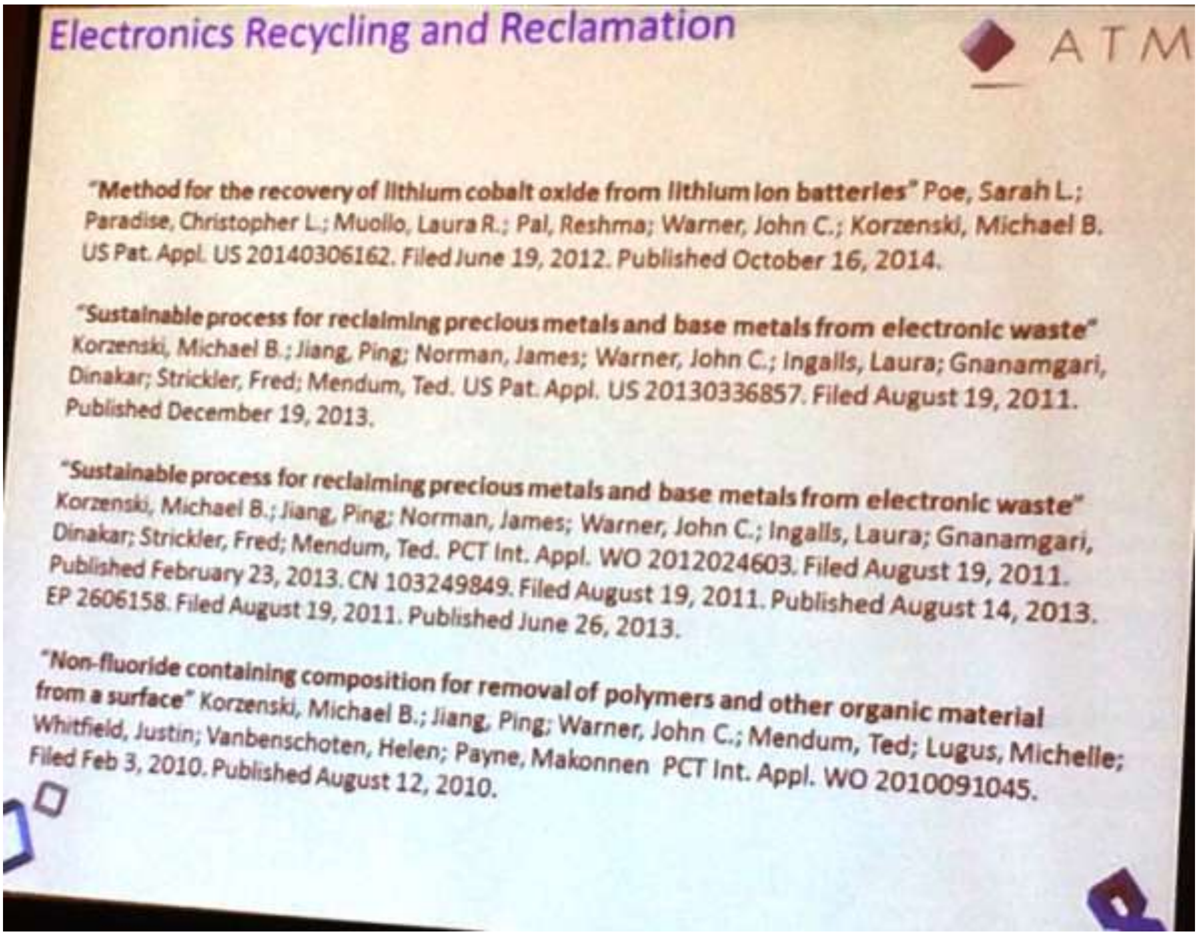
Hair Color Restoration

"Formulation and Processes for Hair Coloring" Warner, John C.; Muollo, Laura; Stewart, Amie. US Patent 8,828,100. Filed Oct. 14, 2013. Published September 9, 2014.

Construction Materials: Wood Composites

"Lignocellulosic Compositions and Methods of Making Same" Warner, John C. et al. US Patent Filed

Ocean Plastics Recycling and Reclamation



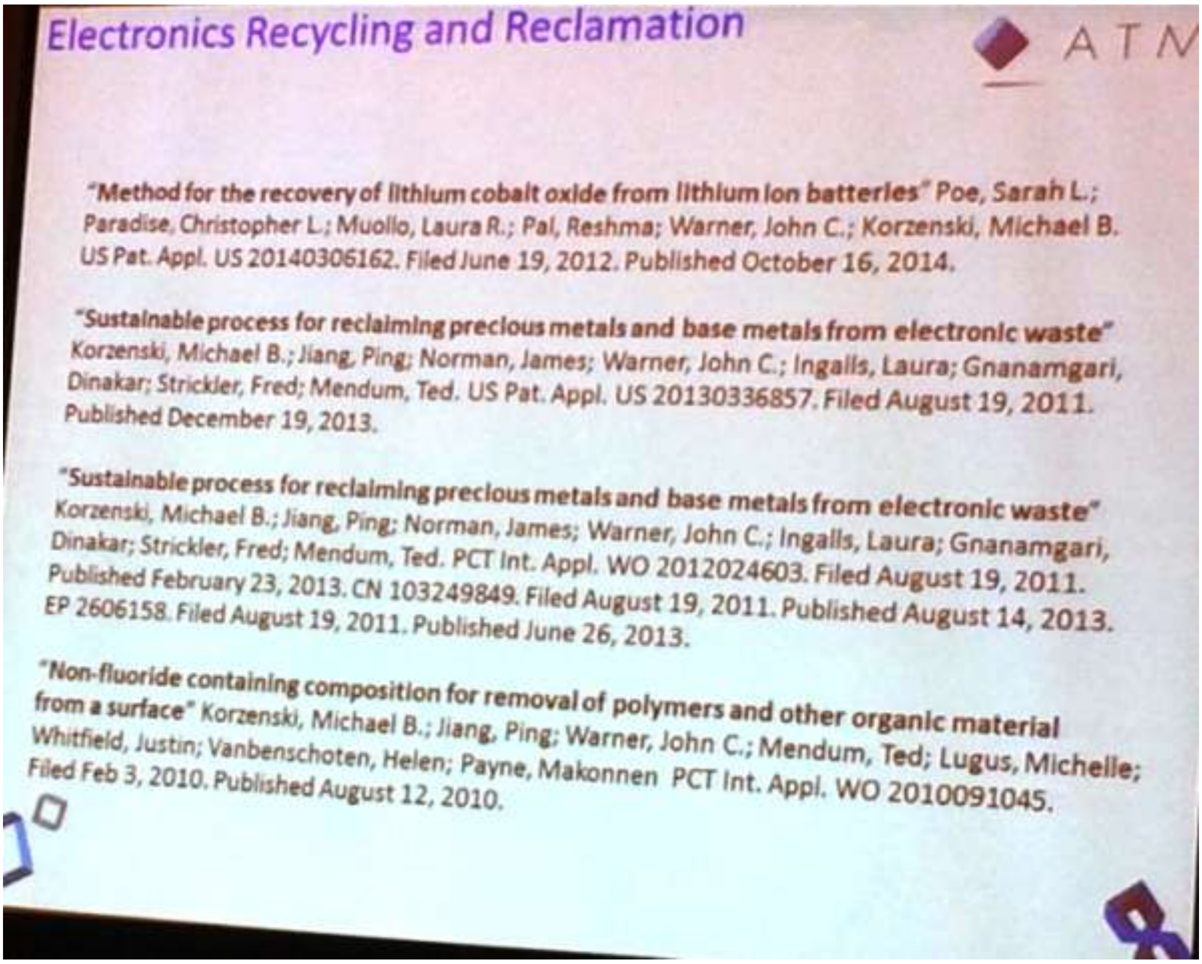
Electronics Recycling and Reclamation

"Method for the recovery of lithium cobalt oxide from lithium ion batteries" Poe, Sarah L.; Paradise, Christopher L.; Muollo, Laura R.; Pal, Reshma; Warner, John C.; Korzenski, Michael B. US Pat. Appl. US 20140306162. Filed June 19, 2012. Published October 16, 2014.

"Sustainable process for reclaiming precious metals and base metals from electronic waste" Korzenski, Michael B.; Jiang, Ping; Norman, James; Warner, John C.; Ingalls, Laura; Gnanamgari, Dinakar; Strickler, Fred; Mendum, Ted. US Pat. Appl. US 20130336857. Filed August 19, 2011. Published December 19, 2013.

"Sustainable process for reclaiming precious metals and base metals from electronic waste" Korzenski, Michael B.; Jiang, Ping; Norman, James; Warner, John C.; Ingalls, Laura; Gnanamgari, Dinakar; Strickler, Fred; Mendum, Ted. PCT Int. Appl. WO 2012024603. Filed August 19, 2011. Published February 23, 2013. CN 103249849. Filed August 19, 2011. Published August 14, 2013. EP 2606158. Filed August 19, 2011. Published June 26, 2013.

"Non-fluoride containing composition for removal of polymers and other organic material from a surface" Korzenski, Michael B.; Jiang, Ping; Warner, John C.; Mendum, Ted; Lugus, Michelle; Whitfield, Justin; Vanbenschoten, Helen; Payne, Makonnen PCT Int. Appl. WO 2010091045. Filed Feb 3, 2010. Published August 12, 2010.



Electronics Recycling and Reclamation

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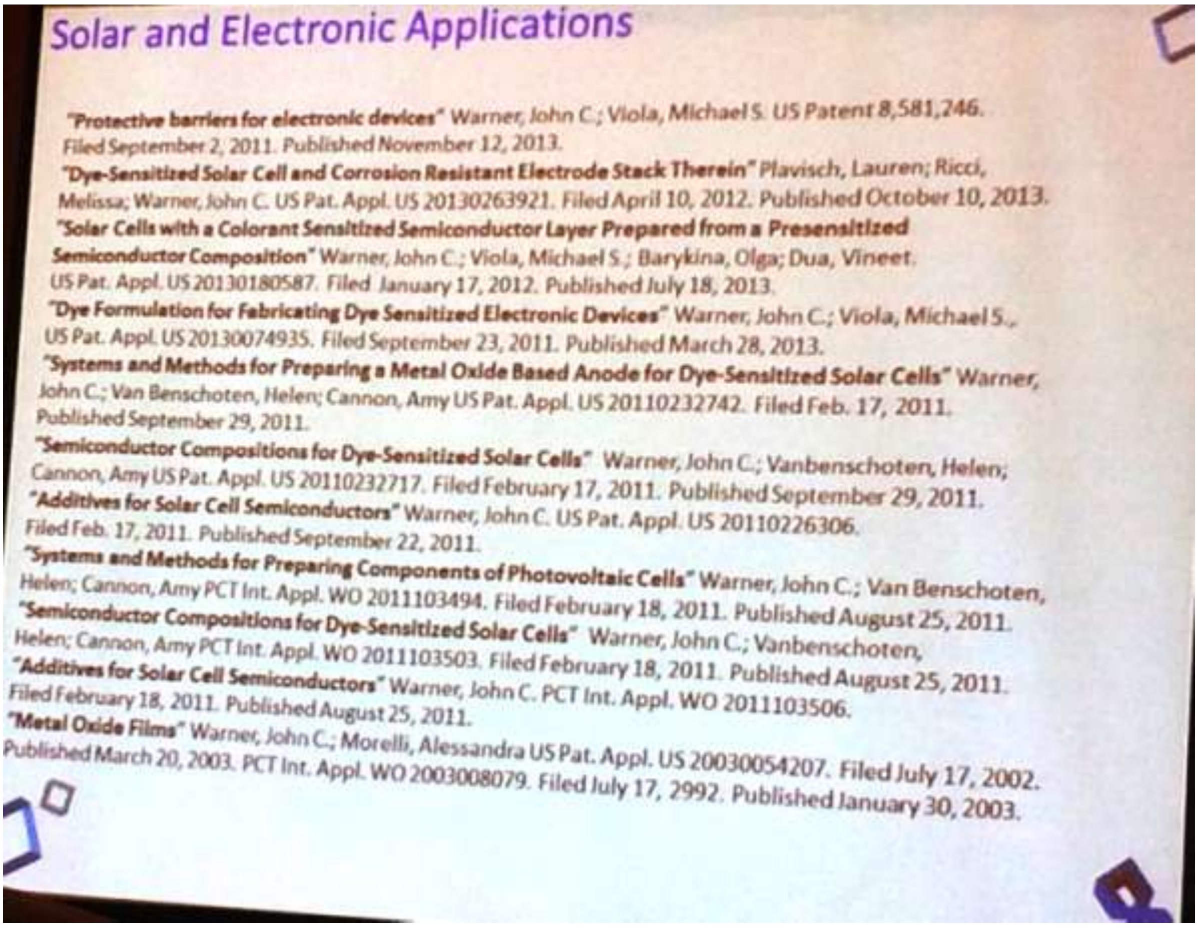


Solar and Electronic Applications

"Protective barriers for electronic devices" Warner, John C.; Viola, Michael S. US Patent 8,581,246. Filed September 2, 2011. Published November 12, 2013.

"Dye-Sensitized Solar Cell and Corrosion Resistant Electrode Stack Therein" Plavisch, Lauren; Ricci, Melissa; Warner, John C. US Pat. Appl. US 20130263921. Filed April 10, 2012. Published October 10, 2013.

"Solar Cells with a Colorant Sensitized Semiconductor Layer Prepared from a Presensitized Semiconductor Composition" Warner, John C.; Viola, Michael S.; Barykina, Olga; Dua, Vineet. US Pat. Appl. US 20130180587. Filed January 17, 2012. Published July 18, 2013.

"Dye Formulation for Fabricating Dye Sensitized Electronic Devices" Warner, John C.; Viola, Michael S., US Pat. Appl. US 20130074935. Filed September 23, 2011. Published March 28, 2013.

"Systems and Methods for Preparing a Metal Oxide Based Anode for Dye-Sensitized Solar Cells" Warner, John C.; Van Benschoten, Helen; Cannon, Amy US Pat. Appl. US 20110232742. Filed Feb. 17, 2011. Published September 29, 2011.

"Semiconductor Compositions for Dye-Sensitized Solar Cells" Warner, John C.; Vanbenschoten, Helen; Cannon, Amy US Pat. Appl. US 20110232717. Filed February 17, 2011. Published September 29, 2011.

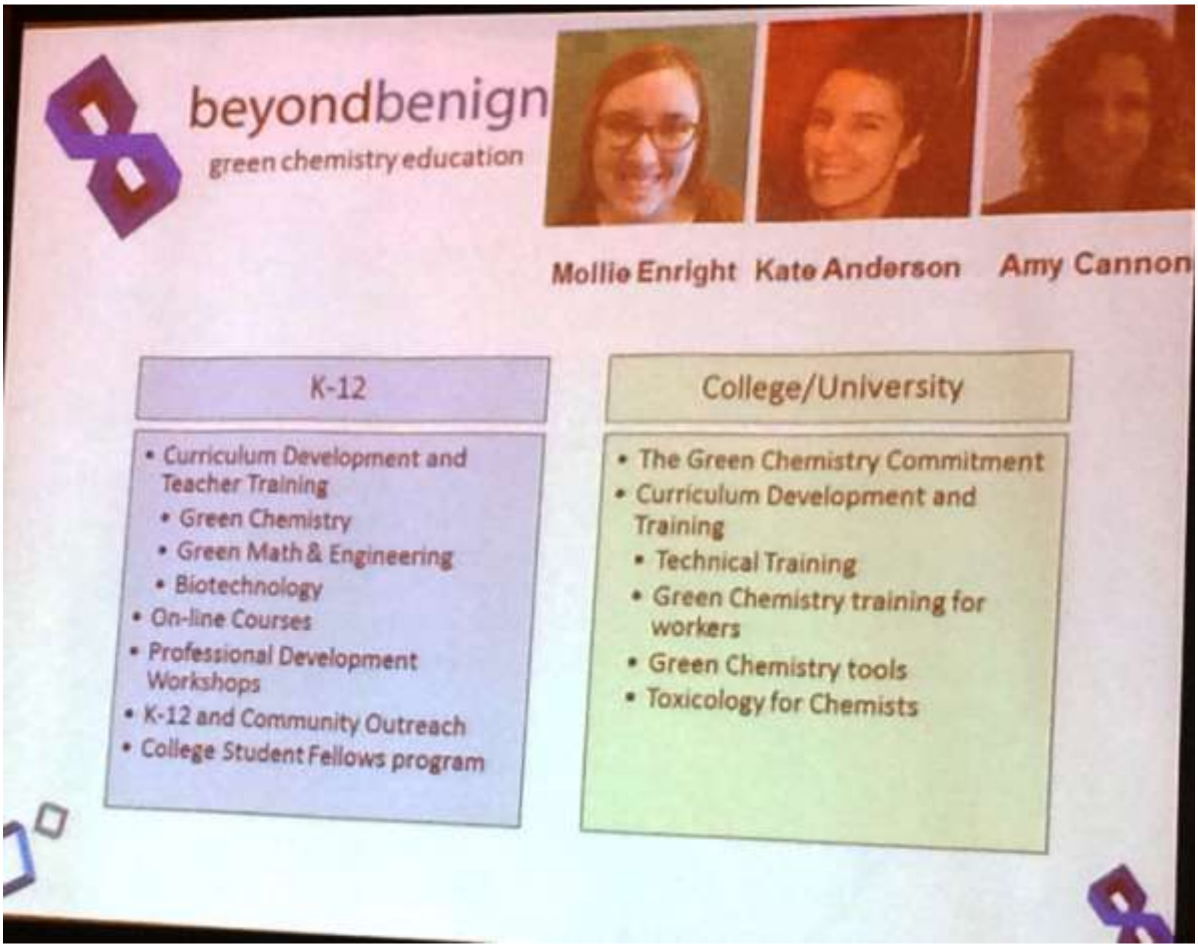
"Additives for Solar Cell Semiconductors" Warner, John C. US Pat. Appl. US 20110226306. Filed Feb. 17, 2011. Published September 22, 2011.

"Systems and Methods for Preparing Components of Photovoltaic Cells" Warner, John C.; Van Benschoten, Helen; Cannon, Amy PCT Int. Appl. WO 2011103494. Filed February 18, 2011. Published August 25, 2011.

"Semiconductor Compositions for Dye-Sensitized Solar Cells" Warner, John C.; Vanbenschoten, Helen; Cannon, Amy PCT Int. Appl. WO 2011103503. Filed February 18, 2011. Published August 25, 2011.

"Additives for Solar Cell Semiconductors" Warner, John C. PCT Int. Appl. WO 2011103506. Filed February 18, 2011. Published August 25, 2011.

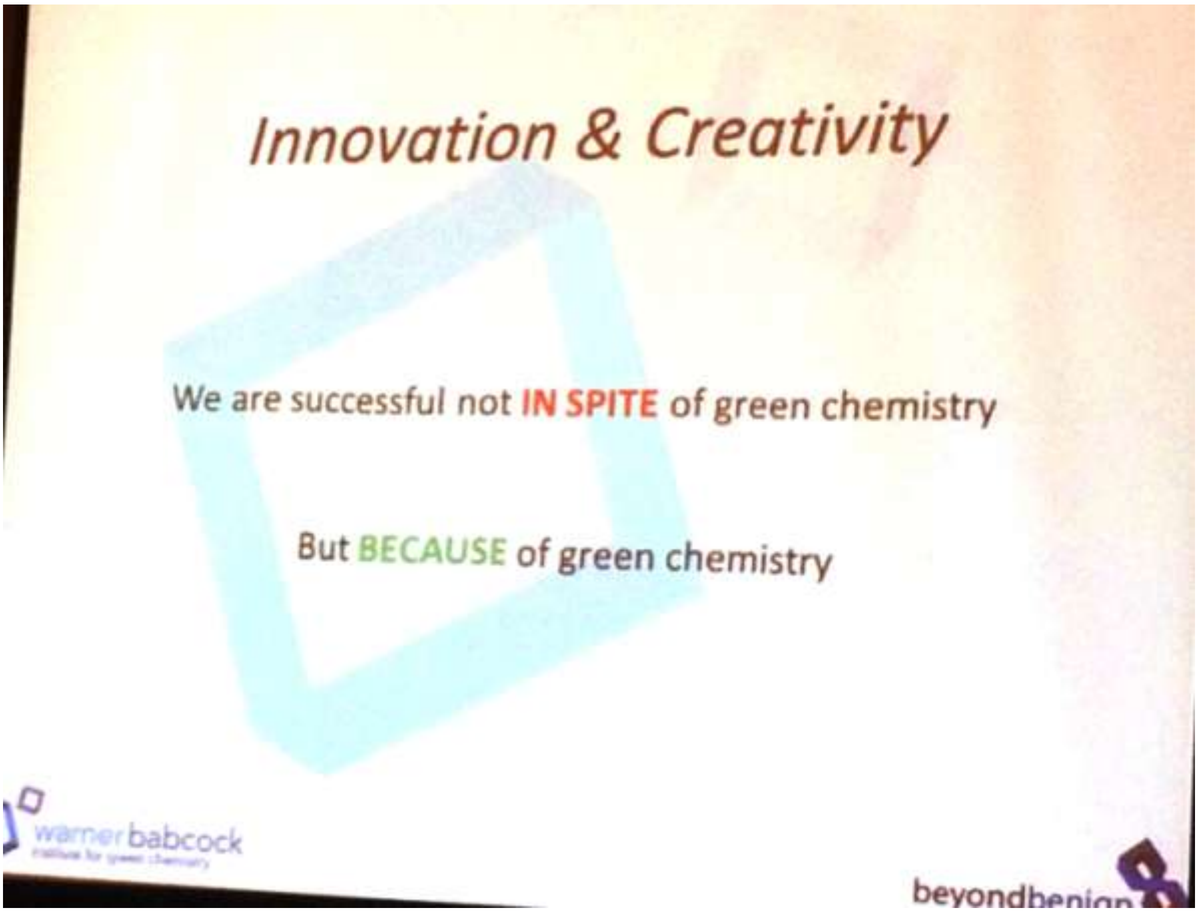
"Metal Oxide Films" Warner, John C.; Morelli, Alessandra US Pat. Appl. US 20030054207. Filed July 17, 2002. Published March 20, 2003. PCT Int. Appl. WO 2003008079. Filed July 17, 2992. Published January 30, 2003.



beyondbenign
green chemistry education

Mollie Enright **Kate Anderson** **Amy Cannon**

K-12	College/University
- Curriculum Development and Teacher Training - Green Chemistry - Green Math & Engineering - Biotechnology - On-line Courses - Professional Development Workshops - K-12 and Community Outreach - College Student Fellows program	- The Green Chemistry Commitment - Curriculum Development and Training - Technical Training - Green Chemistry training for workers - Green Chemistry tools - Toxicology for Chemists



Innovation & Creativity

We are successful not **IN SPITE** of green chemistry

But **BECAUSE** of green chemistry

3.2.2 將植物細胞轉化為綠色藥物工廠 (Evolving plant cells to function as green pharmaceutical factories)

演講者：John Littleton, Ph.D.

機構名稱：University of Kentucky, USA

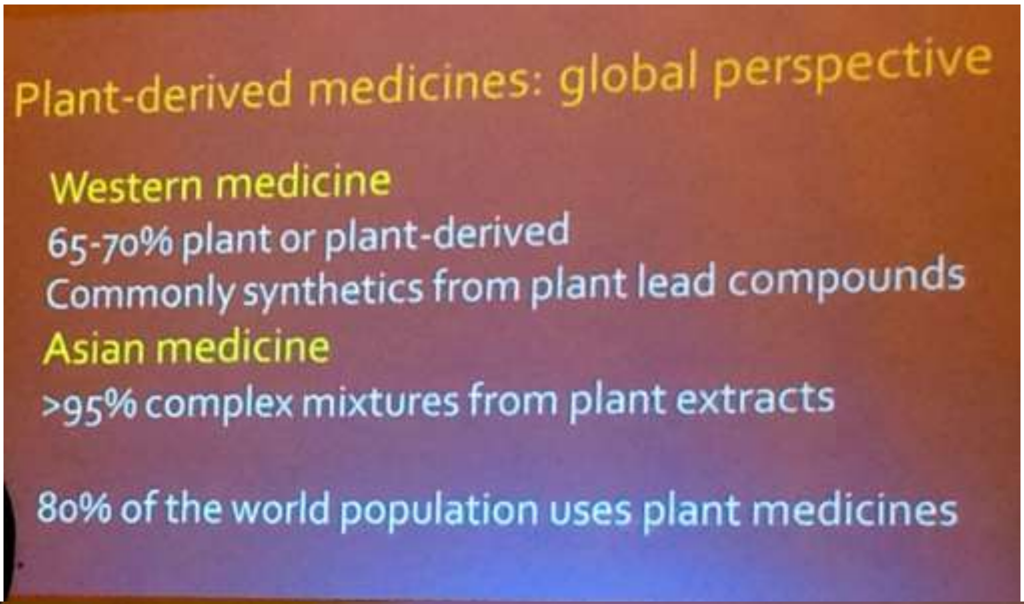
演講摘要：

西方國家藥物約 65-70%為植物來源或植物衍生物，亞洲國家則高達 95%為複合性植物配方，目前全球超過 80%人口使用植物衍生藥物。現代藥物除了普遍的化學合成方式外，可藉植物合成或得具更廣泛生物活性的化合物。具療效的植物化合物大部分屬於植物代謝產物，是隨著生存競爭經過幾千年來演化而來。例如特定植物代謝物可與草食性昆蟲中樞神經特定蛋白質結合，殺死攝入的昆蟲，而植物族群中因突變而傾向產生此類代謝物者，由於較能防止被攝食，而得以生存繁衍。此類達爾文適者生存法則，恰似現今藥廠研發單位使用的組合式化學合成 (Combinational Chemical Synthesis, CCS)：藉由高通量藥物篩選 (High Throughput Pharmacological Screening, HTPS)，由整個藥物化合物庫中「演化」出可針對治療標靶蛋白質加以結合的化合物。Littleton 博士改造植物代謝途徑，利用植物複雜而優越的生物合成能力篩選具有結合特定蛋白質能力的代謝物。為了證明這個看似簡單的概念，其團隊培育出特殊基改植物，在特定環境下只有能合成與目標蛋白質結合之代謝物的植株細胞才能生存，藉此技術配合類似 HTPS 篩選技術，製造出一個隨機功能獲得性突變 (random gain-of-function mutation) 的植物細胞庫 (類似 CCS 的概念)，再將整個基因庫細胞培養在非自然選擇性環境，用以篩選能大量生合成具有結合特定治療標靶蛋白質能力代謝物的植物細胞，這些代謝物可能原本在野生株少量表現，但隨機功能獲得性突變可能活化部分原本未表現基因，而修飾原先代謝途徑，進而產生具全新活性的代謝物，藉此目標導向演化 (target-directed evolution) 技術，將產生獲得特殊突變而全新具療效的植株，同時這類新代謝物也將具智產權保護。

基於以上概念，Littleton 博士團隊由模式植物菸草中，藉由農桿菌進行主動標記式突變 (Activation Tagging Mutagenesis, ATM)， 篩選可大量生產尼古丁的隨機功能獲得性突變植株：於 10,000 株突變株中得到 2 株分別具有 20 倍及 100 倍尼古丁活性，其中 1 株染色體具有 1 個 ATM 突變，尼古丁生合成量不變，顯示該植株可產生某種全新、具有類似尼古丁活性的代謝物，因此進行該代謝物鑑定及專利申請與技術移轉；另一株染色體具有 2 個 ATM 突變，外觀性狀大幅改變且可產生 5 倍以上尼古丁，其突變研究結果也可供不同植物系統研究參考。

另一個例子為甘草根 (Licorice root) 萃取物，含有類黃酮 (flavonoid) 可藉活化雌激素接受器 (estrogen receptor, ER)，改善更年期症狀；然而 ER 分為兩型，若活化 ERalpha 會增加罹患乳癌機率，因此或能將類黃酮活性導向 ERbeta 則會提升更年期症狀治療的安全性。因此 Littleton 博士團隊使用甘草 (licorice, *Glycyrrhiza Glabra*) 為模式植物，針對 ERbeta 蛋白選殖得到大量生產 (5 倍以上) 類黃酮的植株，然而由於此植株分泌之類黃酮對於兩種接受器皆有活性，Littleton 博士團隊再次設計實驗，將第二階段選殖流程改為篩選能夠分泌對 ERalpha 蛋白結合力較低類黃酮代謝物之植株，也顯示該選殖系統的靈活性與穩定性。

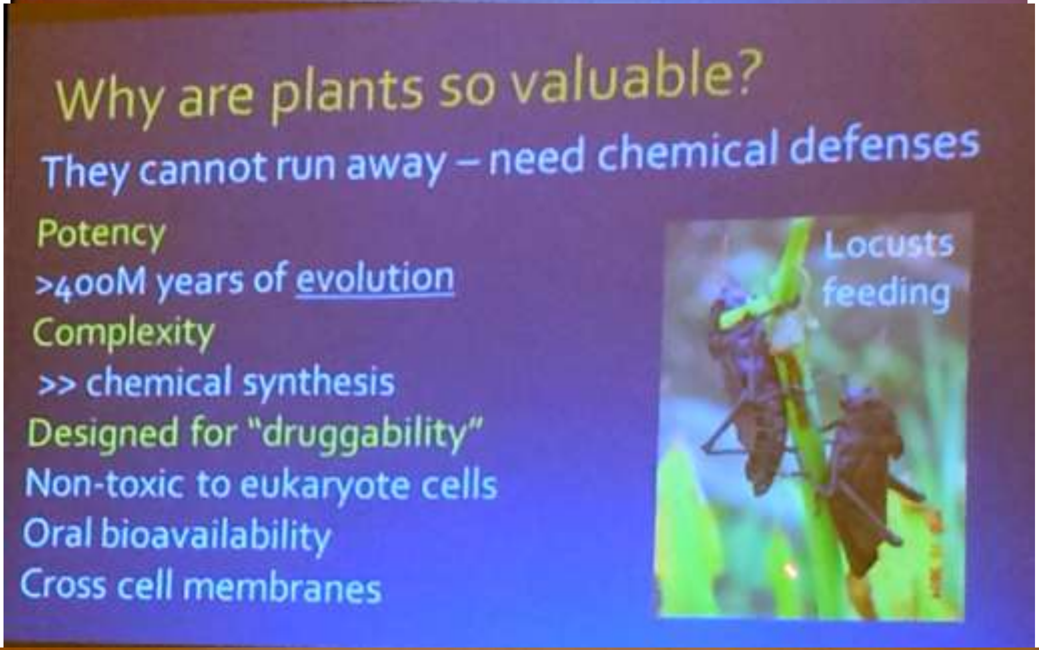
Littleton 博士的研究是以植物為出發點，合成現今化學技術較難合成的代謝物，並以生物方式進行高通量篩選，建立穩定而具靈活度的篩選流程，除得到具療效植株外，也有機會發現能製造全新具生物活性代謝物的植株，更方便智產權申請與保護，無論在學理上或應用層次皆具極高價值，過程中完全使用植物系統，也符合綠色化學理念，對於本所植物相關領域高值化研究，具有參考及合作價值。以下將報告內容重要投影片列出：



Plant-derived medicines: global perspective

Western medicine
65-70% plant or plant-derived
Commonly synthetics from plant lead compounds
Asian medicine
>95% complex mixtures from plant extracts

80% of the world population uses plant medicines

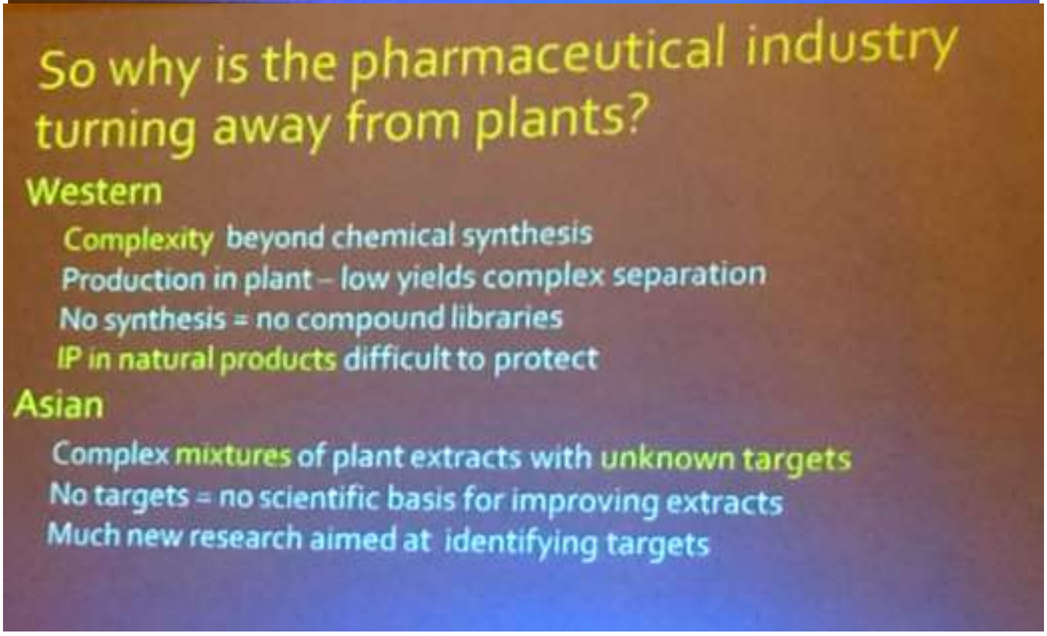


Why are plants so valuable?

They cannot run away – need chemical defenses

Potency
>400M years of evolution
Complexity
>> chemical synthesis
Designed for "druggability"
Non-toxic to eukaryote cells
Oral bioavailability
Cross cell membranes

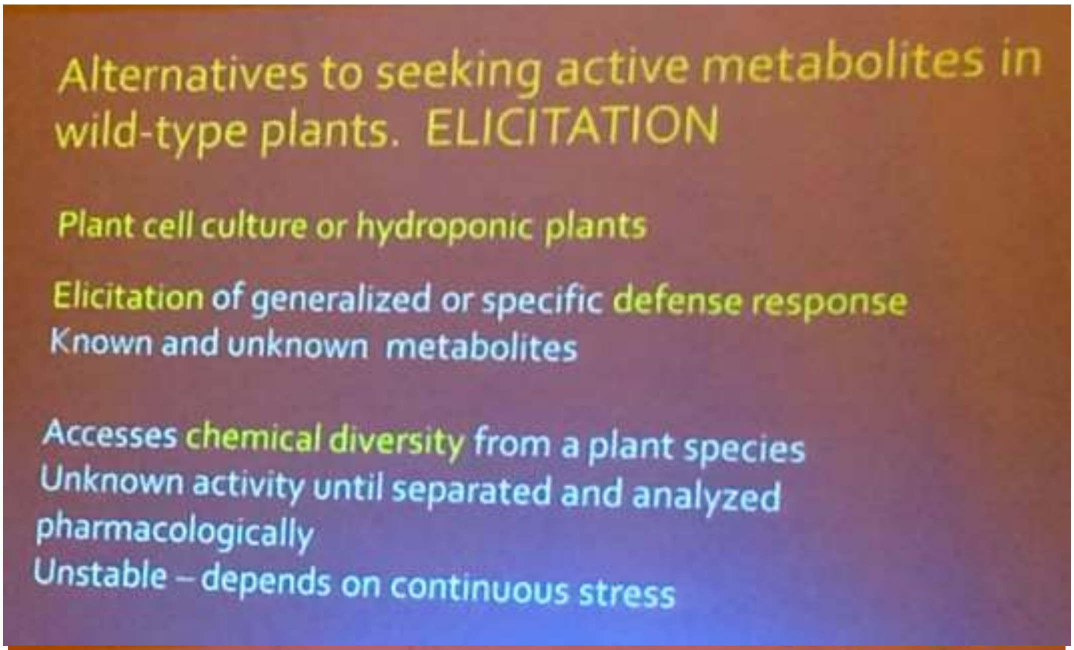
Locusts feeding



So why is the pharmaceutical industry turning away from plants?

Western
- Complexity beyond chemical synthesis
- Production in plant – low yields complex separation
- No synthesis = no compound libraries
- IP in natural products difficult to protect

Asian
- Complex mixtures of plant extracts with unknown targets
- No targets = no scientific basis for improving extracts
- Much new research aimed at identifying targets

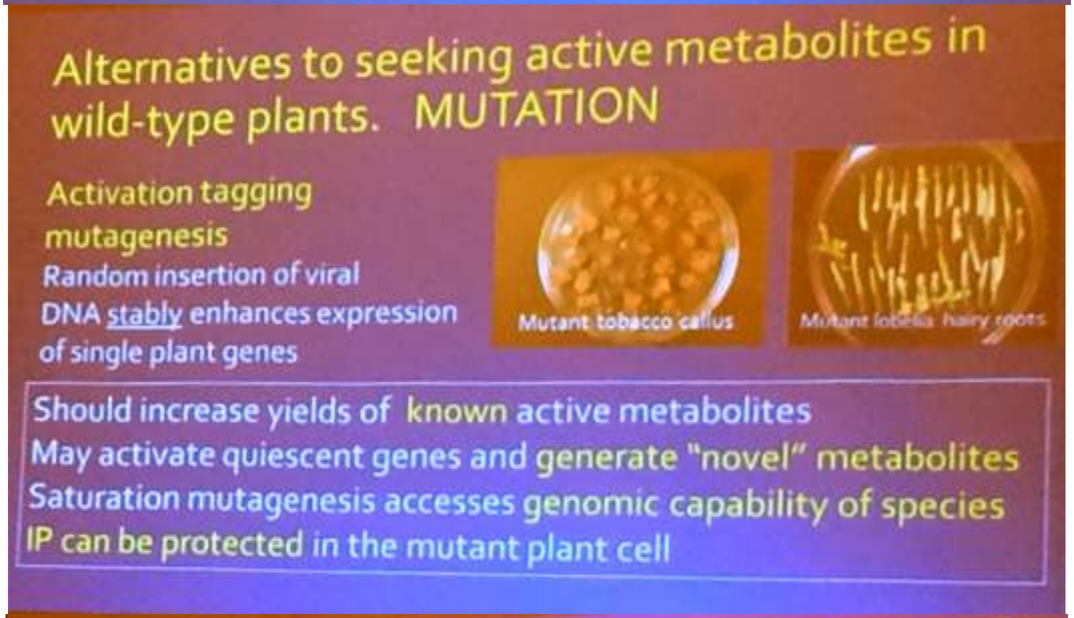


Alternatives to seeking active metabolites in wild-type plants. ELICITATION

Plant cell culture or hydroponic plants

Elicitation of generalized or specific defense response
Known and unknown metabolites

Accesses chemical diversity from a plant species
Unknown activity until separated and analyzed pharmacologically
Unstable – depends on continuous stress



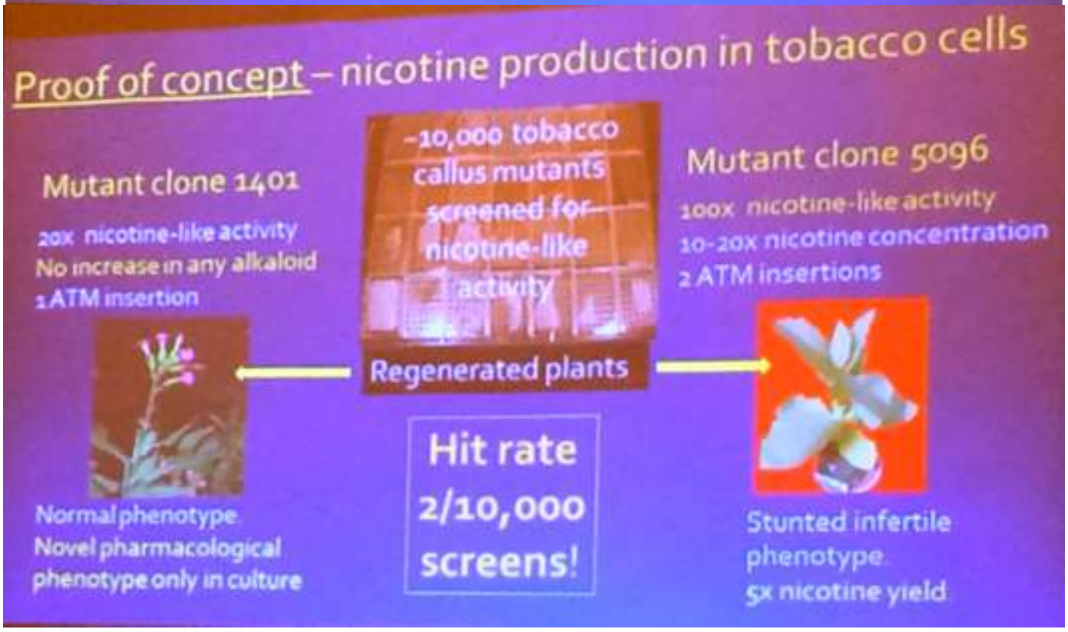
Alternatives to seeking active metabolites in wild-type plants. MUTATION

Activation tagging mutagenesis
Random insertion of viral DNA stably enhances expression of single plant genes

Mutant tobacco callus

Mutant lobelia hairy roots

Should increase yields of known active metabolites
May activate quiescent genes and generate "novel" metabolites
Saturation mutagenesis accesses genomic capability of species
IP can be protected in the mutant plant cell



Proof of concept – nicotine production in tobacco cells

~10,000 tobacco callus mutants screened for nicotine-like activity

Mutant clone 1401
20x nicotine-like activity
No increase in any alkaloid
1 ATM insertion

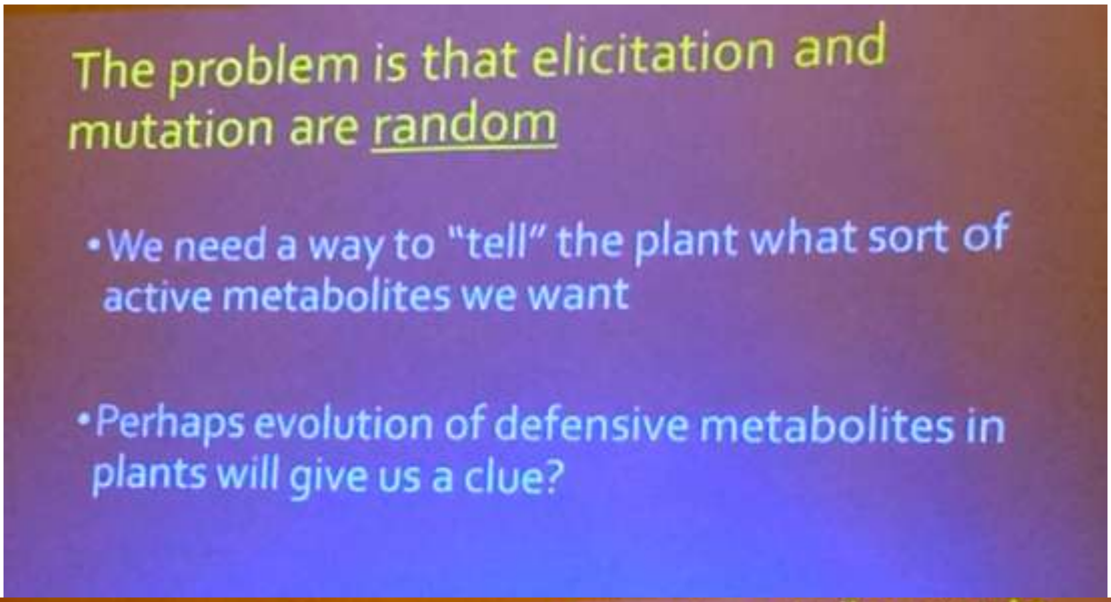
Mutant clone 5096
100x nicotine-like activity
10-20x nicotine concentration
2 ATM insertions

Regenerated plants

Normal phenotype
Novel pharmacological phenotype only in culture

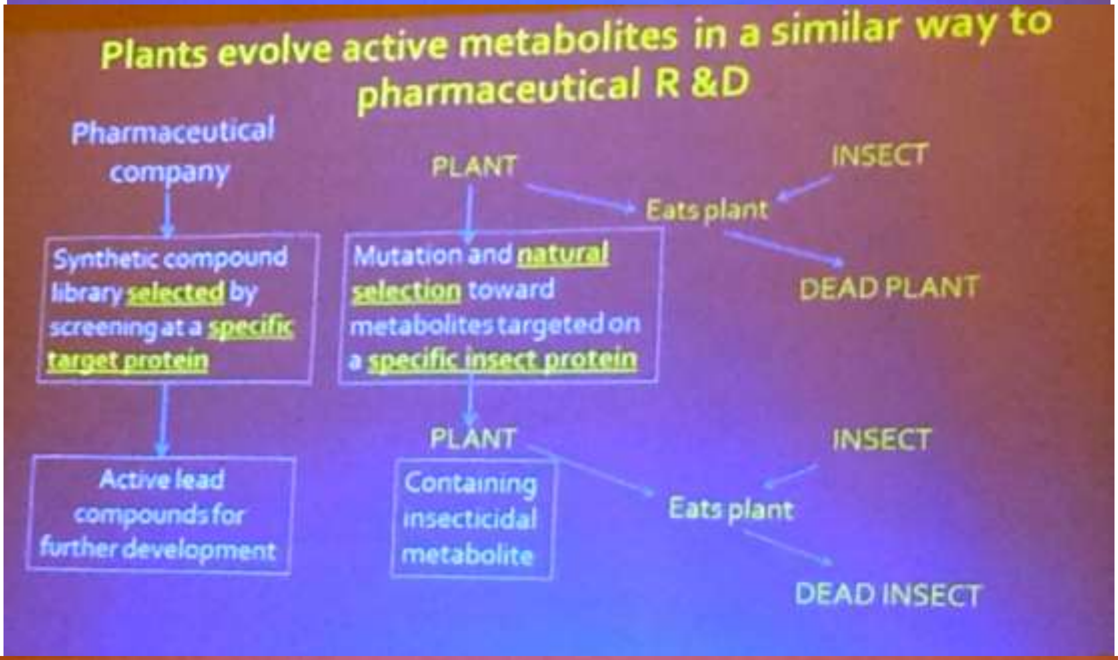
Hit rate 2/10,000 screens!

Stunted infertile phenotype
5x nicotine yield



The problem is that elicitation and mutation are <u>random</u>

- We need a way to "tell" the plant what sort of active metabolites we want
- Perhaps evolution of defensive metabolites in plants will give us a clue?



Plants evolve active metabolites in a similar way to pharmaceutical R &D

Pharmaceutical company

Synthetic compound library **selected** by screening at a **specific target protein**

Active lead compounds for further development

PLANT

Mutation and **natural selection** toward metabolites targeted on a **specific insect protein**

PLANT

Containing insecticidal metabolite

INSECT

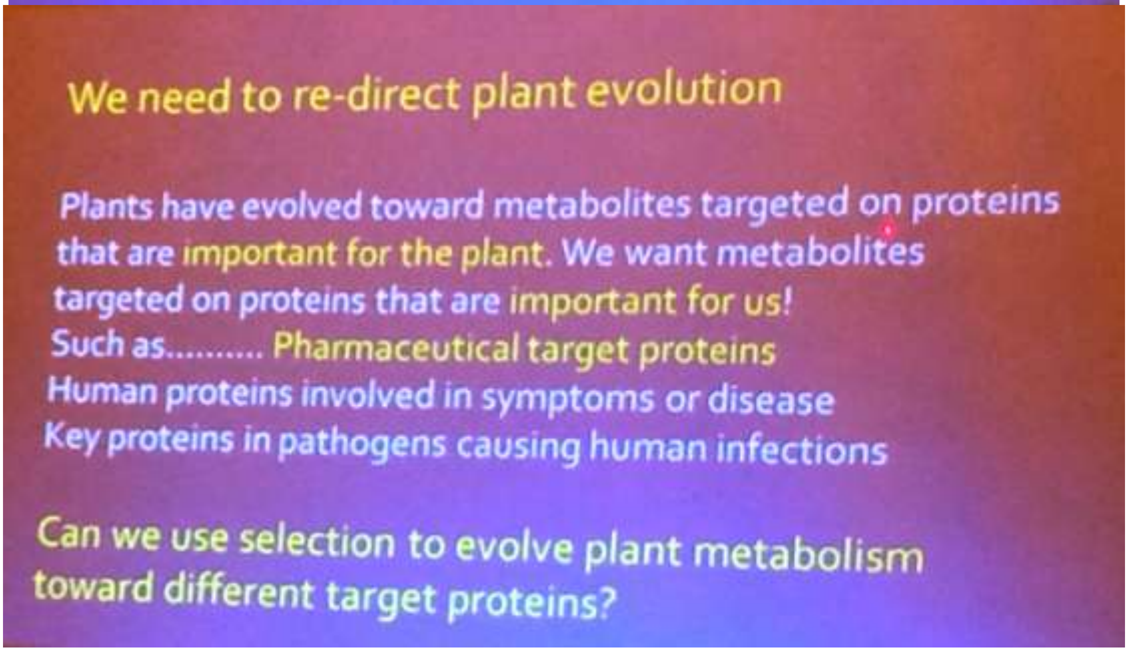
Eats plant

DEAD PLANT

INSECT

Eats plant

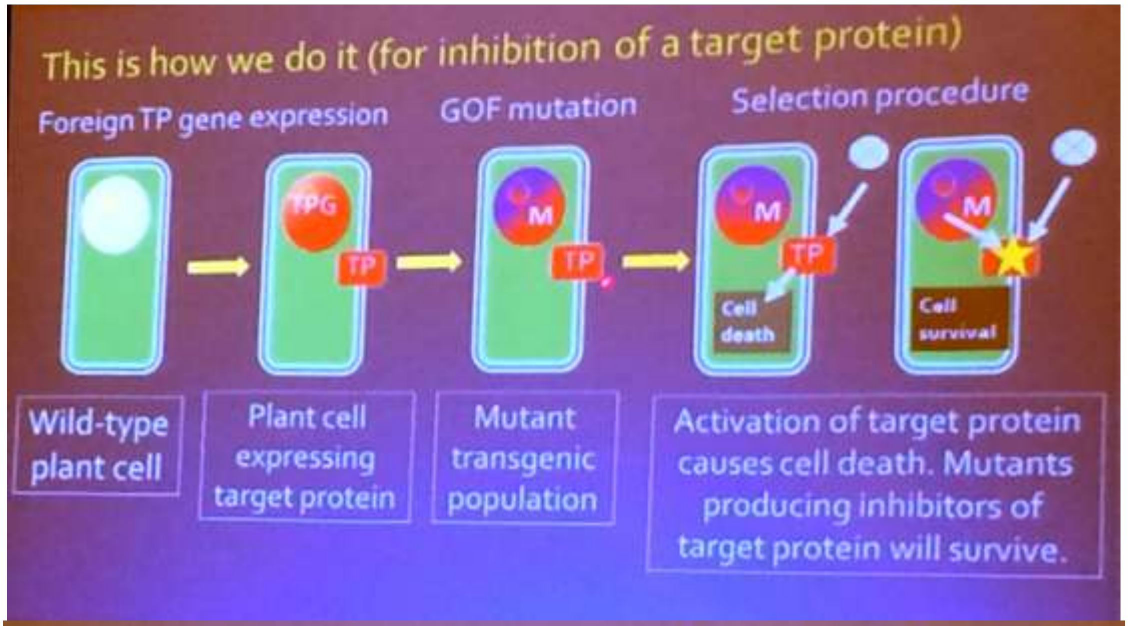
DEAD INSECT



We need to re-direct plant evolution

Plants have evolved toward metabolites targeted on proteins that are important for the plant. We want metabolites targeted on proteins that are important for us!
Such as.......... Pharmaceutical target proteins
Human proteins involved in symptoms or disease
Key proteins in pathogens causing human infections

Can we use selection to evolve plant metabolism toward different target proteins?



This is how we do it (for inhibition of a target protein)

Foreign TP gene expression

GOF mutation

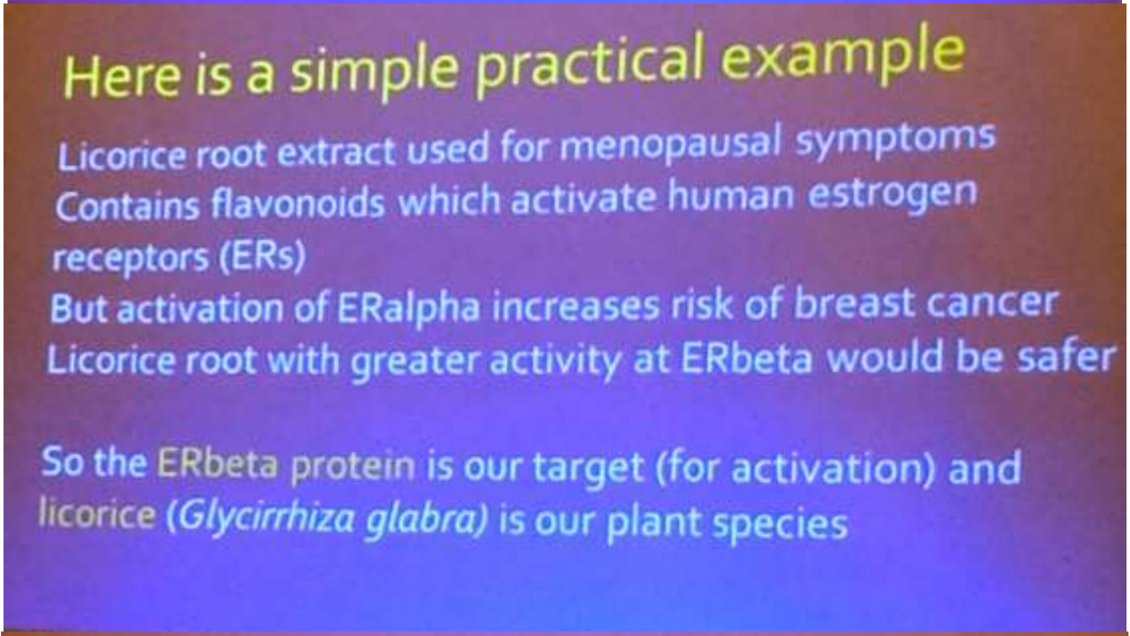
Selection procedure

Wild-type plant cell

Plant cell expressing target protein

Mutant transgenic population

Activation of target protein causes cell death. Mutants producing inhibitors of target protein will survive.



Here is a simple practical example

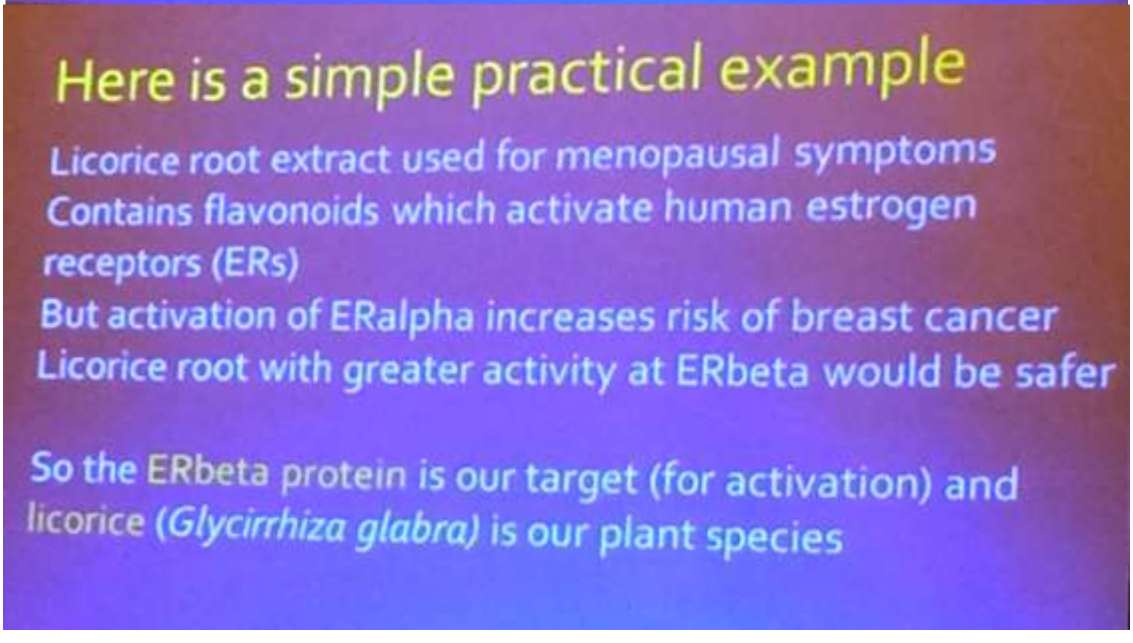
Licorice root extract used for menopausal symptoms

Contains flavonoids which activate human estrogen receptors (ERs)

But activation of ERalpha increases risk of breast cancer

Licorice root with greater activity at ERbeta would be safer

So the ERbeta protein is our target (for activation) and licorice (*Glycirrhiza glabra)* is our plant species



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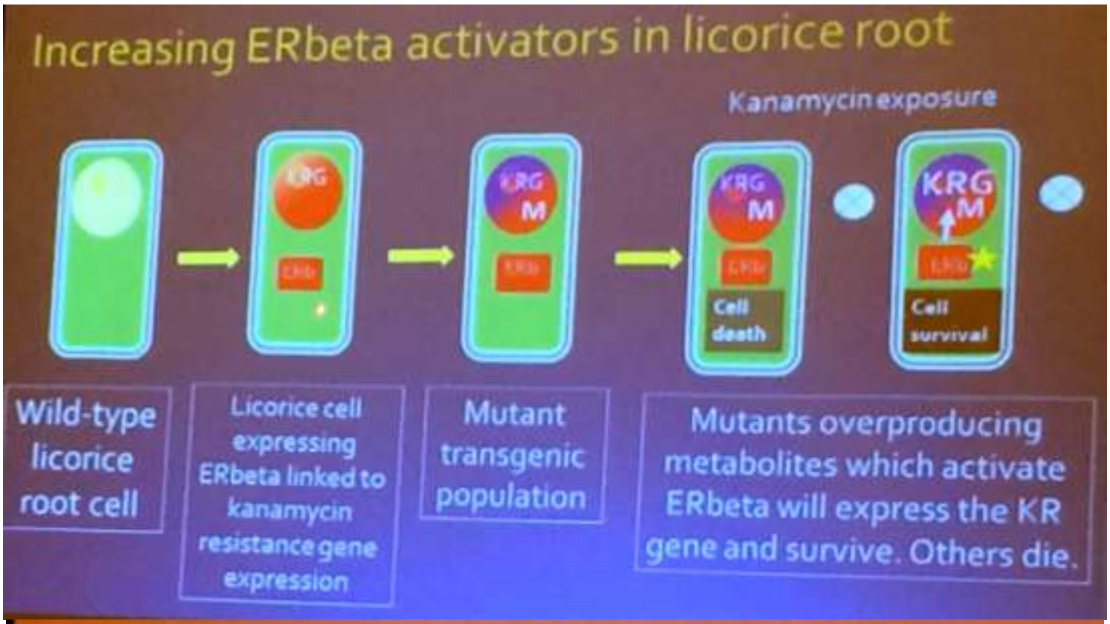


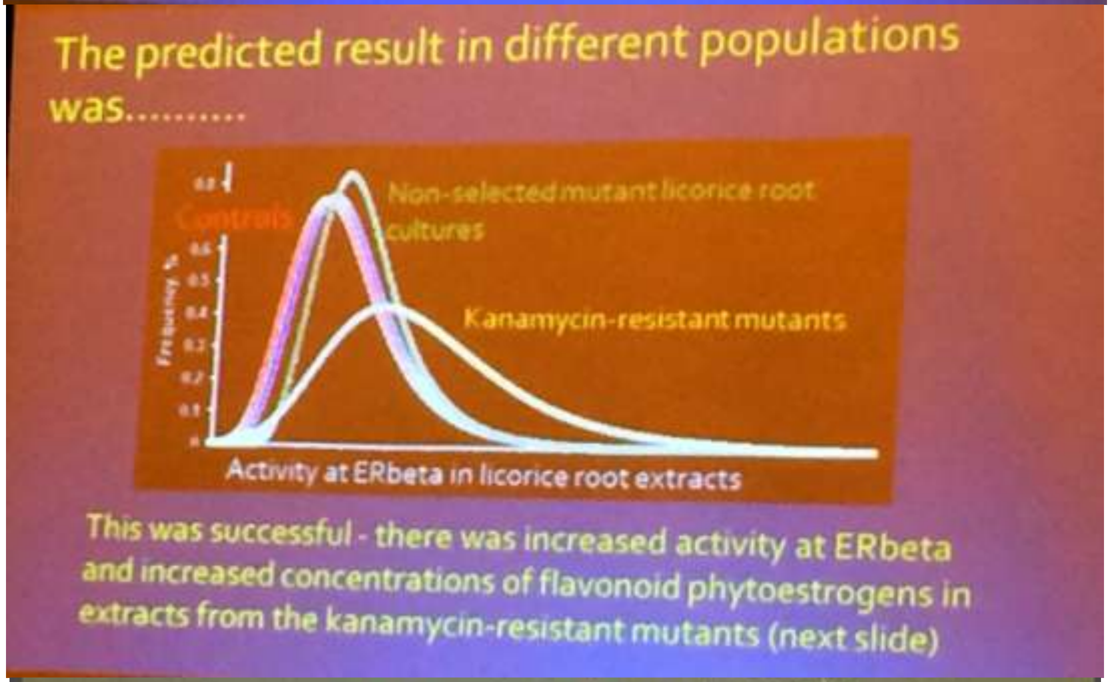
Increasing ERbeta activators in licorice root

Wild-type licorice root cell

Licorice cell expressing ERbeta linked to kanamycin resistance gene expression

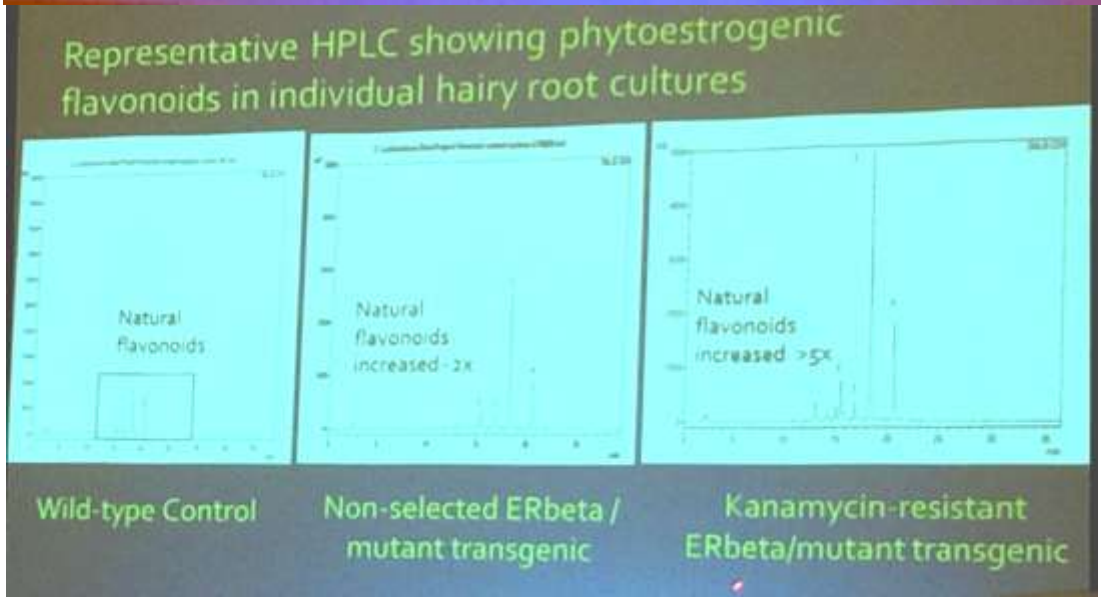
Mutant transgenic population

Mutants overproducing metabolites which activate ERbeta will express the KR gene and survive. Others die.



The predicted result in different populations was..........

This was successful - there was increased activity at ERbeta and increased concentrations of flavonoid phytoestrogens in extracts from the kanamycin-resistant mutants (next slide)

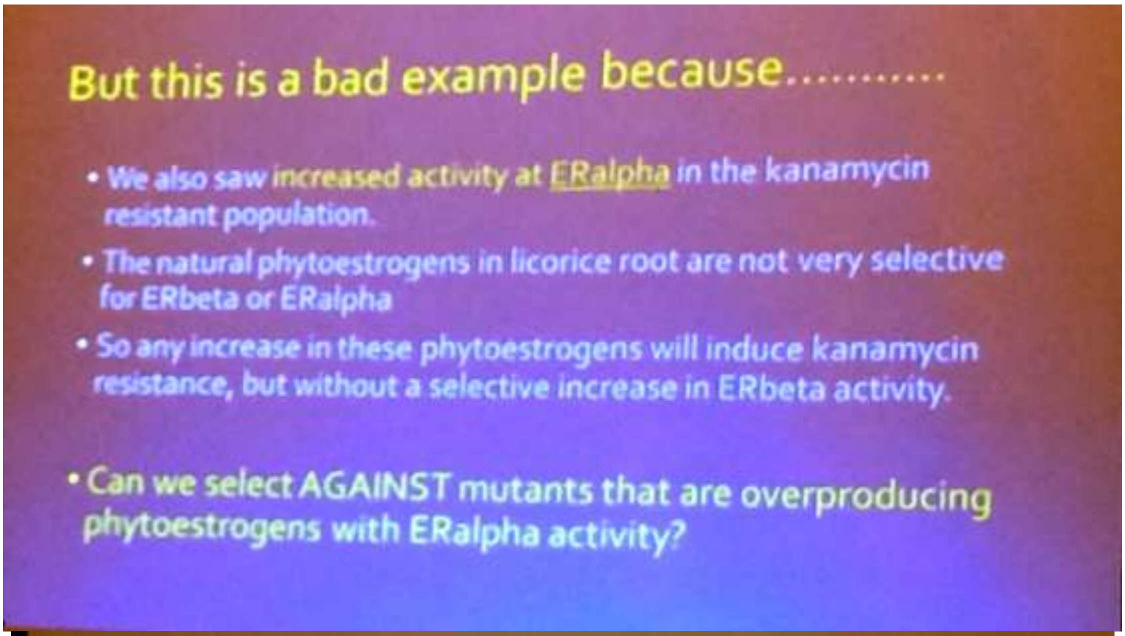


Representative HPLC showing phytoestrogenic flavonoids in individual hairy root cultures

Wild-type Control

Non-selected ERbeta / mutant transgenic

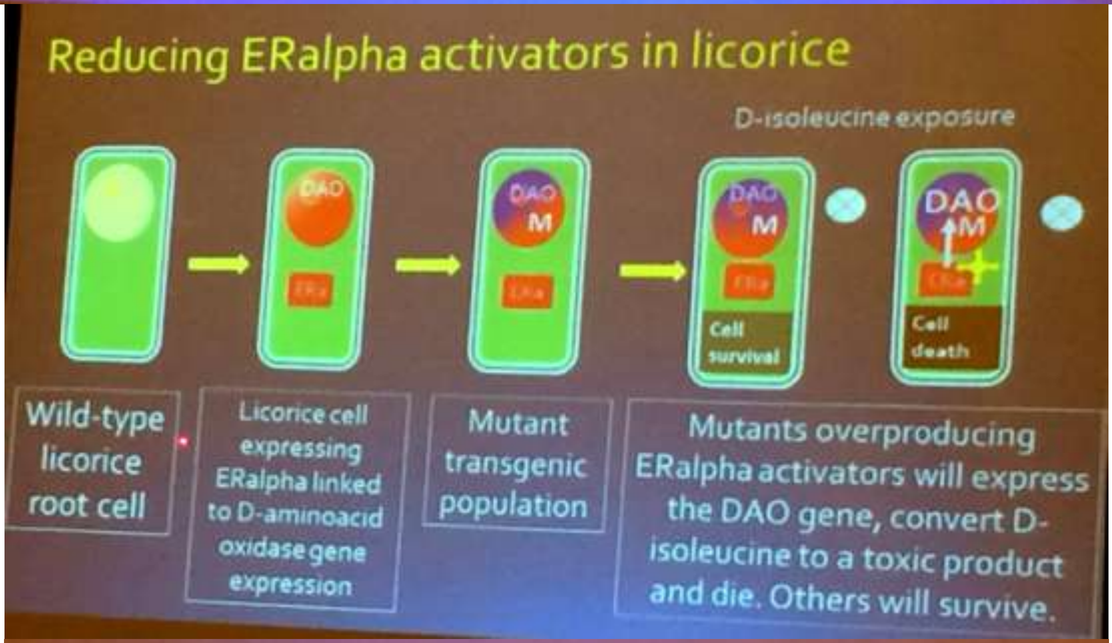
Kanamycin-resistant ERbeta/mutant transgenic



But this is a bad example because..........

- We also saw increased activity at ERalpha in the kanamycin resistant population.
- The natural phytoestrogens in licorice root are not very selective for ERbeta or ERalpha
- So any increase in these phytoestrogens will induce kanamycin resistance, but without a selective increase in ERbeta activity.

- Can we select AGAINST mutants that are overproducing phytoestrogens with ERalpha activity?



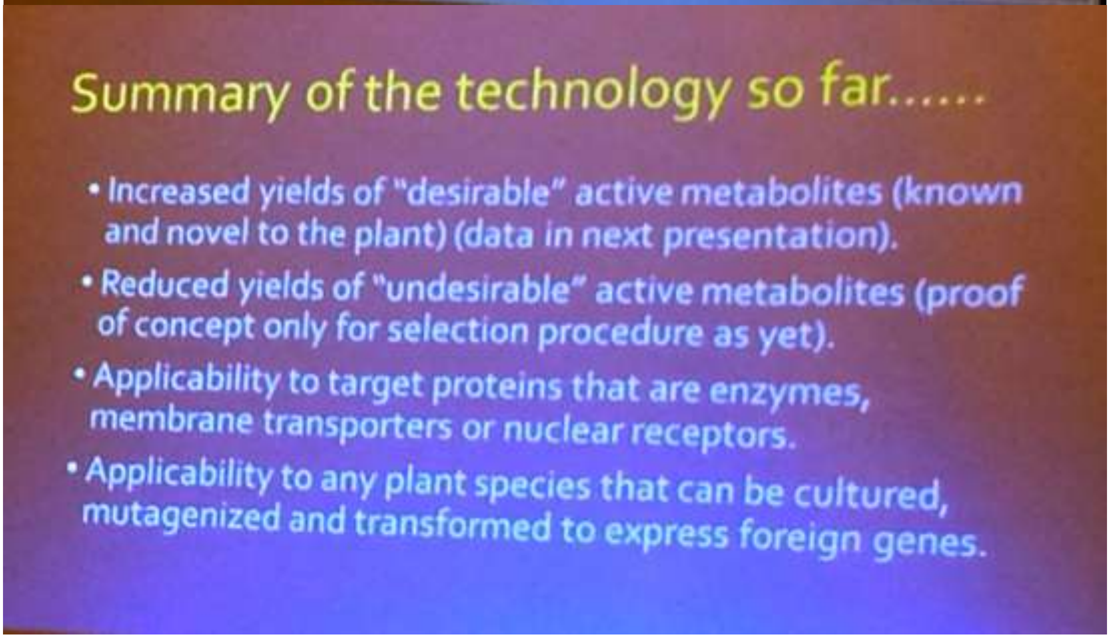
Reducing ERalpha activators in licorice

Wild-type licorice root cell

Licorice cell expressing ERalpha linked to D-aminoacid oxidase gene expression

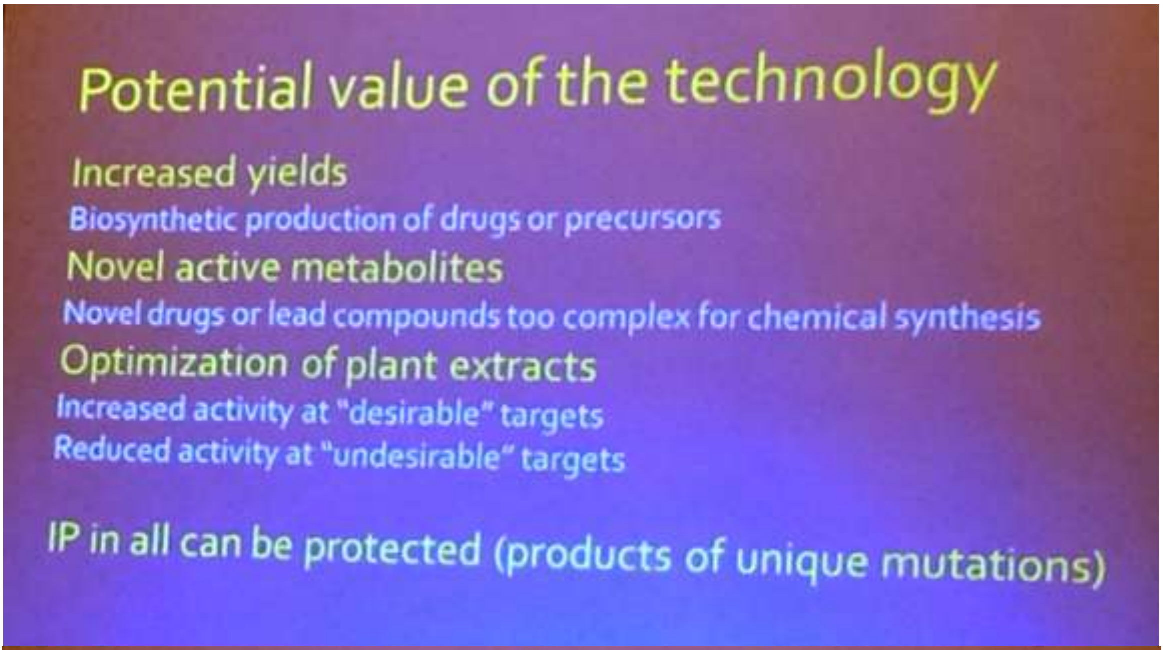
Mutant transgenic population

Mutants overproducing ERalpha activators will express the DAO gene, convert D-isoleucine to a toxic product and die. Others will survive.



Summary of the technology so far......

- Increased yields of "desirable" active metabolites (known and novel to the plant) (data in next presentation).
- Reduced yields of "undesirable" active metabolites (proof of concept only for selection procedure as yet).
- Applicability to target proteins that are enzymes, membrane transporters or nuclear receptors.
- Applicability to any plant species that can be cultured, mutagenized and transformed to express foreign genes.



Potential value of the technology

Increased yields

Biosynthetic production of drugs or precursors

Novel active metabolites

Novel drugs or lead compounds too complex for chemical synthesis

Optimization of plant extracts

Increased activity at "desirable" targets

Reduced activity at "undesirable" targets

IP in all can be protected (products of unique mutations)

Technology transfer is next…………

The plant genome has an extraordinary capacity for biosynthesis.

This technology could unlock it.

Plant cells are green pharmaceutical factories just waiting to be told what we want them to produce.

This technology could tell them.

3.2.3 地區特性是否扮演化學永續性全球化之重要角色? (Are regional features a key to globalize sustainability in chemistry?)

演講者：Lothar Brecker, Ph.D.

機構名稱：University of Vienna, Austria

演講摘要：

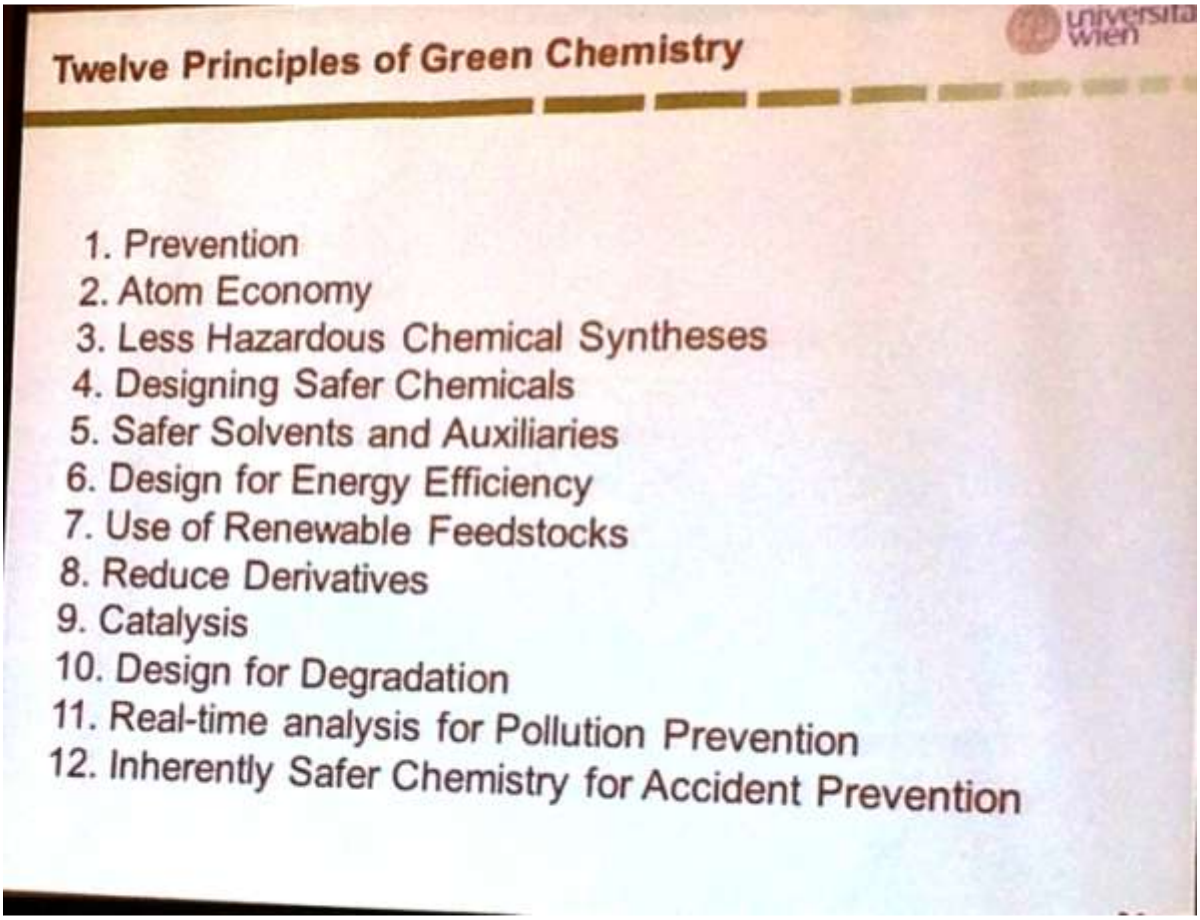
Littleton 博士的演講內容相對較為宏觀，主要圍繞綠色化學相關研究如何達到永續性及全球化等議題。首先他引用 Warner 博士所著綠色化學的 12 項

原則，與現今許多工業化國家發展永續性能源產業所遵循的原則相比較，發現大方向之外，許多國家格外強調區域性特色發展；因此制訂再生能源政策時，若能考慮不同區域特色並加以採納，則在環境保護、區域與國家整體經濟發展上，較能取得事半功倍之效。總而言之，我們也亟需制訂一個可通用全球的永續性能源產業發展宗旨，此宗旨必須兼顧區域特色發展之彈性，這有待人類的智慧遠見及拋棄多餘政治性考量的勇氣。

Littleton 博士實驗室主要利用 NMR 技術研究酵素與受質結合能力、小分子間交互作用、天然化合物的結構等等，共發表超過 90 篇學術論文，產量豐富。演講最後 Littleton 博士以山竹 (Mangosteen, 學名 *Garcinia mangostana*) 為例，說明區域特性重要性：山竹原產於馬來群島中的巽他群島和摩鹿加群島，由於盛產於南洋熱帶地區，有「熱帶果后」之稱。在馬來西亞、新加坡和泰國，榴槤和山竹被視為「夫妻果」，故此相對於稱為「果王」的榴槤而言，山竹就是「果后」。其果皮為黑紫色或粉紅色，很厚，味苦，一般不食用；果肉為白色，瓣狀，外觀頗似蒜瓣，可食用，味道濃郁，清涼甜美，口感柔和，有質感。其外果皮包含具有收斂作用的一系列多酚類物質，包括氧雜蒽酮和單寧酸，這些物質可以確保果實在未成熟時不受昆蟲、真菌、植物病毒、細菌和動物的侵害；外果皮中的紅色素，亦可用來製黃色染料。因此，對於每年生產大量山竹的區域，外果皮成為方便取得且便宜的生質料源，這類立足農業卻可多元發展至工業、紡織業甚至醫療業的區域性經濟，將在未來永續能源開發上扮演至為重要的角色。

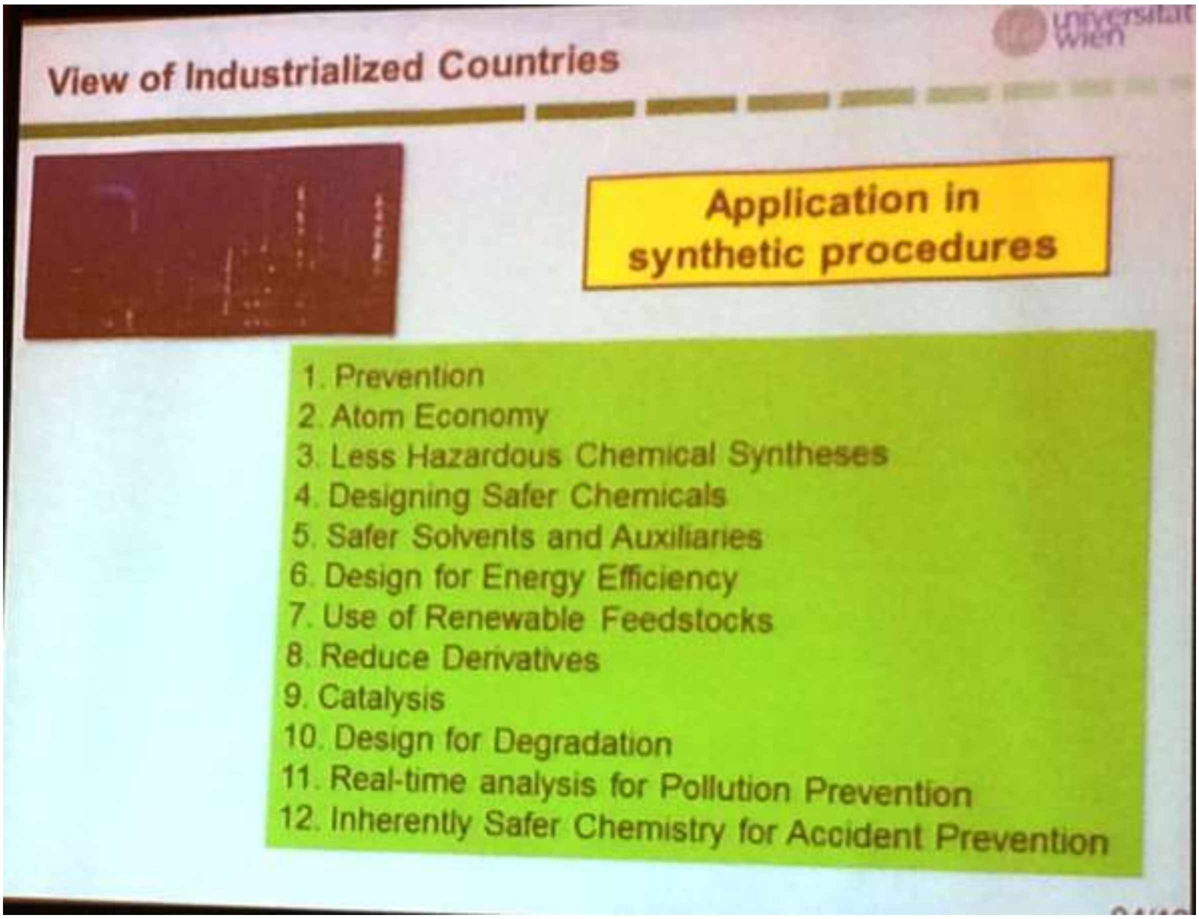
整體而言，Littleton 博士的演講進一步闡述 Warner 博士所提的綠色化學理念，也再次強調制訂政策必須考量的多種面向，也提供區域性經濟在國家發展再生能源時可扮演角色的例子，值得我國政策制訂借鏡。以下將報告內容重要投影片列出：

Local and Regional Aspects



Twelve Principles of Green Chemistry

1. Prevention
2. Atom Economy
3. Less Hazardous Chemical Syntheses
4. Designing Safer Chemicals
5. Safer Solvents and Auxiliaries
6. Design for Energy Efficiency
7. Use of Renewable Feedstocks
8. Reduce Derivatives
9. Catalysis
10. Design for Degradation
11. Real-time analysis for Pollution Prevention
12. Inherently Safer Chemistry for Accident Prevention



View of Industrialized Countries

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Application in synthetic procedures

1. Prevention
2. Atom Economy
3. Less Hazardous Chemical Syntheses
4. Designing Safer Chemicals
5. Safer Solvents and Auxiliaries
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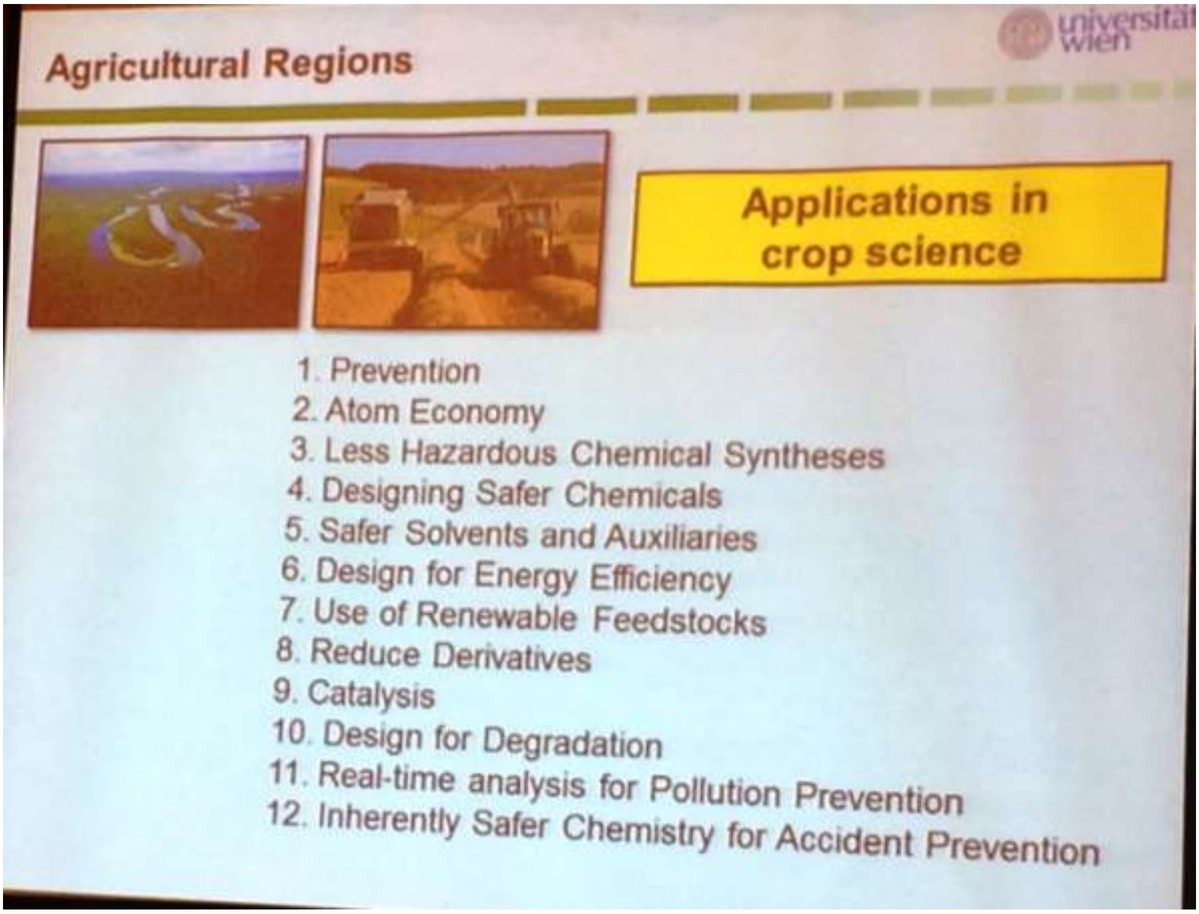

Agricultural Regions

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Applications in crop science

1. Prevention
2. Atom Economy
3. Less Hazardous Chemical Syntheses
4. Designing Safer Chemicals
5. Safer Solvents and Auxiliaries
6. Design for Energy Efficiency
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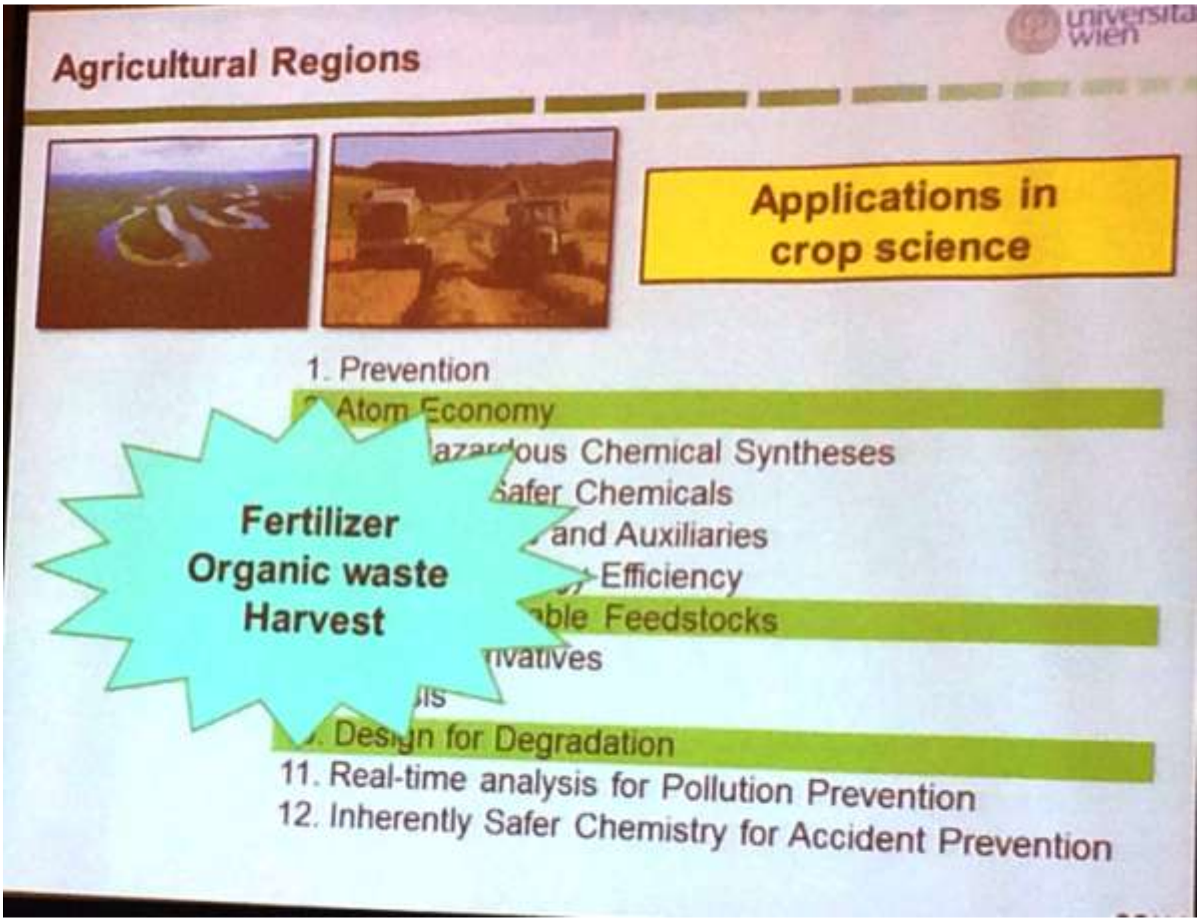
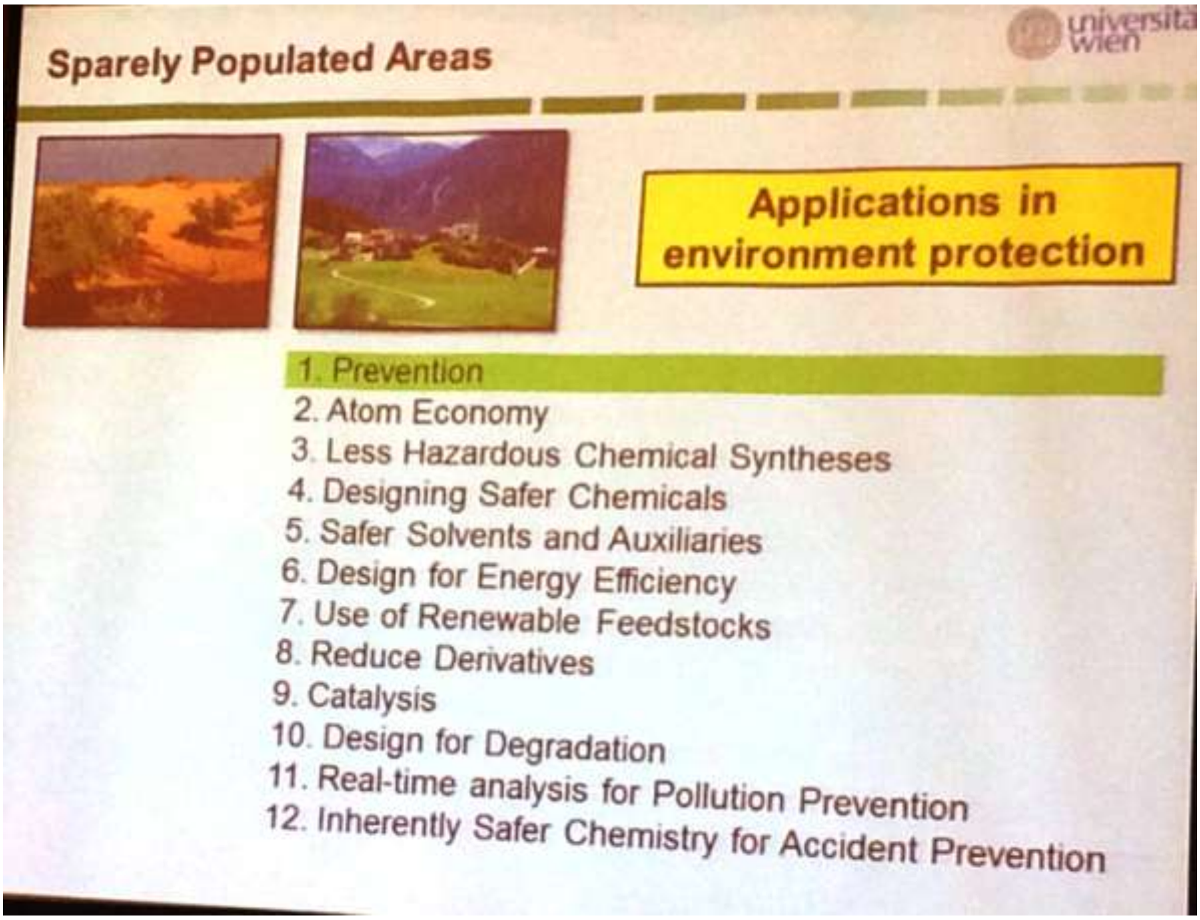


Agricultural Regions

Applications in crop science

1. Prevention
Atom Economy
azardous Chemical Syntheses
afer Chemicals
and Auxiliaries
Efficiency
ble Feedstocks
ivatives
is
Design for Degradation
11. Real-time analysis for Pollution Prevention
12. Inherently Safer Chemistry for Accident Prevention

Fertilizer
Organic waste
Harvest



Sparely Populated Areas

Applications in environment protection

1. Prevention
2. Atom Economy
3. Less Hazardous Chemical Syntheses
4. Designing Safer Chemicals
5. Safer Solvents and Auxiliaries
6. Design for Energy Efficiency
7. Use of Renewable Feedstocks
8. Reduce Derivatives
9. Catalysis
10. Design for Degradation
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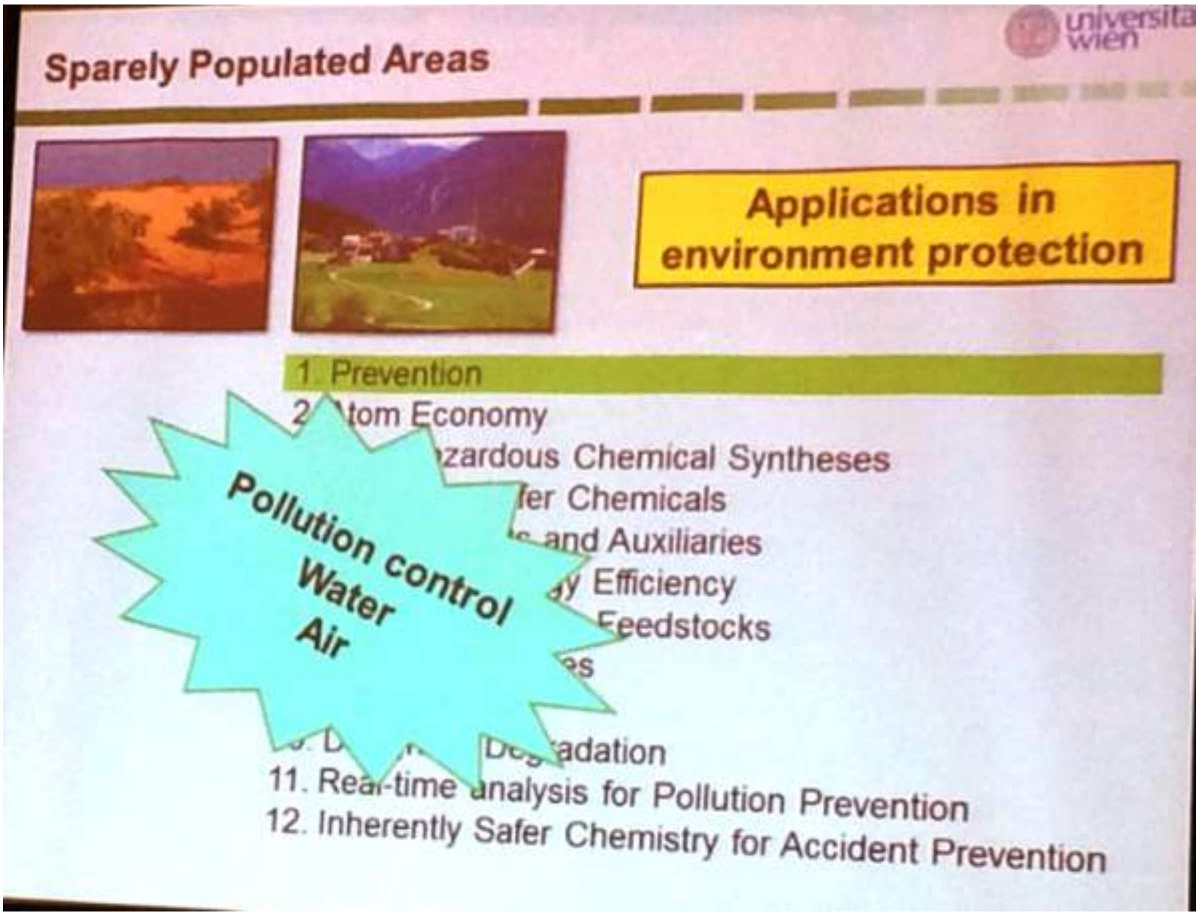
12. Inherently Safer Chemistry for Accident Prevention



Sparely Populated Areas

Applications in environment protection

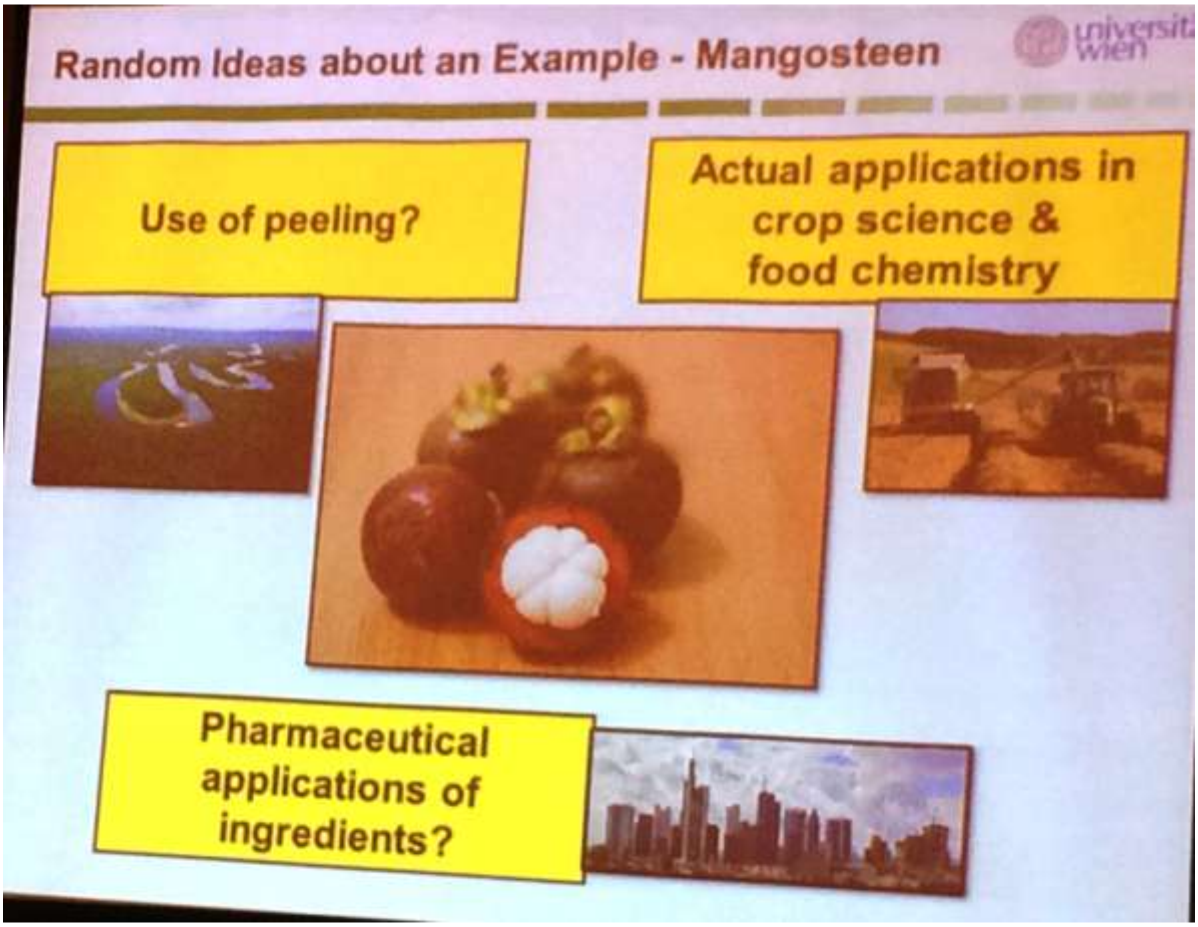
1. Prevention
2 tom Economy
zardous Chemical Syntheses
fer Chemicals
and Auxiliaries
y Efficiency
Feedstocks
es
Degradation
11. Real-time analysis for Pollution Prevention
12. Inherently Safer Chemistry for Accident Prevention

Pollution control
Water
Air

Can we Combine These Points of View?

Sustainability

Joined Solutions
in
Chemical Applications



Random Ideas about an Example - Mangosteen

Use of peeling?

Actual applications in crop science & food chemistry

Pharmaceutical applications of ingredients?

3.3 專題演講

3.3.1 綠色化學與全球化用藥：嶄新化學研究如何提升人類免疫缺乏症候群、瘧疾及肝炎的治療 (Green Chemistry and global access to medicines: New chemistry for access to HIV, Malaria, and Hepatitis medicines)

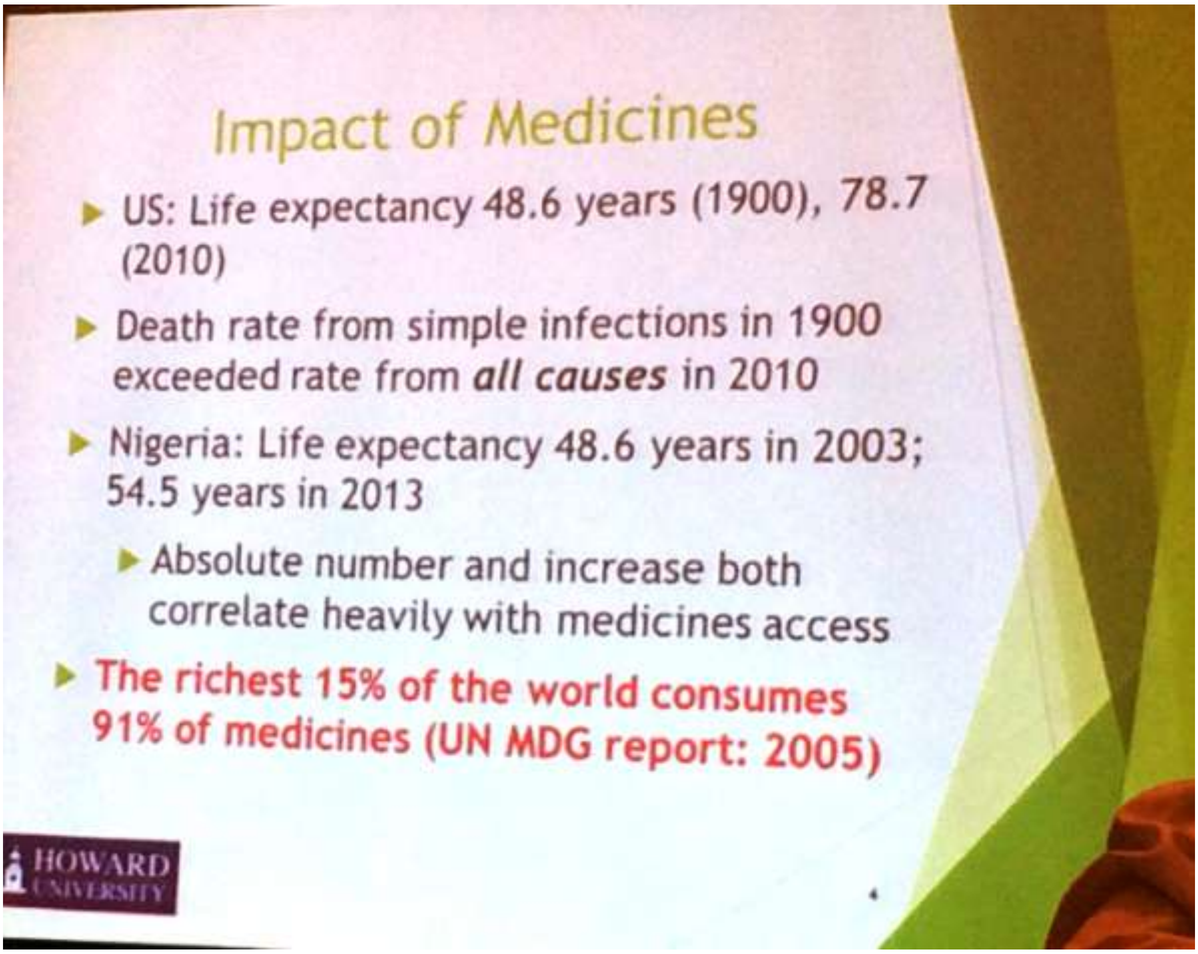
演講者：Joseph M. Fortunak, Ph.D.

機構名稱：Howard University, USA

演講摘要：

Fortunak 博士投身學界前曾任職杜邦藥廠 (Dupont Pharmaceuticals) 且曾任亞培實驗室全球化學研發主持人 (Head of Global Chemical Development at Abbott Labs)，業界經歷超過 21 年，現為美國霍華德大學化學與藥物科學系教授，實驗室進行嶄新化學研究，研發目標之一，為降低低收入和中等收入國家 (low- and middle-income countries, LMICs) 1400 萬 HIV/AIDS 患者的醫療花費。

Fortunak 博士的演講指出，根據 2005 年聯合國千禧年發展目標報告書 (United Nations Millenium Development Goals: Progress Report)，世界上 15%最富有的人口平均消耗 91%藥物，經過十年，這個情況僅有些許改善：世界衛生組織所列基本藥物目錄 (World Health Organization’s “Essential Medicine List”) 內大部份藥物，已經由大量製造、不同型式授權、降低價格，在 LMICs 較為普及，其中 HIV/AIDS、瘧疾、C 型肝炎藥物的價格通常為高收入國家價格 1%以下，然而這樣的價格還是太高，因此需要實驗室針對不同藥物內有效藥物成份 (Active Pharmaceutical Ingredients, APIs) 合成製程進行改造。Fortunak 博士實驗室針對數種 APIs，包括 HIV 蛋白酶抑制物 Darunavir 及 Atazanavir、肝炎藥物、瘧疾用藥 (Amodiaquine, Piperaquine 及 Lumefantrine) 等研發更環保價格更低廉的合成方法，包括對於 Darunavir 及 Atazanavir 兩個鄰近對掌性中心 (chiral center) 進行同步有機催化，並能有效控制其立體結構化學特性 (stereochemistry, 藥物立體結構對於藥效有直接影響因此極為重要) 之催化步驟研發等。以下將報告內容重要投影片列出：



Impact of Medicines

- US: Life expectancy 48.6 years (1900), 78.7 (2010)
- Death rate from simple infections in 1900 exceeded rate from ***all causes*** in 2010
- Nigeria: Life expectancy 48.6 years in 2003; 54.5 years in 2013
  - Absolute number and increase both correlate heavily with medicines access
- **The richest 15% of the world consumes 91% of medicines (UN MDG report: 2005)**

1. Work with NGOs and producers:

Lowest sustainable prices for LMICs

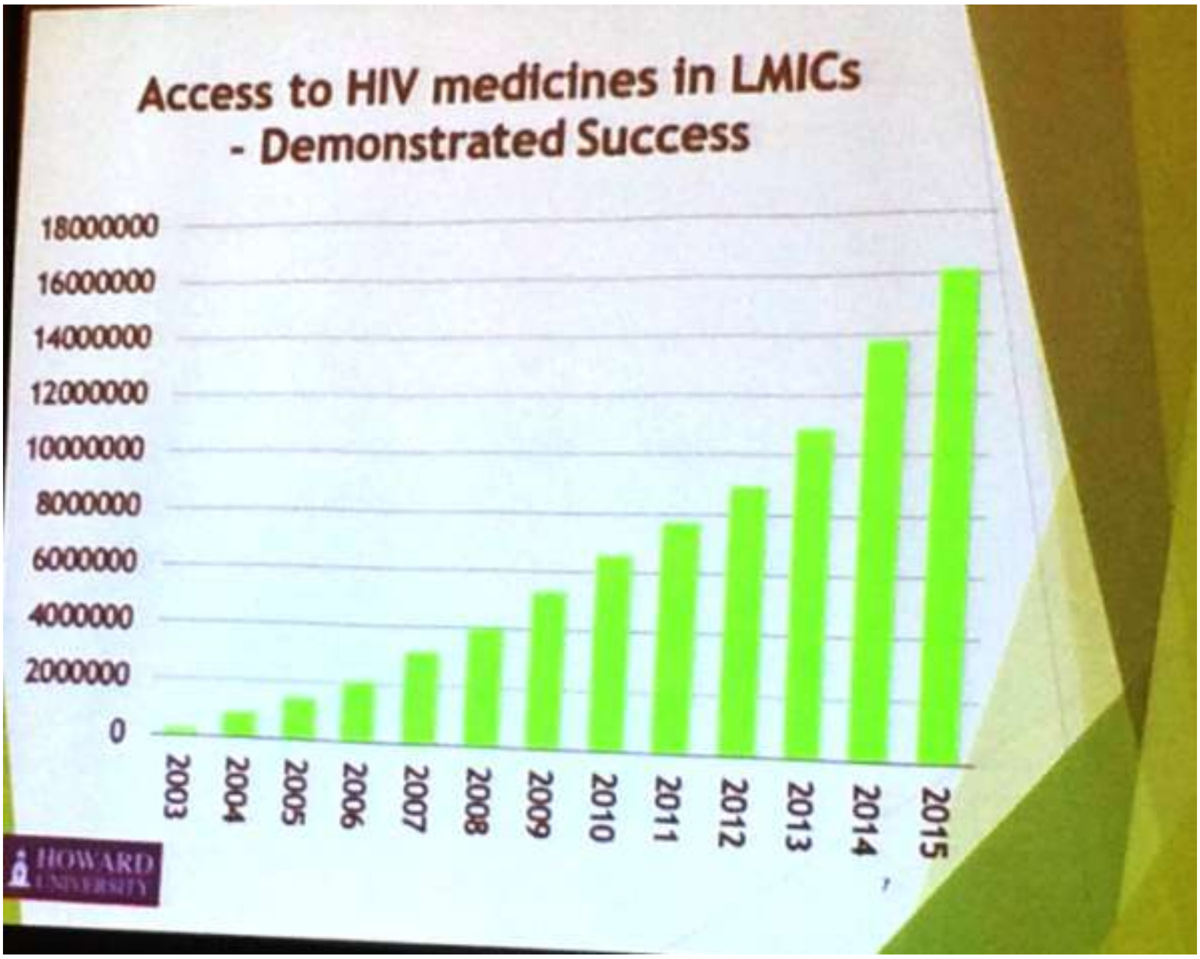
==================================

2. Improve regional manufacturing and regulation:

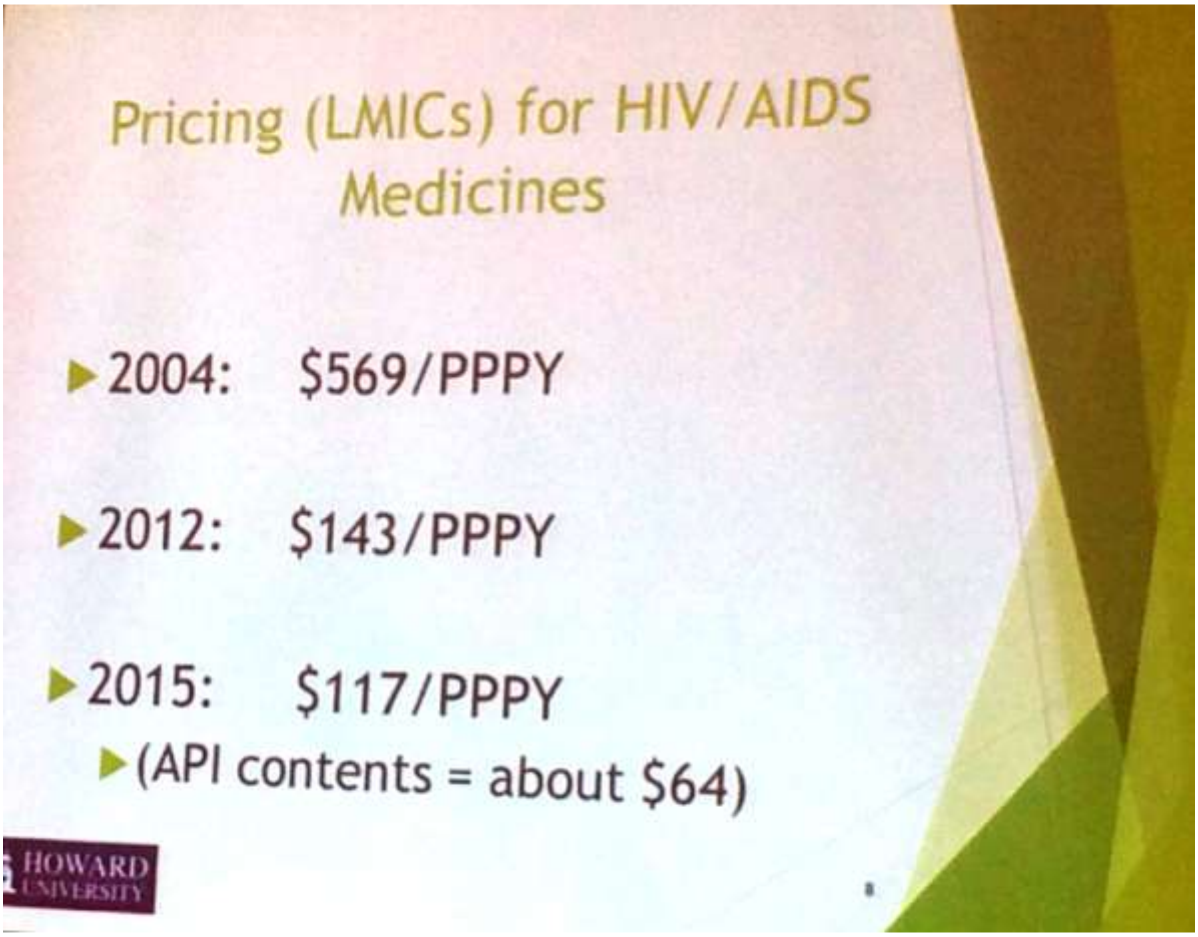
Assure quality, increase supply, expand beyond AIDS, TB, malaria...

= End dependence,

Create jobs, economic development

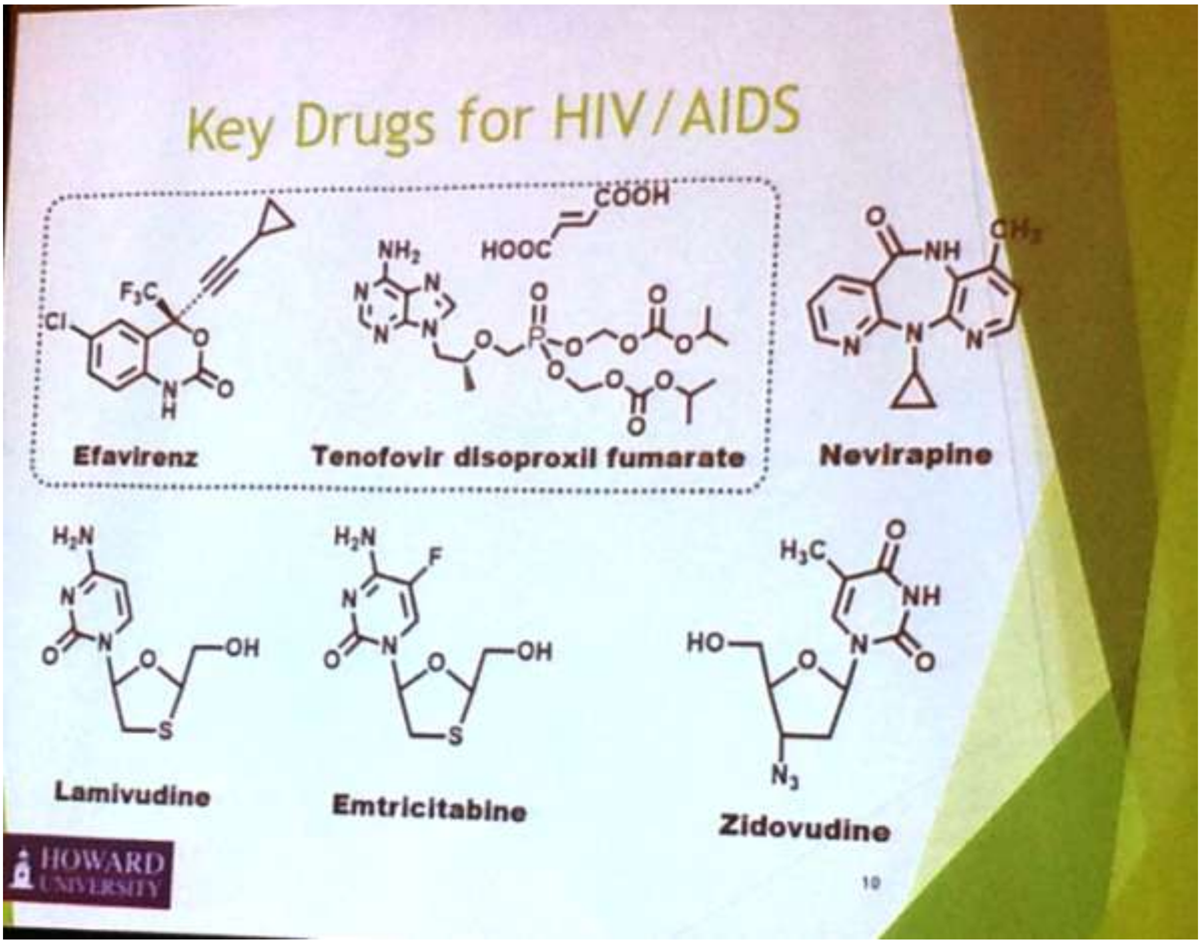


Access to HIV medicines in LMICs - Demonstrated Success



Pricing (LMICs) for HIV/AIDS Medicines

- 2004: $569/PPPY
- 2012: $143/PPPY
- 2015: $117/PPPY
  - (API contents = about $64)



Key Drugs for HIV/AIDS

Efavirenz

Tenofovir disoproxil fumarate

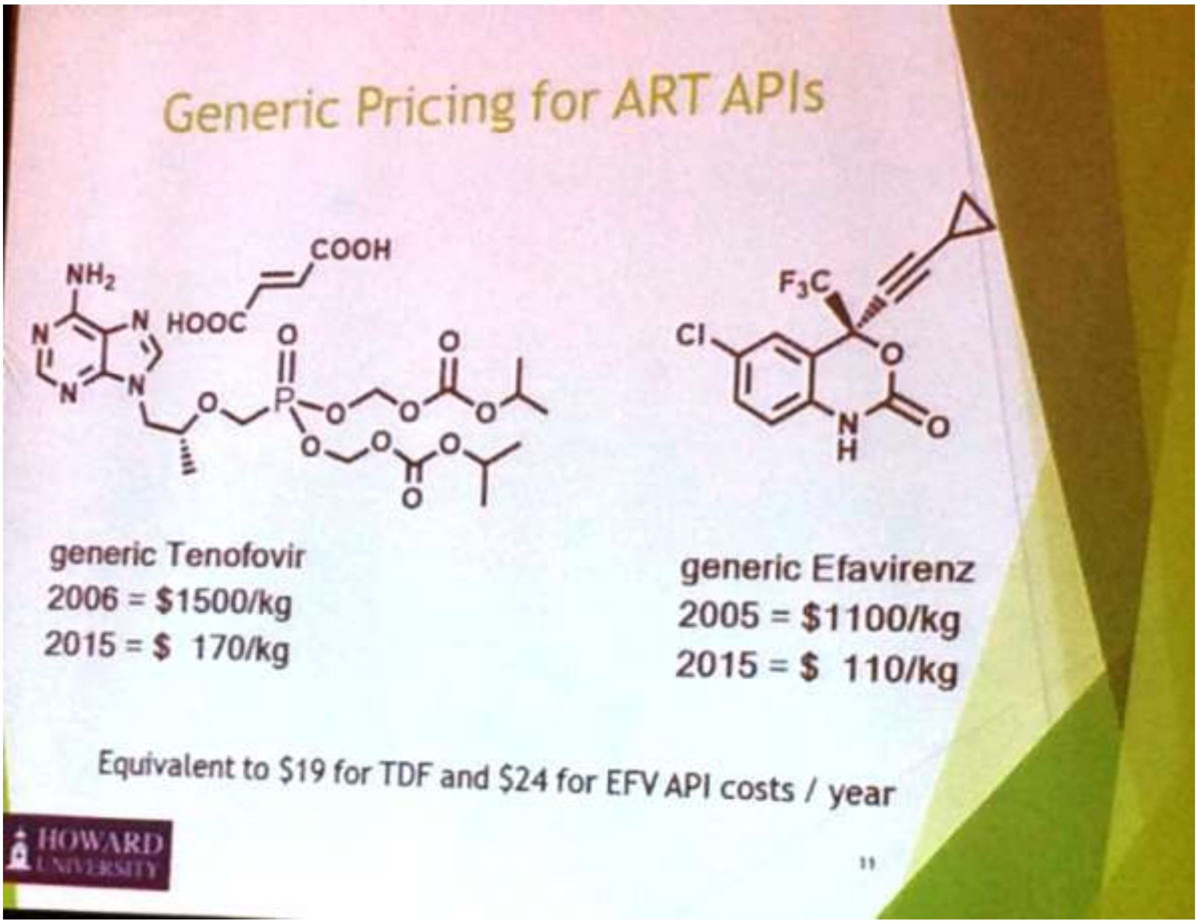
Nevirapine

Lamivudine

Emtricitabine

Zidovudine

HOWARD UNIVERSITY



Generic Pricing for ART APIs

generic Tenofovir
2006 = $1500/kg
2015 = $ 170/kg

generic Efavirenz
2005 = $1100/kg
2015 = $ 110/kg

Equivalent to $19 for TDF and $24 for EFV API costs / year

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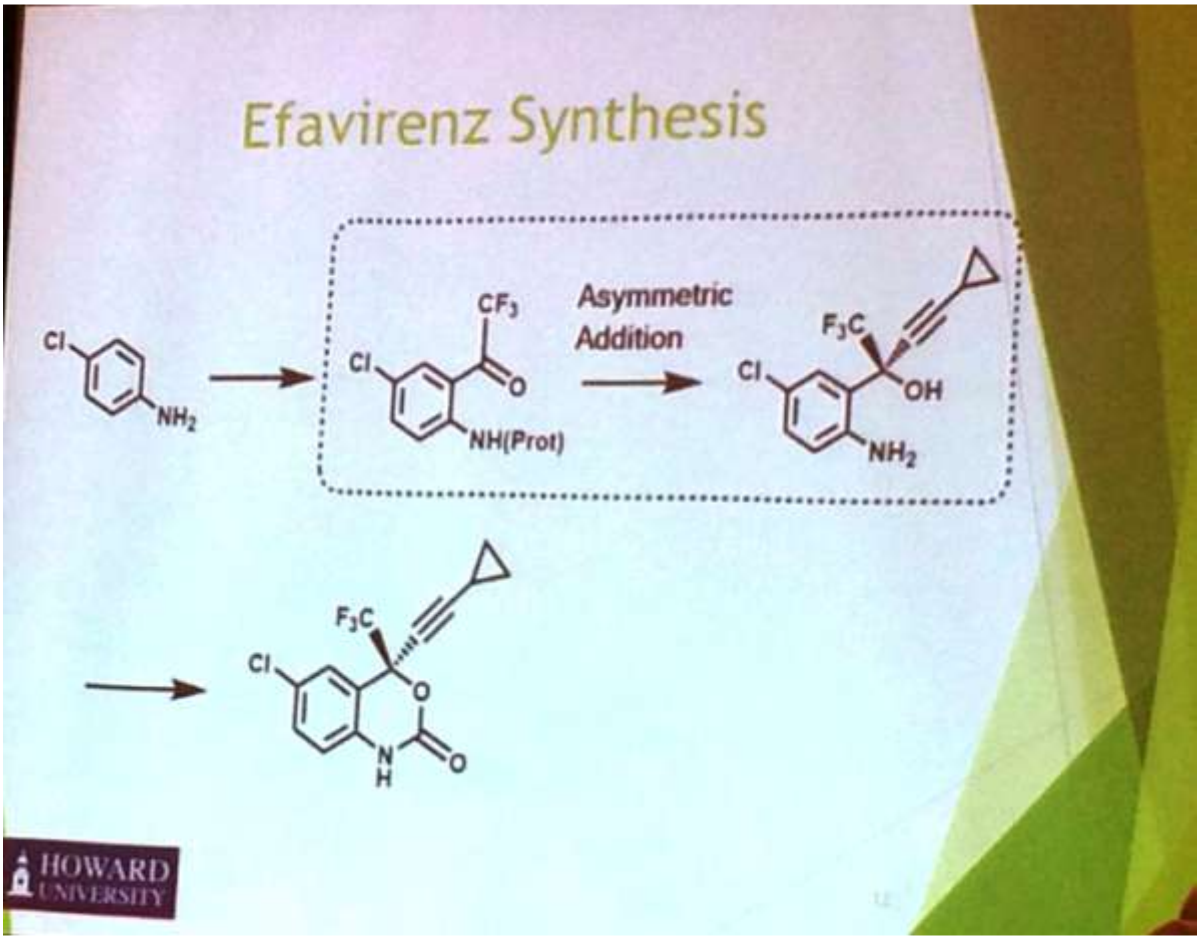
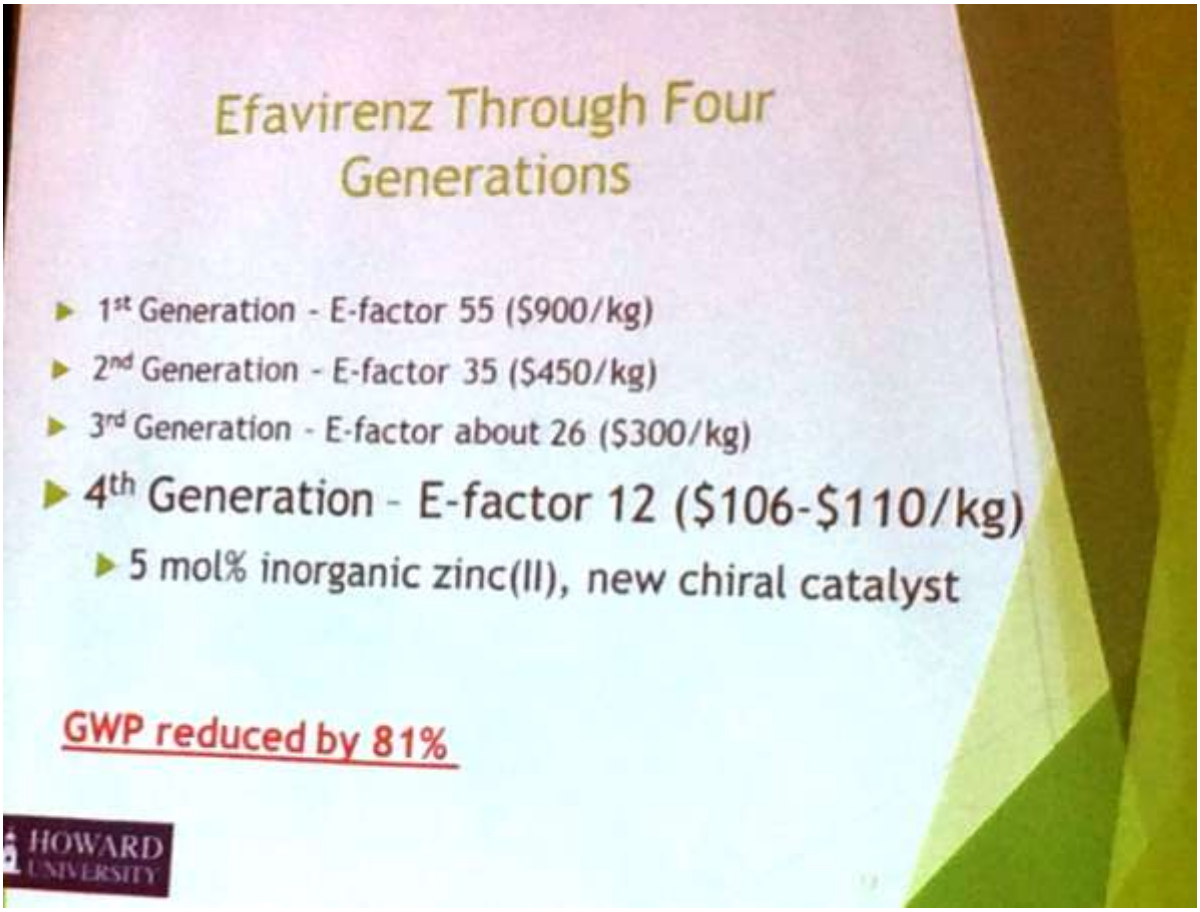


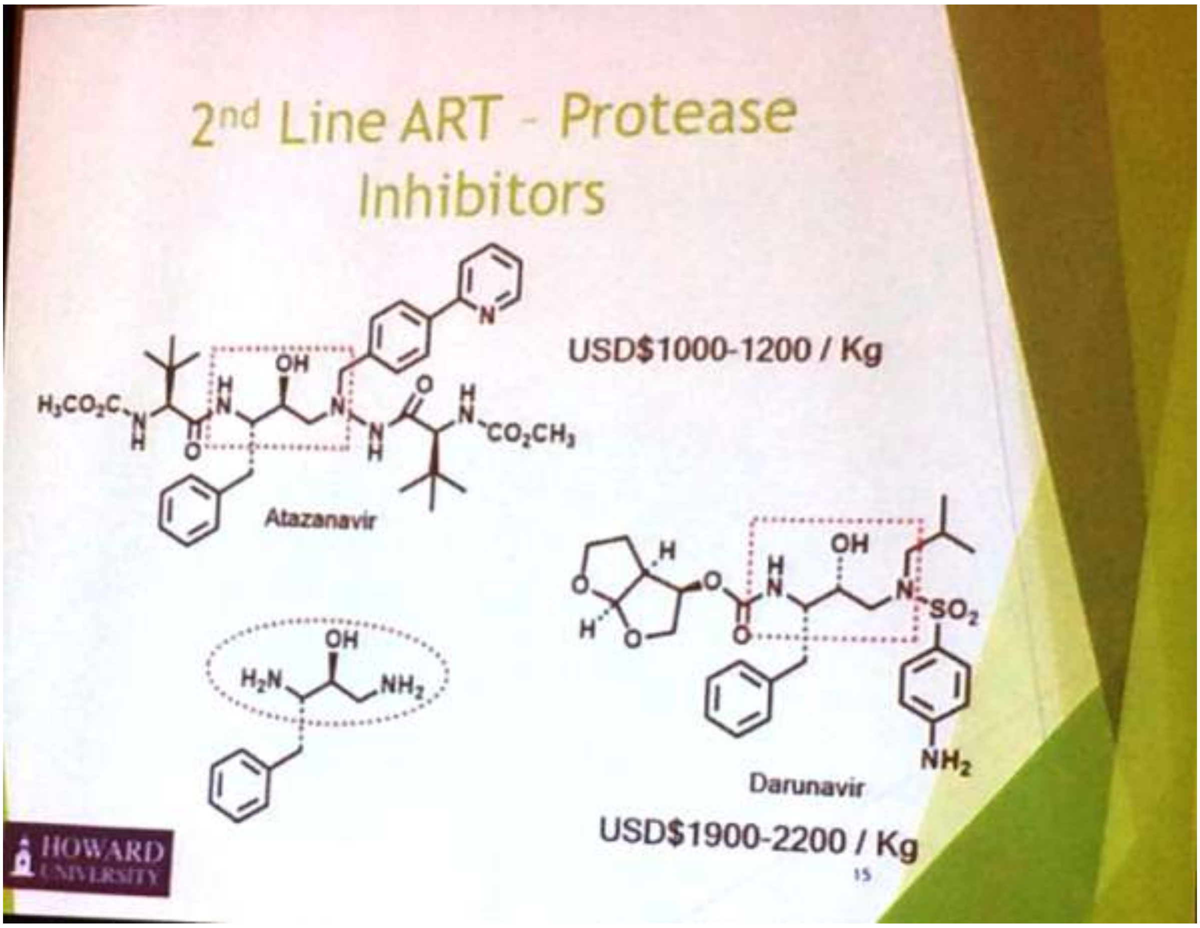
Efavirenz Synthesis



Efavirenz Through Four Generations

- 1st Generation - E-factor 55 ($900/kg)
- 2nd Generation - E-factor 35 ($450/kg)
- 3rd Generation - E-factor about 26 ($300/kg)
- 4th Generation - E-factor 12 ($106-$110/kg)
  - 5 mol% inorganic zinc(II), new chiral catalyst

GWP reduced by 81%



2nd Line ART - Protease Inhibitors

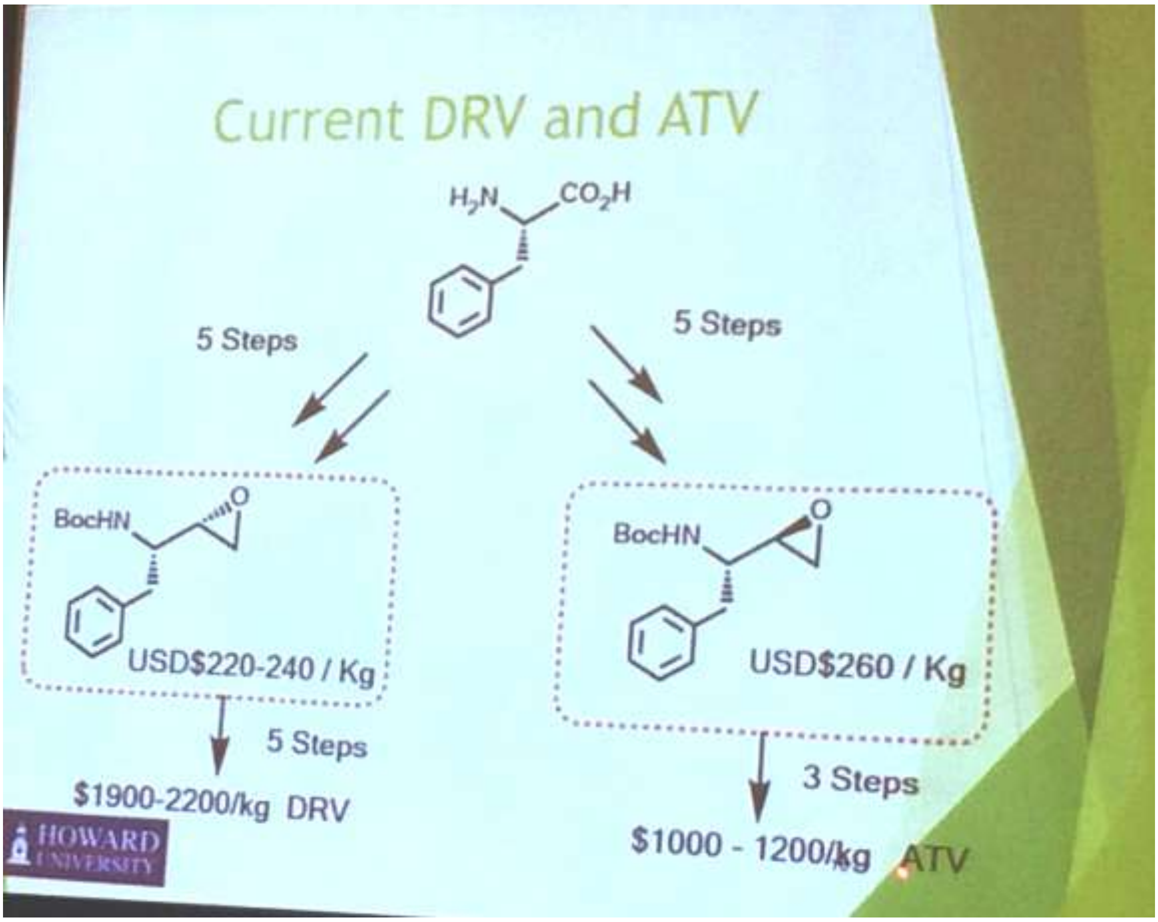
USD$1000-1200 / Kg

Atazanavir

Darunavir

USD$1900-2200 / Kg

15



Current DRV and ATV

5 Steps

5 Steps

USD$220-240 / Kg

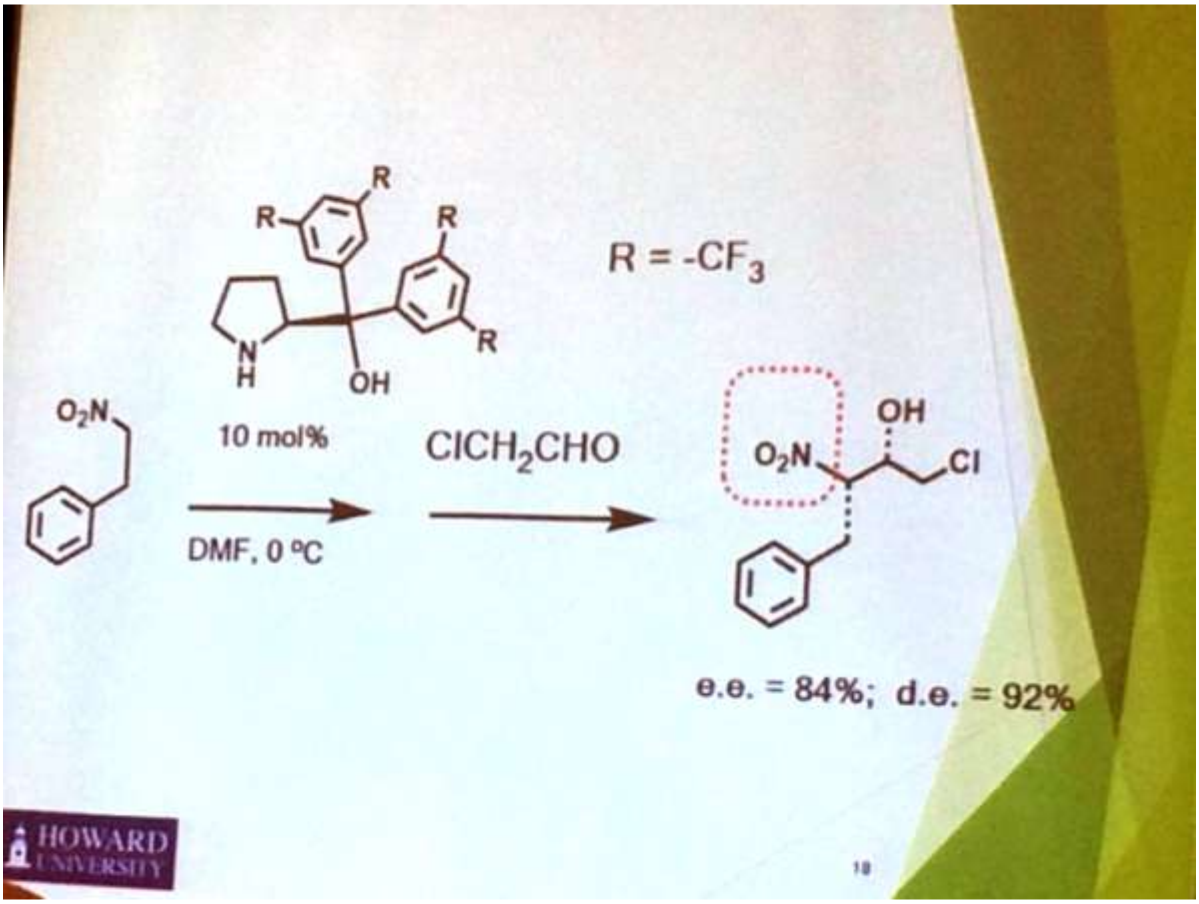
USD$260 / Kg

5 Steps

3 Steps

$1900-2200/kg DRV

$1000 - 1200/kg ATV



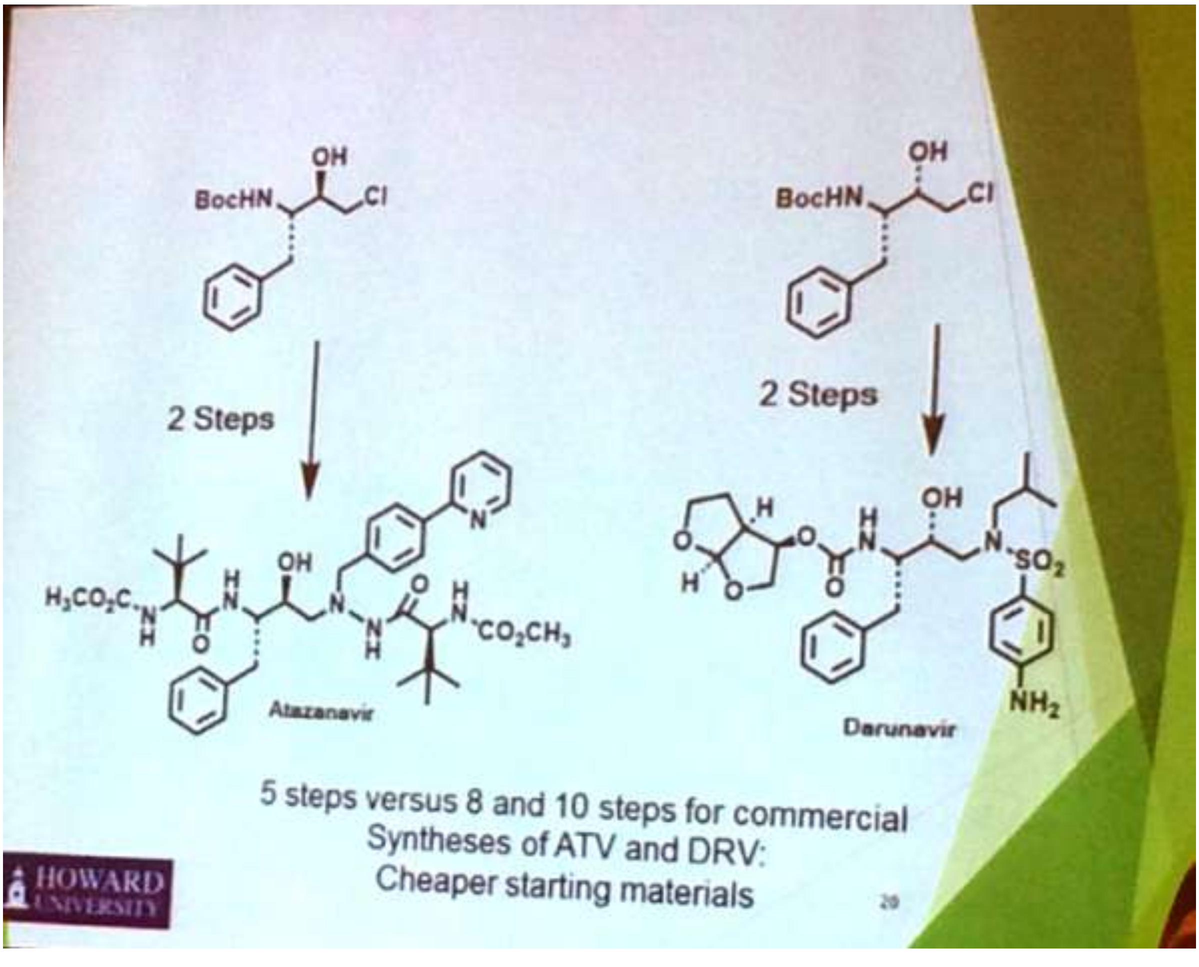
R = $-CF_3$

10 mol%

DMF, 0 °C

$ClCH_2CHO$

e.e. = 84%; d.e. = 92%



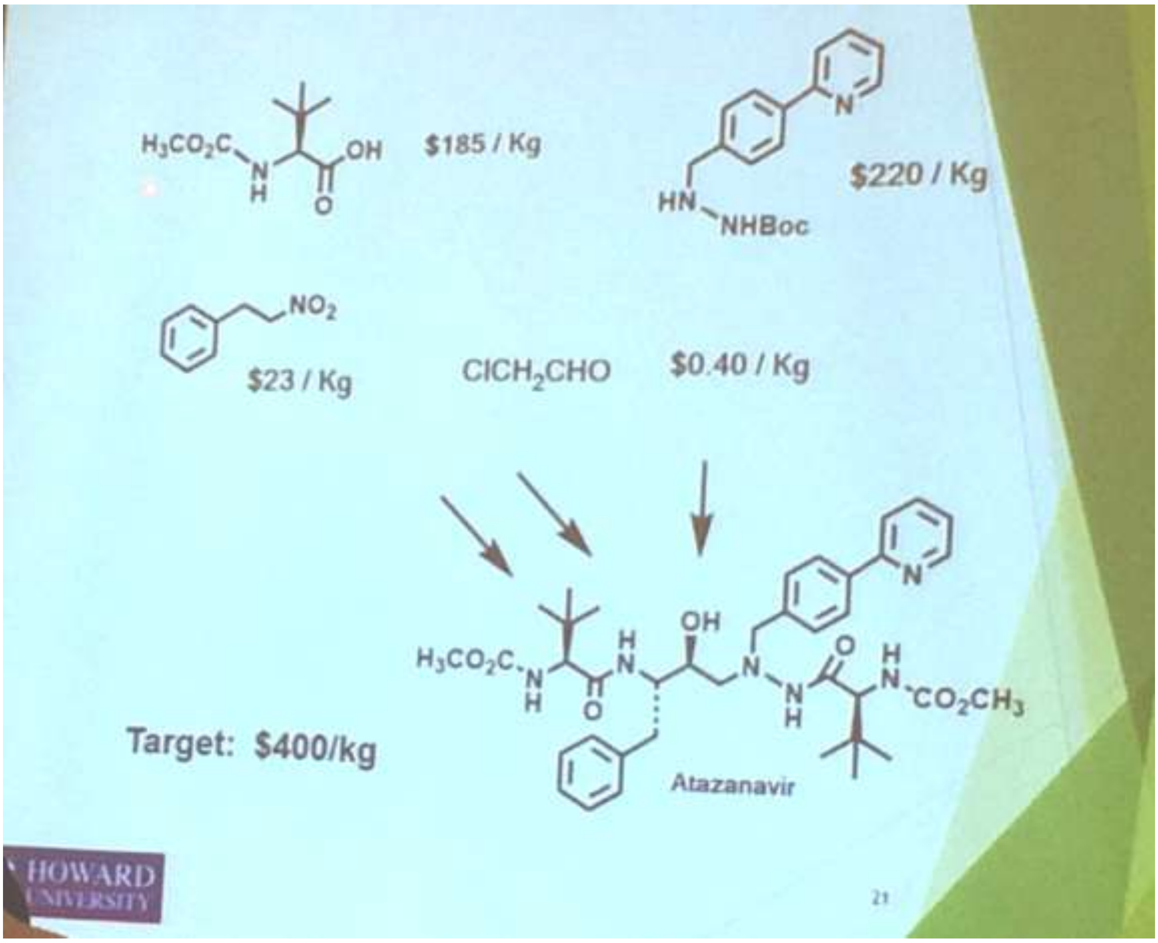
2 Steps

2 Steps

Atazanavir

Darunavir

5 steps versus 8 and 10 steps for commercial
Syntheses of ATV and DRV:
Cheaper starting materials



$185 / Kg

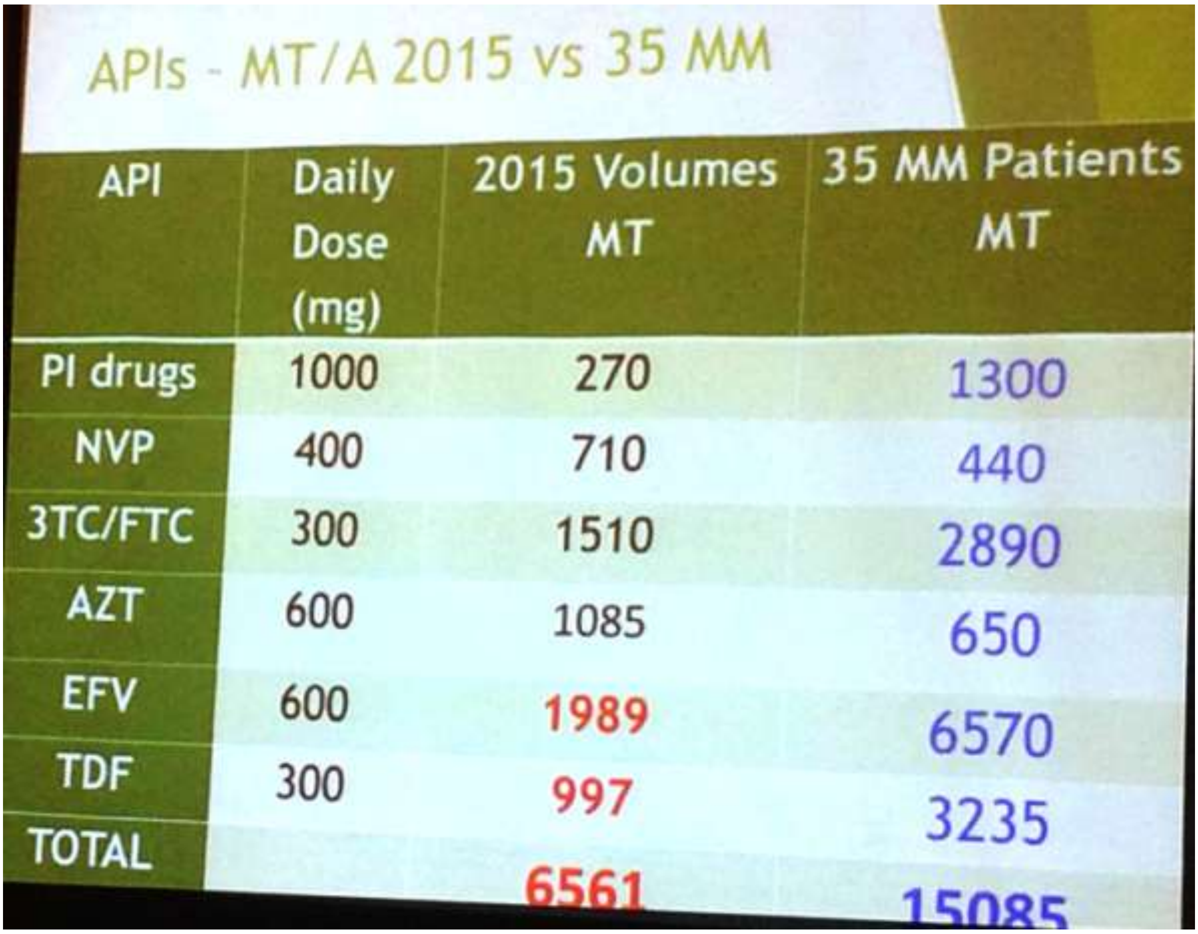
$220 / Kg

$23 / Kg

$ClCH_2CHO$ $0.40 / Kg

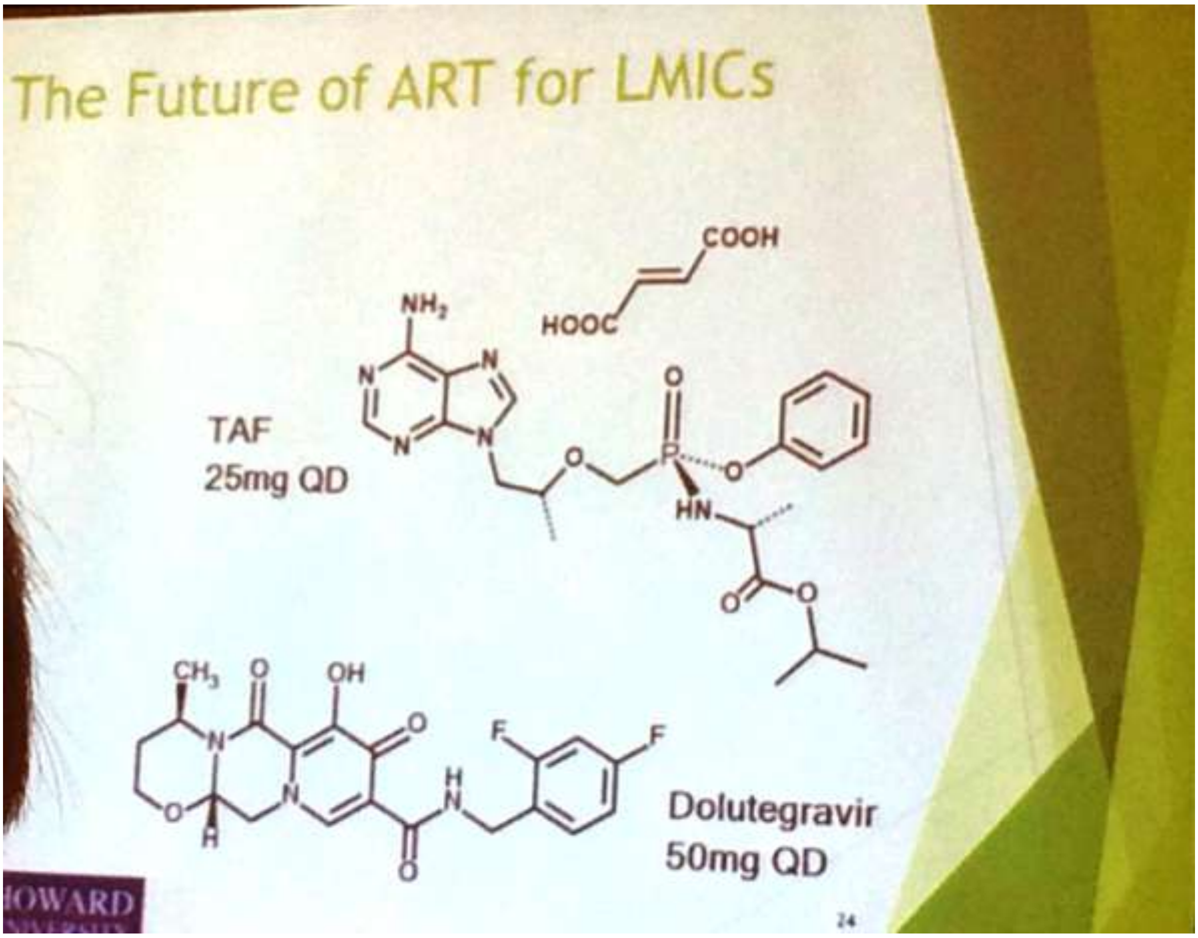
Target: $400/kg

Atazanavir



APIs - MT/A 2015 vs 35 MM

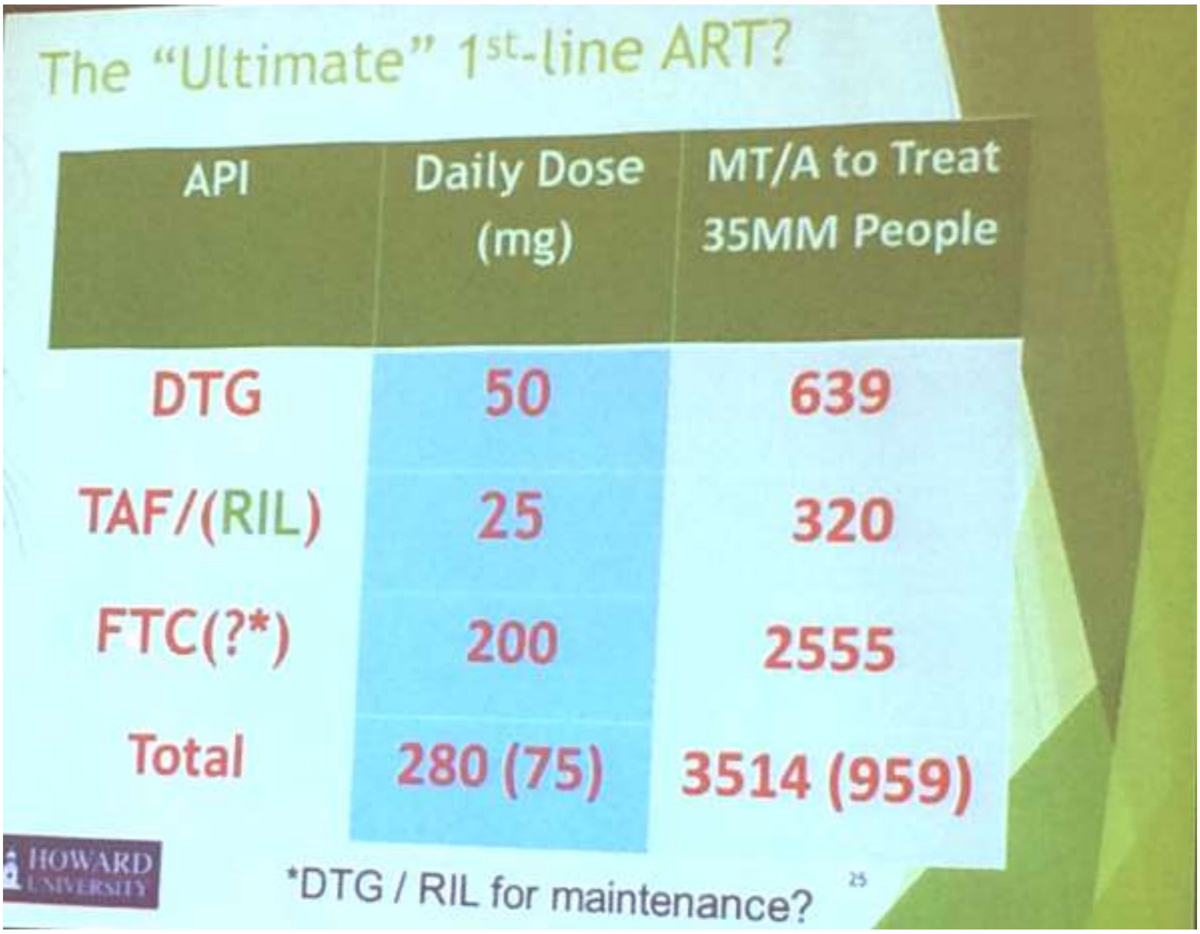
API	Daily Dose (mg)	2015 Volumes MT	35 MM Patients MT
PI drugs	1000	270	1300
NVP	400	710	440
3TC/FTC	300	1510	2890
AZT	600	1085	650
EFV	600	1989	6570
TDF	300	997	3235
TOTAL		6561	15085



The Future of ART for LMICs

TAF
25mg QD

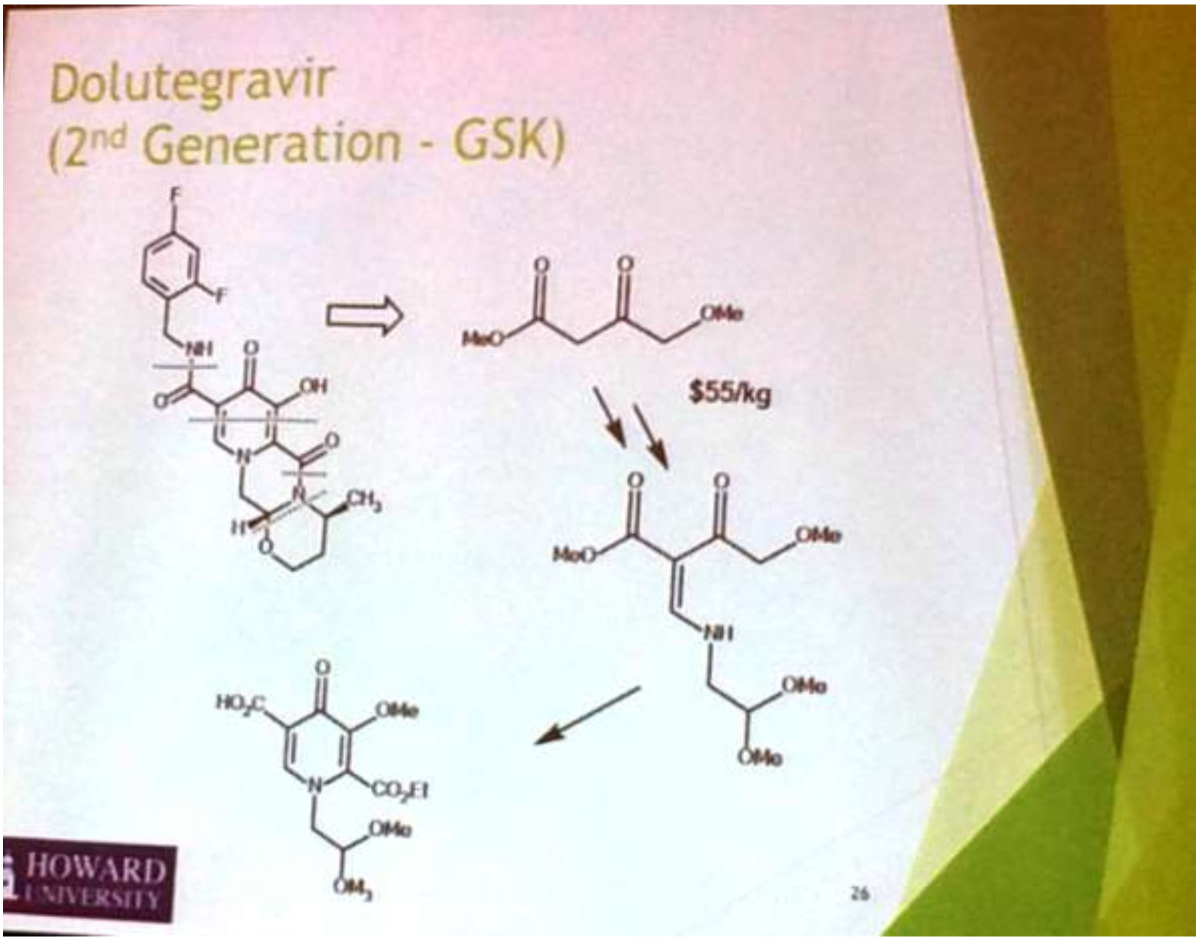
Dolutegravir
50mg QD



The “Ultimate” 1st-line ART?

API	Daily Dose (mg)	MT/A to Treat 35MM People
DTG	50	639
TAF/(RIL)	25	320
FTC(?*)	200	2555
Total	280 (75)	3514 (959)

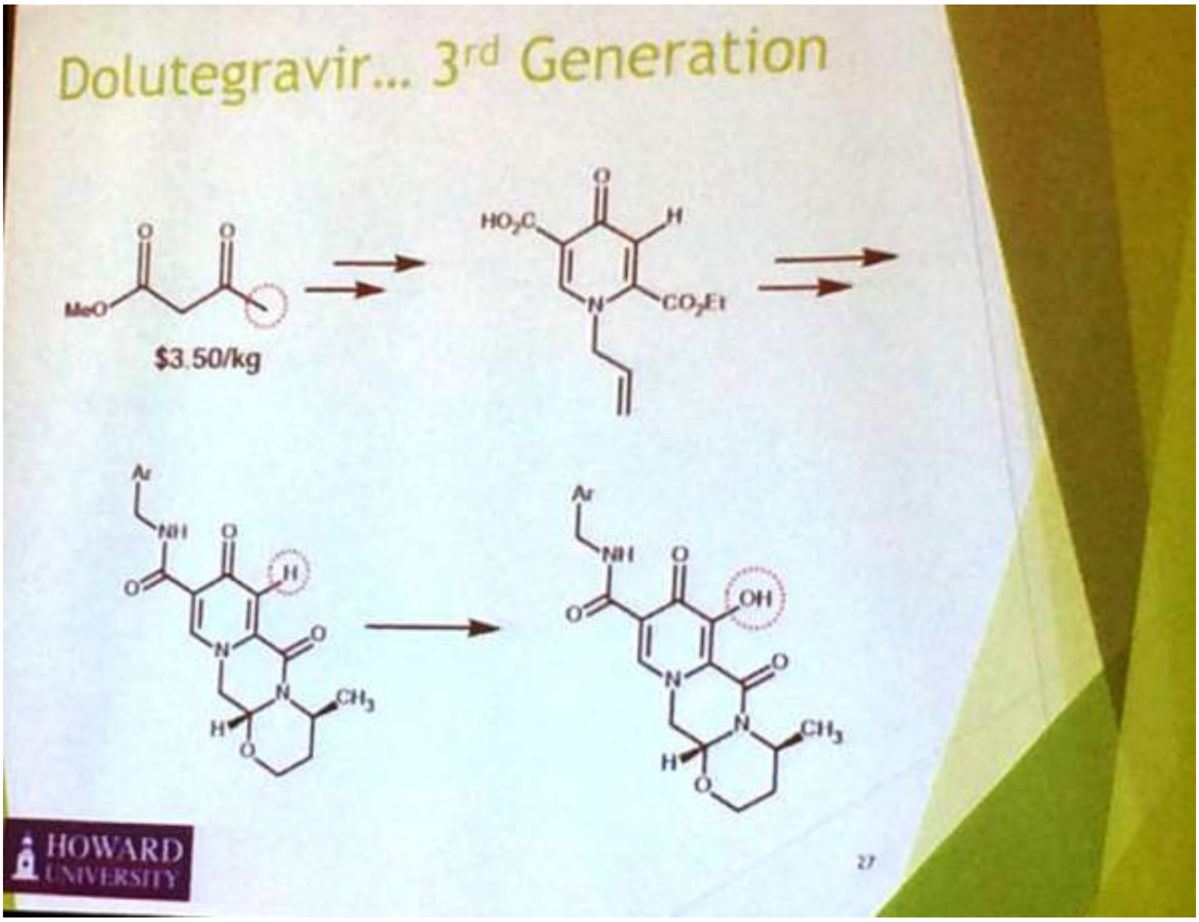
*DTG / RIL for maintenance?



Dolutegravir
(2nd Generation - GSK)

$55/kg

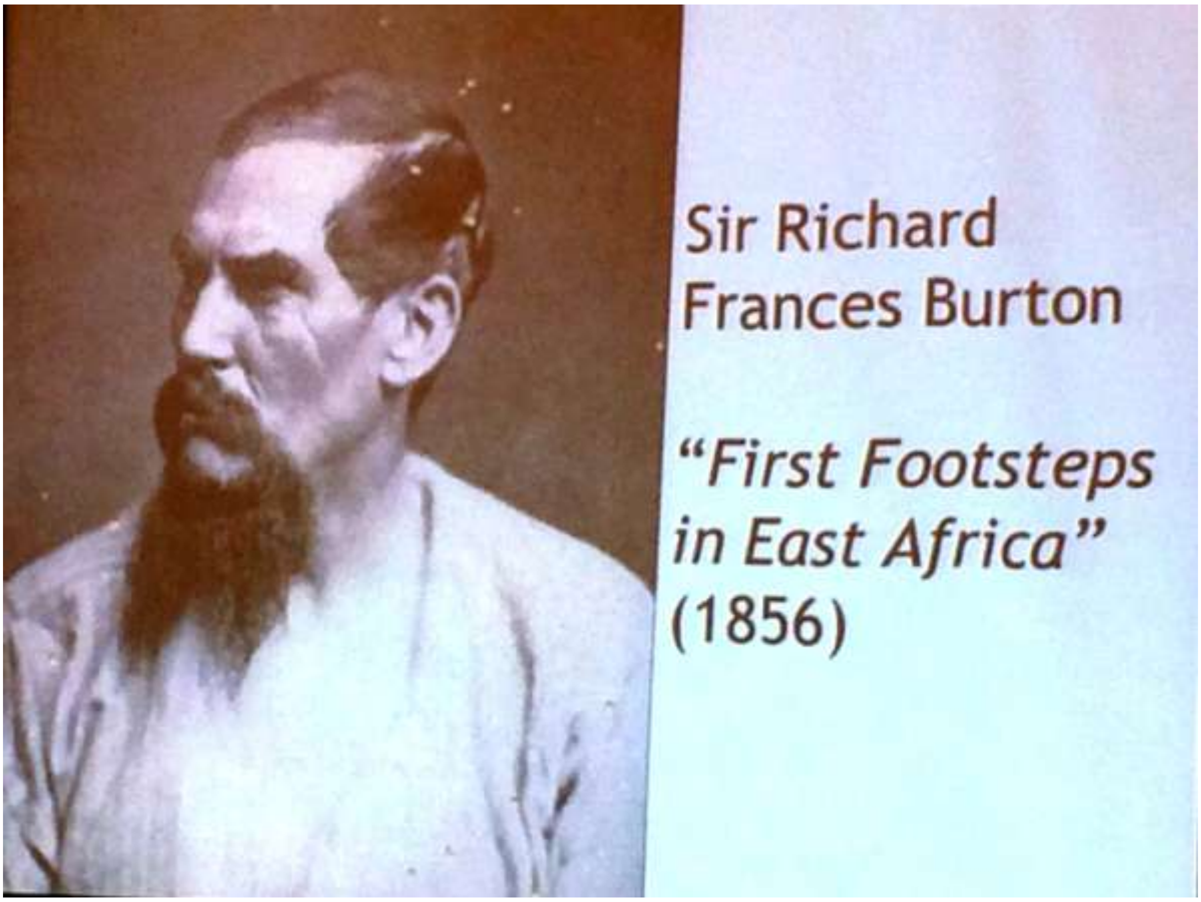
HOWARD UNIVERSITY



Dolutegravir... 3rd Generation

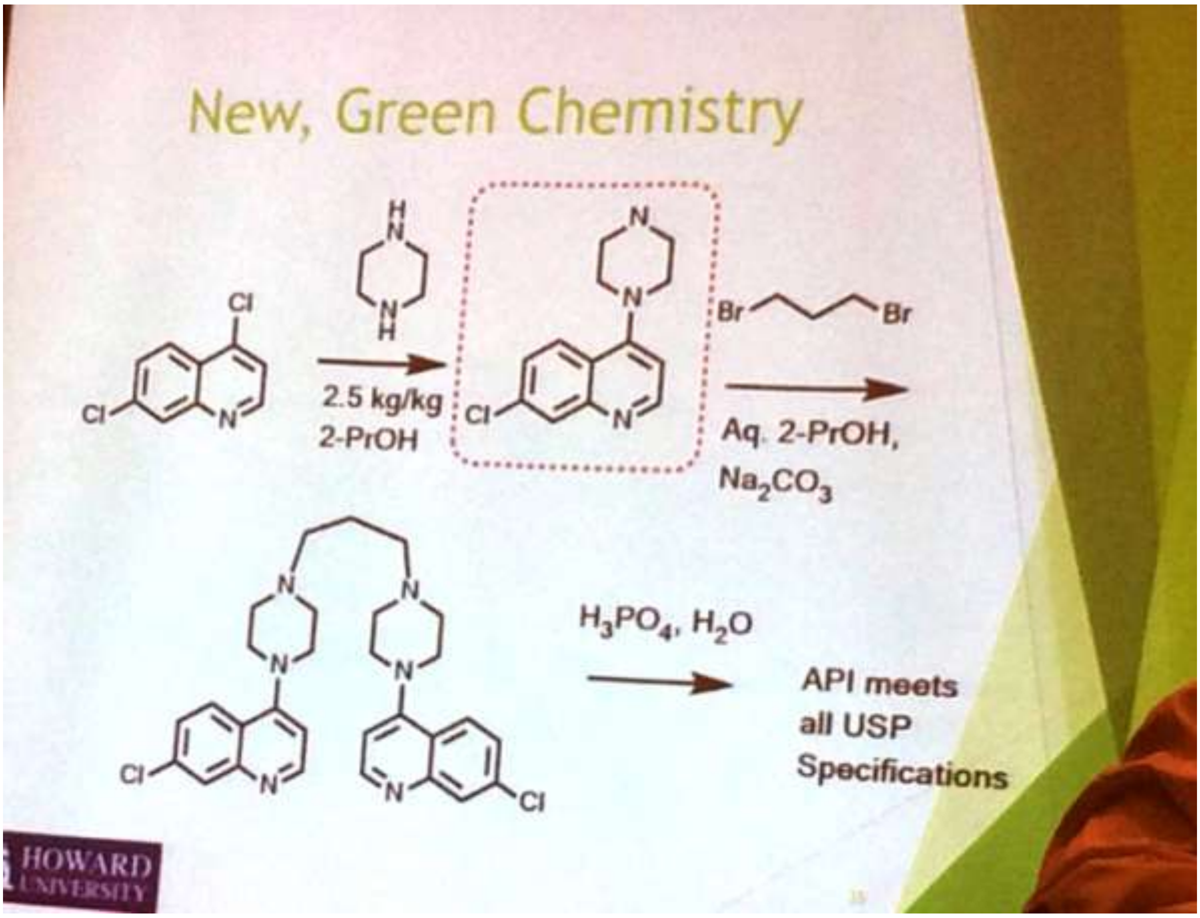
$3.50/kg

HOWARD UNIVERSITY



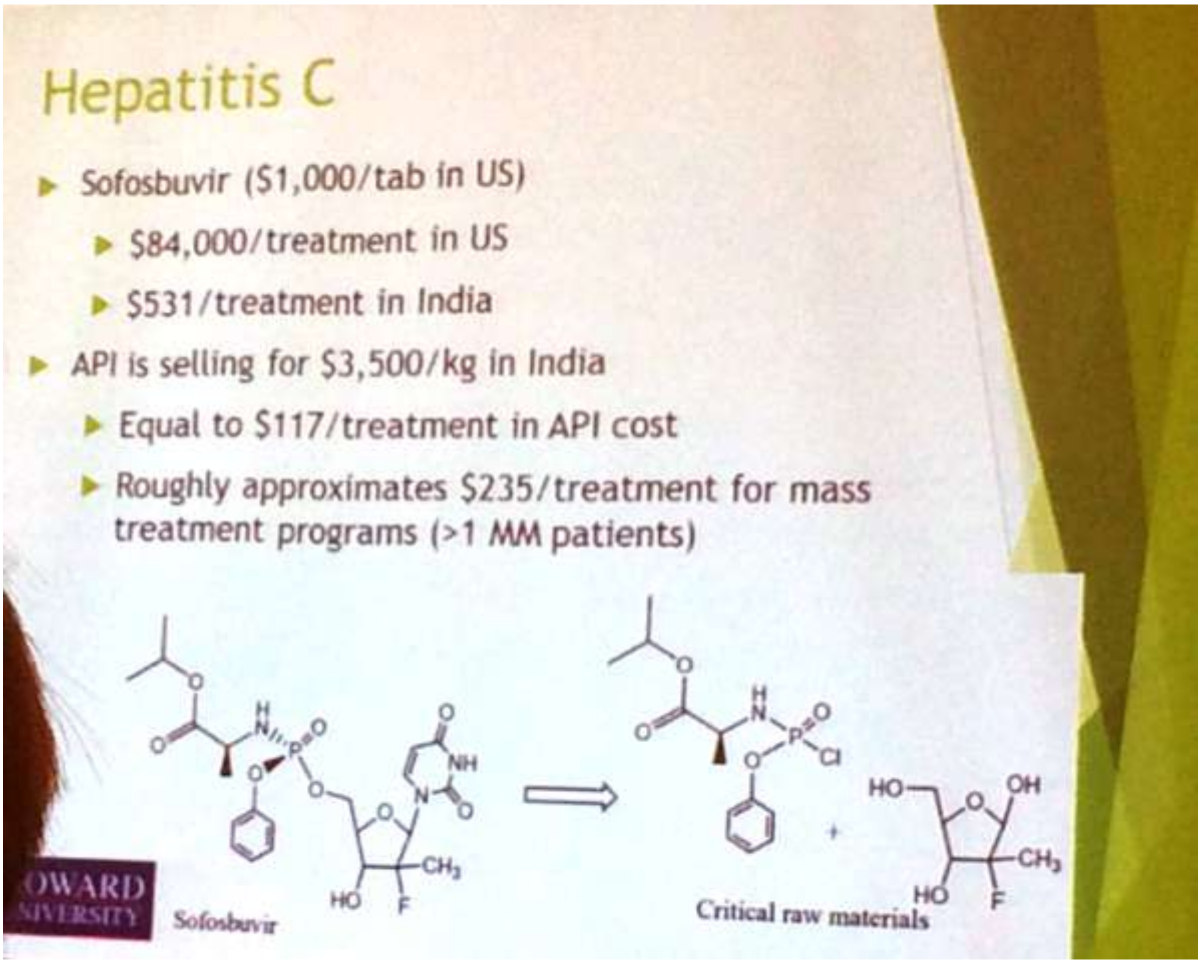
Sir Richard Frances Burton

“First Footsteps in East Africa” (1856)



New, Green Chemistry

API meets all USP Specifications

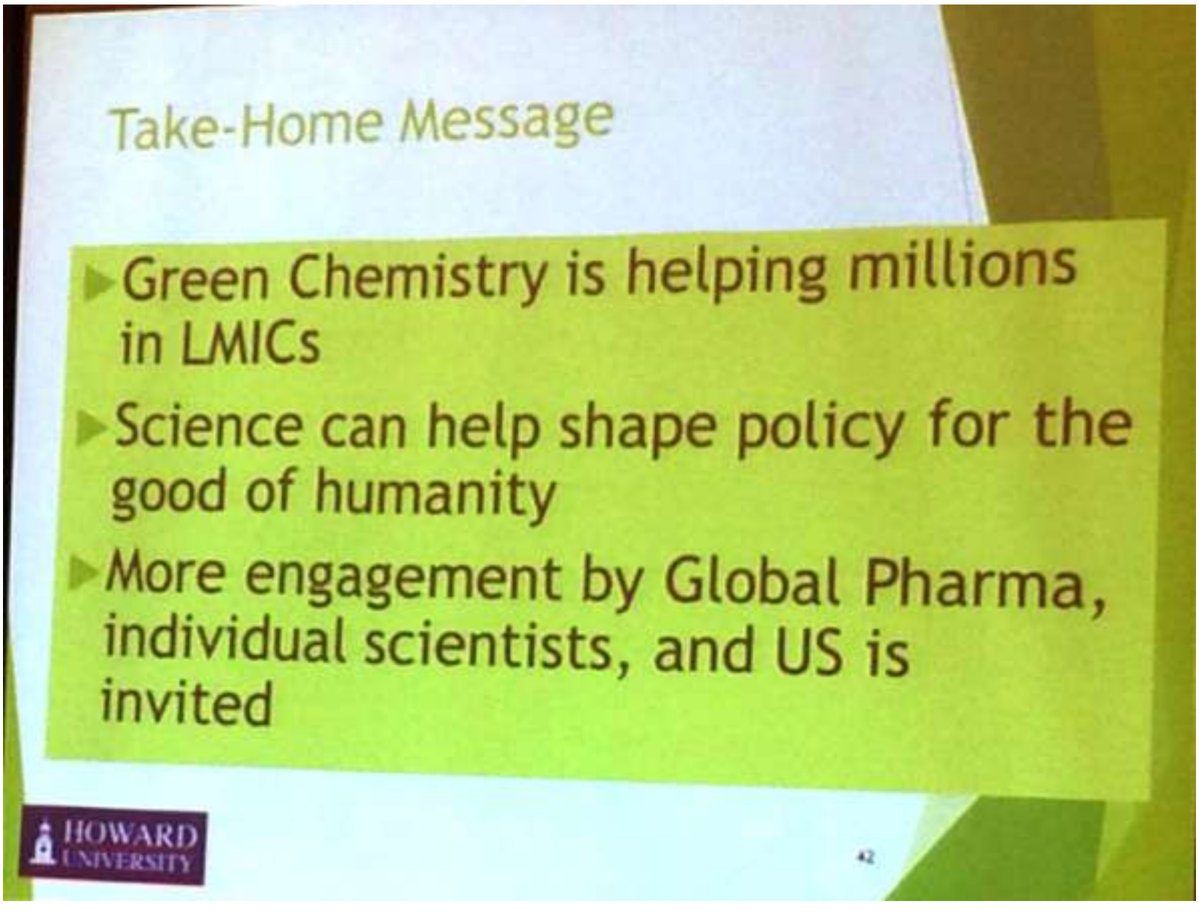


Hepatitis C

- Sofosbuvir ($1,000/tab in US)
  - $84,000/treatment in US
  - $531/treatment in India
- API is selling for $3,500/kg in India
  - Equal to $117/treatment in API cost
  - Roughly approximates $235/treatment for mass treatment programs (>1 MM patients)

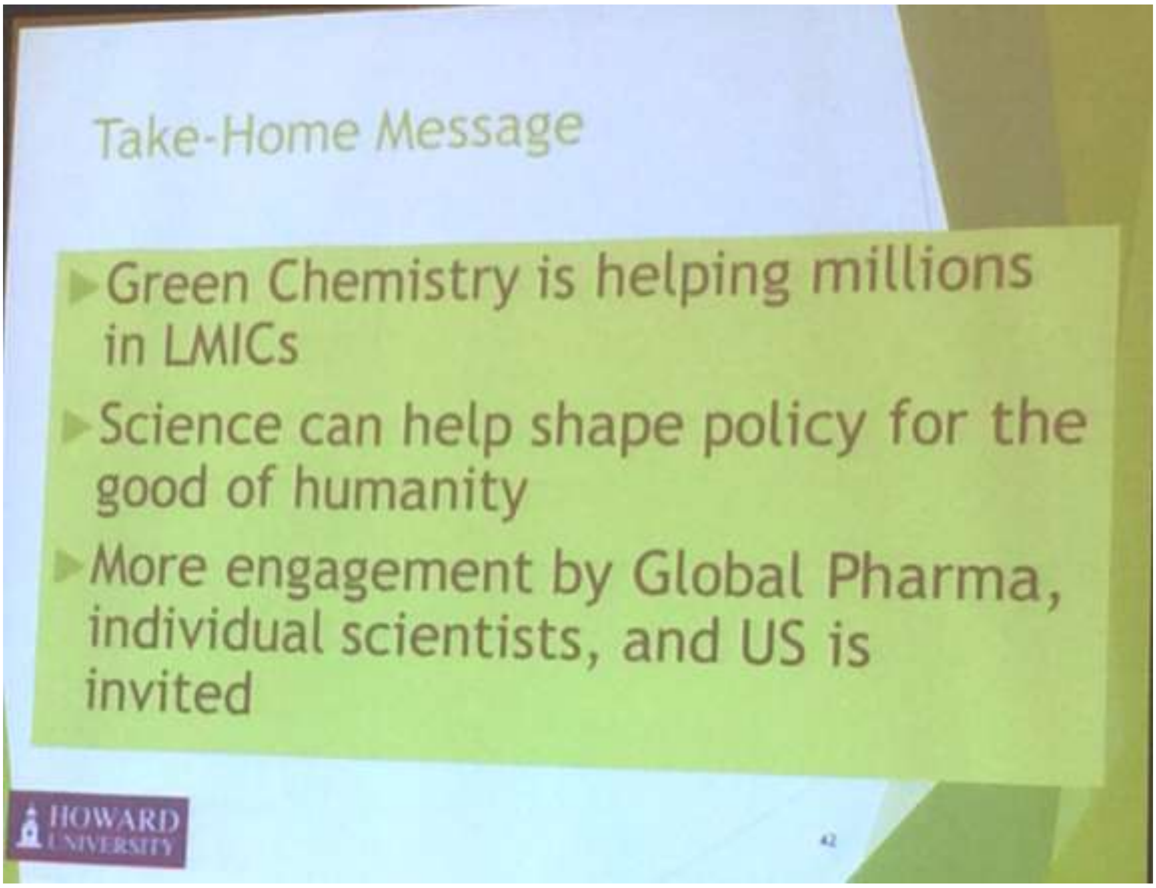
Sofosbuvir

Critical raw materials



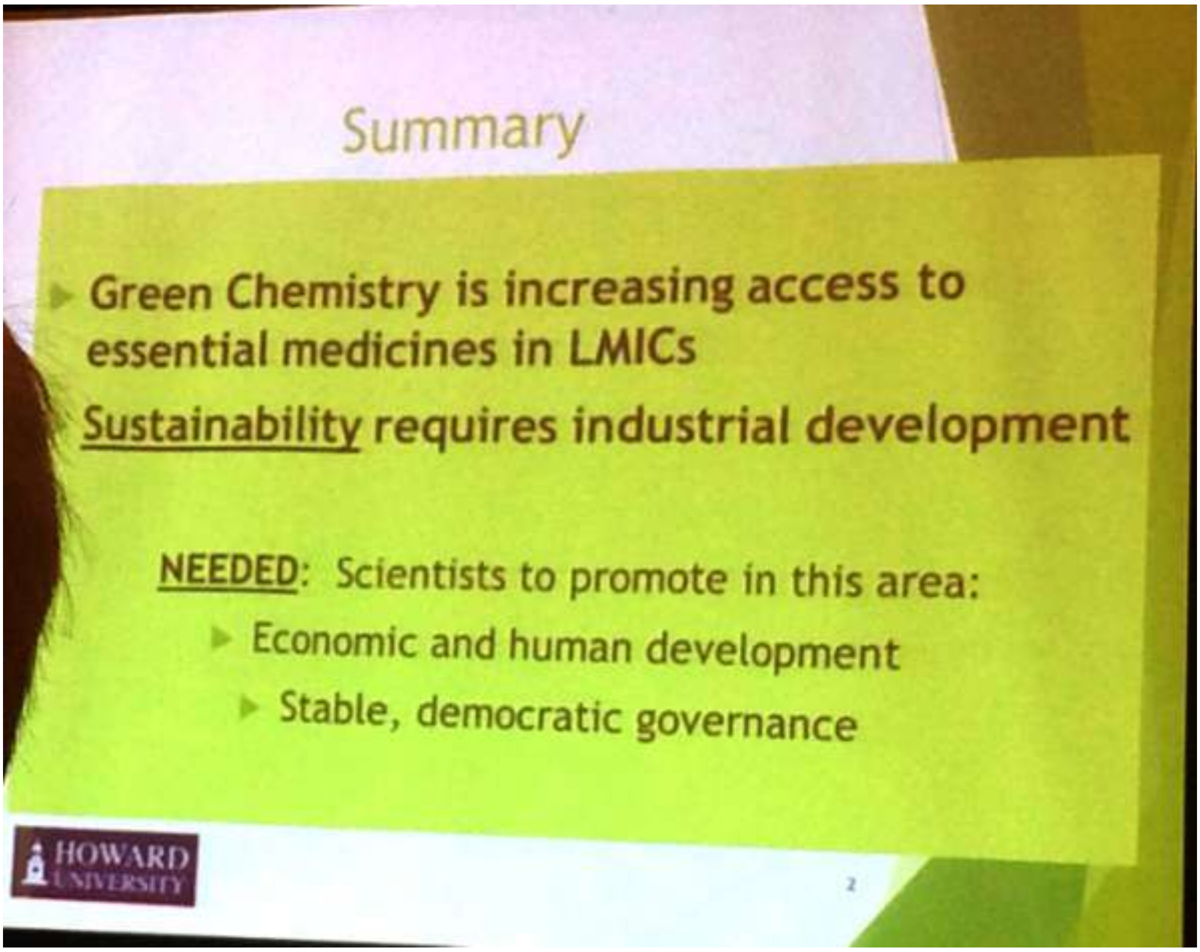
Take-Home Message

- Green Chemistry is helping millions in LMICs
- Science can help shape policy for the good of humanity
- More engagement by Global Pharma, individual scientists, and US is invited



Take-Home Message

- Green Chemistry is helping millions in LMICs
- Science can help shape policy for the good of humanity
- More engagement by Global Pharma, individual scientists, and US is invited



Summary

- **Green Chemistry is increasing access to essential medicines in LMICs**

Sustainability requires industrial development

NEEDED: Scientists to promote in this area:
  - Economic and human development
  - Stable, democratic governance

3.3.2 綠色化學與高等教育 (Green Chemistry in higher education)

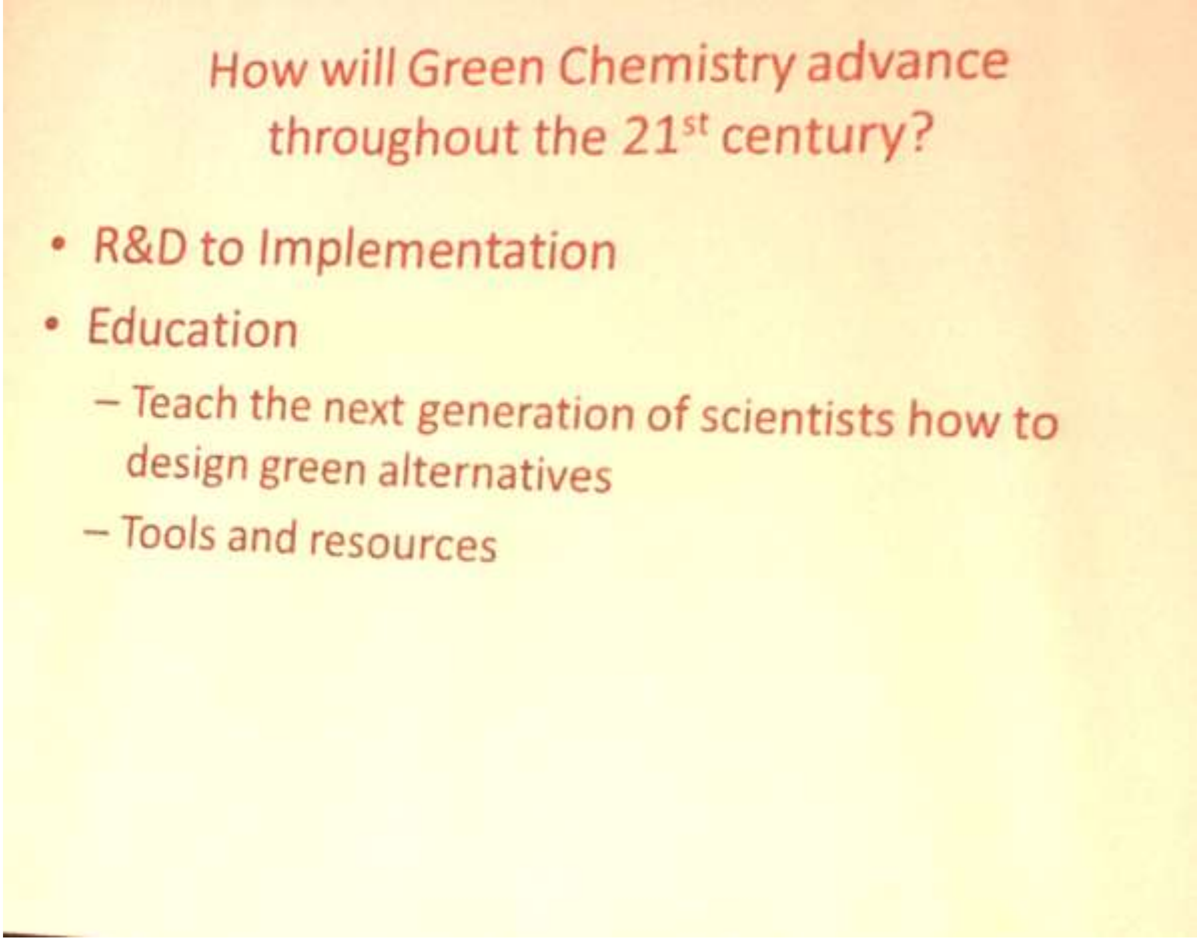
演講者：Amy S. Cannon, Ph.D.

機構名稱：Beyond Benign, USA

演講摘要：

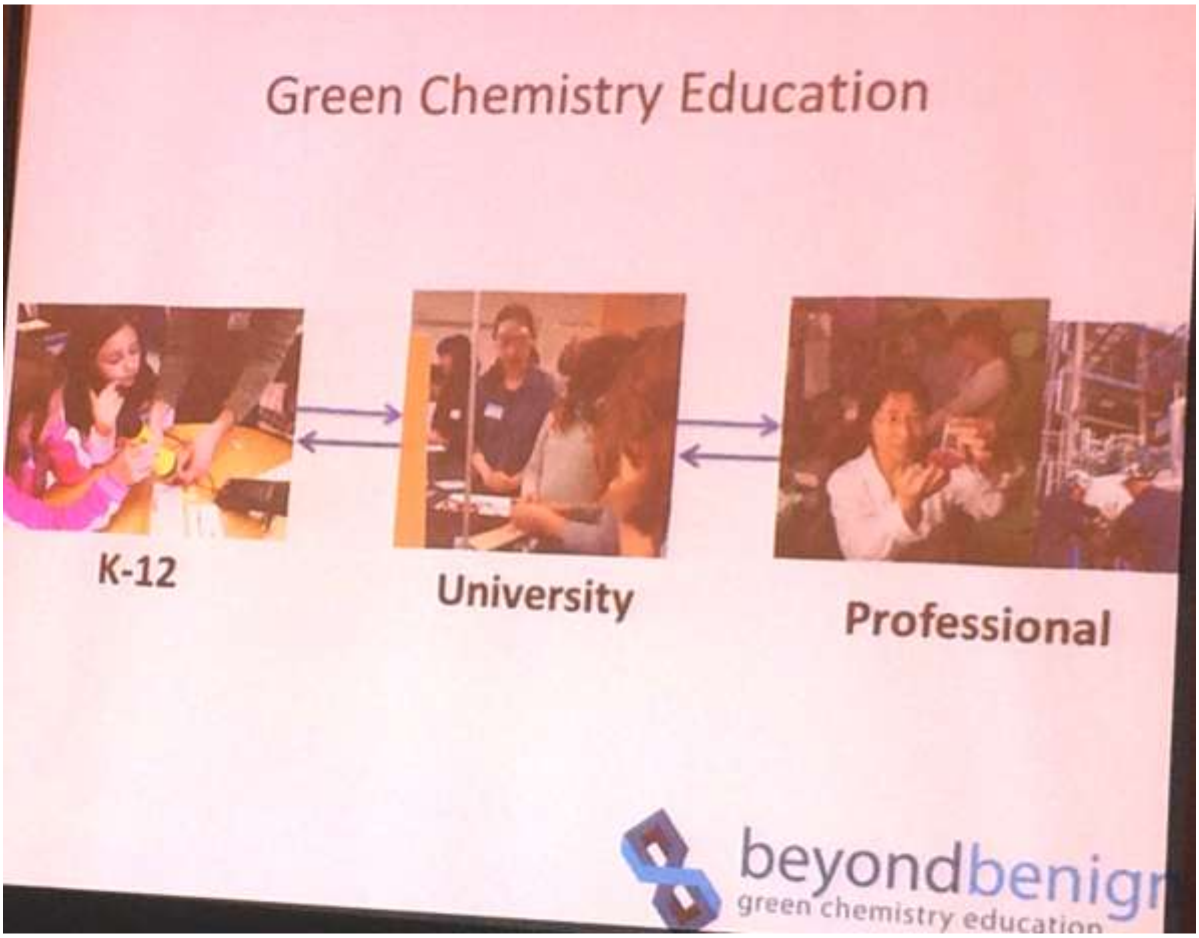
Cannon 博士為世界上第一位綠色化學博士，同時具有學界 (Assistant Professor and Director of Outreach and Community Education at the Center for Green Chemistry at UMass Lowell) 及業界經歷 (Analytical Chemist at Gillette Company and Scientist at Rohm and Hass Company)，以研究者身份投身教育工作，創立專為綠色化學教育設立的非營利組織「Beyond Benign」，針對美國 K-12 (約為高中以下) 及高等 (大專以上) 教育化學學科導入綠色化學的觀念。

Cannon 博士演講中指出，綠色化學涵蓋所有降低汙染及危險性的產品製造及設計，然而許多化學家在接受初等或高等教育時，往往忽略此概念，投入職場後也缺乏吸收相關知識的機會。為了培育未來具有綠色化學觀念的化學家，並為其投身職場做準備，整個教育系統必須有所改進。隨著環保及永續性概念逐步普及，未來從分子設計學家、化學家至工程師，都必須具有降低製程或產品汙染的基本常識，因此，由培訓具備綠色化學概念師資開始，Cannon 博士講解 Beyond Benign 機構大力推行的「綠色化學承諾計畫 (Green Chemistry Commitment Program)」，包含化學教師們所需的課程設計與教學方法等概念，期待下一代年輕科學家們，因為具有綠色化學背景，進入業界後，為人們設計更安全更永續的產品及製程。以下將報告內容重要投影片列出：



How will Green Chemistry advance throughout the 21st century?

- R&D to Implementation
- Education
  - Teach the next generation of scientists how to design green alternatives
  - Tools and resources

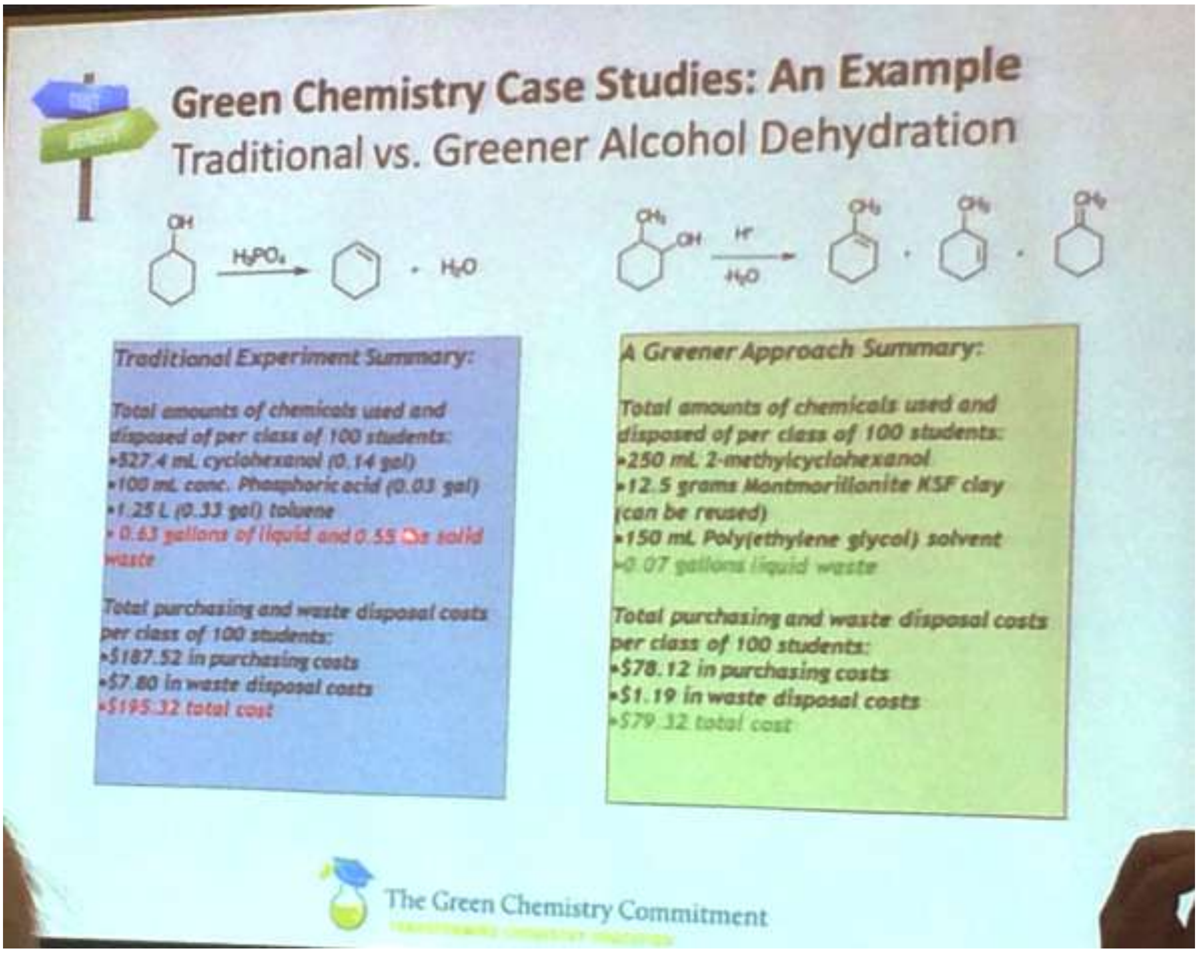


Green Chemistry Education

K-12

University

Professional



Green Chemistry Case Studies: An Example
Traditional vs. Greener Alcohol Dehydration

Traditional Experiment Summary:

Total amounts of chemicals used and disposed of per class of 100 students:
- *527.4 mL cyclohexanol (0.14 gal)*
- *100 mL conc. Phosphoric acid (0.03 gal)*
- *1.25 L (0.33 gal) toluene*
- *0.63 gallons of liquid and 0.55 [illegible] solid waste*

Total purchasing and waste disposal costs per class of 100 students:
- *$187.52 in purchasing costs*
- *$7.80 in waste disposal costs*
- *$195.32 total cost*

A Greener Approach Summary:

Total amounts of chemicals used and disposed of per class of 100 students:
- *250 mL 2-methylcyclohexanol*
- *12.5 grams Montmorillonite KSF clay (can be reused)*
- *150 mL Poly(ethylene glycol) solvent*
- *0.07 gallons liquid waste*

Total purchasing and waste disposal costs per class of 100 students:
- *$78.12 in purchasing costs*
- *$1.19 in waste disposal costs*
- *$79.32 total cost*

The Green Chemistry Commitment

3.3.3 加氫催化實務 (Practical catalytic hydrogenation)

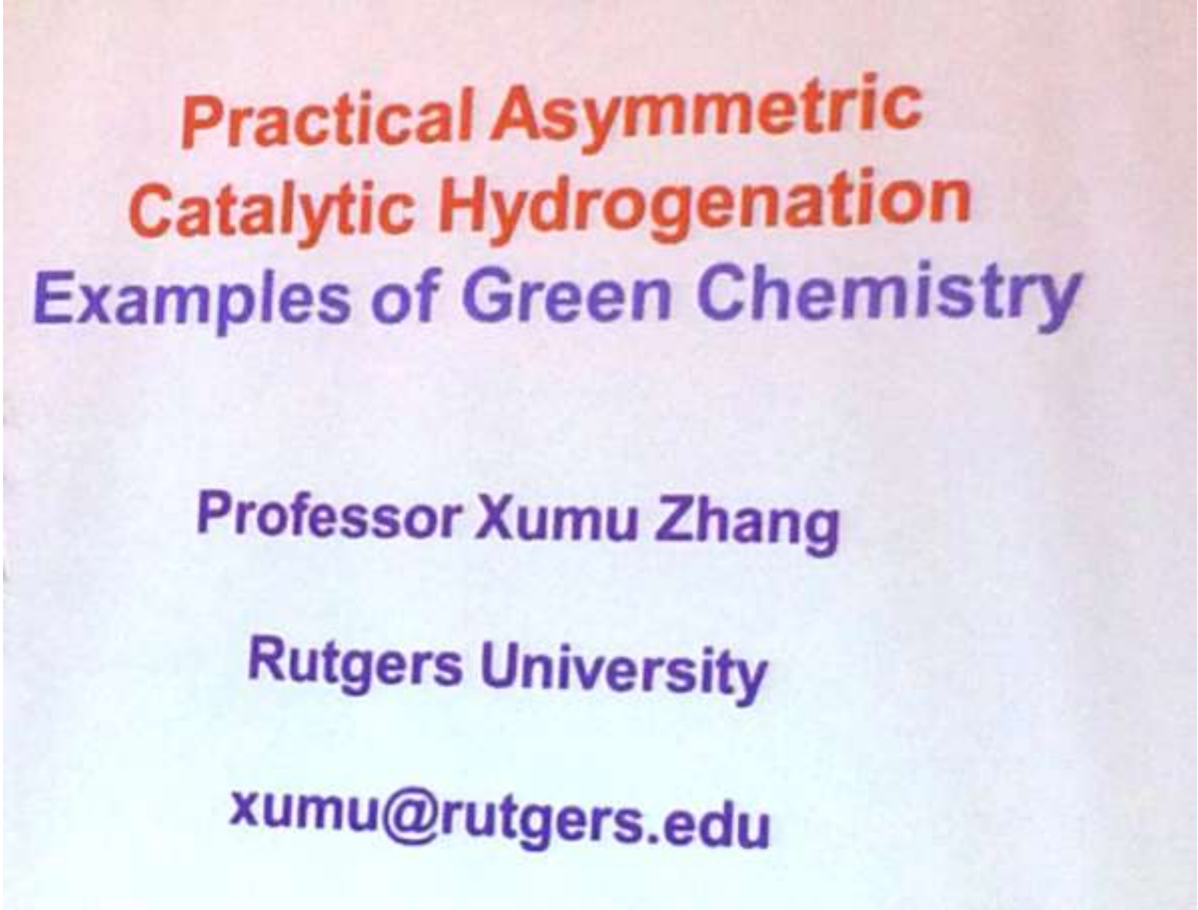
演講者：Xumu Zhang, Ph.D. (張緒穆博士)

機構名稱：Rutgers, The State University of New Jersey, USA

演講摘要：

張博士主要研究領域為非對稱催化 (Asymmetric catalyst)，利用有機合成、無機合成、金屬有機化學、過渡金屬元素催化並產生具生物活性化合物，原在賓州州立大學化學系任職並升至教授，現為紐澤西州立羅格斯大學教授。

張教授以 2001 年諾貝爾獎得主 William Knowles 在 1960~1970 年間，關於非對稱加氫催化研究開場，說明該領域 40 年來進步之處與尚待研究的項目，隨後張教授說明該團隊如何將非對稱加氫研究，由實驗室放大至工業級規模。由於非對稱催化技術應用廣泛，包括不同藥物光學異構物等，因此被稱為新世代催化技術 (next generation catalyst)。以下將報告內容重要投影片列出：

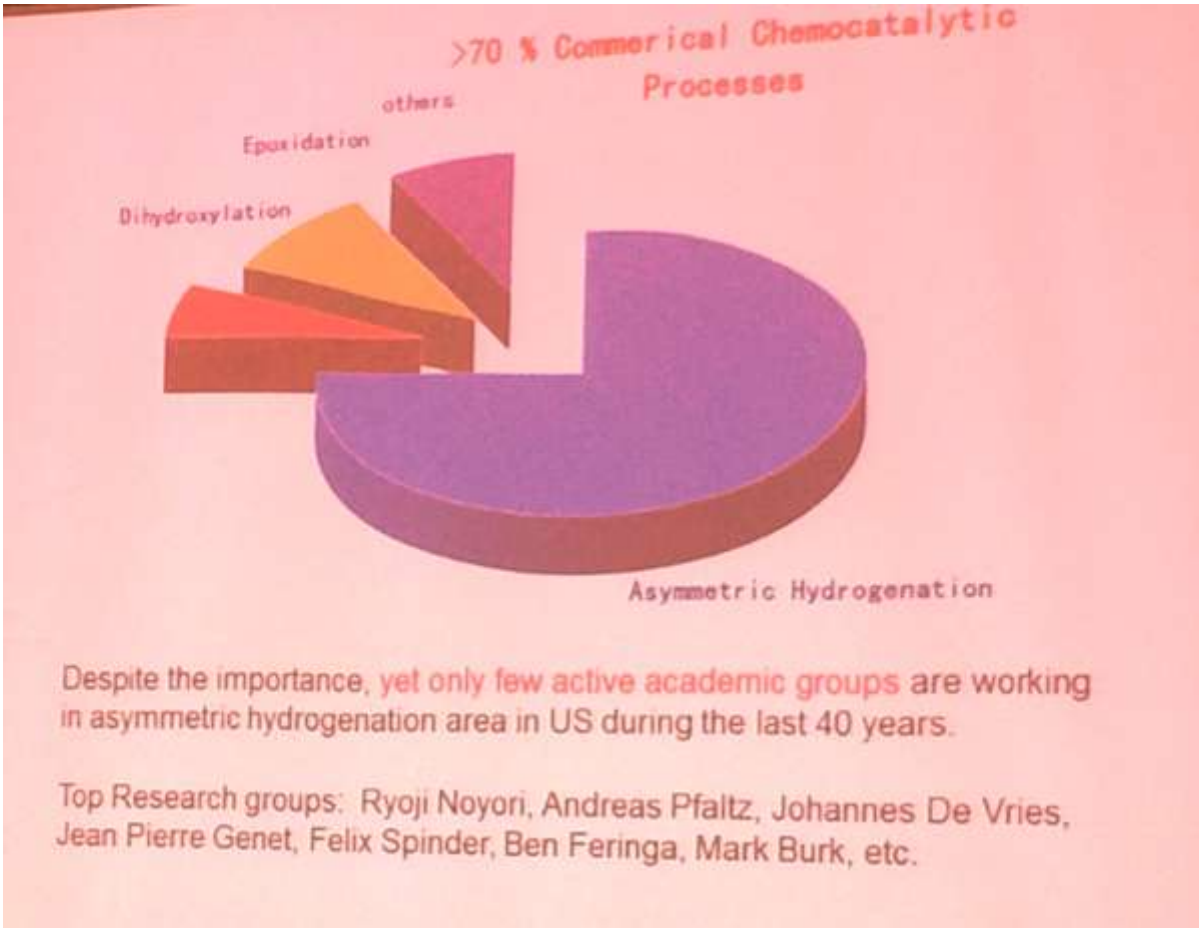


Practical Asymmetric Catalytic Hydrogenation
Examples of Green Chemistry

Professor Xumu Zhang

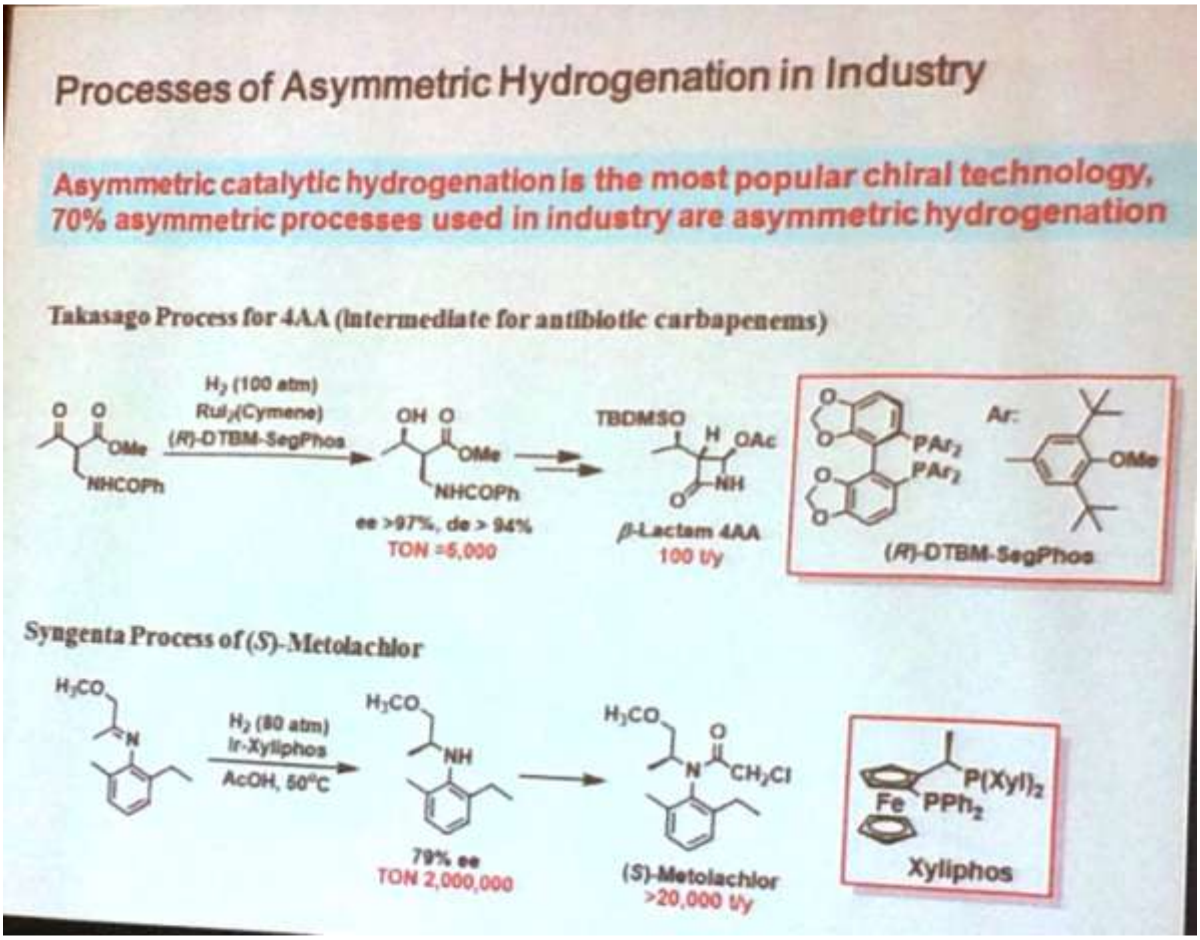
Rutgers University

xumu@rutgers.edu



Despite the importance, yet only few active academic groups are working in asymmetric hydrogenation area in US during the last 40 years.

Top Research groups: Ryoji Noyori, Andreas Pfaltz, Johannes De Vries, Jean Pierre Genet, Felix Spinder, Ben Feringa, Mark Burk, etc.

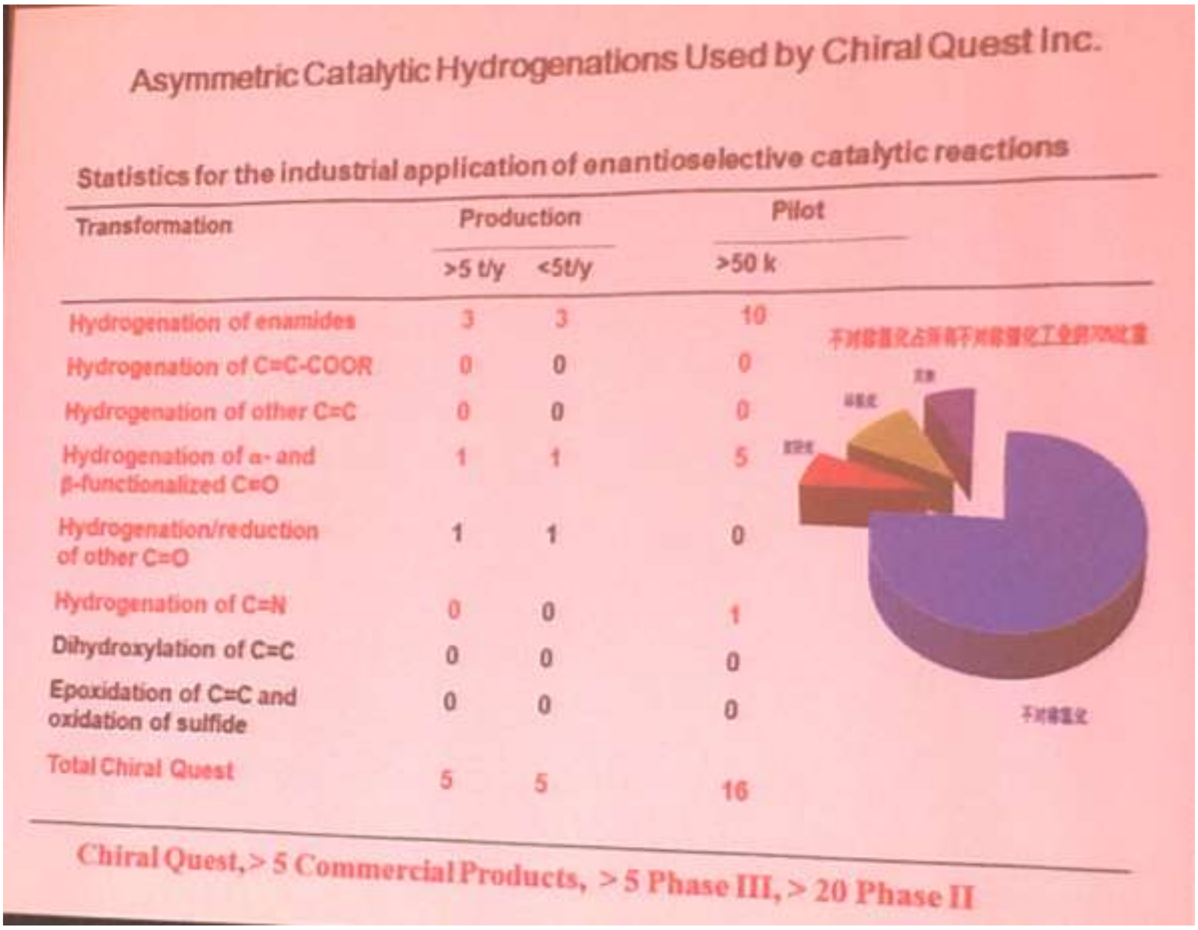


Processes of Asymmetric Hydrogenation in Industry

Asymmetric catalytic hydrogenation is the most popular chiral technology, 70% asymmetric processes used in industry are asymmetric hydrogenation

Takasago Process for 4AA (intermediate for antibiotic carbapenems)

Syngenta Process of (*S*)-Metolachlor

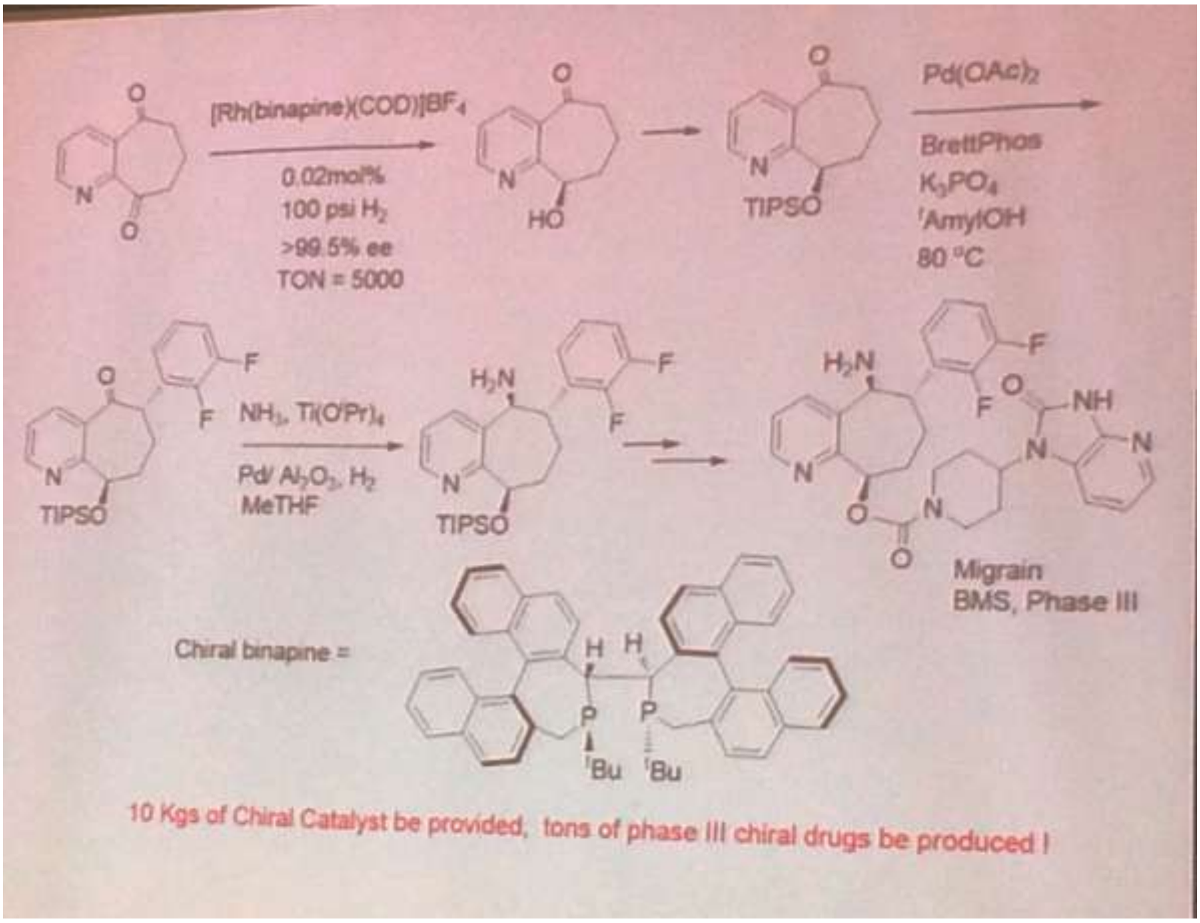


Asymmetric Catalytic Hydrogenations Used by Chiral Quest Inc.

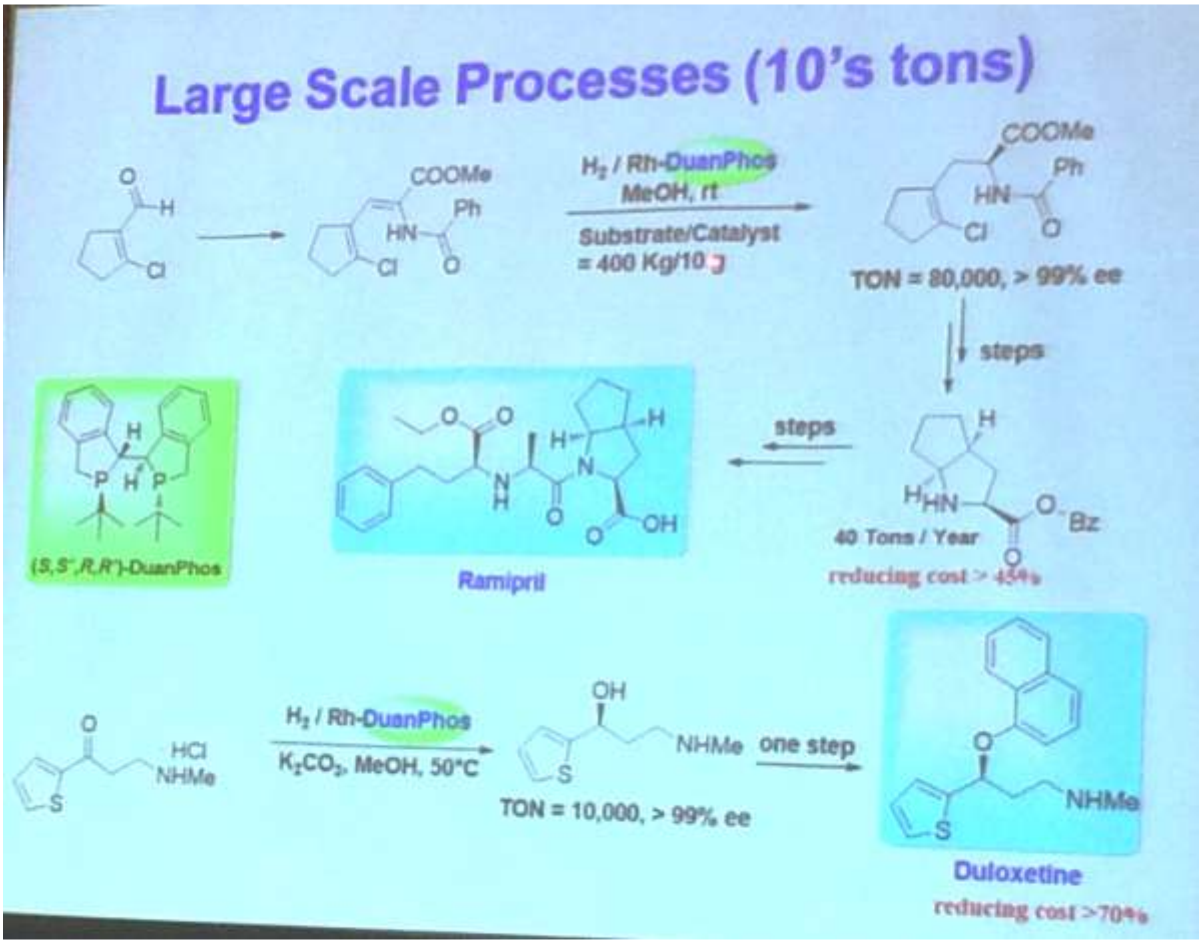
Statistics for the industrial application of enantioselective catalytic reactions

Transformation	Production		Pilot
	>5 t/y	<5t/y	>50 k
Hydrogenation of enamides	3	3	10
Hydrogenation of C=C-COOR	0	0	0
Hydrogenation of other C=C	0	0	0
Hydrogenation of α- and β-functionalized C=O	1	1	5
Hydrogenation/reduction of other C=O	1	1	0
Hydrogenation of C=N	0	0	1
Dihydroxylation of C=C	0	0	0
Epoxidation of C=C and oxidation of sulfide	0	0	0
Total Chiral Quest	5	5	16

Chiral Quest, > 5 Commercial Products, > 5 Phase III, > 20 Phase II



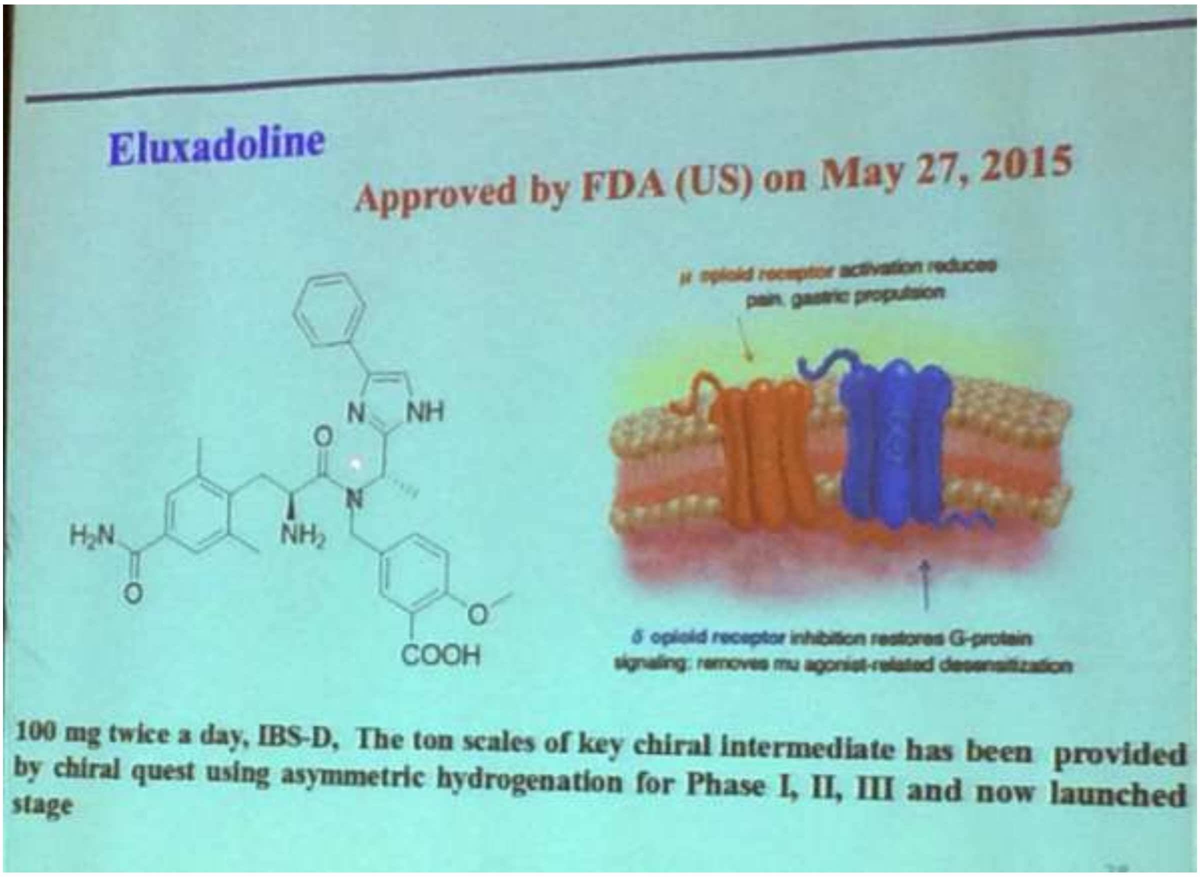
10 Kgs of Chiral Catalyst be provided, tons of phase III chiral drugs be produced !



Large Scale Processes (10's tons)

reducing cost > 45%

reducing cost >70%



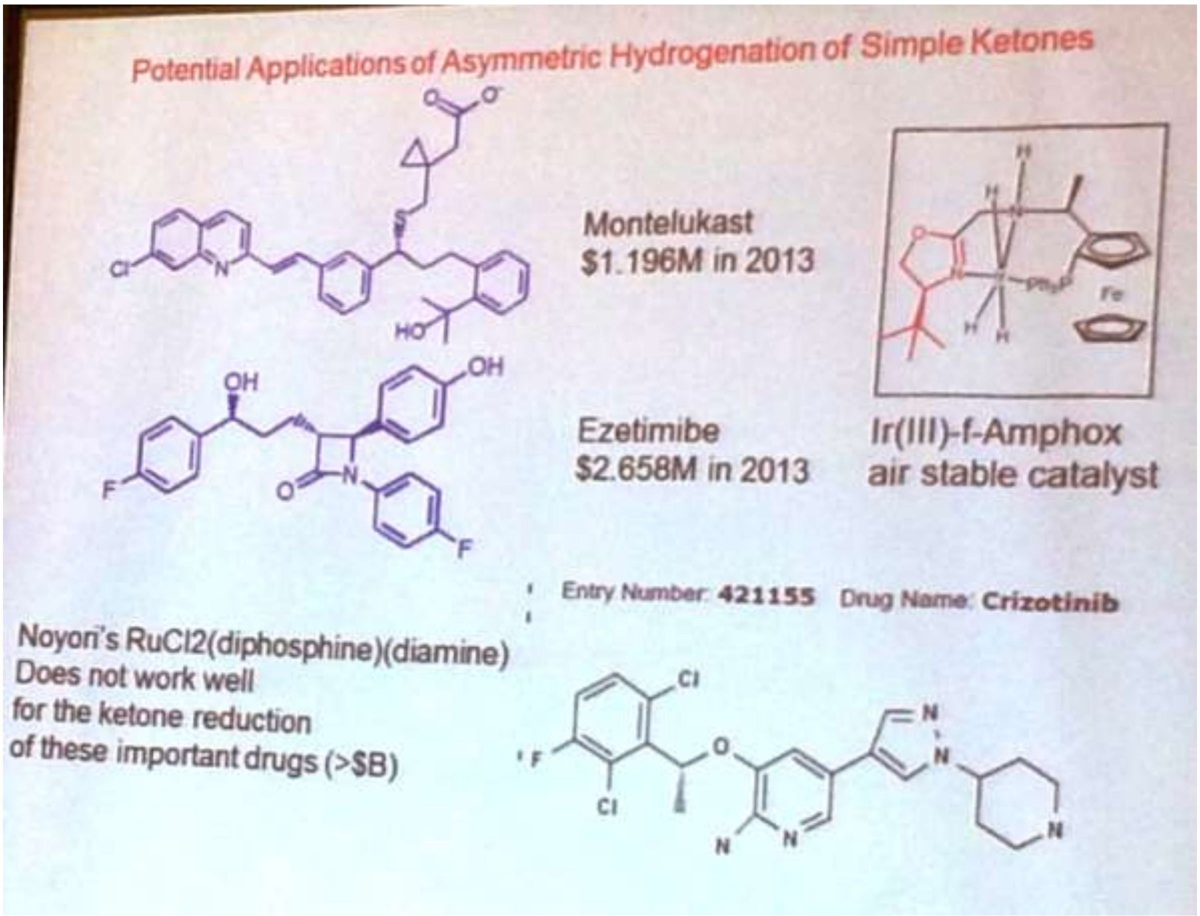
Eluxadoline

Approved by FDA (US) on May 27, 2015

μ opioid receptor activation reduces pain, gastric propulsion

δ opioid receptor inhibition restores G-protein signaling; removes mu agonist-related desensitization

100 mg twice a day, IBS-D, The ton scales of key chiral intermediate has been provided by chiral quest using asymmetric hydrogenation for Phase I, II, III and now launched stage



Potential Applications of Asymmetric Hydrogenation of Simple Ketones

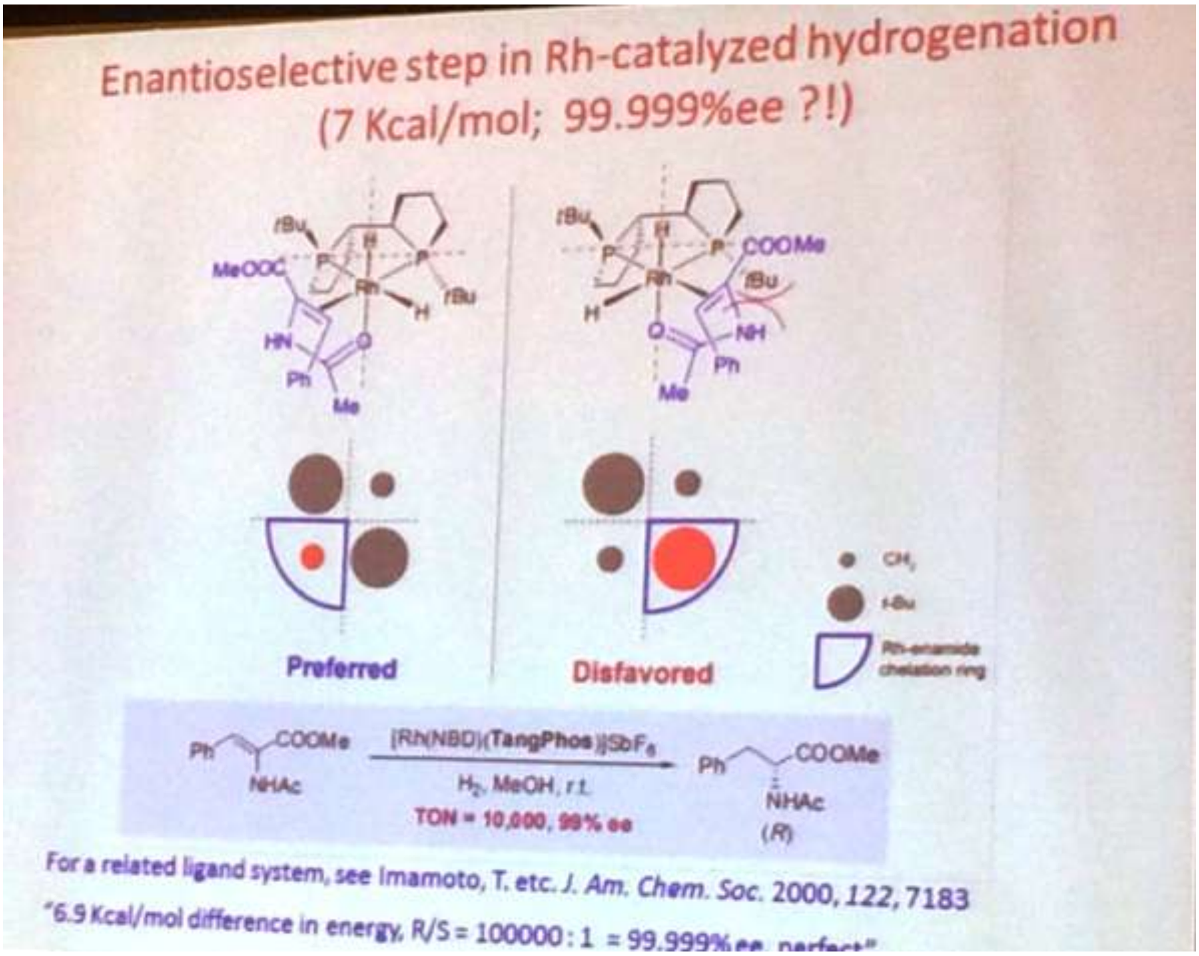
Montelukast
\$1.196M in 2013

Ezetimibe
\$2.658M in 2013

Ir(III)-f-Amphox
air stable catalyst

Entry Number: **421155** Drug Name: **Crizotinib**

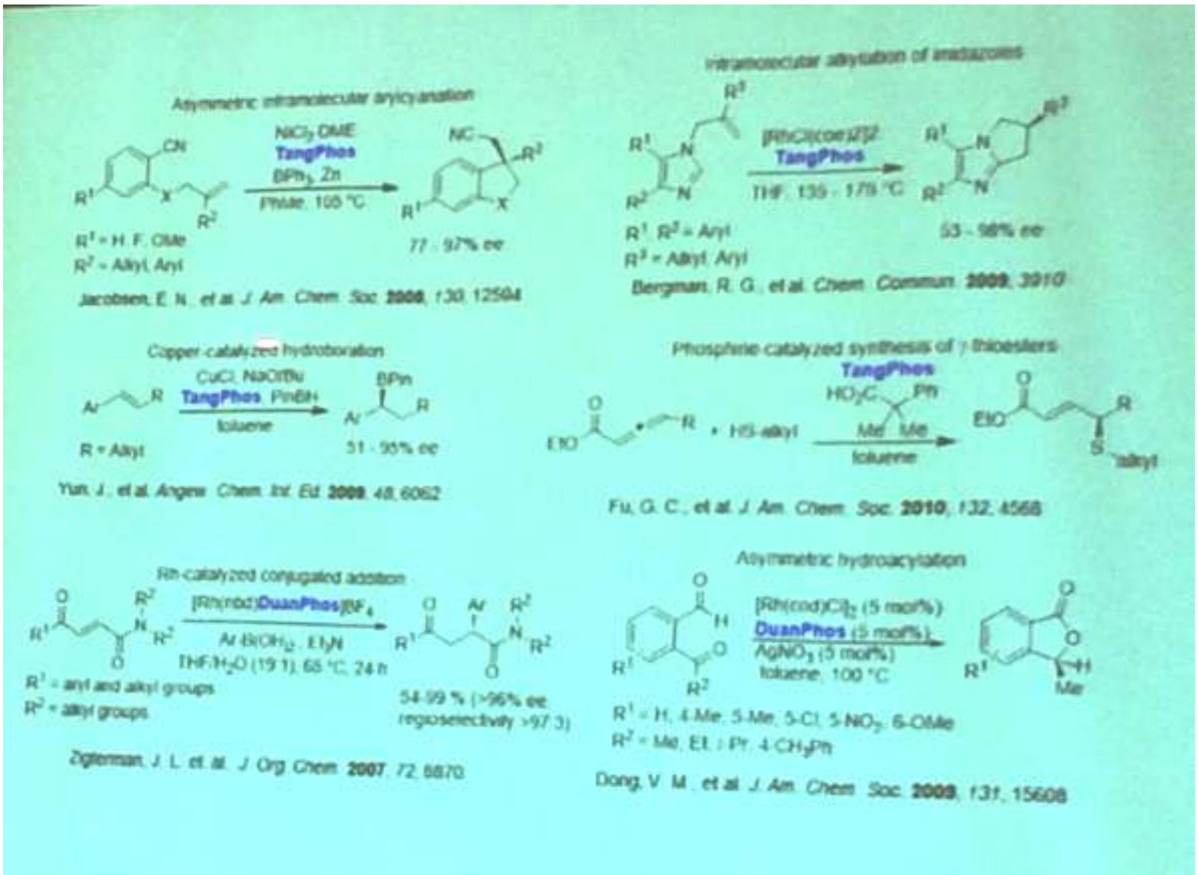
Noyori's RuCl2(diphosphine)(diamine)
Does not work well
for the ketone reduction
of these important drugs (>\$B)



Enantioselective step in Rh-catalyzed hydrogenation (7 Kcal/mol; 99.999%ee ?!)

For a related ligand system, see Imamoto, T. etc. *J. Am. Chem. Soc.* 2000, *122*, 7183

"6.9 Kcal/mol difference in energy, R/S = 100000 : 1 = 99.999%ee, perfect"



Asymmetric intramolecular arylcyanation

Jacobsen, E. N., et al. *J. Am. Chem. Soc.* **2008**, *130*, 12594

Intramolecular alkylation of imidazoles

Bergman, R. G., et al. *Chem. Commun.* **2009**, *3010*

Copper-catalyzed hydroboration

Yun, J., et al. *Angew. Chem. Int. Ed.* **2009**, *48*, 6062

Phosphine catalyzed synthesis of γ-thioesters

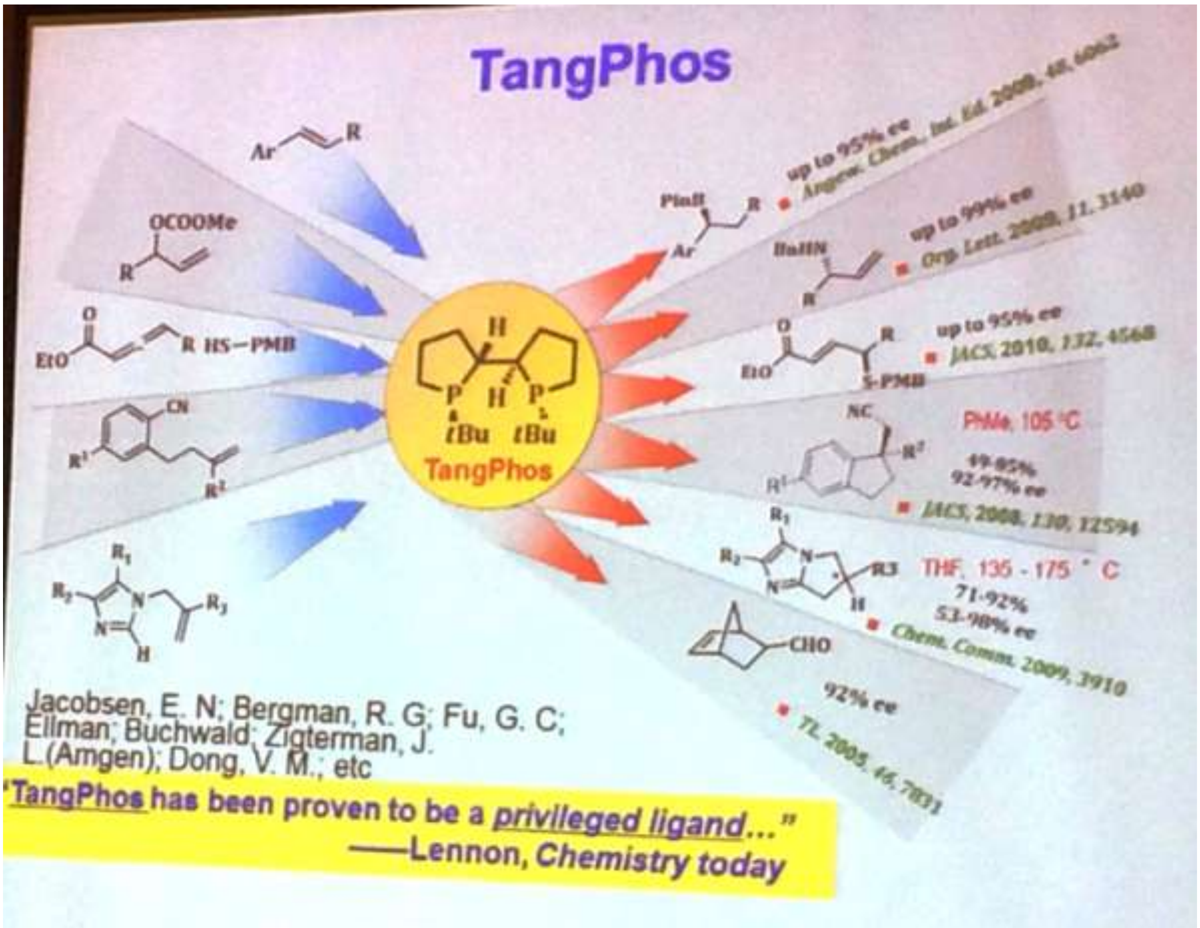
Fu, G. C., et al. *J. Am. Chem. Soc.* **2010**, *132*, 4568

Rh-catalyzed conjugated addition

Zigterman, J. L. et al. *J. Org. Chem.* **2007**, *72*, 8870

Asymmetric hydroacylation

Dong, V. M., et al. *J. Am. Chem. Soc.* **2009**, *131*, 15608



TangPhos

TangPhos

up to 95% ee
Angew. Chem., Int. Ed. 2009, 48, 6062

up to 99% ee
Org. Lett. 2009, 11, 3140

up to 95% ee
JACS, 2010, 132, 4568

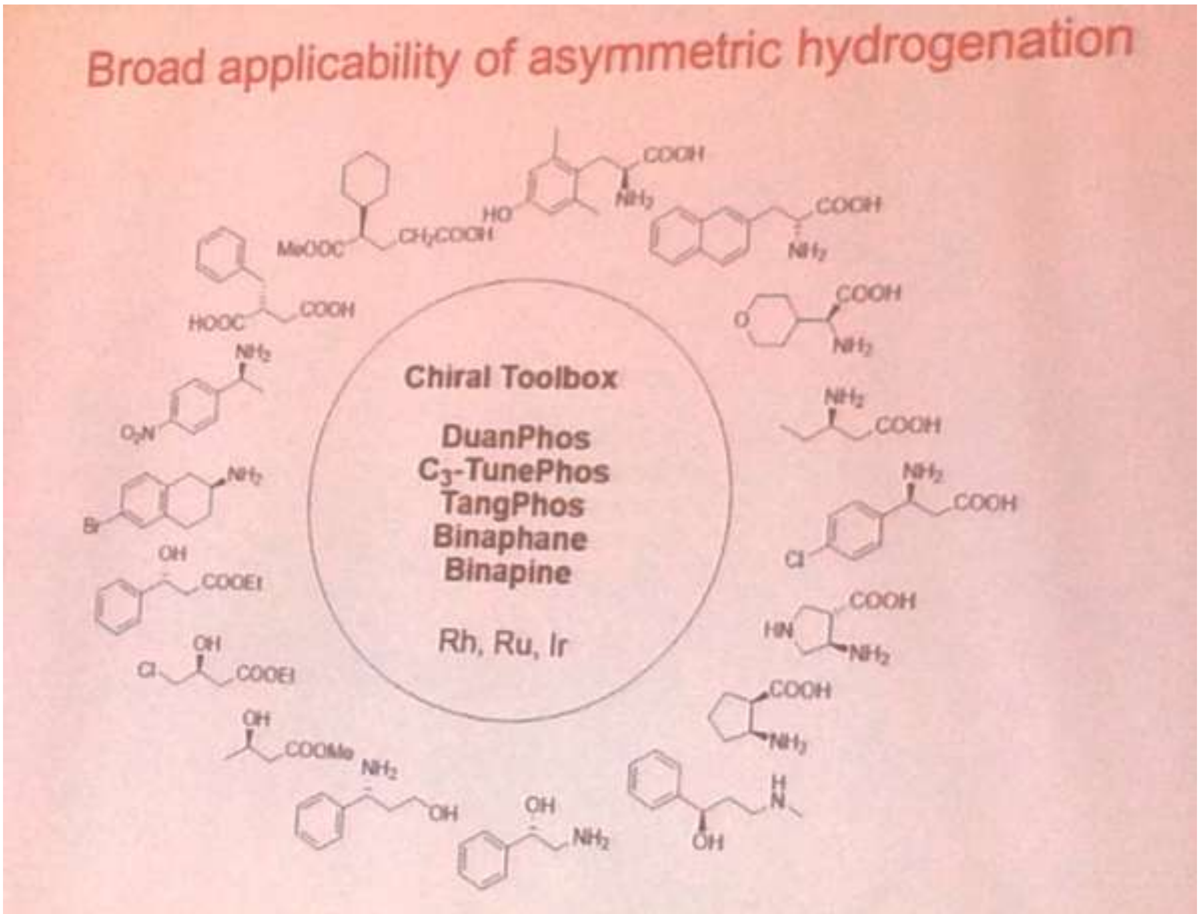
PhMe, 105 °C
49-85%
92-97% ee
JACS, 2008, 130, 12594

THF, 135 - 175 ° C
71-92%
53-98% ee
Chem. Comm. 2009, 3910

92% ee
TL 2005, 46, 7831

Jacobsen, E. N; Bergman, R. G; Fu, G. C;
Ellman; Buchwald; Zigterman, J.
L.(Amgen); Dong, V. M., etc

"**TangPhos** has been proven to be a ***privileged ligand***…"
—Lennon, *Chemistry today*

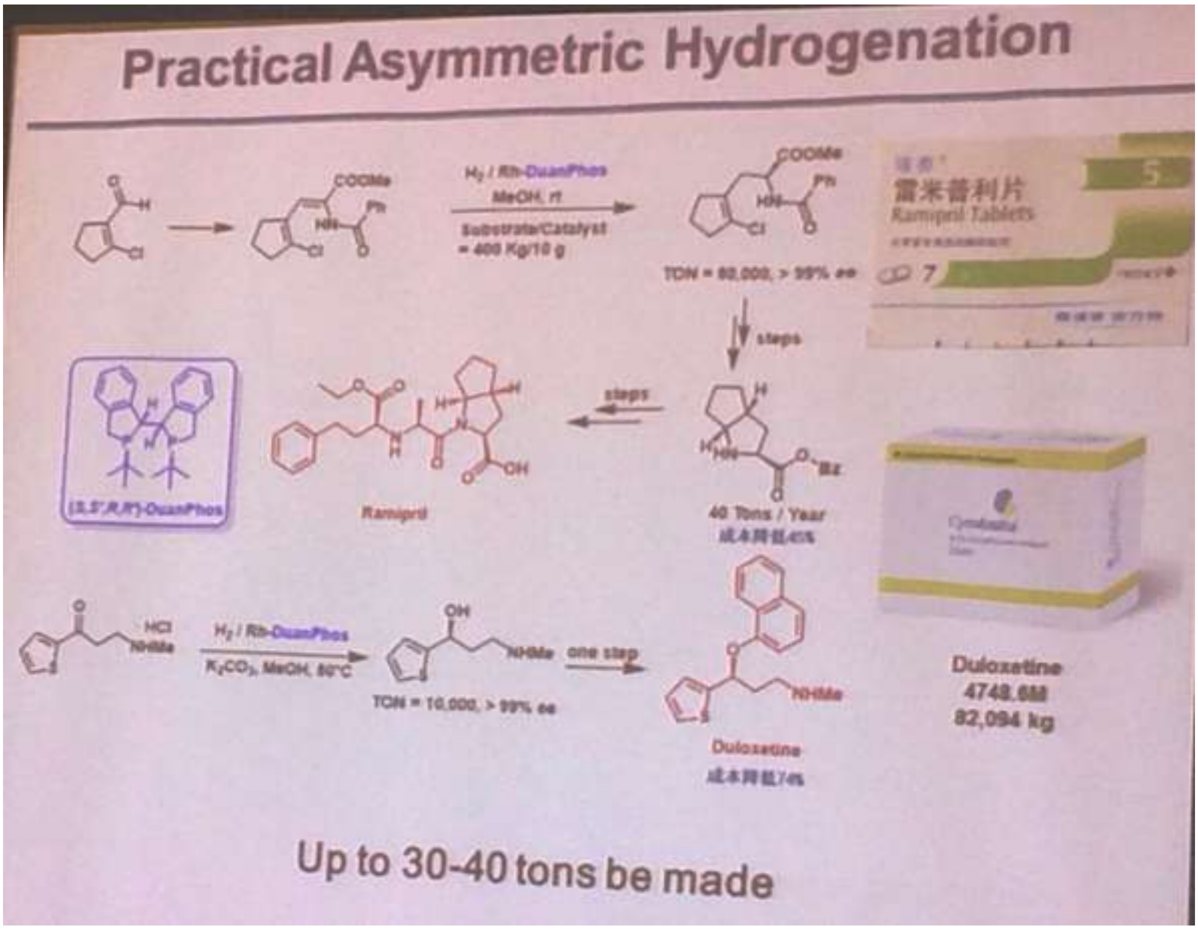


Broad applicability of asymmetric hydrogenation

Chiral Toolbox

DuanPhos
C_3-TunePhos
TangPhos
Binaphane
Binapine

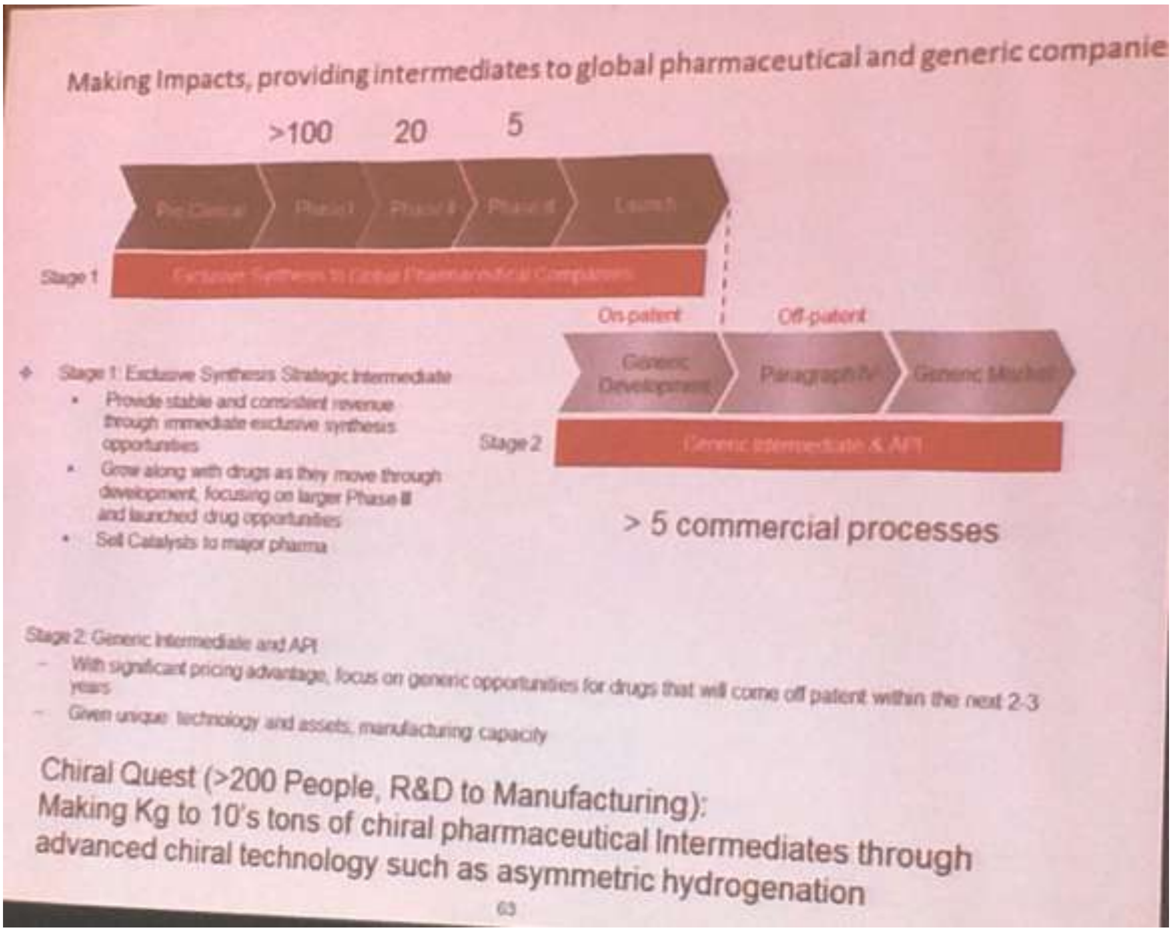
Rh, Ru, Ir



Practical Asymmetric Hydrogenation

Duloxetine
4748.6M
82,094 kg

Up to 30-40 tons be made



Making Impacts, providing intermediates to global pharmaceutical and generic companie

>100 20 5

Pre Clinical › Phase I › Phase II › Phase III › Launch

Stage 1 Exclusive Synthesis to Global Pharmaceutical Companies

On patent | Off-patent

Generic Development › Paragraph IV › Generic Market

Stage 2 Generic Intermediate & API

- Stage 1: Exclusive Synthesis Strategic Intermediate
  - Provide stable and consistent revenue through immediate exclusive synthesis opportunities
  - Grow along with drugs as they move through development, focusing on larger Phase III and launched drug opportunities
  - Sell Catalysis to major pharma

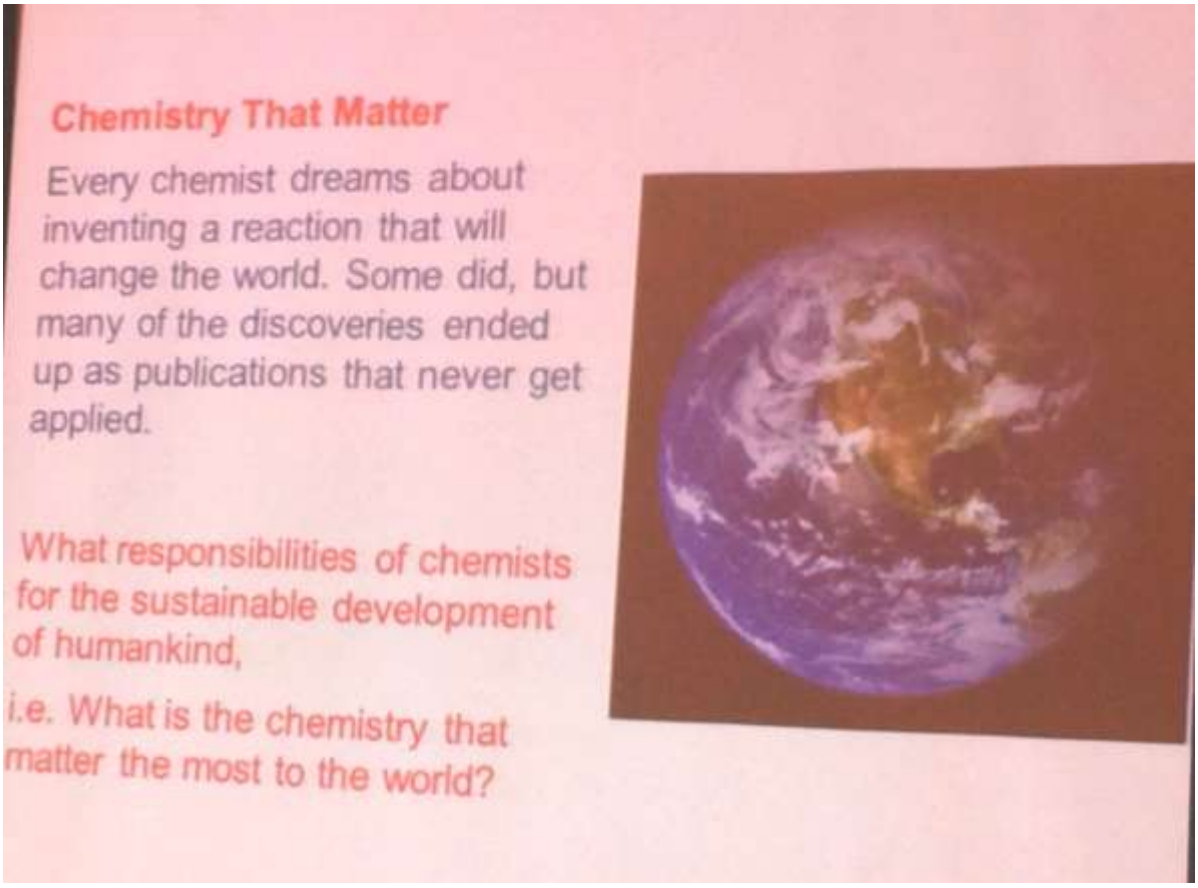
> 5 commercial processes

Stage 2: Generic Intermediate and API

- With significant pricing advantage, focus on generic opportunities for drugs that will come off patent within the next 2-3 years
- Given unique technology and assets, manufacturing capacity

Chiral Quest (>200 People, R&D to Manufacturing):
Making Kg to 10's tons of chiral pharmaceutical Intermediates through advanced chiral technology such as asymmetric hydrogenation

63



Chemistry That Matter

Every chemist dreams about inventing a reaction that will change the world. Some did, but many of the discoveries ended up as publications that never get applied.

What responsibilities of chemists for the sustainable development of humankind,

i.e. What is the chemistry that matter the most to the world?

3.3.4 二價銅離子與雙噁唑啉錯合物作為非對稱異質催化劑之應用研究 (Asymmetric heterogeneous catalysts based on copper(II) complexes with bis(oxazoline) ligands)

演講者：Ana Rosa Silva, Ph.D.

機構名稱：Aveiro University, Portugal

演講摘要：

Silva 博士致力於非對稱異質催化、綠色化學、同質/異質液相氧化催化技術等研究。催化劑的利用具有分子經濟效益 (atom economic, 為綠色化學 12 項原則之一) 且可降低成本，因此也屬於綠色化學分支之一；非對稱催化具有使用極少量適當對掌性催化劑 (chiral catalyst) 即可獲得大量高鏡像純度 (enantiopure) 化合物之特性。雙噁唑啉 (bis(oxazoline)) 為非對稱催化反應中常用對掌性催化劑之一，利用其與過渡元素錯合物的不同組合，可以催化具有

高度鏡像選擇性的反應，得到高鏡像純度化合物。其中又以二價銅離子對於烯烴類環丙烷化 (cyclopropanation) 及氮丙啶化 (aziridination) 以及二醇類 (1,2-diol) 反應動力學上解析度 (kinetic resolution) 具有高催化效果；然而，其缺點為價格昂貴，因此許多研究者致力於發展可回收並重覆使用的此類觸媒。Silva 博士藉由共價修飾方式將觸媒固定化，測試不同多孔性材料對於觸媒穩定性及催化活性之差異。以下將報告內容重要投影片列出：

university of aveiro
theoria poiesis praxis

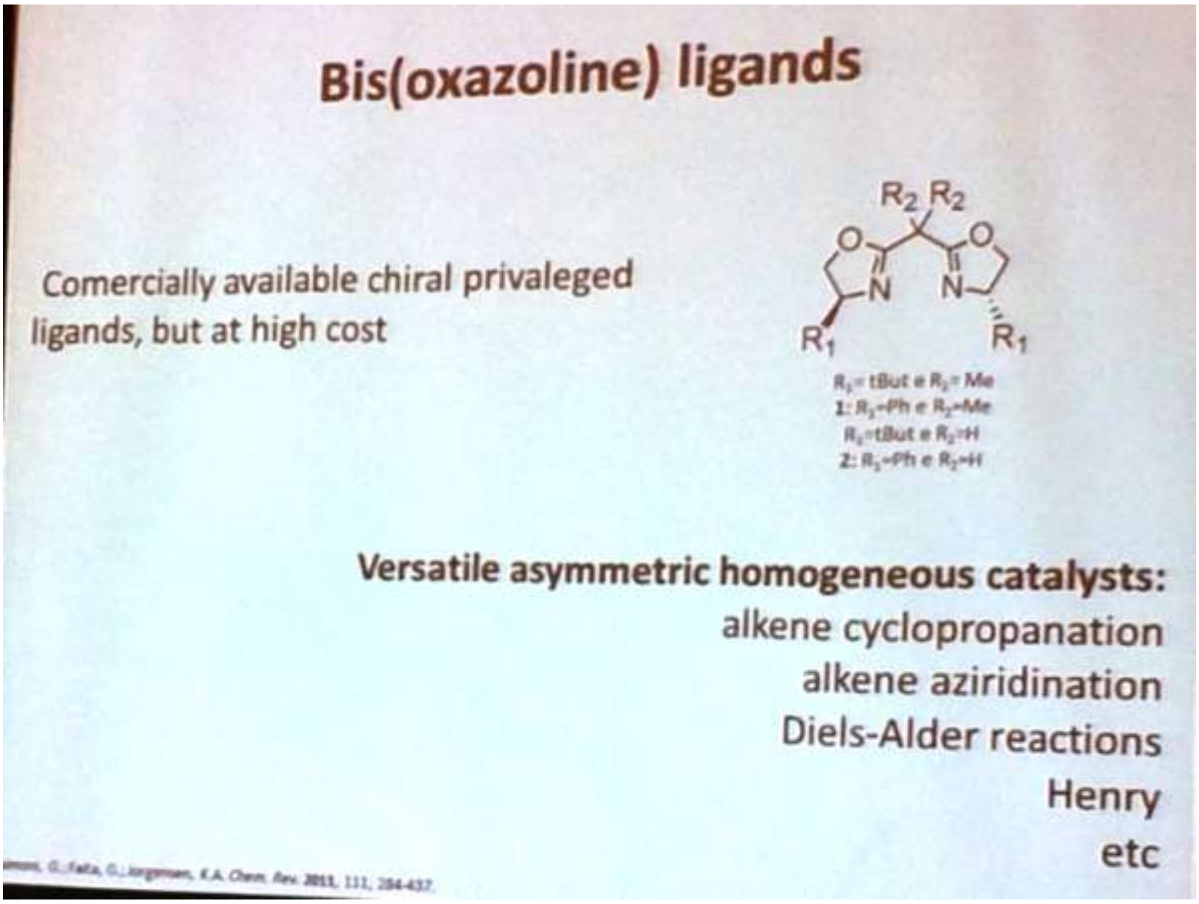
ciceco
centre for research in ceramics & composite materials

FACULDADE
DE CIÊNCIAS

Asymmetric heterogeneous catalysts based on copper(II) complexes with bis(oxazoline) ligands

Ana Rosa Silva

Department of Chemistry, CICECO, University of Aveiro, Portugal



Bis(oxazoline) ligands

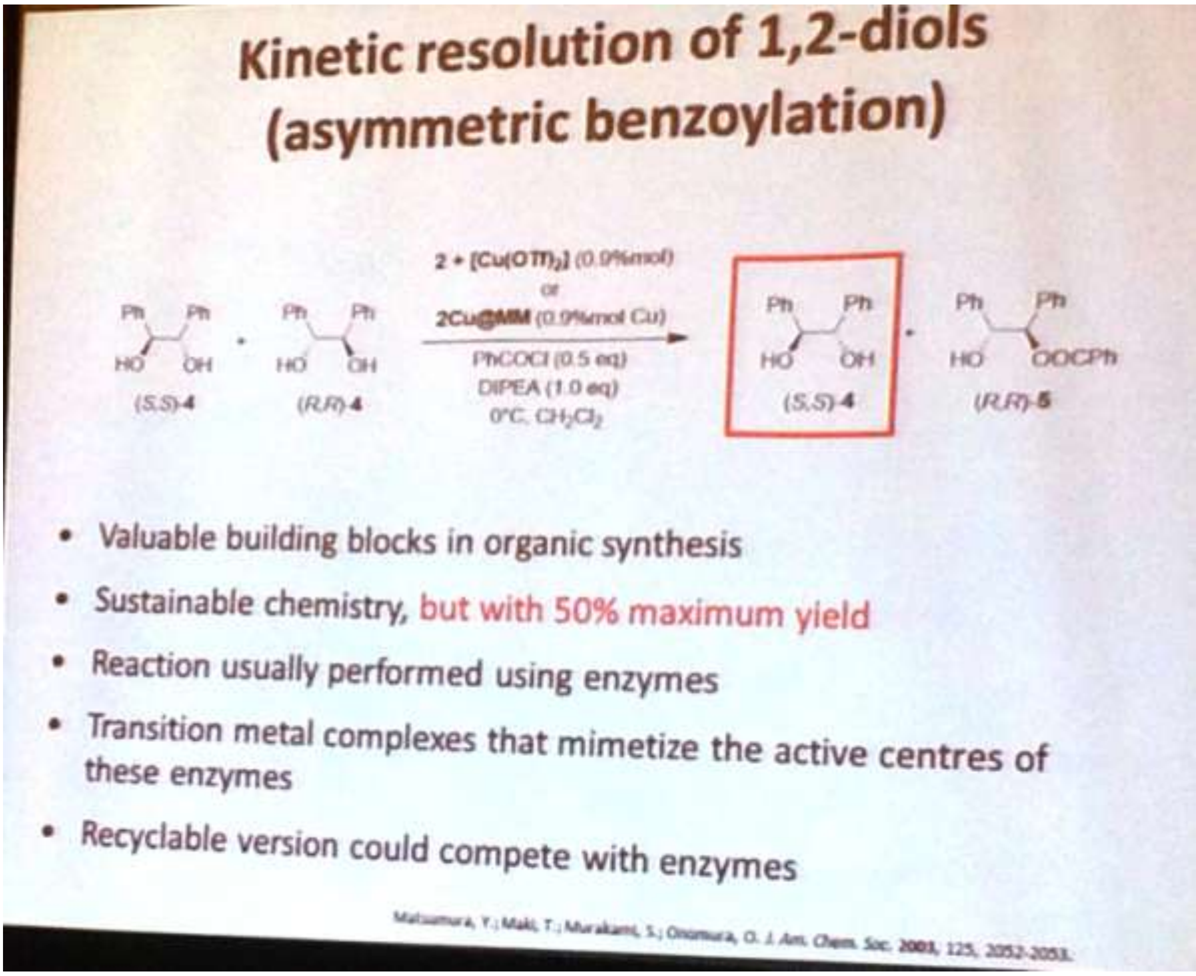
Comercially available chiral privaleged ligands, but at high cost

R_1 = tBut e R_2 = Me
1: R_1=Ph e R_2=Me
R_1=tBut e R_2=H
2: R_1=Ph e R_2=H

Versatile asymmetric homogeneous catalysts:

alkene cyclopropanation
alkene aziridination
Diels-Alder reactions
Henry
etc

G.; Faita, G.; Jorgensen, K.A. *Chem. Rev.* **2011**, 111, 284-437.

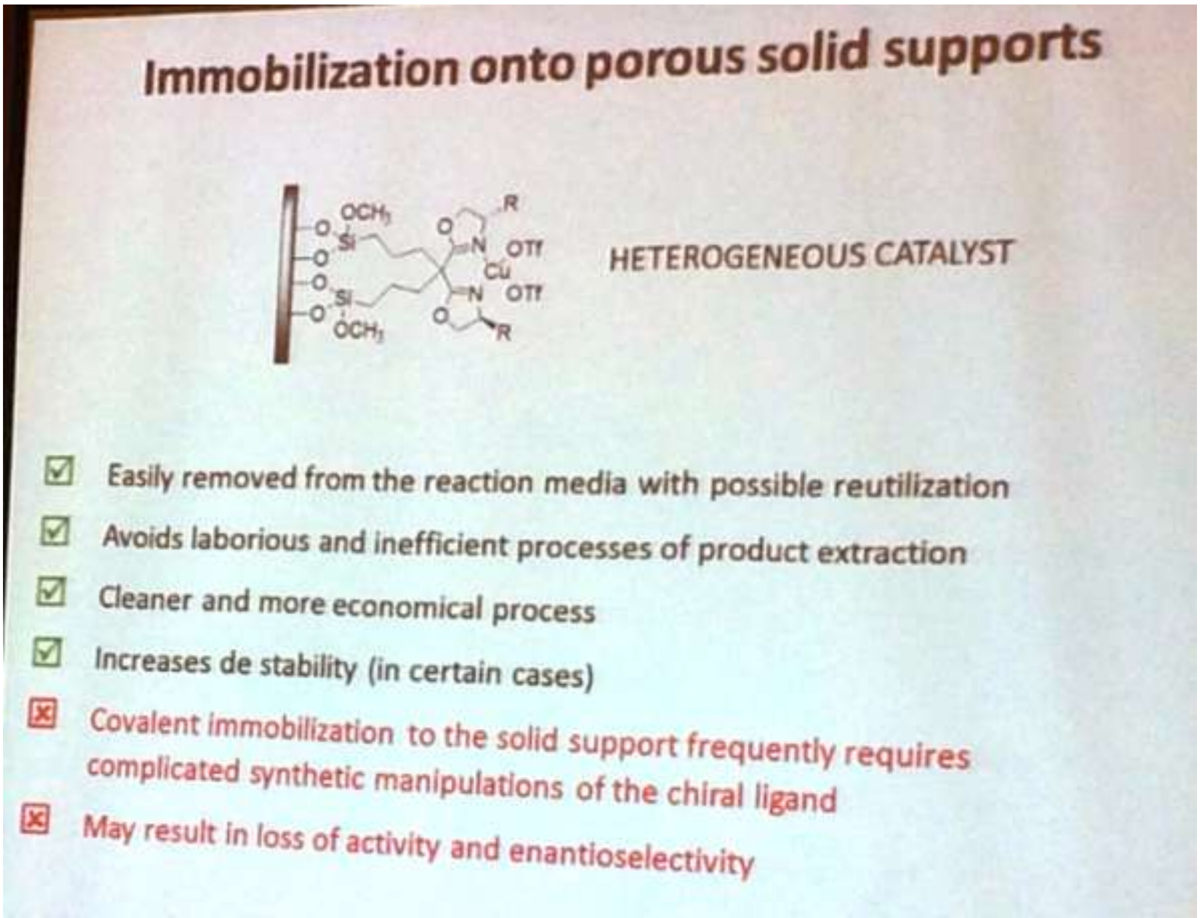


Kinetic resolution of 1,2-diols (asymmetric benzoylation)

2 + $[Cu(OTf)_2]$ (0.9%mol)
or
2Cu@MM (0.9%mol Cu)
PhCOCl (0.5 eq)
DIPEA (1.0 eq)
0°C, CH_2Cl_2

- Valuable building blocks in organic synthesis
- Sustainable chemistry, but with 50% maximum yield
- Reaction usually performed using enzymes
- Transition metal complexes that mimetize the active centres of these enzymes
- Recyclable version could compete with enzymes

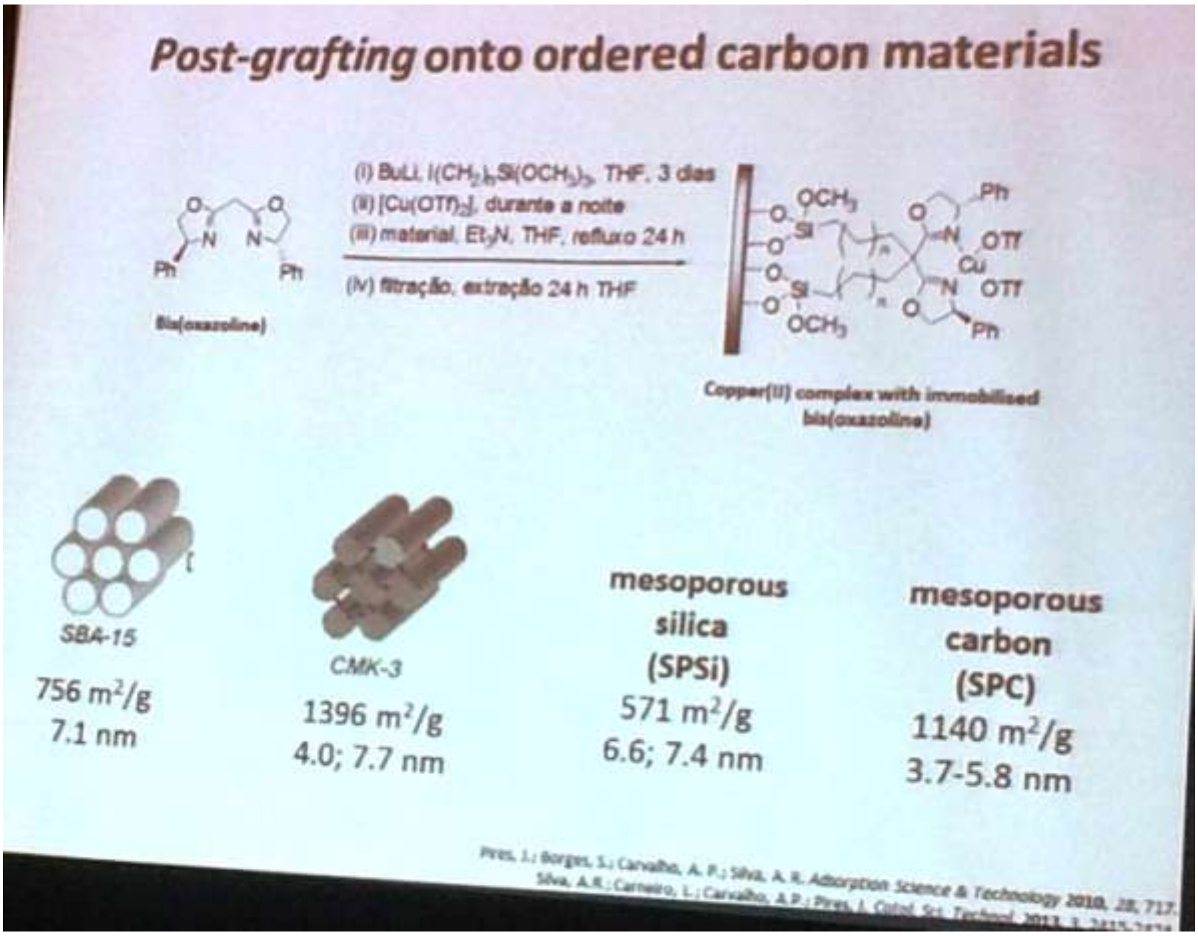
Matsumura, Y.; Maki, T.; Murakami, S.; Onomura, O. *J. Am. Chem. Soc.* **2003**, 125, 2052-2053.



Immobilization onto porous solid supports

HETEROGENEOUS CATALYST

- ☑ Easily removed from the reaction media with possible reutilization
- ☑ Avoids laborious and inefficient processes of product extraction
- ☑ Cleaner and more economical process
- ☑ Increases de stability (in certain cases)
- ☒ Covalent immobilization to the solid support frequently requires complicated synthetic manipulations of the chiral ligand
- ☒ May result in loss of activity and enantioselectivity



Post-grafting onto ordered carbon materials

(i) BuLi, $I(CH_2)_nSi(OCH_3)_3$, THF, 3 dias
(ii) $[Cu(OTf)_2]$, durante a noite
(iii) material, Et_3N, THF, refluxo 24 h
(iv) filtração, extração 24 h THF

Bis(oxazoline)

Copper(II) complex with immobilised bis(oxazoline)

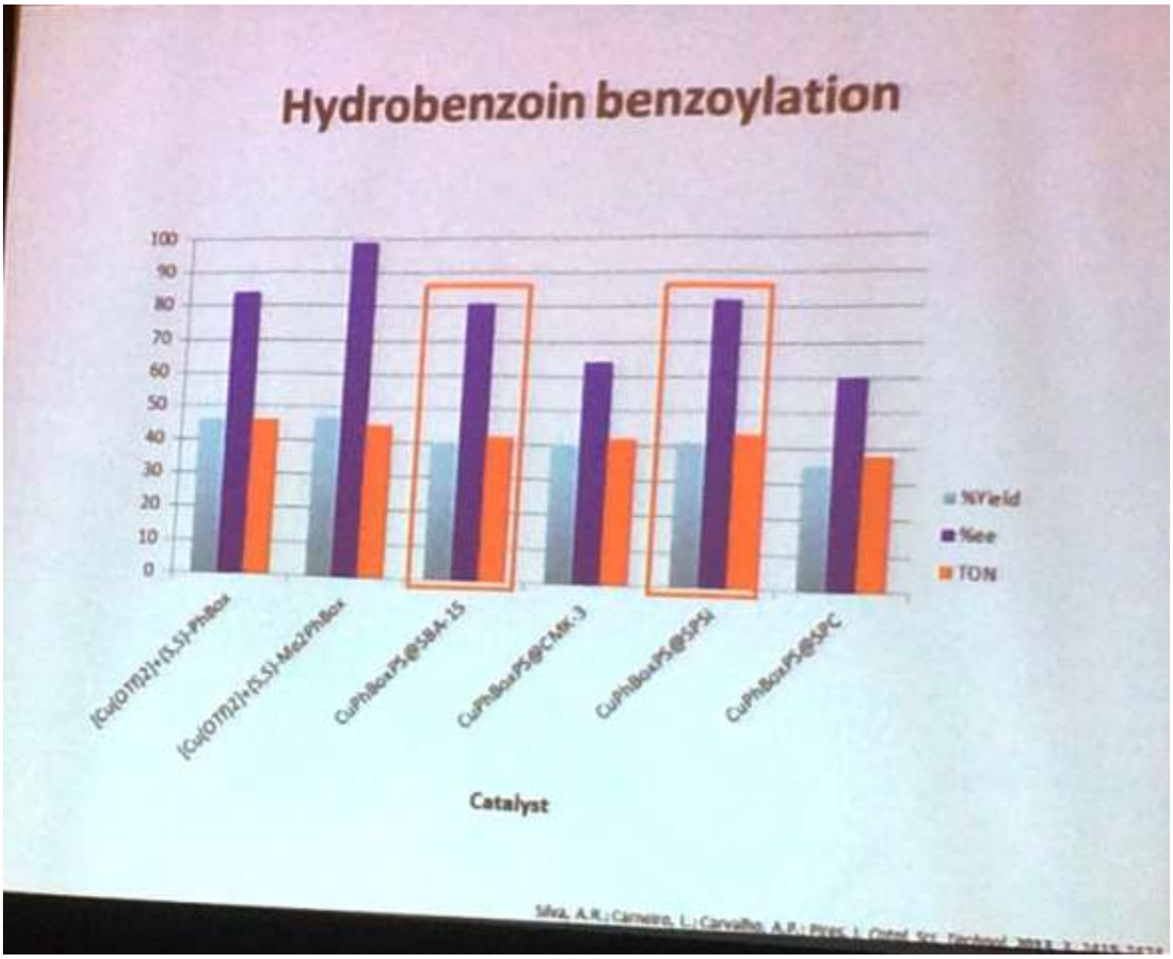
SBA-15
756 m^2/g
7.1 nm

CMK-3
1396 m^2/g
4.0; 7.7 nm

mesoporous silica (SPSi)
571 m^2/g
6.6; 7.4 nm

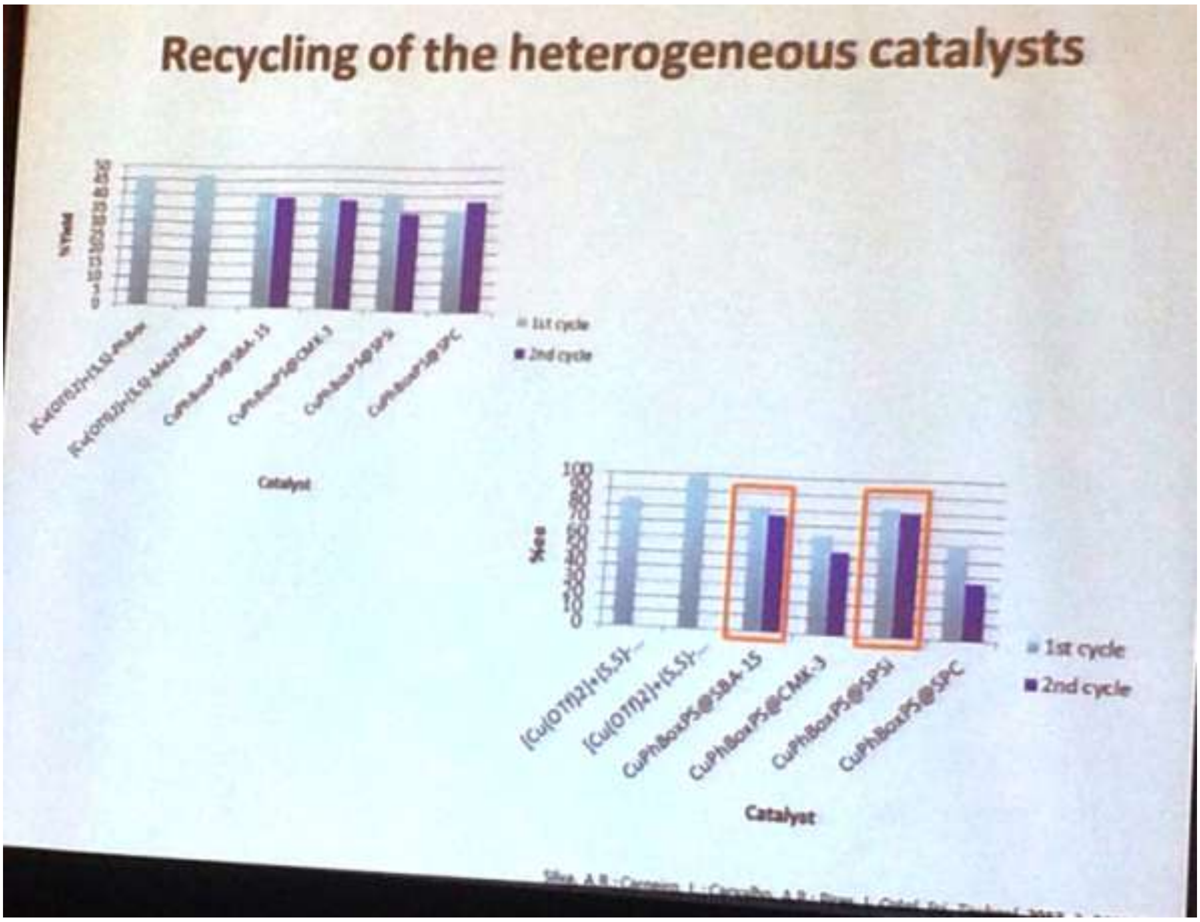
mesoporous carbon (SPC)
1140 m^2/g
3.7-5.8 nm

Pires, J.; Borges, S.; Carvalho, A. P.; Silva, A. R. *Adsorption Science & Technology* **2010**, *28*, 717.
Silva, A.R.; Carneiro, L.; Carvalho, A.P.; Pires, J. *Catal. Sci. Technol.* **2013**, *3*, 2415-2424



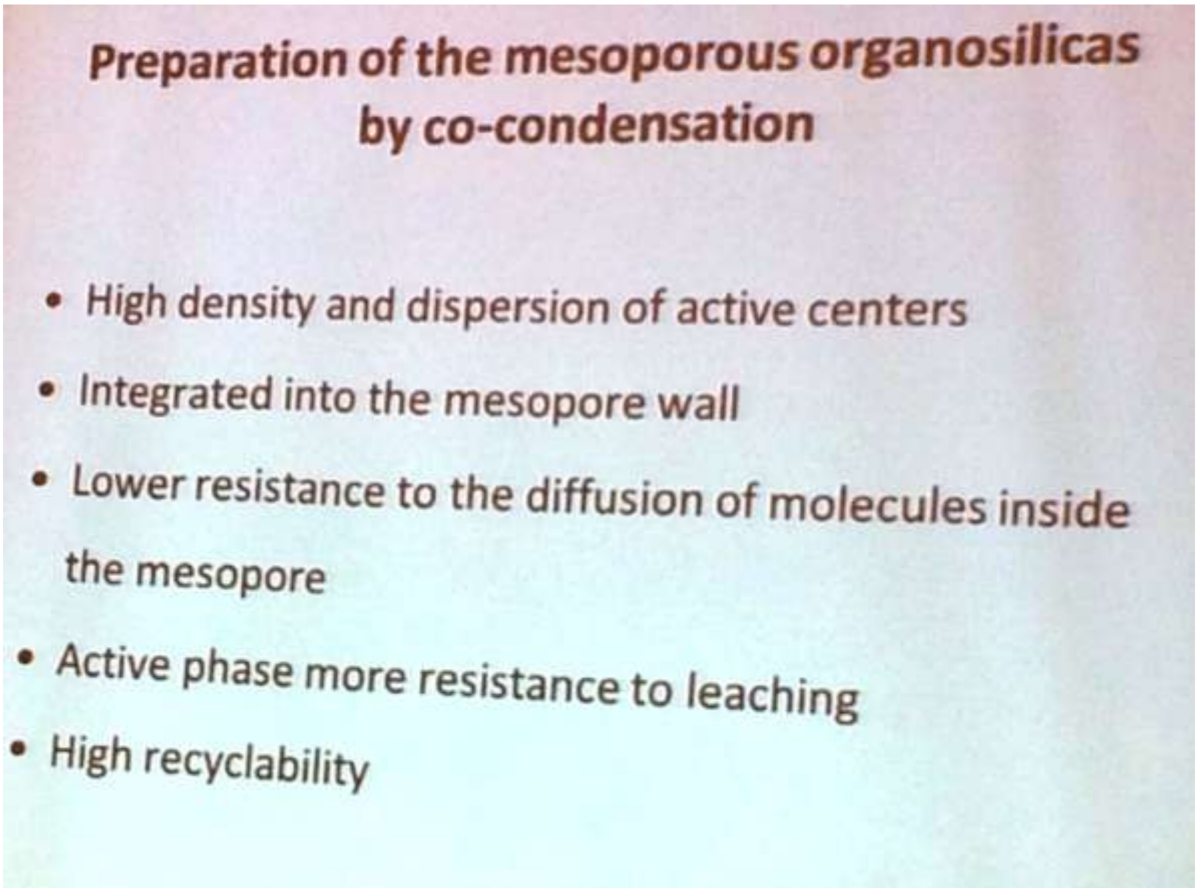
Hydrobenzoin benzoylation

Silva, A.R.; Carneiro, L.; Carvalho, A.P.; Pires, J. Catal. Sci. Technol. 2013, 3, 2415-2424



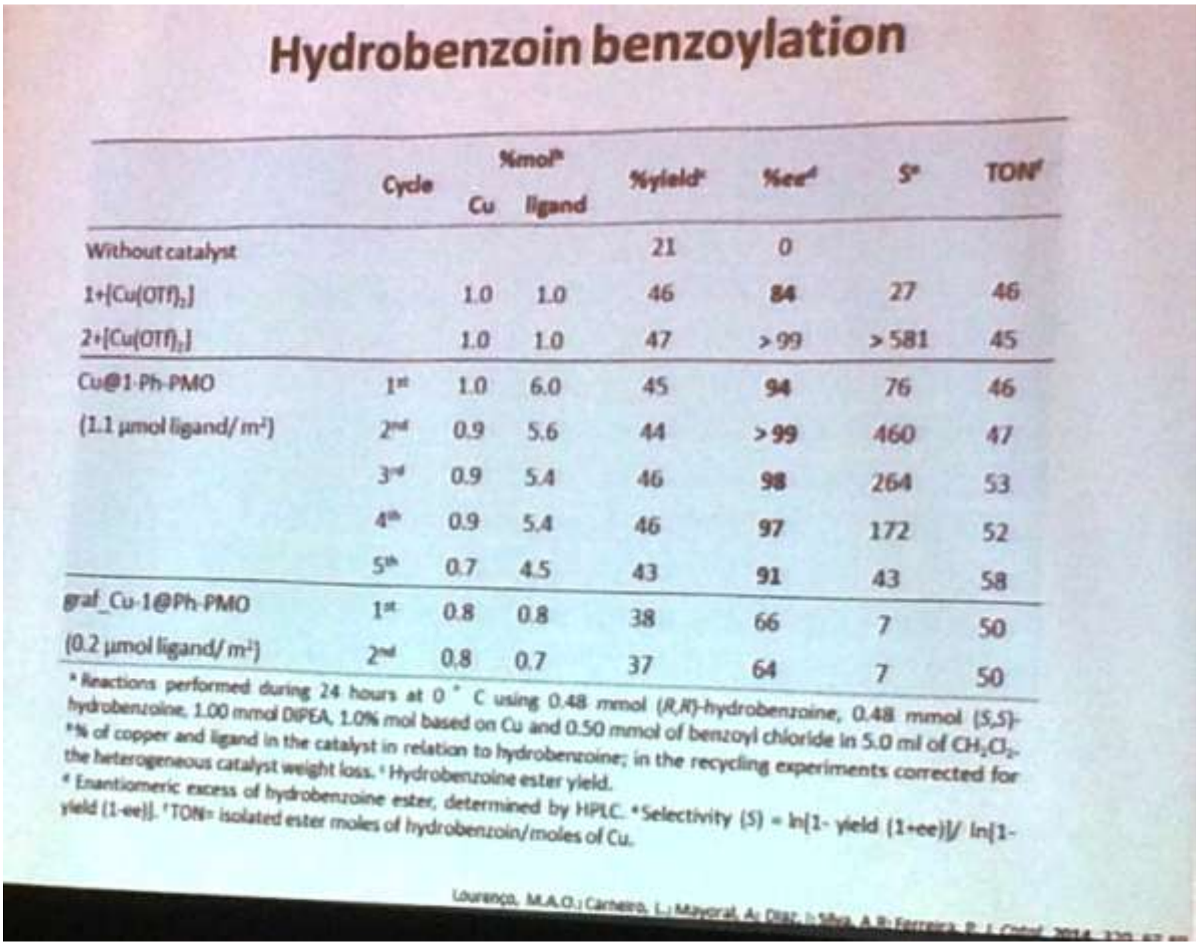
Recycling of the heterogeneous catalysts

Silva, A.R.; Carneiro, L.; Carvalho, A.P.; Pires, J. Catal. Sci. Technol.



Preparation of the mesoporous organosilicas by co-condensation

- High density and dispersion of active centers
- Integrated into the mesopore wall
- Lower resistance to the diffusion of molecules inside the mesopore
- Active phase more resistance to leaching
- High recyclability

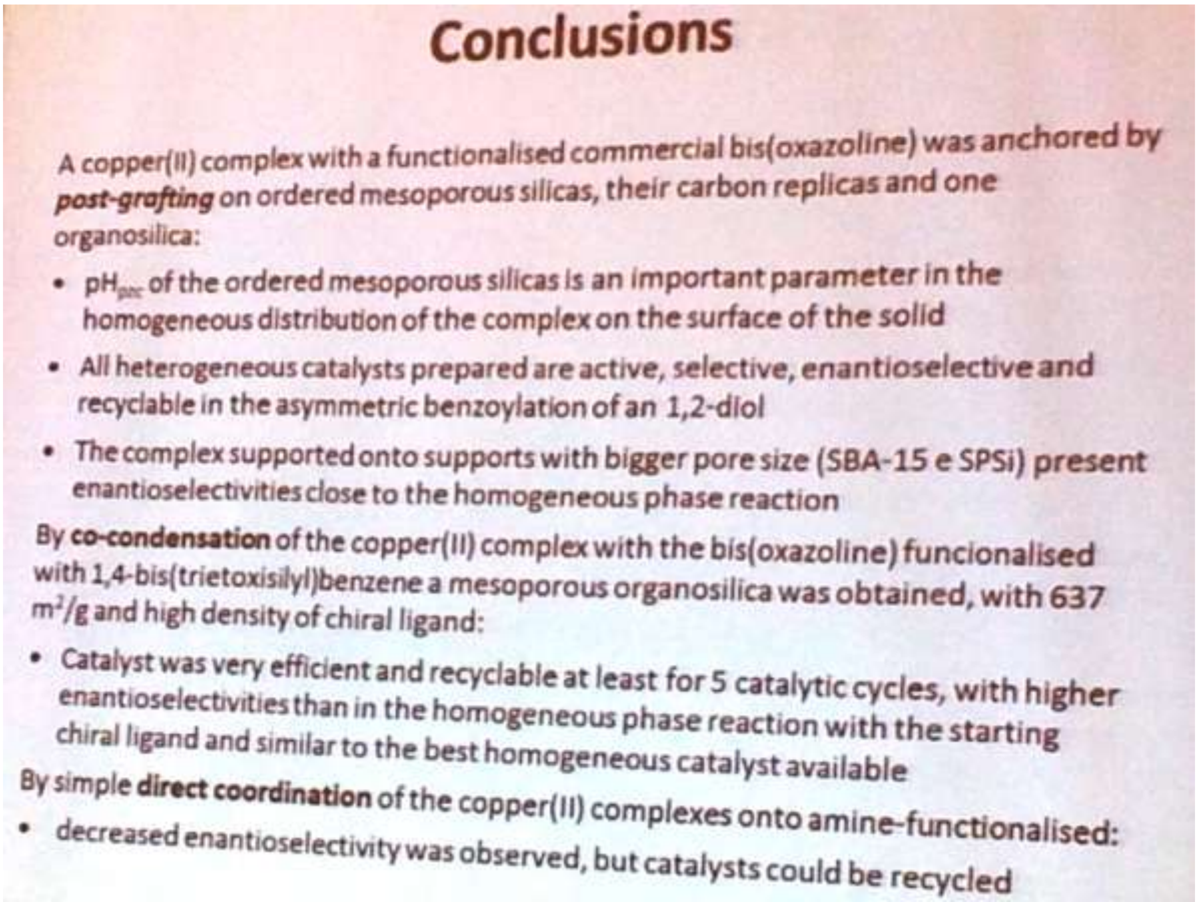


Hydrobenzoin benzoylation

	Cycle	%mol[b]		%yield[c]	%ee[d]	S[e]	TON[f]
		Cu	ligand				
Without catalyst				21	0		
1+[Cu(OTf)$_2$]		1.0	1.0	46	**84**	27	46
2+[Cu(OTf)$_2$]		1.0	1.0	47	>99	>581	45
Cu@1-Ph-PMO	1st	1.0	6.0	45	**94**	76	46
(1.1 μmol ligand/m^2)	2nd	0.9	5.6	44	**>99**	460	47
	3rd	0.9	5.4	46	**98**	264	53
	4th	0.9	5.4	46	**97**	172	52
	5th	0.7	4.5	43	**91**	43	58
graf_Cu-1@Ph-PMO	1st	0.8	0.8	38	66	7	50
(0.2 μmol ligand/m^2)	2nd	0.8	0.7	37	64	7	50

[a] Reactions performed during 24 hours at 0 ° C using 0.48 mmol (*R,R*)-hydrobenzoine, 0.48 mmol (*S,S*)-hydrobenzoine, 1.00 mmol DIPEA, 1.0% mol based on Cu and 0.50 mmol of benzoyl chloride in 5.0 ml of CH_2Cl_2. [b] % of copper and ligand in the catalyst in relation to hydrobenzoine; in the recycling experiments corrected for the heterogeneous catalyst weight loss. [c] Hydrobenzoine ester yield.
[d] Enantiomeric excess of hydrobenzoine ester, determined by HPLC. [e] Selectivity (S) = ln[1- yield (1+ee)]/ ln[1-yield (1-ee)]. [f] TON= isolated ester moles of hydrobenzoin/moles of Cu.

Lourenço, M.A.O.; Carneiro, L.; Mayoral, A.; Diaz, I.; Silva, A.R.; Ferreira, P. J. Catal. 2014, 320, 67



Conclusions

A copper(II) complex with a functionalised commercial bis(oxazoline) was anchored by ***post-grafting*** on ordered mesoporous silicas, their carbon replicas and one organosilica:

- pH_{pzc} of the ordered mesoporous silicas is an important parameter in the homogeneous distribution of the complex on the surface of the solid
- All heterogeneous catalysts prepared are active, selective, enantioselective and recyclable in the asymmetric benzoylation of an 1,2-diol
- The complex supported onto supports with bigger pore size (SBA-15 e SPSi) present enantioselectivities close to the homogeneous phase reaction

By **co-condensation** of the copper(II) complex with the bis(oxazoline) funcionalised with 1,4-bis(trietoxisilyl)benzene a mesoporous organosilica was obtained, with 637 m^2/g and high density of chiral ligand:

- Catalyst was very efficient and recyclable at least for 5 catalytic cycles, with higher enantioselectivities than in the homogeneous phase reaction with the starting chiral ligand and similar to the best homogeneous catalyst available

By simple **direct coordination** of the copper(II) complexes onto amine-functionalised:

- decreased enantioselectivity was observed, but catalysts could be recycled

3.3.5 綠色化學的利基應用：綠色光阻的發展 (Green Chemistry in niche applications: Development of “green” photoresists)

演講者：Frank Wiesbrock, Ph.D.

機構名稱：Polymer Competence Center Leoben, Austria

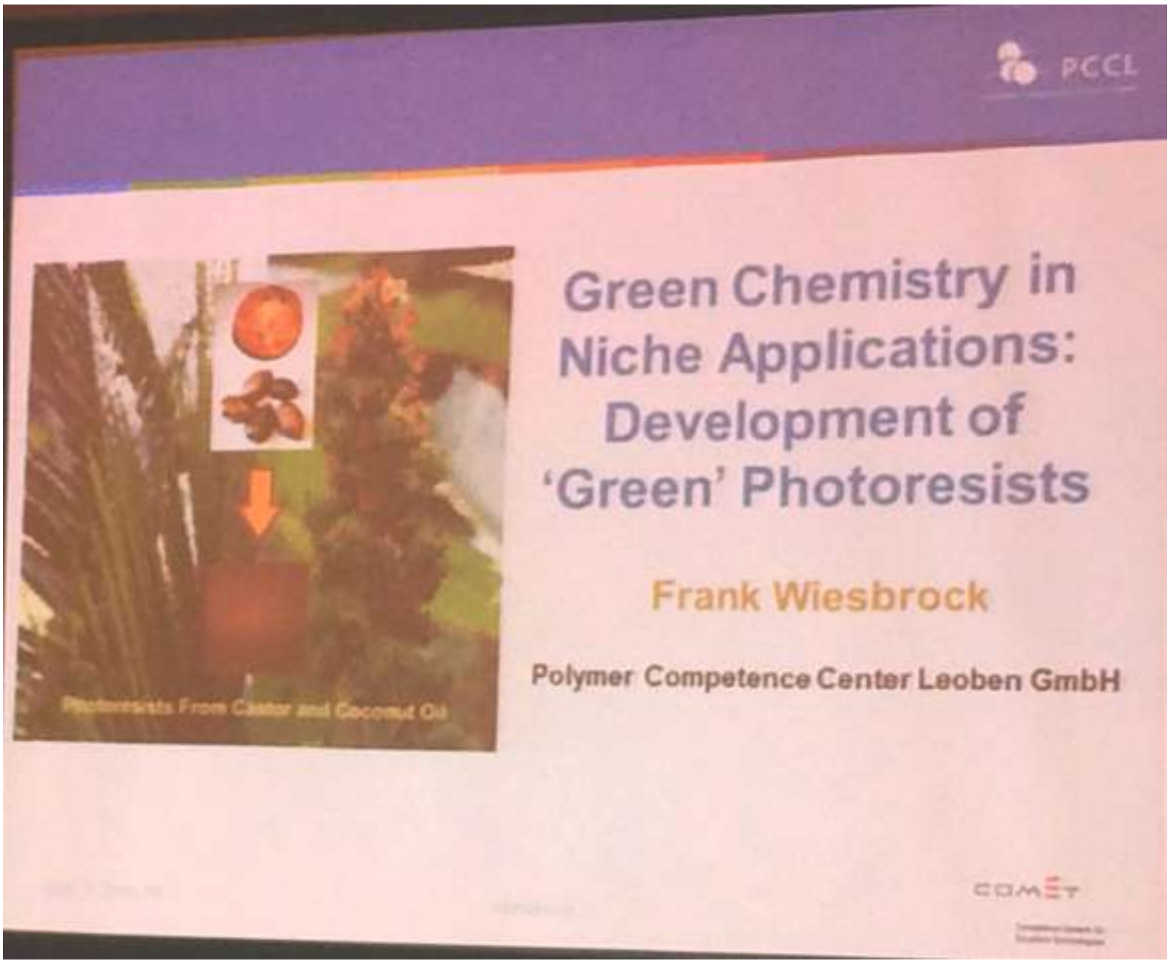
演講摘要：

僅管全世界廣泛認為化學材料的選擇與合成應該朝向環保方面發展，現實中此類綠色概念往往只在少數利基應用上實現，這包含光阻 (photoresist)。光阻亦稱為光刻膠或光阻劑，是指通過紫外光、深紫外光、電子束、離子束、X 射線等光照或輻射，其溶解度發生變化的耐蝕刻薄膜材料，是光刻工藝中的關鍵材料，主要應用於集成電路和半導體分立器件的細微圖形加工；Wiesbrock 博士的研究重點，即為利用更環保的配方及合成步驟製造光阻。

由於可以製造 2.5 及 3D 微結構,高分子聚合光阻 (polymer-based photoresist) 應

用相當廣泛，包括晶圓製造、實驗室晶片技術 (lab-on-a-chip manufacturing)、表面精整加工 (surface finishing) 等。其中負性光刻膠 (negative photoresist) 之曝光部分因交聯固化反應 (cross-linking) 而不溶於顯影液，而未曝光部分溶於顯影液，可將與掩膜上相反的圖形複製到襯底上。

Wiesbrock 博士團隊開發一種水溶性光阻，可減少製程中揮發性有機溶劑使用並申請專利 (WO 2013/036979)，近期更研發由再生材料製作的光阻，使得光阻在綠色化學上應用邁進一大步：他們分別利用蓖麻油及椰子油中的十一烯酸 (undecenoic acid) 及葵酸 (羊酯酸，decanoic acid)，與乙醇胺 (ethanol amine) 合成雙噁唑啉 (2-oxazoline) 單體，再經過共同聚合反應 (copolymerization) 製作達 300 公克等級的光阻；為達到一定能源效率，該團隊使用離子液體配合吸收微波輻射，等卻後聚合物沉澱即可回收，並可重複利用離子液體。Wiesbrock 博士團隊也藉由該聚合物與四級硫 (tetrathiol) 行硫基-乙烯基交聯固化反應，測試聚合物之可應用性，並達到 1 微米解析度。以下將報告內容重要投影片列出：



PCCL

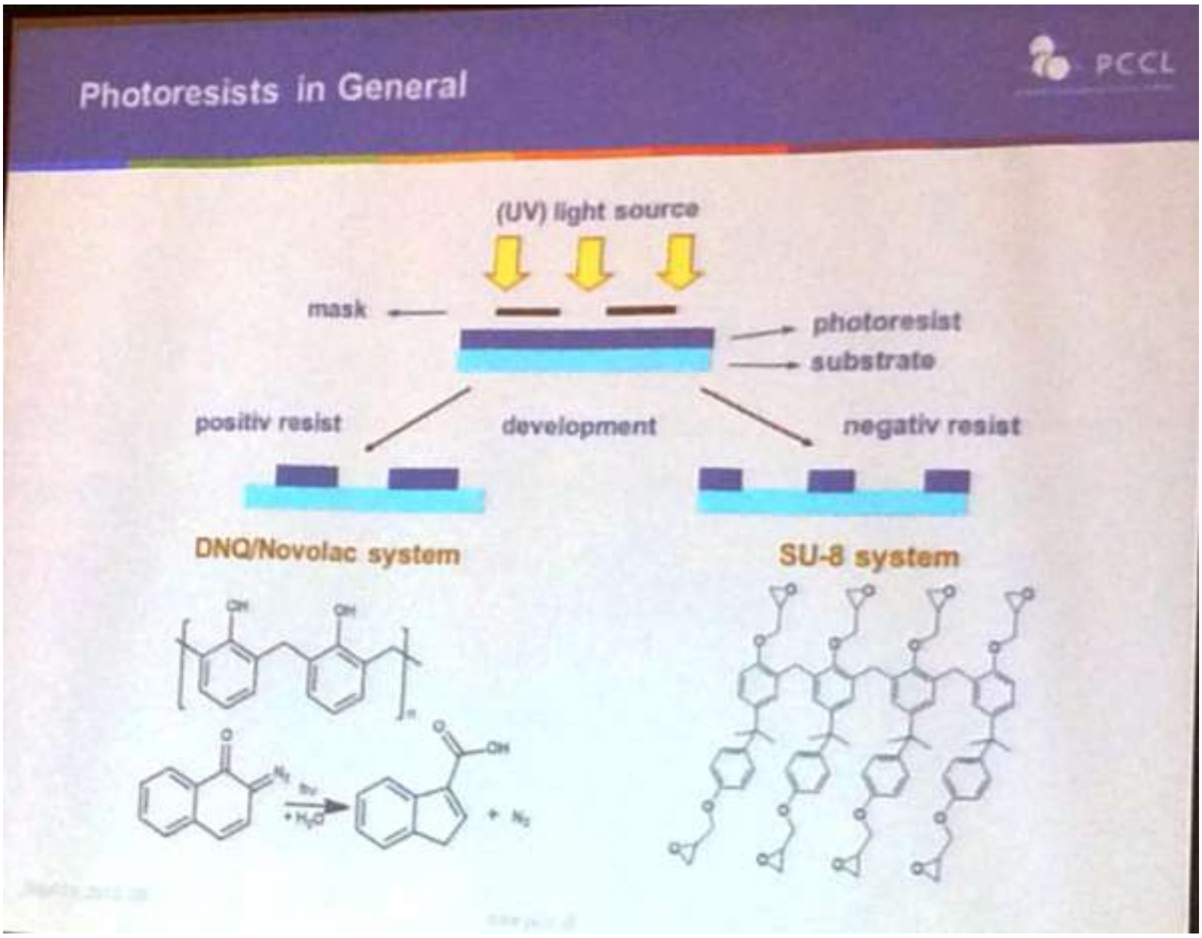
Green Chemistry in Niche Applications: Development of 'Green' Photoresists

Frank Wiesbrock

Polymer Competence Center Leoben GmbH

Photoresists From Castor and Coconut Oil

COMET



PCCL

Photoresists in General

(UV) light source

mask

photoresist

substrate

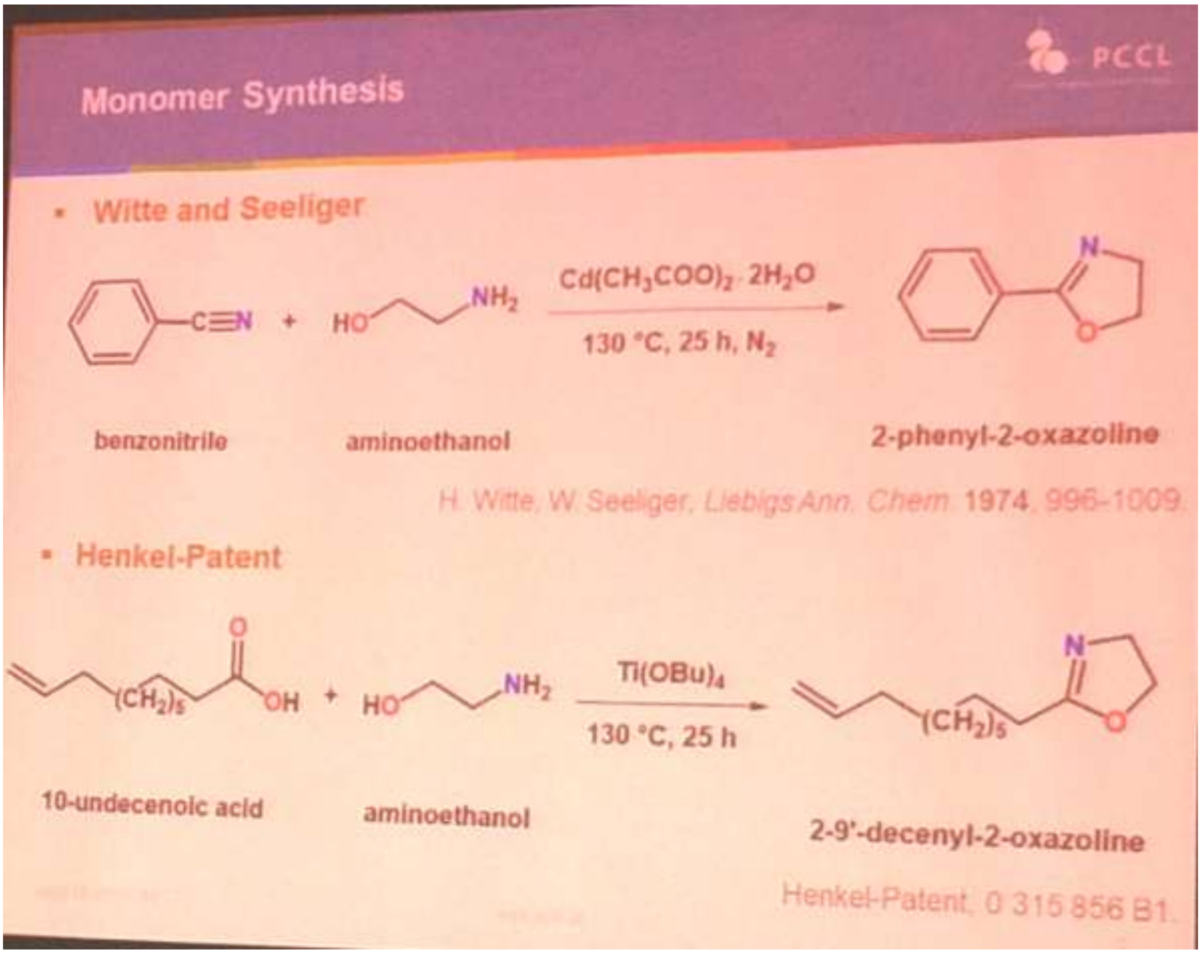
positiv resist

development

negativ resist

DNQ/Novolac system

SU-8 system



Monomer Synthesis

- Witte and Seeliger

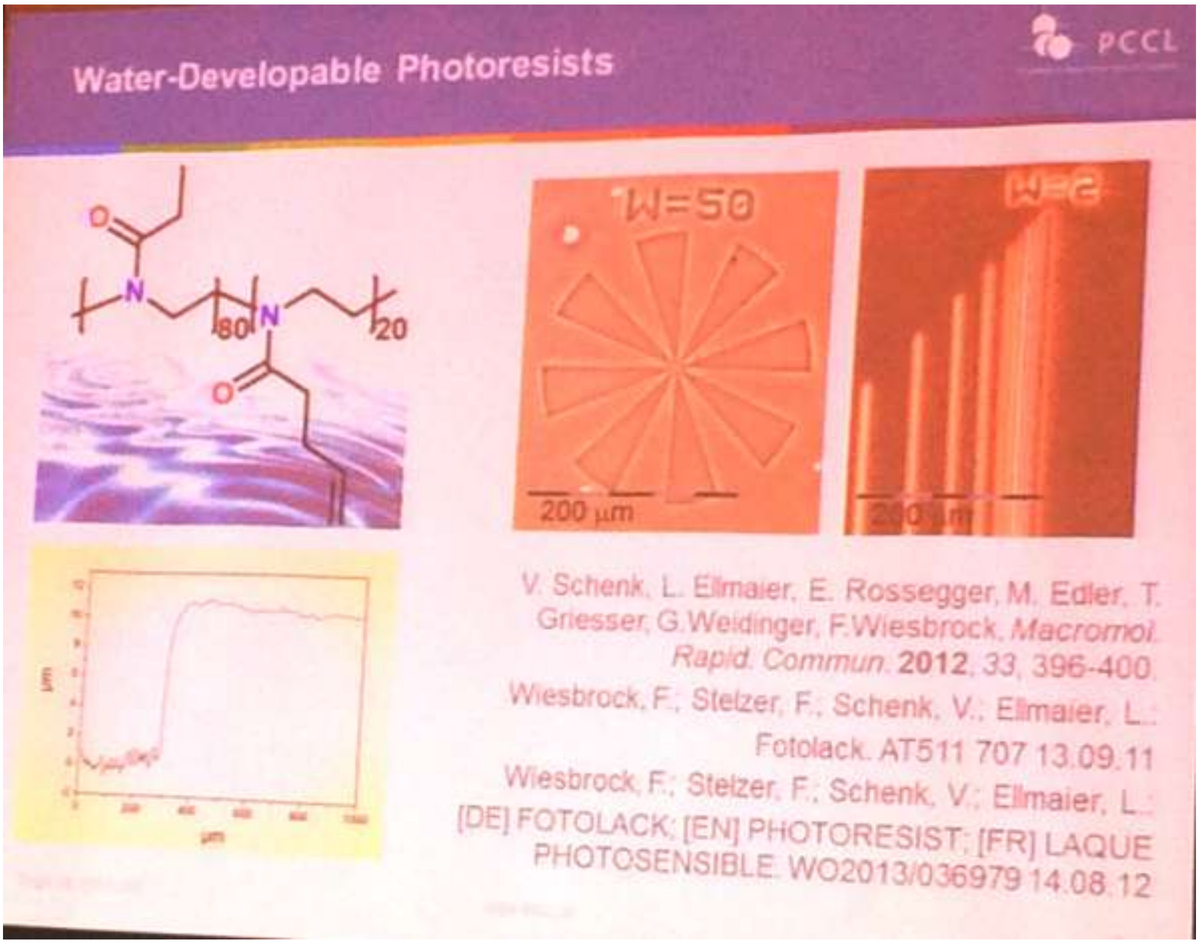
benzonitrile **aminoethanol** **2-phenyl-2-oxazoline**

H. Witte, W. Seeliger, *Liebigs Ann. Chem.* **1974**, 996-1009.

- Henkel-Patent

10-undecenoic acid **aminoethanol** **2-9'-decenyl-2-oxazoline**

Henkel-Patent, 0 315 856 B1.

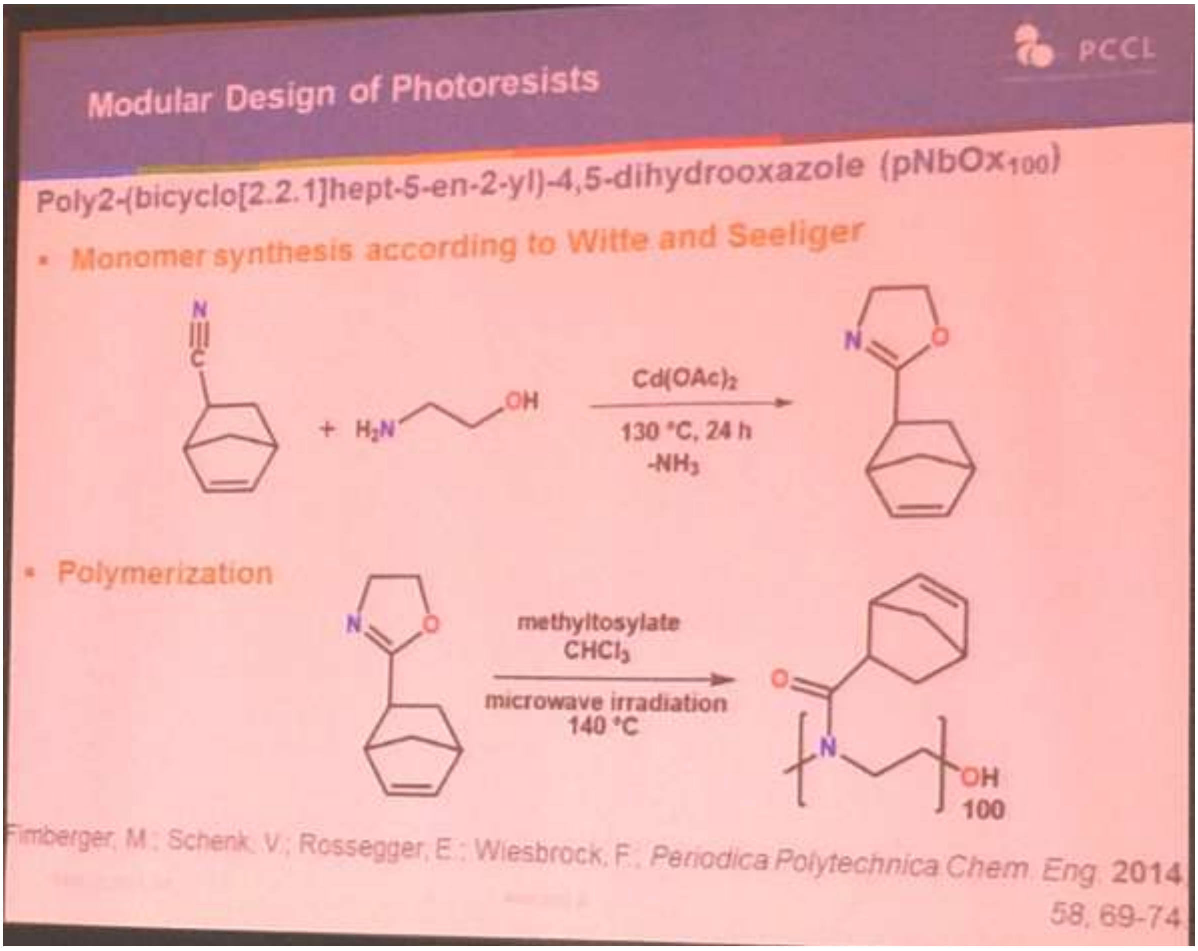


Water-Developable Photoresists

V. Schenk, L. Ellmaier, E. Rossegger, M. Edler, T. Griesser, G. Weidinger, F. Wiesbrock, *Macromol. Rapid. Commun.* **2012**, *33*, 396-400.

Wiesbrock, F.; Stelzer, F.; Schenk, V.; Ellmaier, L.: Fotolack. AT511 707 13.09.11

Wiesbrock, F.; Stelzer, F.; Schenk, V.; Ellmaier, L.: [DE] FOTOLACK; [EN] PHOTORESIST; [FR] LAQUE PHOTOSENSIBLE. WO2013/036979 14.08.12



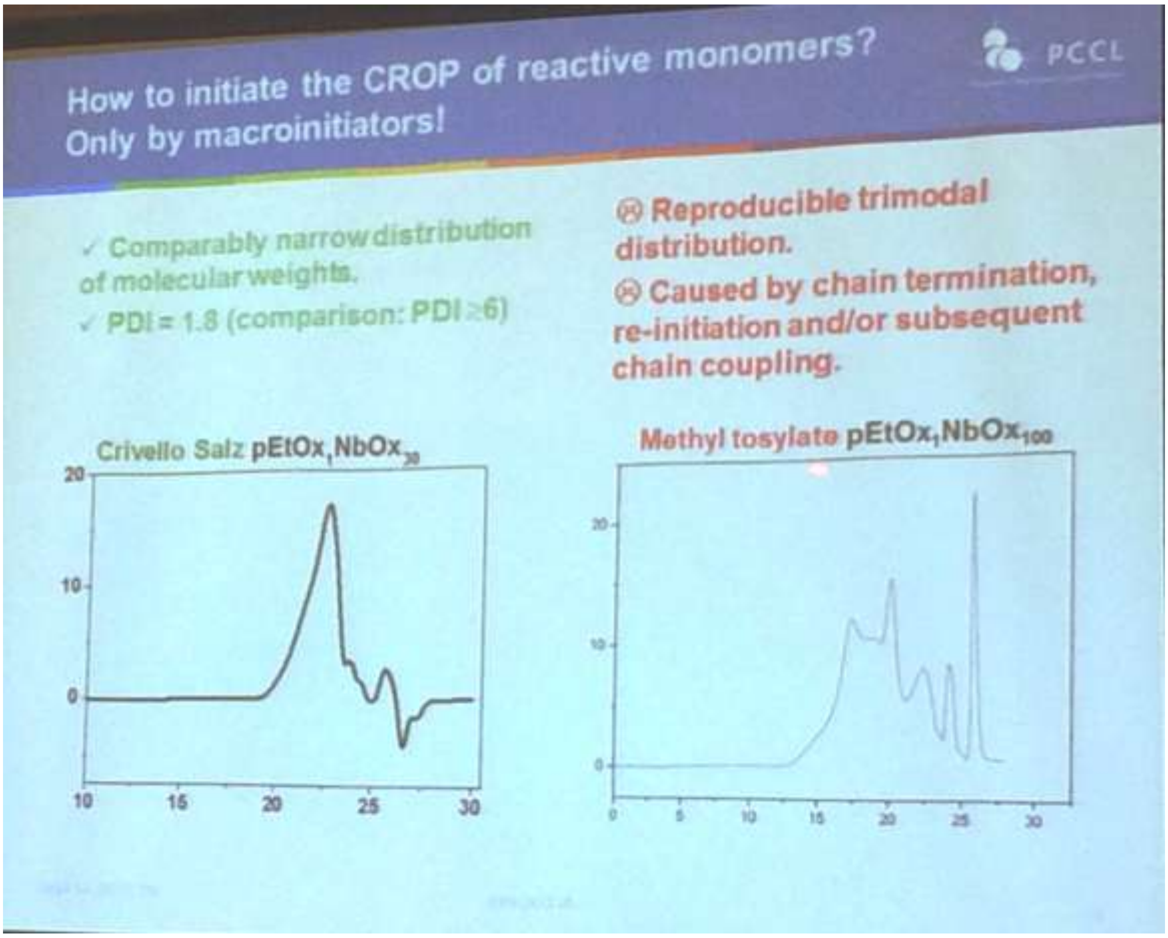
Modular Design of Photoresists

Poly2-(bicyclo[2.2.1]hept-5-en-2-yl)-4,5-dihydrooxazole (pNbOx$_{100}$)

- Monomer synthesis according to Witte and Seeliger

- Polymerization

imberger, M.; Schenk, V.; Rossegger, E.; Wiesbrock, F.; *Periodica Polytechnica Chem. Eng.* **2014** 58, 69-74



How to initiate the CROP of reactive monomers? Only by macroinitiators!

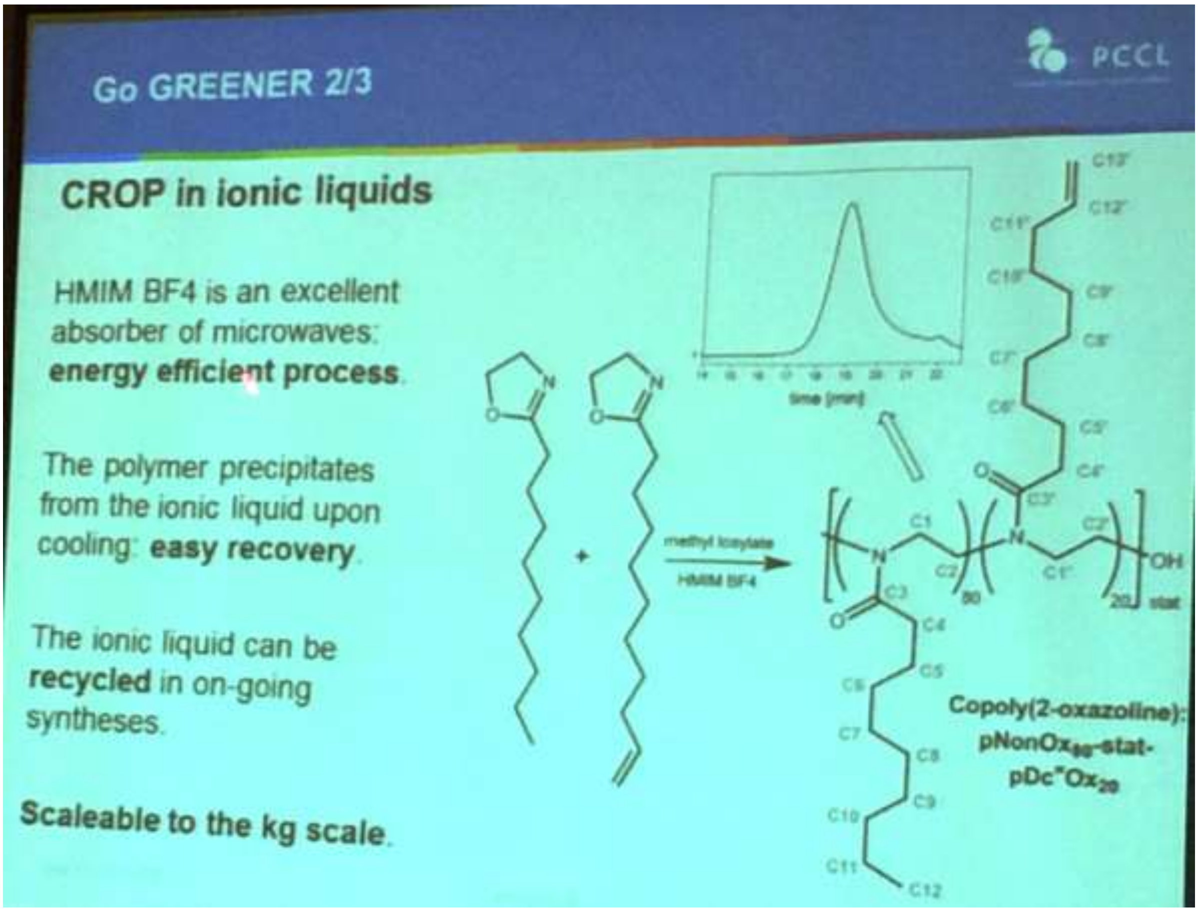
- ✓ Comparably narrow distribution of molecular weights.
- ✓ PDI = 1.8 (comparison: PDI ≥6)

☹ Reproducible trimodal distribution.

☹ Caused by chain termination, re-initiation and/or subsequent chain coupling.

Crivello Salz pEtOx$_1$NbOx$_{30}$

Methyl tosylate pEtOx$_1$NbOx$_{100}$



Go GREENER 2/3

CROP in ionic liquids

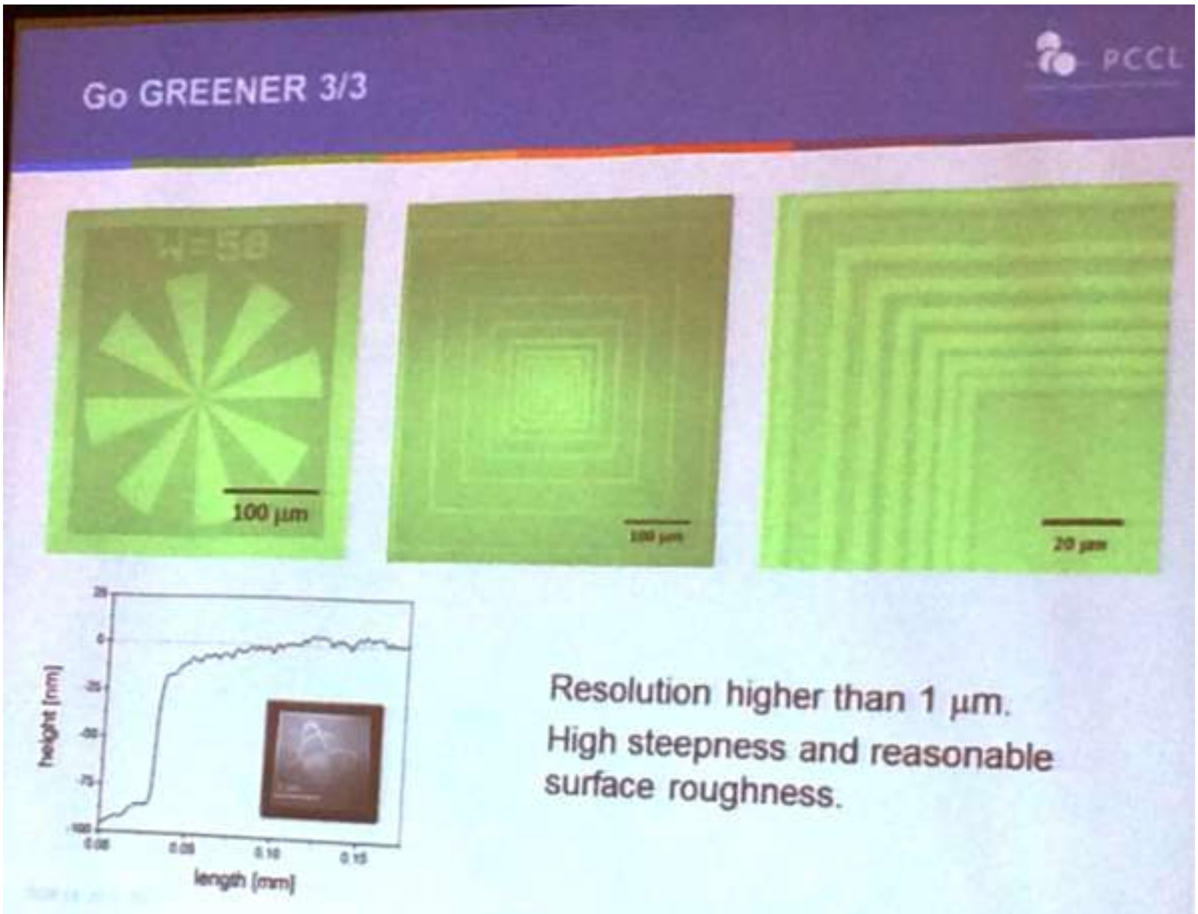
HMIM BF4 is an excellent absorber of microwaves: **energy efficient process**.

The polymer precipitates from the ionic liquid upon cooling: **easy recovery**.

The ionic liquid can be **recycled** in on-going syntheses.

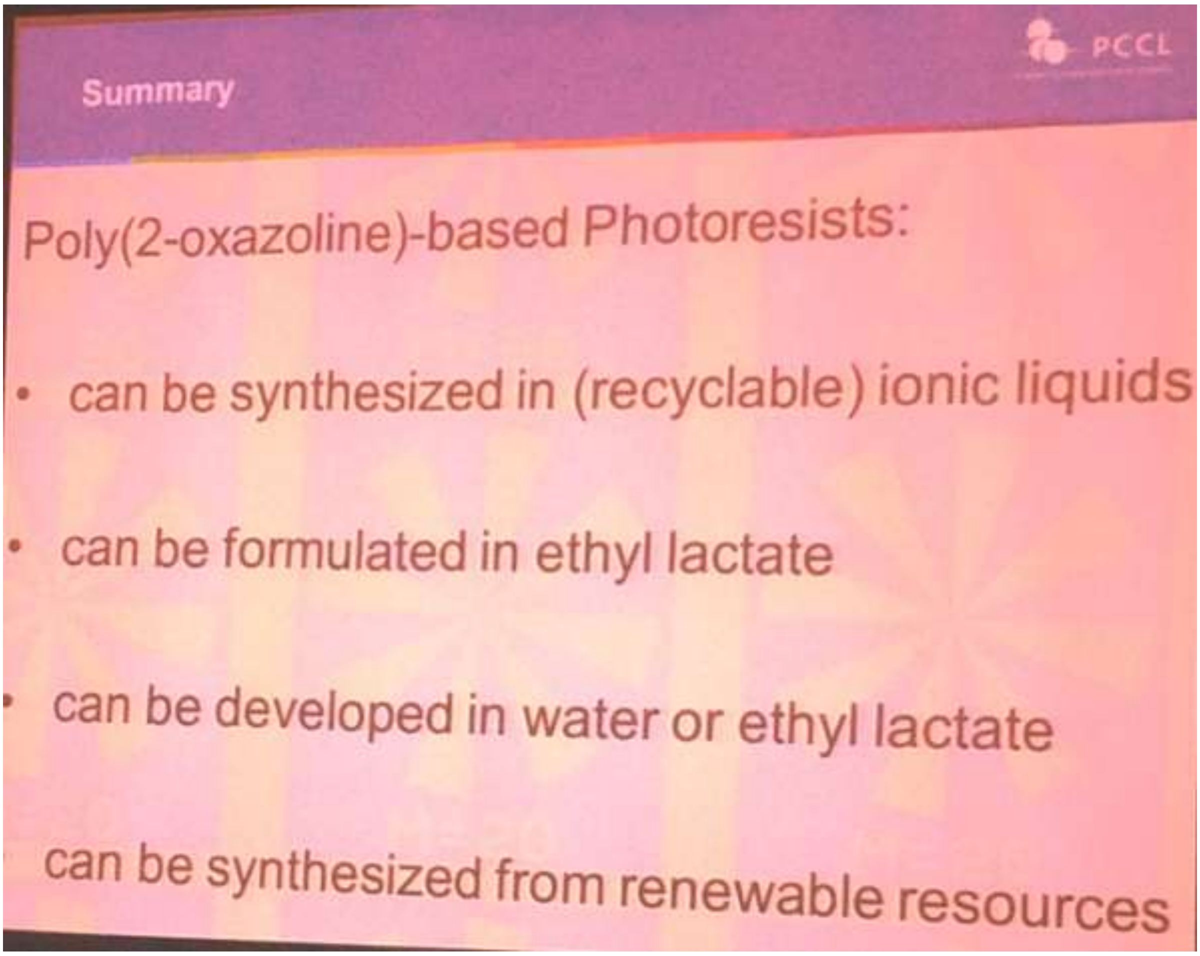
Scaleable to the kg scale.

Copoly(2-oxazoline): $pNonOx_{80}$-stat-$pDc^{=}Ox_{20}$



Go GREENER 3/3

Resolution higher than 1 µm.
High steepness and reasonable surface roughness.



PCCL

Summary

Poly(2-oxazoline)-based Photoresists:

- can be synthesized in (recyclable) ionic liquids
- can be formulated in ethyl lactate
- can be developed in water or ethyl lactate
- can be synthesized from renewable resources

3.4 論文海報發表

3.4.1 分離可應用於生物復育之耐受重金屬細菌 (Isolation and characterization of heavy metal tolerant bacteria for the purpose of bioremediation)

發表者：Finola Fung-Khee

機構名稱：Borough of Manhattan Comminuty College, USA

演講摘要：

重金屬如鉛、鋅、銅、鎳等的累積可能造成都會區或工業區水源及土壤汙染，這類環境汙染造成的生物效應包括生長抑制、畸形突變、微生物相改變及動物族群不正常消長。重金屬毒性也可能造成人類健康危機，如神經系統退化、生殖系統及泌尿系統異常等等。在重金屬汙染區生長的細菌，往往具藉由特殊基因表現使其適應汙染環境並生長，它們可能具有高度重金屬耐受性，也因此成為生物復育的良好素材

(Nancharaiah, Venkata Mohan et al. 2015)。

此篇壁報論文中，作者發現由紐約市布魯克林區 Newtown Creek 分離的特殊細菌，可以耐受重金屬，因此將收集到的 15 株菌株進行生物復育能力的測試與評估，發現所有微生物皆可生長於含 4 mM 至 20 mM $Pb(NO_3)_2$, $Ni(NO_3)_2$ 或 $Cu(SO_4)_2$ 的培養基。由於許多抗重金屬基因可能藉由質體 (plasmid) 型式在不同細菌菌株間傳遞(Bolan, Kunhikrishnan et al. 2014)，因此該團隊針對數隻菌株中所含質體進行抽取與定序分析，未來工作包括鑑定質體上抗重金屬基因序列，進一步探討重金屬抗性機制；另外也將比較植物生長在添加或未添加重金屬抗性菌種土壤上的生長情形，以確認此類微生物行生物復育的潛力。

此項研究可作為本公司進行廠區土壤及水源復育相關研究之參考，由於高雄廠區關閉在即，許多土地需要進行環境評估及復育，可能耗時 5~20 年，為了更有效的除去土壤中汙染源，我們需要多管齊下以節省時間，此類生物復育概念並不陌生，若能在高雄廠區完成，除了彰顯本公司研究單位研發能量，更能提升企業形象，提供公司朝向綠色能源發展的極佳範例。

3.4.2 利用固體廢棄物吸收有機汙染物，作為環保復育的替代方案 (Uptake of organic pollutants by solid wastes as an eco-friendly remediation alternative)

發表者：Kateryna Zhdanova[1], Tenzing Japhe[1], Loretta Roberson[2] and Abel E. Navarro[1]

機構名稱：[1]Borough of Manhattan Comminuty College, USA; [2]University of Puerto Rico-Rio Piedras, USA

演講摘要：

有機汙染物涵蓋不同類型的化合物：染劑 (dye)，多環芳香烴碳氫化合物 (polycyclic aromatic hydrocarbons, PAHs)，藥物 (pharmaceuticals)，含酚化合物 (phenolic compounds) 及其他。雖然含酚化合物在環境復育時通

常被忽略，它們不僅廣泛存在於工業廢水、對人體健康有害、更被美國環保署列為新興汙染源之一，因此收到高度關注。

此篇壁報論文中，作者利用泡茶後剩下的黃春菊 (Chamomile)、綠茶 (green tea)、薄荷草等廢棄物，作為室溫環境下 2-氯酚 (2-chlorophenol) 的生物性吸收劑，並利用酸鹼性及單位質量吸收率等平衡常數作為評估依據。結果顯示 pH 值對於 2-氯酚的吸收能力影響最大，在大約 pH 9 時吸收效果最好，此外吸收效果以黃春菊葉最佳，薄荷葉次之，再其次為綠茶。二價離子例如鉛、銅離子，以及聚乙二醇 (polyethylene glycol) 等帶離子性及共價性分子，對於 2-氯酚的吸收能力具有些許影響。本研究結果顯示，木質纖維所組成的固體廢棄物，有作為吸受劑的良好潛力，同時可生物降解並在價格上具有競爭力，可應用於生物復育上。

如同上一則壁報論文，本研究對於減低環境汙染及提升本公司形象具有良好啟發效果，尤其適合煉研所環境資源組或綠能所環保科技組投入研究，並應用於高雄廠區環境整治。

4 心得與建議

4.1 心得

本次研討會為時共三天，包括主題演講、專題演講、學者交流討論、壁報發表討論及競賽，甚至包含 YouTube 線上直播，個人心得分為以下兩方面：

4.1.1 研討會規模與內容：

以學術觀點來看，本次研討會類似學術界享譽以久的 Gordon Research Conference：通常主題範圍非常專一，以小型學術研討會模式，聚集少數各界菁英在一起討論，激發嶄新想法。因此有別於傳統大型研討會類似大海撈針式搜尋感興趣的題目及講者，小型研討會可以讓某類領域專家集中能量，對於特定議題即時討論。除此之外，這次得以與深耕綠色化學多年的學界、產業界、教育界研究者交流，分享研究成果，經驗相當難得，本研討會所具備的廣度又較 Gordon Research Conference 更高，使我得窺綠色化學各分支領域的不同層次及不同面相。本次研討會亦具備專業領域之深度，以化學界為例，聚集許多化學專家，專長領域包括有機化學、無機化學、觸媒與催化劑、高分子合成、材料化學等；針對綠色化學應用，也有關於處理土壤污染及水污染的專家蒞臨現場，並分享重金屬除污、微生物生物復育等相關研究。因此本次研討會具備橫向及縱向的深度，個人於會議中及壁報論文發表時與學者的討論，感到收穫相當豐富。

4.1.2 國際交流制度建立：

另一方面體會是，西方社會對於科學研究相當重視，亦比東方社會更早建構評量制度、教育與技能訓練、學術交流、產業與商業化應用等系統，因此知識與技術得以不斷累積，然後等待適當成熟時間點，突破性創新的產生便能迅速發展成產業，開拓市場並獲利。相較之下，亞洲社會雖然近一世紀來努力學習西方制度，大都只學得表面制度而非精髓：許多來自歐美的制度或系統，在亞洲或者更精確的說在台灣，往往流於形式，執政者不在乎，一般民眾更不在乎。然而大多

數人都不在乎時，這些制度的引進不啻是一種資源浪費？隨著網路的發達，資訊交流更加快速，但訊息氾濫使我們難以仔細思考甚麼才真正適合中油公司或適合台灣；除了物質生活外，我們更需要全面教育提昇全民素質，使綠色化學等概念確實傳達給每個人。因此，國內需要更多與國際專家資訊交流的平台，而研討會就是最快而有效的方式，若能積極參與或舉辦國際性研討會，除快速累積知識與人脈外，也能提高中油公司的可見度，搭上國際化的列車。

4.2 建議

本人去年任職於中油公司前，自求學時代至美國工作期間，有多次參加國際研討會經驗，相較之下，關於本次參加研討會有以下建議：

4.2.1 簡化出國申請與處理之行政流程：

雖然中油公司排名在全球前五百大企業之列，進入公司後本人卻感到許多制度與行政流程相當冗長、缺乏彈性與效率。以本次出國參加研討會發表論文為例，除了與學界業界專家交流，更是增加本公司綠能所可見度、提升企業形象的大好機會，卻因為複雜的行政流程，預訂九月份為出國日期，卻得在二月份開始處理研討會費用、發表論文內容陳核、機票費用、論文發表費用詢價等事宜，機票又因為四月份機場稅調漲而影響最初估價、內部文件的陳核曠日廢時，出國相關規定在六月份與八月底一再更改，十月份臨時告知回國報告繳交期限縮短等，處理這些事務佔去大部分可用來做研究的時間，拖慢研究員的研發腳步，也澆熄對研究的熱情。內部承辦人員對於出國案的處理，也往往標準不一，各自陳述，申請文件一改再改，公文往來頻繁，行政效率低落，公司內部封閉保守的心態，並且與國外公司、學術單位或研究機構，也缺乏正式溝通管道。期待本公司未來能提升行政效率，以便朝國際化道路邁進。

4.1.1 加強國際交流與合作：

各國政府、全球各大石油公司、化學公司、農業公司，無不積極發展再生能源，且多數已經累積數十年經驗，綠能科技研究所身為中油在再生能源方面主要研究單位，年資尚淺，需要更積極的向外交流、評估不同嶄新研究領域的發展性，找尋具有潛力的研究課題。台灣地狹人稠，在資源上勢必無法與泱泱大國競爭，必須尋求高值化或藉合作方式走向國際；策略聯盟的概念近年來逐漸在亞洲國家間興起與落實，例如泰國、日本等國家，依據各國不同的地理位置與自然資源，透過產業合作發展生質能研究與扶植相關企業，達到互惠雙贏的局面。生質能與化學品公司間，合作更密切、頻繁。例如 DuPont 與 Genomatica 公司互相技術授權 1,4-丁二醇醱酵生產技術 (自然界微生物無法自行合成 1,4-丁二醇，但 Genomatica 利用代謝及合成生物學方式成功改造大腸桿菌生成 1,4-丁二醇(Yim, Haselbeck et al. 2011))、Genomatica 又與 Eni、Novamont 合作發展丁二醇轉丁二烯技術；BASF 與 Mitsubishi Chemical 策略聯盟，並與 Metabolix、CJ CheilJedang 合作發展丁二醇轉 THF 技術；Lanza Tech 與國內李長榮公司及大陸中國鋼鐵合作，利用煉鋼爐煙道氣成份作為碳源，發展微生物厭氧醱酵技術生產酒精及 2,3-丁二醇(Kopke, Mihalcea et al. 2011)，同時 Lanza Tech 亦與與 Invista 合作開發一步化 2,3-丁二醇轉為丁二烯技術。諸如此類合作模式，皆基於公司本身及合作夥伴的技術與未來發展方向，獲取最佳的發展策略及市場取向，值得本公司踏足生質能產業的借鏡。

4.1.2 綠色化學與環保議題發展：

本公司高廠關閉在即，除了廠區人員安置、設備轉移之外，各界最關注的無非高廠土地如何最佳化利用。然而，數十年的煉油製程歷史，意味著未來環境評估與土壤整治還有一段很長的路要走。針對環境汙染防治方面，建議公司整合各部門人力，與市政府及後勁地區居民共同協商，尋求能在中油公司永續經營前提下，不偏袒經濟發展及環境保護任何一方的解決方案，畢竟未完成整治的土地，是不可能安

心蓋屋居住的。中油公司若可針對土壤整治方面，以土壤及地下水整治工程處為主，偕同綠能所與煉研所同仁，共同提供實務及研究方面協助，規畫整治相關事宜，不僅是企業負責任的表現，更能證明本公司發展策略可兼顧經濟與環保，有助於提升公司整體形象。這也是本次研討會上眾多學者不斷呼籲的重要概念：綠色化學是求得經濟與環境永續的重要法則。

5 參考資料

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