出國報告（出國類別：其他）

參加「2016 第四屆廣州核酸國際論壇學術研討會」赴大陸報告

服務機關：核能研究所
姓名職稱：楊浚泓　研究助理
派赴國家：中國大陸
出國期間：105 年 11 月 8 日~105 年 11 月 11 日
報告日期：105 年 12 月 8 日

摘 要

本次出國公差目的是赴中國大陸廣州參加 2016 第四屆廣州核酸國際論壇學術研討會，蒐集國際最新核酸藥物開發與其在診斷與治療領域上的發展新知與研究成果，與國際專家學者進行交流與討論，出國公差自 105 年 11 月 08 日至 11 月 11 日止共計 4 日。

核酸藥物應用於診斷與治療上因為具有高專一性、高靈敏性、低毒性等優勢，已成為最新熱門之藥物開發標的之一，無論是在病毒治療、先天性疾病或是肝臟腫瘤的治療上，都有其應用價值，為本所發展新穎核醫藥物或肝臟疾病診療藥物的重要目標之一。廣州核酸國際論壇為每年集合全球核酸領域知名專家學者就最新技術、方法及研究成果進行交流與討論，今年是第四屆，發表主題涵蓋非編碼 RNA 國際最新研究、尖端核酸技術開發與應用、核酸診斷與標誌物發現以及核酸治療與藥物開發等領域。這些議題對於本所發展核醫應用於核酸藥物上的可能提供豐富的參考資料。

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一、目　的

(一)、　本次同位素組研究助理楊浚泓赴中國大陸廣州目的為參加 2016 第四屆廣州核酸國際論壇學術研討會，蒐集國際最新核酸藥物開發與其在診斷與治療領域上的發展新知與研究成果，與國際專家學者進行交流與討論，出國公差自 105 年 11 月 08 日至 11 月 11 日止共計 4 日。

(二)、　楊員應邀參加第四屆廣州核酸論壇學術交流會，會議共計兩個整天，由 18 位國際核酸研究專家學者與核酸藥物開發藥廠進行專題演講，全程參與蒐集核酸藥物的最新技術、方法及研究成果並與與會人員進行交流與討論。

(三)、　「廣州核酸論壇學術交流會」，為自 2013 年以來每年舉辦之一系列非營利性的國際核酸科學領域最新研究與應用和尖端技術研討會，主題包含核酸領域的新概念、新技術、新進展，將涵蓋 DNA/RNA 生物學，核酸相關的新技術（新一代測序，生物資訊學，核酸分離與檢測，基因合成，核酸奈米結構與技術，基因組編輯及其它），非編碼 RNA（miRNA，piRNA，lncRNA 等等)，核酸的結構與功能（核酶，染色質動力學，RNA 編輯，DNA 複製，RNA 加工與轉運，基因組的完整性和轉錄後調控等等），核酸治療與診斷（基因沉默，反義核酸，適配體，miRNA，RNA 疫苗，mRNA 治療，基因檢測，FISH 檢測，核酸檢測等等）。這些議題對於本所發展核醫應用於核酸藥物上的可能提供豐富的參考資料。

二、過　程

(一)、　行程表：

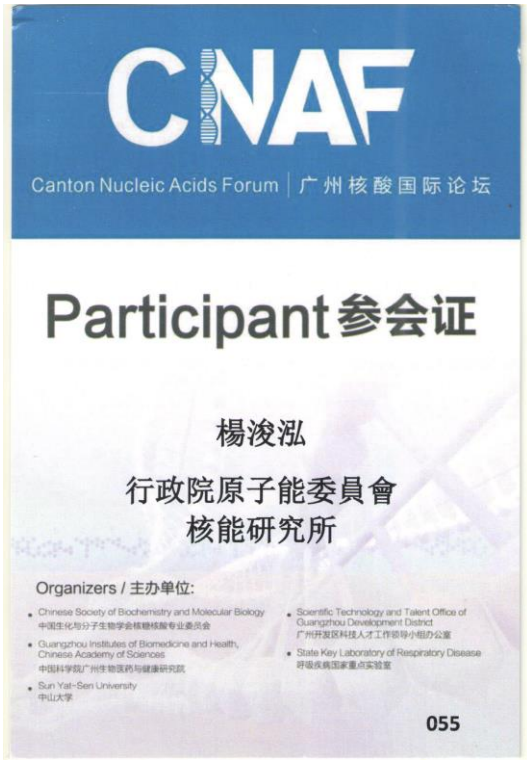
赴中國大陸廣州參加第四屆廣州核酸論壇學術研討會主要行程與內容如下：

日期	地點	內容
105/11/08	台灣→大陸廣州	去程：台灣桃園國際機場→中國大陸廣州白雲國際機場→研討會會場
105/11/09	大陸廣州	大會首日 上午：開幕式、4 場主題報告 下午：5 場主題報告
105/11/10	大陸廣州	大會次日 上午：4 場主題報告 下午：5 場主題報告、閉幕式
105/11/11	大陸廣州→台灣	回程：研討會會場→中國大陸廣州白雲國際機場→台灣桃園國際機場

(二)、　研討會地點：

廣州翡翠皇冠假日酒店(廣東省廣州市蘿崗區凝彩路 28 號)

(三)、 會議識別證：



(四)、 會議邀請函：

LETTER OF INVITATION

August 4, 2016,

Dear Sir or Madam,

Please be informed that Dr. CHUN-HUNG YANG is invited to attend the 4th Canton Nucleic Acids Forum held in Guangzhou on November 9-10, 2016. Related information is listed as below:

Name as in passport	CHUN-HUNG YANG
Gender	Male
Date of birth	1985.10.18
Passport number	309952490
Area	Taiwan
Affiliation	Division of Isotope Applications, Institute of Nuclear Energy Research(INER), Atomic Energy Council, Taiwan
Job title	Research Assistant
Dates of travel (from…to…)	From Nov. 8 to Nov. 11

We would appreciate if you could kindly allow him to come so that he can make the trip.

Thank you for your kind consideration.

Yours truly,

Guangzhou RiboBio Co Ltd

(五)、　會議簡介：

第四屆廣州核酸國際論壇於 2016 年 11 月 09 日至 10 日在羊城廣州科學城召開。本屆論壇由中國生化與分子生物學會核糖核酸專業委員會、中科院廣州生物醫藥與健康研究院、廣州開發區科技人才工作領導小組辦公室、呼吸疾病國家重點實驗室、中山大學主辦，由廣州市銳博生物科技有限公司承辦。核酸科學是當前新興國際生物醫學領域的和熱門研究方向，發展迅速，對推動精準醫學研究和人類健康起到重要作用。本屆論壇旨在為中外科學家提供一個尖端交流平臺，共同分享和探討本領域的最新研究成果、應用前景及產業化方向。

主辦單位：

中國生化與分子生物學會核糖核酸專業委員會

中國科學院廣州生物醫藥與健康研究院

廣州開發區科技人才工作領導小組辦公室

呼吸疾病國家重點實驗室

中山大學

(六)、　第四屆廣州核酸國際論壇學術研討會紀要

第四屆廣州核酸國際論壇學術研討會於 2016 年 11 月 9-10 日於中國廣州召開，本次會議共三百餘人出席(**圖一**)、共有 18 位核酸研究領域專家學者進行專題演講報告。由 2006 年諾貝爾獎獲得者 Mello 教授開幕致辭(**圖二**)。

圖一、第四屆廣州核酸國際論壇出席人員

圖二、Mello 教授開幕致詞

大會主題報告共 18 個主題，茲整理重點如下：

第一天：

<u>第一場演講</u>題目: Combating resistance to antibacterial and anti-parasite ribosomal antibiotics

講者： **Ada Yonath PhD** (2009 年因對核醣體功能與結構的傑出貢獻獲得諾貝爾化學獎)

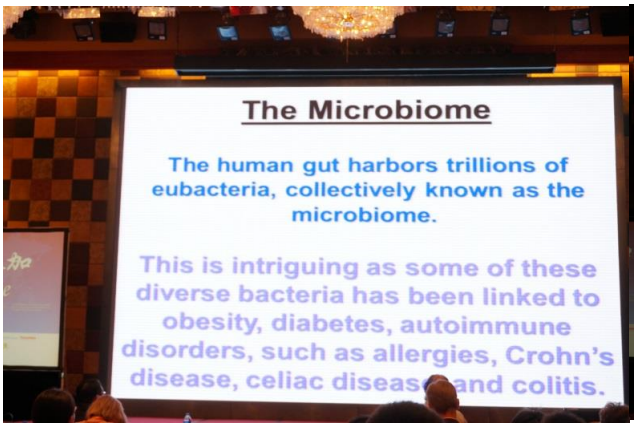
演講重點：Ada 先是簡單的介紹了由 DNA→RNA→Protein 的著名中心法則(central dogma)，由於 RNA 轉譯為蛋白質是藉由核醣體的轉譯作用，因此關於轉譯的任何步驟被打斷都有可能阻止細胞的正常生理功能，也因此有超過 40%的抗生素作用機轉是抑制核醣體的生物合成作用，例如阻止 tRNA 進入 A 位、阻止 amide bond 成形、打斷 elongation 等等，所以微小(500~1000Da)的抗生素就能阻斷整個巨大的核醣體(~2,500,000Da)的功能。而現今最困擾人類醫療的問題就在於細菌的抗藥性，而具抗藥性基因多樣性的細菌似乎天然就存在世上，科學家研究從未攝取過現代西方社會食物與醫藥的南美亞馬遜 Yanomami 族，令人驚訝的是這些住在叢林中的原始部落人類其腸道細菌亦具有多種抗藥性基因，難道抗藥性問題永遠無法克服嗎?Ada 為我們介紹了幾個重要的訊息顯示並非如此悲觀：

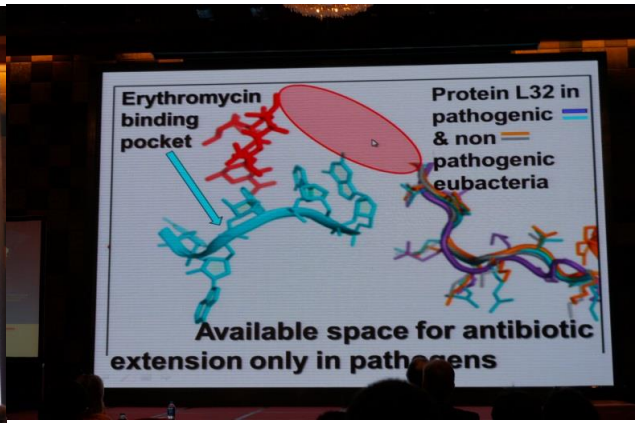
1. <u>抗生素的效率有可能被提升</u>：由於抗生素主要結合在核醣體的結構都相當近似，這可能源自於核醣體結構的保守性，因此如 pleuromutilin 這類首先在 1951 年被發現於某真菌的抗生素，其三環結構一直沒有改變，但這些年來僅僅改變其一個 14 號碳上的延伸結構，即能避免其抗藥性，這些延伸結構都有相似的氫鍵結合位置。
2. <u>抗生素的選擇性有可能被增加</u>：可以藉由分析致病菌與非致病菌其抗生素結合位置空間的差異，改變抗生素的結構使其只能插入致病菌的核醣體結構中，即能提升其選擇性。
3. <u>利用致病菌的核醣體結構模型預測新的抗生素結合位</u>：Ada 團隊藉由分析不同物種的核醣體蛋白 RPL3 序列，找出致病菌與其他物種不同的序列結構，並預測其可能的抗生素結合位共有 25 個，其中 16 個位置結合後可抑制蛋白的生成，且由於這些位置不牽涉初級核醣體功能(decoding、peptide bond formation 等)，因此理論上這些致病菌在演化

上不會保有這些位置的修飾，也不會具有抗藥性基因的存在，是相當具有新藥發展設計的結合位。

4. 對環境友善的抗生素設計：現有的抗生素大多是真核生物無法分解的小分子化合物，容易累積在我們的環境中，未來針對上述有潛力發展新穎抗生素的結合位，我們可以利用如核酸、胜肽等材料做抗生素，如此就具有可分解性，對環境更為友善。

要達到上述效果，我們勢必要有非常大量的致病菌核醣體「結構」資訊，以 X-ray 分析結晶的方法顯然太慢(結晶極為耗時)，CryoEM(冷凍電子顯微鏡)或許是目前最快可獲知蛋白結構的方法，這些結構資料庫的建立將對未來抗生素藥物的發展突破產生重要的助益。

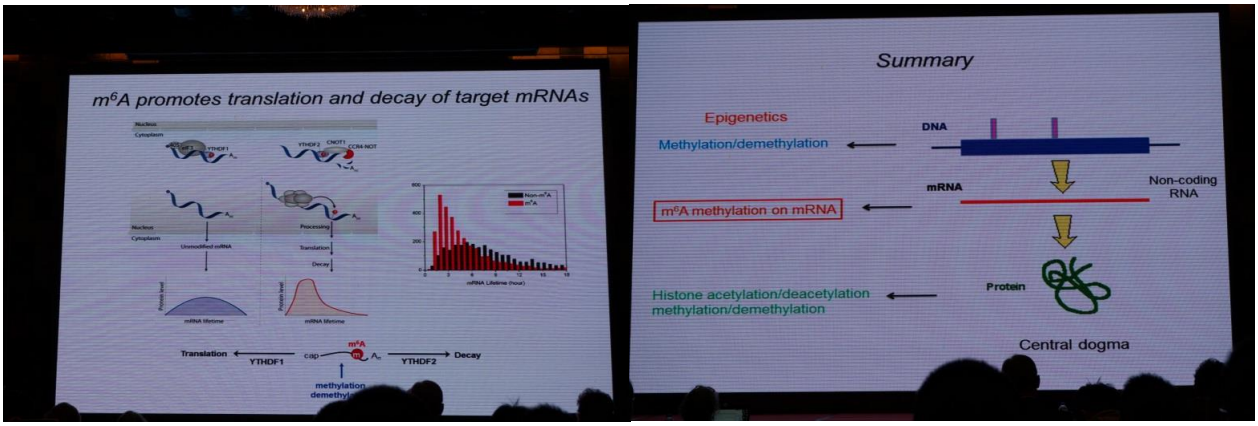




第二場演講題目：RNA methylation in gene expression regulation

講者：**Chuan H. E. PhD** (霍華休斯醫學中心、芝加哥大學教授)

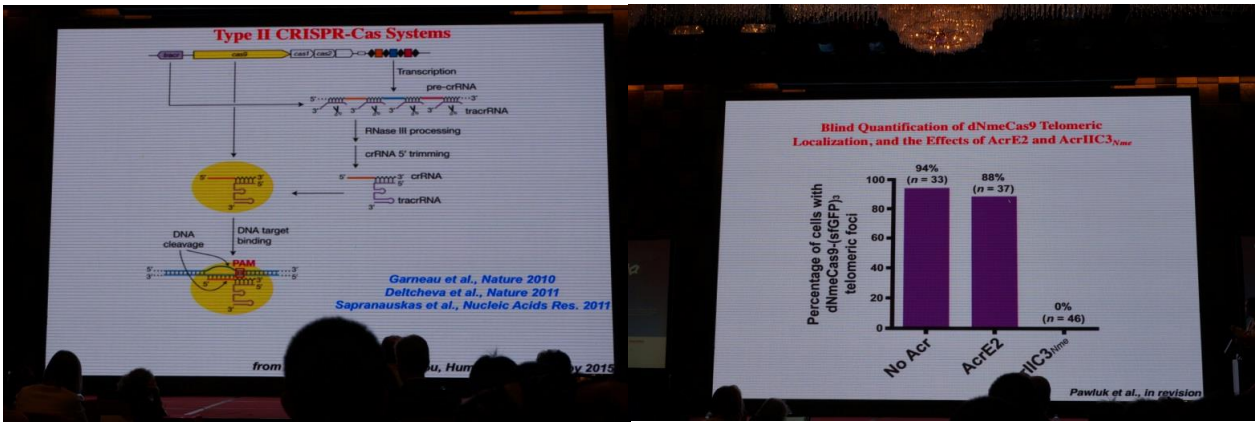
演講重點：本講者介紹的是較少被提及的 RNA 甲基化修飾之研究，我們常聽到 DNA 的甲基化/去甲基化修飾、蛋白質(如 Histone)的 acetylation/deacetylation 等與基因表現調控相關的修飾，卻很少注意在 RNA 上各種化學修飾代表的意義。mRNA 有一種常見的甲基修飾：m^6A，1970 年代被發現在各種生物的 mRNA 上都有這樣的內生性修飾存在，每個 mRNA 上約有 3~5 個 m^6A 修飾，。2011 年，講者的團隊發現第一個 RNA demethylase --- FTO/ALKBH5，這個基因剔除的小鼠會比正常小鼠體型略小，顯示其在發育上扮演的腳色，講者的研究團隊發現一類 YTH domain family(YTHDF)的蛋白會讀取 mRNA 上的 m^6A 修飾，並將被修飾的 mRNA 比其他更快速的被 processed→送出細胞核→進行轉譯，也就是加速其表現，這個功能對於胚胎的早期發育相當重要，這個發現對於 mRNA 修飾在表觀遺傳學(Epigenetics)的所扮演的角色有了新的研究面向，對於這種修飾的了解越多，也有幫助於未來核酸藥物修飾的設計工作。



<u>第三場演講</u>題目：Genetic interference and genome editing by Neisseria meningitides Cas9

講者：**Erik Sontheimer, PhD** (麻省醫學大學 RNA 治療研究所教授)

演講重點：CRISPR/Cas9（Clustered, Regularly Interspaced, Short Palindromic Repeats/ CRISPR-Associated Protein 9）是近期相當熱門的 DNA/RNA 修飾工具，起源於 1987 年科學家在細菌體內發現的特殊核酸內切酶系統，會辨認外來 DNA 並將其切割降解，被認為是細菌對抗病毒的自我防禦機制之一，而在 2012 年科學家解開 Cas9 對於其目標 DNA 的辨認機制，發現 Cas9 會與其導引 RNA（small-guiding RNA）結合後得到辨認目標序列的能力，從而結合並切割目標 DNA，科學家只需要修改導引 RNA 的序列，即可改變 Cas9 的專一性，命令其轉而裁切另一不同序列的 DNA。而講者的研究主要在於當以 Cas9 剪切完目標 DNA 後，如何「關閉(off switch)」這個剪切作用，過去的研究只知道 TypeI 的 CRISPR 系統可被 Acr 蛋白關閉，講者透過找出與其相似的其他序列，篩選出 *Neisseria meningitides* (Nme，奈瑟氏菌屬的腦膜炎細菌) 的 AcrII 蛋白，可用以有效調控 TypeII 的 Cas9 基因剪切作用，對於未來 TypeII 的 CRISPR/Cas9 系統應用於基因治療上有很大的幫助。

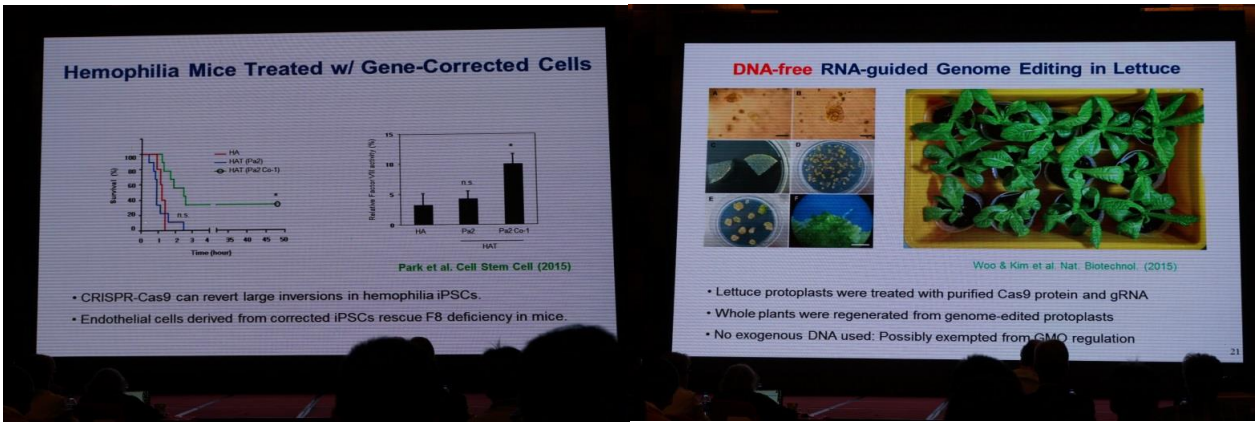


<u>第四場演講</u>題目：CRISPR RNA-guided Genome Editing in Human Stem Cells, Animals, and Plants

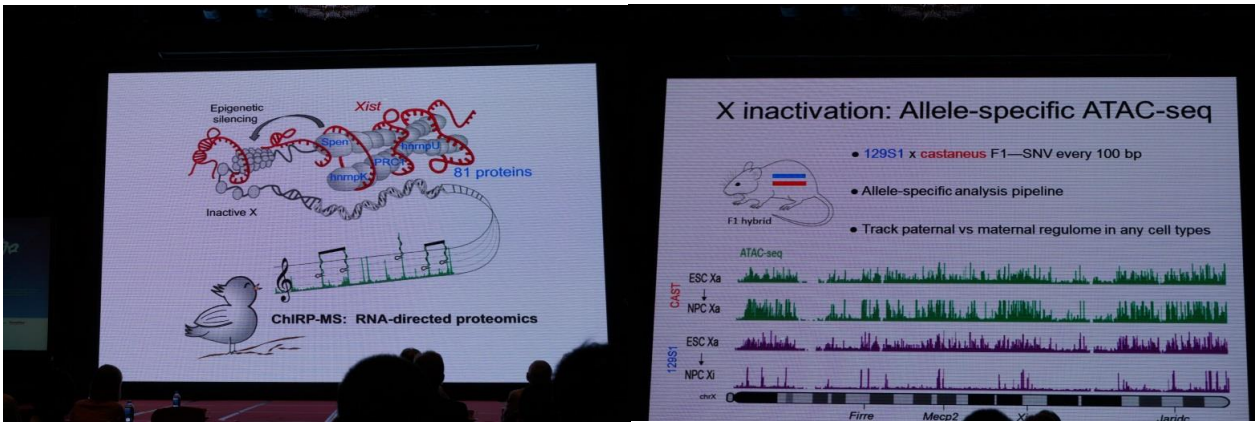
講者：**Jin-Soo Kim, PhD** (南韓首爾大學基因體工程中心主任教授)

演講重點：金教授的演講主要也是以 CRISPR/Cas9 的基因剪切技術為主，首先介紹了此系統的優點之一就是相比其他 DNA 內切酶，有較低的「脫靶效應(off-targeting effect)」

存在，可降低出現非預期基因剪切的機率。而該單位的研究成果包含以 Cas9 修飾後的自體 iPS 細胞(Induced pluripotent stem cells，誘導性多功能幹細胞)進行細胞療法，這是從病人身上取出體細胞，經過刺激使其還原(reprogramming)成 iPS 幹細胞，並將此幹細胞的基因已 Cas9 系統進行修復後，重新植入病人體內進行細胞治療的方法，目前該團隊以此方法成功使部分血友病(hemophilia)模式小鼠被治癒。另外，該技術也可用於植物的基因改造上，研究團隊利用 Cas9 技術修改菸草原生質體(protoplast)的基因，並將其重新培育成整株植物，這樣的基因修改植株並不含外源基因，某種程度上可減低對於以動物基因轉殖入植物體內的道德疑慮。



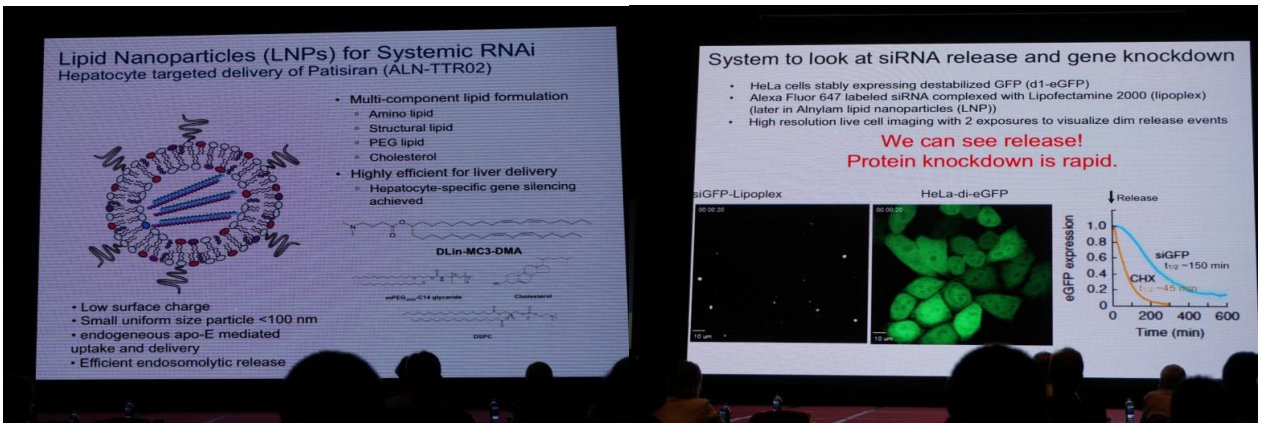
<u>第五場演講</u>題目：Genome Regulation by Long Noncoding RNAs (lncRNA).
講者：**Howard Chang, MD, PhD** (美國史丹佛大學教授，霍華休斯醫學中心)
演講重點：非編碼 RNA 在體內的功能一直存在非常多的謎團與未知，過去我們已經知道，所有雌性哺乳動物其中一個 X 染色體，其轉錄功能都會被抑制使其 X 染色體體基因的表現量與雄性一致，這條不活化的 X 染色體(Xi)會被壓縮成緊密的 Barr body，而「異染色質化(heterochromatinized)」，已知在雌性之體細胞中 Xi 性染色體會附著一稱為 Xist 的 RNA(Xi-specific transcript)分子以及特殊的組織蛋白，使整條 Xi 染色體的基因不表現，這種 RNA 與染色質間的交互作用顯現了長鏈非編碼 RNA 對於基因調控的重要性。講者的研究團隊在 2011 年開發出 ChIRP 技術，該技術可以在 whole gemome-wide 內鑑定 RNA 與染色質的交互作用。後來又將 ChIRP 進行改造，發布了稱為 dChIRP（domain-specific ChIRP）的新技術，該技術可以在天然環境下剖析 lncRNA 不同結構域的功能，後來在 ChIRP 的基礎上又再開發了質譜分析技術 ChIRP-MS。這是一種 RNA 導向的蛋白質組學技術（RNA-directed proteomics），能夠全面鑑定特定非編碼 RNA 的結合蛋白。這種細胞在基因組外的重新編程向我們展示了體細胞狀態在表觀遺傳學上的可塑性。而 lncRNA 被認為在表觀遺傳學調控中具有重要的作用。



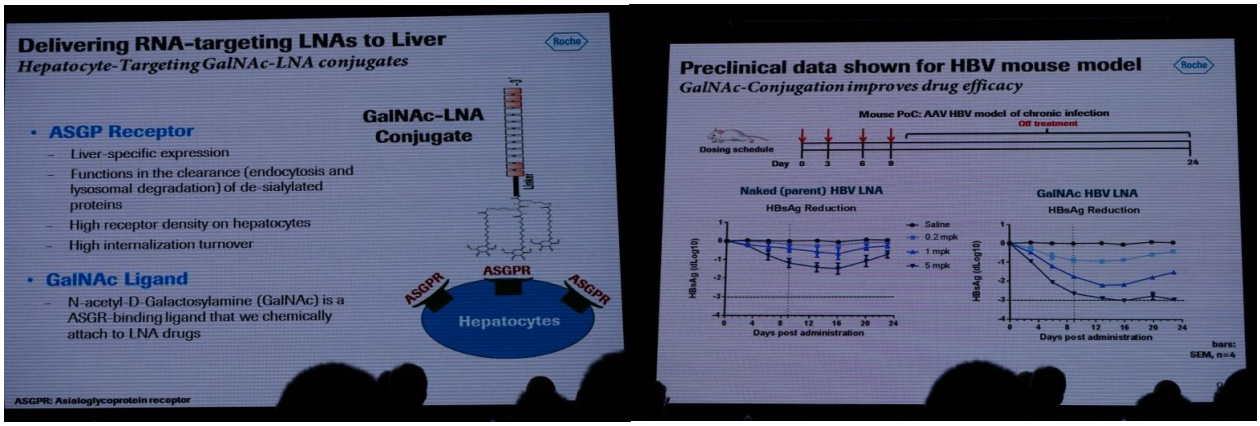
<u>第六場演講</u>題目：The Silent Treatment：Targeted gene knockdown

講者：**Judy Lieberman, MD, PhD** (哈佛醫學院教授)

演講重點：Judy 的研究主要專精於 siRNA 進入細胞的輸送機轉，siRNA 進入細胞主要有兩大瓶頸：1.由胞外通過目標細胞的細胞膜進入 endosome 之中；2.從 endosome 中被釋放到細胞質內並執行其功能。而 siRNA 要發揮功能最重要的就是這個輸送進入細胞內的系統，Alnylam 的 Transthyretin(TTR，轉甲狀腺素)新藥 GalNac-conjugated siRNA (Revusiran)由於加了三鏈 GalNac 的配體，因此進入肝臟的效率更高，可惜的是，這個藥物雖於去年(2015 進入臨床三期)，但在今年(2016/10/05)由於用藥組的 cardiac amyloidosis(心肌澱粉樣變性沉積症)病人比對照組的死亡率高，宣布新藥失敗而放棄，Alnylam 的股價也因此幾乎腰斬，目前另一新藥 Patisran，針對另一類型的 TTR 病症(Familial Amyloidotic Polyneuropathy(FAP)，家族性澱粉樣多發性神經病變)，並採用不同的藥物輸送系統：Lipid nanoparticles (LNPs)正進入臨床三期中，是否能與 Revusiran 有不同的結果備受關注。Judy 的研究團隊利用螢光技術觀察 LNPs 輸送 siRNA 進入細胞的機制，發現許多與 LNPs 進入細胞以及在細胞中被釋放所相關的表面蛋白，並且因為螢光技術而使得 in vitro 實驗中能「看見」siRNA 被釋放的時間，因而能對於此細部的 siRNA 輸送機制進行研究。但此種輸送方法目前仍有許多問題，主要在於效率仍然不高：僅有 7%的 LNPs 能被釋放，而每個進入細胞的 LNPs 僅能釋放 1/2 的所攜 siRNA 分子，等於僅有 3.5%的 RNAi 藥物能真的進入細胞的細胞質中發揮作用。由於過量的 siRNA 可能導致無法預期的副作用，因此持續提升 siRNA 藥物輸送系統的效率是非常重要的研究課題。

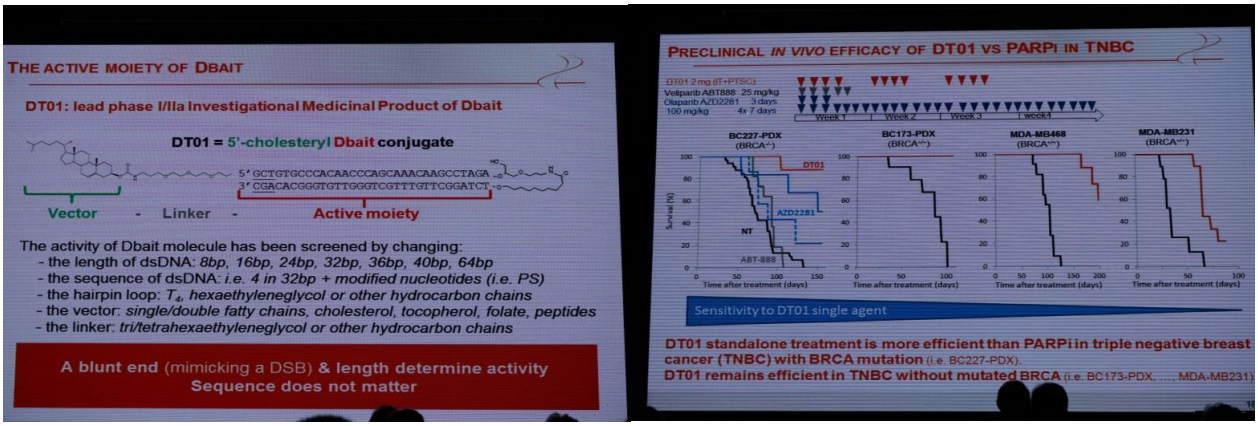


第七場演講題目：New structure-activity Determinants for Locked Nucleic Acids (LNAs)
講者：**Troels Koch, PhD** (Roche RNA 治療部門副總裁)
演講重點：2011 年羅氏投入超過 5 億美元進入 RNA 治療領域，但很快發現其困難遠超出想像而放棄，但在 2014 年，羅氏與 Santaris 公司合作再次跨足 RNA 治療領域，主要就是靠 Santaris 公司的專利—LNA 技術，這個技術可使 RNA 分子有更長的半生期、更好的穩定度與更低的生物毒性與脫靶效應。Koch 此次介紹分為兩大方向，一是有關 LNA 藥物目前的發展，羅氏與 Alnylam 同樣利用將 RNA 藥物接上三鏈 GalNAc 結構，使其能被肝細胞上的 ASGPR 蛋白結合，得到更好的藥物進入肝臟之輸送效率，差別在於 RNA 的結構，Alnylam 幾個月前失敗的 Revusiran 是採用較長的雙股 RNA 結構，而 LNA 則是單股的特殊修飾 RNA，其抑制 RNA 表現的機制亦有不同，羅氏的團隊研究對於 ApoB (與膽固醇過高有關，為低密度脂蛋白(LDL)上主要的蛋白成分之一)與 B 型肝炎設計 GalNAc 修飾之 LNA 藥物，目前已在動物身上取得成功的效果。另一部分的研究則是在透過改變 LNA 藥物 PS 修飾的立體旋光性(chirality)而優化 LNA 藥物的性質，這可能是透過其立體結構的改變使其能與 RNase H 有更好的結合，因此能提升其抑制的效率，在 Alnylam 的新藥失敗後，羅氏能否在 RNA 治療的領域上有所斬獲亦備受大家的期待。



第八場演講題目：Concept of DNA Repair Signal Interfering DNA (siDNA)
講者：**Jian-Sheng Sun, PhD, HDR** (法國國立自然史博物館教授)
演講重點：Jian-Sheng Sun 博士是 Dbait 的發明人之一，所謂 Dbait 是指雙股 DNA(dsDNA)斷裂的「誘餌」，這是第一個訊息干擾 DNA(signal interfering DNA，siDNA)故又被稱 DT01，這種 siDNA 分子是一種短的雙鏈 DNA 分子，目的在於提供假的 DNA 斷裂信號來吸引腫瘤中的 DNA 修復蛋白，從而阻止 DNA 修復酶到真正的 DNA 損傷位點上，等於是以誘餌誘騙腫瘤，使其以為 DNA 的損傷已經超過可承受的範圍，而含有損傷 DNA 的癌細胞持續分裂，最終它們因缺乏阻止細胞分裂的能力而走向自我毀滅的過程，因此亦具有輔助化學治療與放射治療的效果，而正常細胞雖然也會接收到這些 Dbait，但由於正常細胞在偵測到過量的 dsDNA 斷裂訊號時即會停止分裂等待 DNA 修復，因此反而不受影響。目前此藥物已經進入臨床 I/IIa 期，臨床前研究的結果發現，Dbait/DT01 會分布在腫瘤與肝臟，但不會造成肝毒性，也不會增加化療藥物以外的毒性，而且其活性主要作用在腫瘤部位而非正常細胞，另外在多種腫瘤模式動物中均有療效，不限腫瘤的種類，根據針對轉移性黑色素瘤病人的首個人類 I/IIa 期臨床試驗的結果，當瘤內注射和在腫瘤

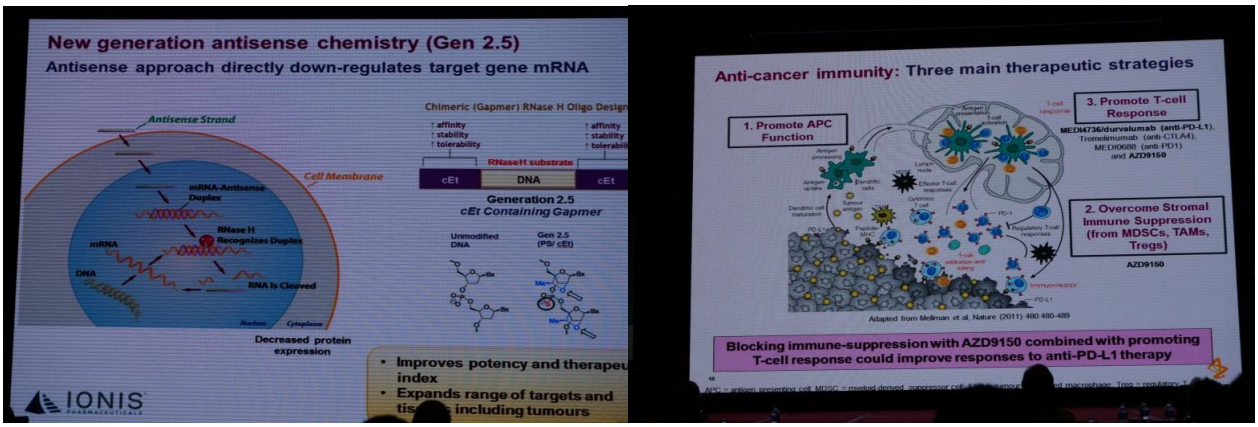
周圍皮下注射時，siDNA 分子具有良好的耐受性和安全性，這些研究結果顯示 Dbait 分子也是未來具有潛力的抗癌藥物發展方向之一。



<u>第 九 場 演 講</u>題 目 ： Therapeutic Antisense Oligonucleotides-Oncology targets – Ligand-conjugated antisense

講者：**Mark Edbrooke, PhD** (AstraZeneca 資深首席科學家)

演講重點：講者首先介紹了其利用 Ionis 公司新一代 RNA 藥物技術所研發的核酸藥物，其一為單股 RNA 結構，並在兩端接上經特殊修飾的短鏈 RNA，提升其活性、穩定度等，首先是一 STAT3 抑制劑 AZD9150 藥物(STAT3 的活化會抑制 T 細胞活性)，是一個 16mer 的單股反義短鏈 RNA，但其單獨使用效果不佳，但最近在一項 1b/2a 臨床試驗中與 durvalumab (PD-L1 的抗體，一種在部分腫瘤大量表現的表面抗原，被認為會抑制 T 細胞的活性) 聯合使用，治療晚期癌症患者。初期的試驗結果令人振奮：在接受第一項聯合療法的 11 名患者中，2 名出現了部分緩解，5 名的病情得到穩定控制，顯示多管齊下的調控免疫活性是可行的癌症治療策略。其二是 AZD4785 藥物，一種 KRAS 的抑制劑，有超過 30%的癌症被發現與 KRAS 蛋白的突變有關，但由於 KRAS 會與 GTP 很好的結合在一起，使得小分子藥物的抑制劑不容易接近，因而發現 KRAS 後 30 多年來，並沒有有效的抑制劑被發現或發明，研究者利用 siRNA 技術去抑制 KRAS 的 mRNA 表現，可有效抑制 LXFA 983 腫瘤之大小，可能是未來治療癌症的新標的。最後不約而同的，AstraZeneca 也發展了以修飾三鏈半乳糖來增加 RNA 藥物進入肝細胞的策略，顯示如何讓 RNA 藥物更有效率的進入細胞確實是所有研究者與藥廠都極感興趣的問題。



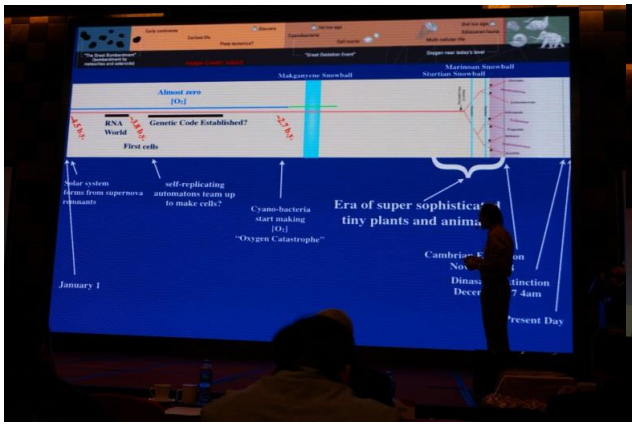
第二天：

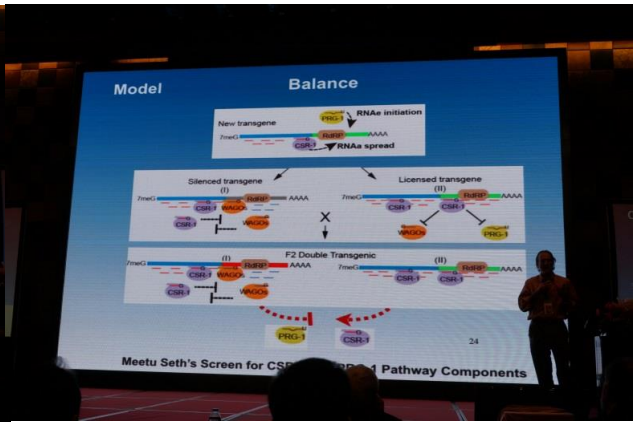
第一場演講題目：**RNA-Guided inheritance**

講者：**Craig Mello, PhD** (2006 年因發現 RNA 干擾現象的傑出貢獻獲得諾貝爾生醫學獎)

演講重點：Craig C. Mello 的父親是位考古學家，時常帶著兒子搜尋恐龍化石與探險，因此引發他對科學的熱愛，演講的開始他也從生物演化的觀點來看 RNA 在遺傳角色的演變，並介紹了以 RNA(而非修飾 DNA)所產生的一種特別遺傳記憶：RNA 誘導表觀沉默，RNA-induced epigenetic silencing (RNAe)，這是通過將外來序列和生物自身先前表達過之 RNA 進行比較，當差異被識別，一種稱為外來 DNA 片段的「表觀記憶」就會產生，並且被遺傳到後代中，永久將此一基因「沉默」下來。最顯著的特點是動物體攜帶有之前基因曾表達過的記憶，這種活性基因的記憶可以作為一種「反沉默（anti-silencing）」信號，保護生物體自體產生的基因不受 RNAe 的影響，甚至在某些情況下，將外來基因加入自身基因體中。研究人員發現，當編碼綠色螢光蛋白(GFP)的外來 DNA 片段，插入到線蟲體內的時候，有些線蟲就會抑制這些新入侵的 DNA，而有些線蟲則會表達 GFP 基因。研究人員深入分析了這種 RNAi 在決策抑制還是表達 GFP 方面的作用，在 RNAi 相關現象中，發現了一種蛋白 Argonaute 會與小分子 RNA 相互作用，利用它們作為識別標靶核苷酸的遺傳記號。

根據這些發現，研究人員提出一個包含有三個獨立 Argonaute 系統的模型，這些系統能共同掃描，識別和沉默外來 DNA，同時保護正常基因的表達。其中一個能結合在 piRNA 上的 Argonaute 蛋白—PRG-1 (Piwi)負責偵測離開細胞核的 RNA 分子，分析這些分子是屬於自體本身，還是外來侵入。如果 PRG-1 和其 piRNAs 輔因子識別出一個外來序列，就會啟動激活第二個 Argonaute 系統，就是 WAGO 系統，導致這一遺傳物質被關閉，不會被表達。這些發現讓我們了解基因調控的遺傳機制遠比我們所想像的更複雜、更多元。



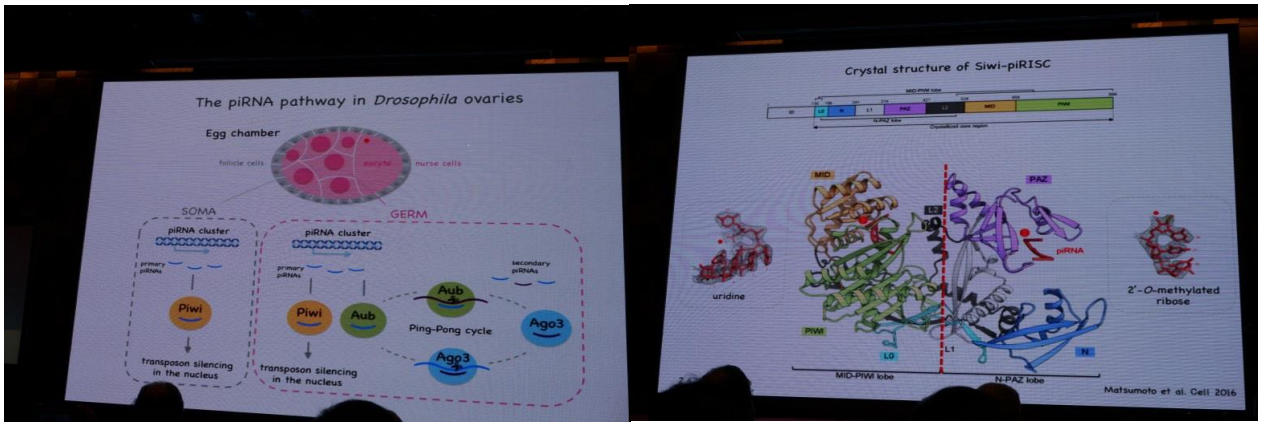


第二場演講題目：PIWI-interacting RNAs in animals

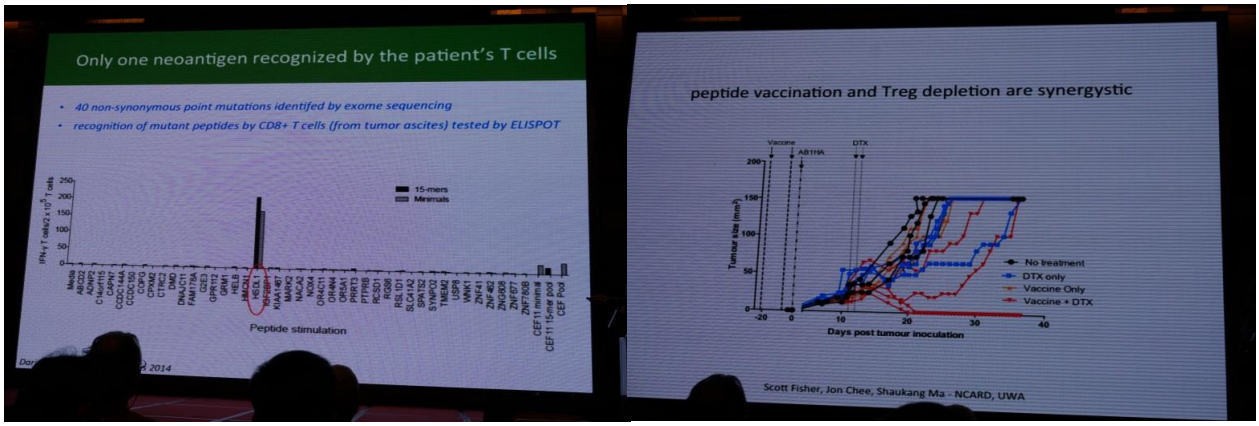
講者：**Mikiko Siomi, PhD** (日本東京大學生物科學系教授)

演講重點：PIWI 蛋白作用 RNA（PIWI-interacting RNAs，piRNAs）是一類小非編碼 RNA 族群，來源於基因組中的 piRNA 簇(piRNA cluster) 或轉位子區域(transposon regions)，由長鏈非編碼基因轉錄出的 RNA 切割產生。成熟的 piRNA 約有 24-32 nt。過去的研究中我們知道，piRNA 在動物界中廣泛存在，在所有的非編碼 RNA 中, piRNA 數量最多，主要存在於生殖系統中。piRNA 作為 PIWI 的嚮導，具有調控靶基因的表達以及轉錄和轉錄後水平的修飾功能。在果蠅卵巢生殖細胞中，piRNA 簇上的轉錄子轉運到胞漿後經過初

級加工途徑形成初級 piRNA，結合到 Piwi 和 Aub 上。而在生殖細胞的初級 piRNA 還會進入次級加工途徑，經 PIWI 家族蛋白(包含 PIWI、Aub 與 Ago3 等)的協同與加工作用，使細胞中的 piRNA 大量擴增，稱為桌球循環(「Ping-Pong」 cycle)，但是目前對桌球循環的細節和具體機制還如一團迷霧般難解，是非常新興的研究領域。Mikiko 教授的研究即在介紹如 PIWI/SIWI 與其 piRNA 結合後的結構，在不同物種間的相似與差異性，希望藉由對於其結構的了解能解開更多 piRNA 在生物體內扮演角色的秘密。



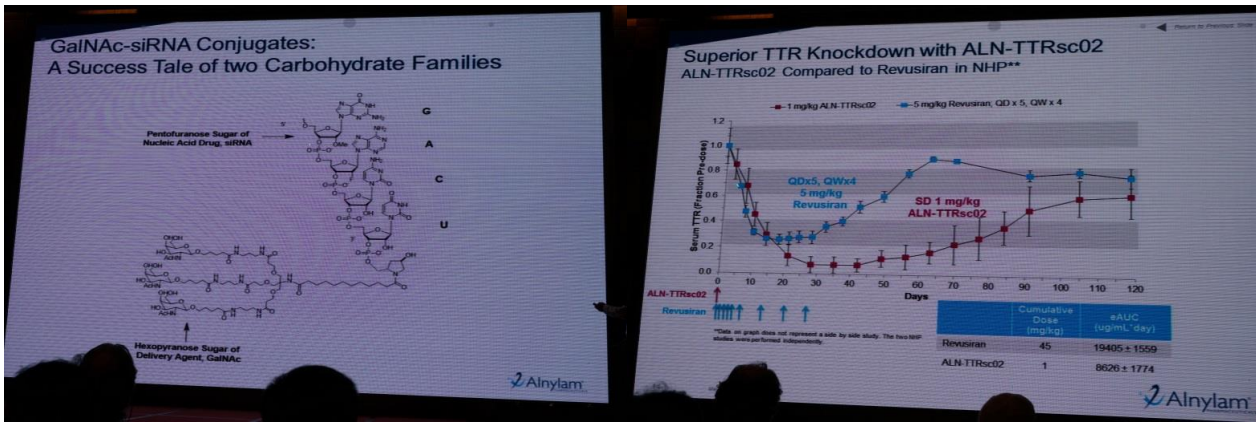
<u>第三場演講</u>題目：Towards T cell Therapeutics：Interrogating the T cell repertoire
講者：**Robert Holt, PhD** (英屬哥倫比亞大學教授)
演講重點：Robert 主要介紹免疫療法的一些故事，從 T 細胞基因庫開始，由於著名的 T 細胞受體(TCR)具有 VDJ 基因重組的機制，使得其具有非常高的多樣性，據研究指出，超過 99%的 TCR 序列在每個個人身上都是獨一無二，有趣的是，整個人類的基因組僅有 1%的不同(約 3 百萬個 SNPs)，但人類的免疫基因庫只有少於 1%是相同的(每個人有超過十億個獨特的 VDJ 鹼基)，因此每個人的免疫反應有時差異非常的大。以腫瘤為例，我們知道在腫瘤周邊的 T 細胞(tumor-infiltrating T cells)越密集，通常病人的存活率也越高，理由是這群 T 細胞既然圍在腫瘤旁邊，想當然爾就是要圍攻腫瘤的，但這些 T 細胞所辨認的抗原為何呢？一個在 12 個不同的癌症種類、3281 顆腫瘤採樣的研究中，總共發現有高達 617,354 種不同的突變，而其中超過 99.5%的突變都僅出現過一次，這些突變會是 T 細胞辨認的關鍵嗎？Robert 介紹了一個個案是卵巢癌的病人，在歷經三次化療後雖一度好轉，但其血液中 CA-125 仍反覆上升，最後死亡，此病人的腫瘤細胞經過分析，發現有 40 個非同義變異（non-synonymous mutation，即突變後胺基酸改變了）存在，但其中僅有一種突變叫 HSDL1 被 CD8+的 T 細胞所辨認，而其他的突變都無法激發免疫反應，因此針對特定突變的 T 細胞療法是否可行？又為何失敗？值得我們思考。
另外，在抗腫瘤的免疫療法除上述 T 細胞對抗原的辨認外，T 細胞本身是否活化也是一大重點，除了上述殺死腫瘤的 T 細胞外，另有一群 T 細胞是專門用來抑制發炎的 regulatory T cell (Treg，調節型 T 細胞)。在感染時若是細菌已經死光了，發炎還持續下去，那麼對正常組織的傷害是很大的，此時就是這群細胞出面阻止發炎的時候，這種現象叫 tolerance。但是在有癌症時，我們希望免疫系統在癌症附近能造成發炎，但這種發炎會被這一群 Treg 所阻止。研究發現缺乏 Treg 的小鼠其腫瘤大小會被明顯的抑制，CD8+的 T 細胞會被大量活化，顯示抑制 Treg 的活性也是癌症的免疫療法能否成功的關鍵因素，隨著我們對於免疫系統的了解越多，就越有可能發展出個人化的癌症免疫療法。



<u>第四場演講</u>題目：RNAi Therapeutics in Human Disease using GalNAc-siRNA Conjugates：How sweet it is to work with sugars.

講者：**Muthiah Manoharan, PhD** (Alnylam 製藥公司資深副總裁)

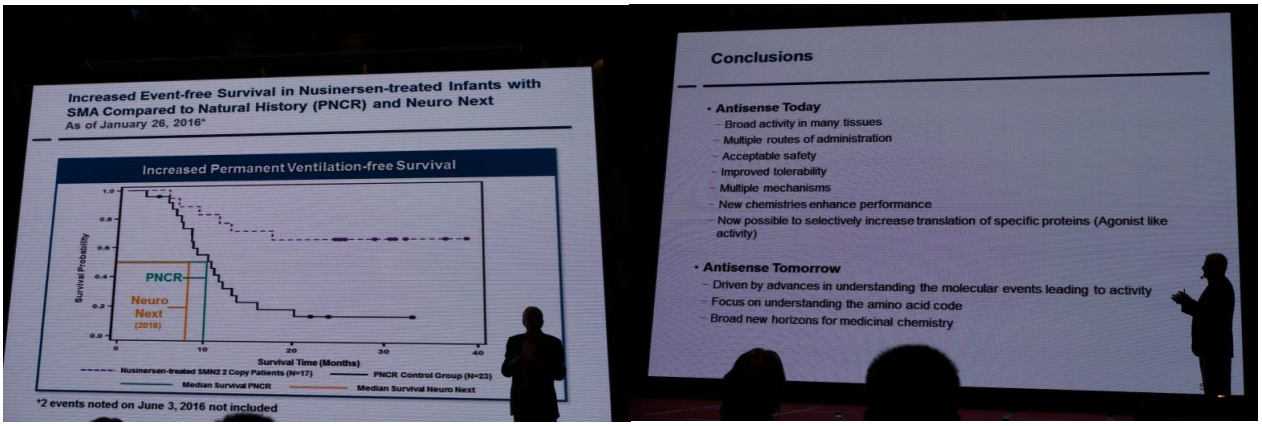
演講重點：在今年 10 月 5 日 Alnylam 的轉甲狀腺素蛋白澱粉樣變性心肌損傷 RNA 新藥 Revusiran 因臨床試驗中有 18 位病人死亡，中期分析顯示用藥組死亡人數偏多，療效也不顯著而宣布失敗股價慘遭腰斬後，Alnylam 似乎急於挽回大眾對於他們研究的信心，除了採用 Lipid-Nanoparticles(LNPs)作為載體的另一進入臨床三期新藥 Patisran 外，也試圖力推新一代的藥物設計技術所產生的新藥—ALN-TTRsc02。其主要與 Revusiran 差異除了適應症的不同，也在於結構的設計上。事實上 Alnylam 的新藥除了 Patisran 外，所有的結構(包含剛失敗的 Revusiran)都是將 siRNA 接上三鏈 GalNAc，使得 siRNA 進入肝臟的效率大增，但除此之外也對 siRNA 本身的結構進行優化與修飾，增進其穩定度，稱為 Enhanced Stabilization Chemistry(ESC)策略，根據講者的資料指出，新藥的結構可讓其被肝細胞上的 ASGPR 辨認而進入肝臟中，相比 Revusiran 來說，其降低血液中 TTR 水平的能力更強且更持久，可以用較低的劑量(5mg/kg→1mg/kg)達到更好的效果，而且降低使用的頻率，使得每年的暴露劑量明顯下降，而 Alnylam 公司下一代的產品幾乎全部都仍採用連接醣分子的這種新結構，顯見其認為 Revusiran 的失敗可能並非連接醣質分子的策略失效所導致，siRNA 本身的結構也是改良的重點，因此醣質分子做為配體(ligand)的優勢與潛力仍被看好。期待新結構能在臨床試驗上帶來好消息。



第五場演講題目：Antisense Technology：Present & Future

講者：**Stanley Crooke, MD, PhD** (Ionis 創辦人、CEO 與董事長)

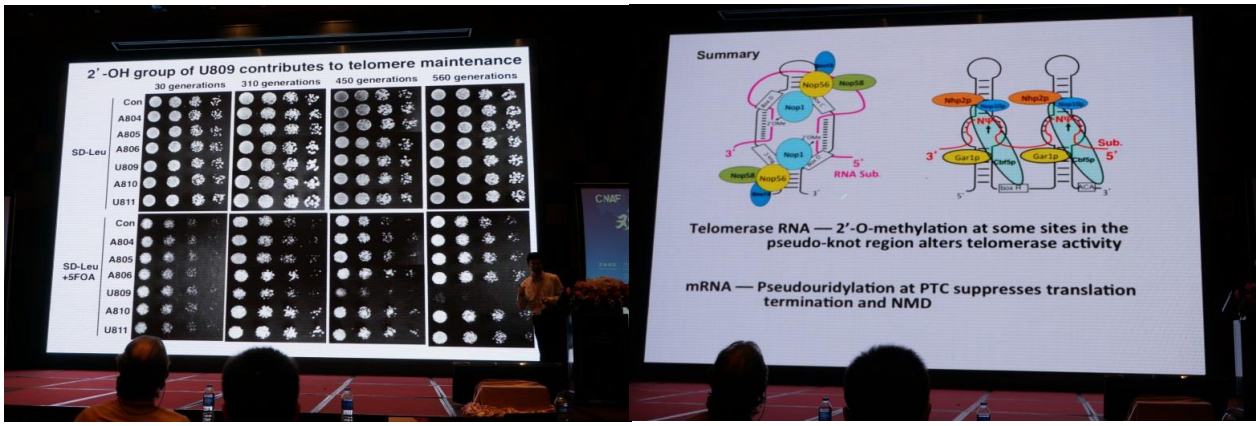
演講重點：Crooke 主要介紹其公司之新藥：脊髓性肌肉萎縮症(Spinal Muscular Atrophy，SMA)的 siRNA 藥物，SMA 是一種遺傳性的神經性肌肉疾病，是嬰幼兒期常見的致死性隱性遺傳病之一，是全球嬰兒死亡率最高的遺傳性疾病。其與著名的「漸凍症」同屬運動神經元退化疾病，不同的是脊髓性肌萎縮症（SMA）主要集中在 5 歲以前發病，而「漸凍症」主要發病時間集中在 40-70 歲，因而脊髓性肌萎縮症（SMA）也被戲稱為「兒童漸凍症」。目前脊髓性肌萎縮症（SMA）尚沒有特效治療方案。根據 Ionis 製藥公布的數據，在 Nusinersen 藥物實驗中，患病嬰兒在生存率、肌肉功能改善等方面都得到持續性提高，安全性及耐藥性方面也沒有重大問題。該藥物完成改善患者運動症狀的後期實驗目標。根據此項結果，相應實驗將中止，患者將在後續實驗中繼續接受藥物。在會中 Crooke 也展示了其人體試驗中的其中一位患者，在剛出生時即患嚴重的第一型 SMA，四肢均無法移動，在用藥治療後，逐漸康復，直到演講前幾天，已經四歲的小男孩已經能騎著小馬玩樂，非常戲劇化的呈現其藥物的效果，SMA 這項絕症是否能被治癒備受期待。另外 Crooke 也簡介新一代藥物開發方向：包含針對 APOC3 進行抑制的治療家族性乳糜血綜合徵(familial chylomicronemia syndrome)新藥、抑制 Factor XI 以預防 靜脈栓塞（venous thrombosis）以及抑制 Glucagon 以治療第二型糖尿病等等，未來的 siRNA 藥物開發會更加多元。



第六場演講題目：RNA-Guided RNA Modification

講者：**Yi-Tao Yu, PhD** (美國羅徹斯特大學醫學與牙醫學院教授)

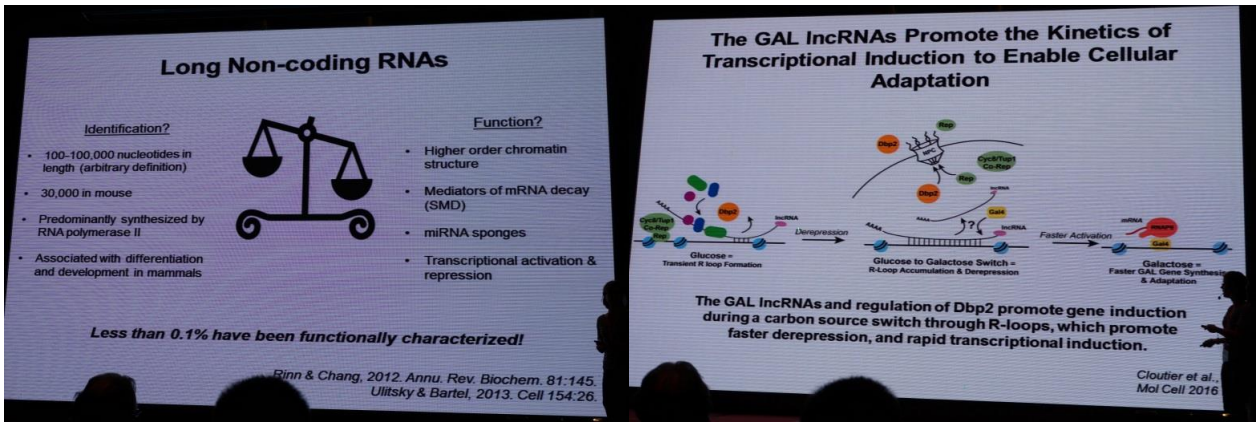
演講重點：Yu 博士主要演講內容專注在 Pseudoridylation 及 2'-O-methylation 這兩種 RNAs 上最常見的修飾類型，並分別由 Pseudouridylase(Box H/ACA RNP) 及 2'-O-methyltransferase(Box C/D RNP)這兩種酵素系統進行修飾工作，其機制是透過 RNA-guided 的方式引導酵素系統到其互補的序列上進行修飾。因此 Yu 博士團隊利用修改 Guided RNA (gRNA)的序列來將修飾的位置進行變化，從而研究這些修飾在 RNA 上所扮演的功能。結果發現，2'-O-methylation 在某些 RNA 的 pseudo-knot 區域會改變 telomerase 的活性，繼而影響細胞的凋亡；而在 mRNA 上的 Pseudoridylation 則會讓一些 nonsense 的密碼子變為 sense 的密碼子，從而改變蛋白轉譯的停止序號區域變為可以繼續轉譯下去，或許可以用來治療一些因 nonsense 突變而造成之疾病，例如： 囊狀纖維化(Cystic fibrosis)、乙型地中海型貧血(Beta Thalassaemia)、賀勒氏症(Hurler syndrome)或某些癌症。



<u>第七場演講</u>題目：Long Non-Coding RNAs Regulate Gene Expression Through Formation Of RNA-DNA Hybrids.

講者：**Elizabeth Tran, PhD** (美國普渡大學教授)

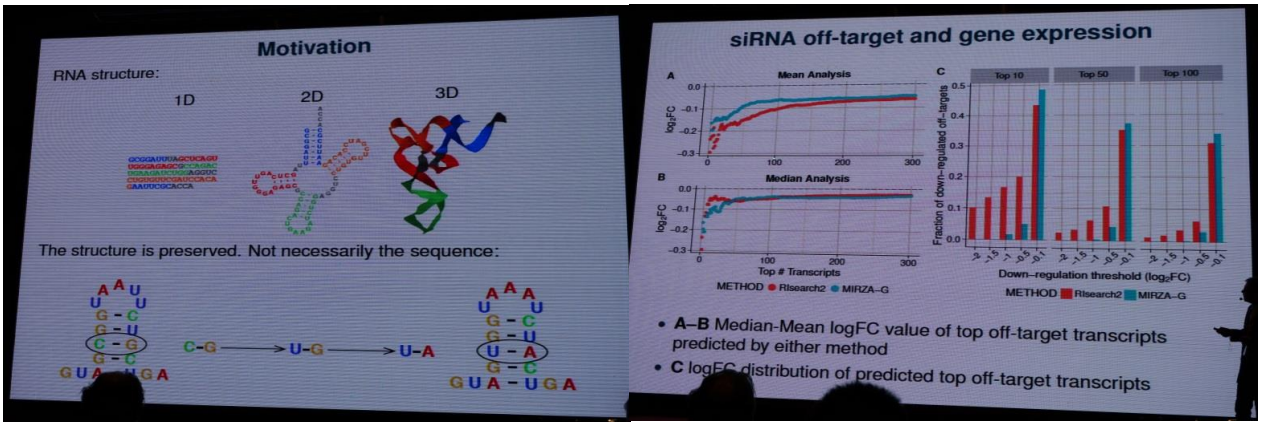
演講重點：長鏈非編碼(Long non-coding，lnc)RNA 曾一度被以為是假的轉錄產物，但如今隨著越來越多的研究，我們已經知道 lncRNA 在真核生物體內扮演多樣的生物化學反應調節者的角色。隨著定序技術的進展，目前的研究已經辨認出在哺乳動物體內有約 50,000-90,000 種 lncRNA，然而個別 lncRNAs 的功能仍然不清楚。講者的研究利用一種出芽酵母菌—*Saccharomyces cerevisiae*，這種酵母菌由於演化上丟失了 microRNA 的調控系統，因此非常仰賴 lncRNA 的功能，提供我們對於 lncRNA 如何調控基因表現前所未有的觀點與模範。利用這個模式講者發現了 Galactose(GAL)基因簇關聯之 lncRNAs 會透過形成 lncRNA-DNA 的互補結構或是 R-loops 來促進轉錄的激發。而這些結構是透過一種在演化上非常保守的 RNA 解旋酶 Dbp2，其功能在於回應環境中的因子對於轉錄激發的需求。GAL lncRNA 會測試 Cyc8 corepressor 離開以及後續的基因環化(looping)，相比於缺乏 GAL lncRNA 的酵母菌，正常的酵母菌在對培養基中具有 galactose 環境的反應要來得更快更迅速，因而產生競爭優勢。由於 GAL lncRNA 可以不需要影響最終平衡的轉錄副本水平，就達到促進轉錄進行的目的，講者因而預測這樣的 lncRNA-loop 結構形成具有演化上的優勢，應該會在更多的轉錄作用轉換上發揮功能，以取得更多適應環境而成長的優勢。



第八場演講題目：Computational analysis of RNA structure and interations in genomic sequence

講者：**Jan Gorodkin, PhD** (丹麥哥本哈根大學非編碼 RNA 技術與健康中心教授)

演講重點：講者重點在介紹利用電腦計算 RNA 的二級結構，這也是目前研究保守性 RNA 二級結構的主要挑戰，因為通常 RNA 的結構都是很保守不變的，而這種不變性似乎與序列的保守性無關，也就是只要能形成相同的結構，RNA 的序列改變也會被保留下來，這就增加了以序列預測結構的困難度。講者試圖以 RNA 結構排比(alignment)策略、CaptureSeq 策略加上結構探測(probing)技術在所選擇的候選 RNA 序列中解決這個難題。同時講者團隊也說明如何利用 RNA 生物資訊技術尋找 RNA-RNA 交互作用的可能方法，採用後綴陣列(suffix-array)實現以及簡化的能量模型並且使分析速度顯著增加，同時這個技術也可以利用來進行 siRNA 脫靶效應以及其抑制效率的預測，使得生物資訊領域在 siRNA 的研究上有更寬廣的應用空間。

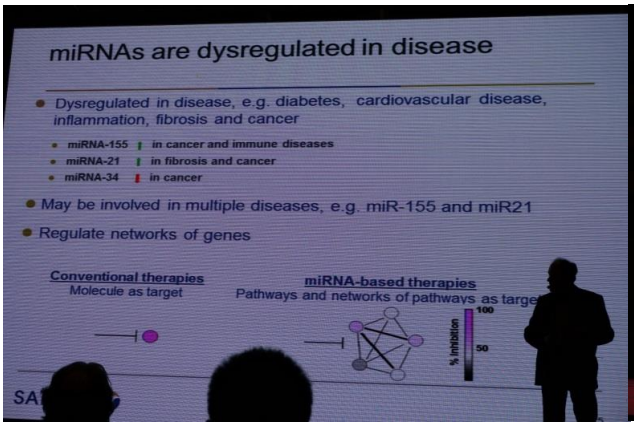


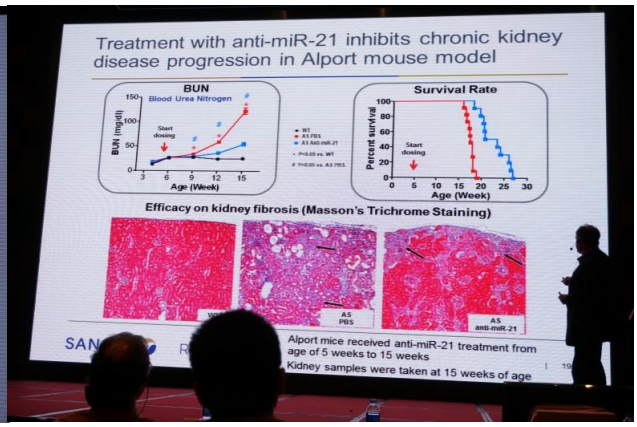
第九場演講題目：MicroRNA Therapeutics for Targeting the Pathways of Human Disease.

講者：Ekkehard Leberer, PhD (Sanofi 資深協理)

演講重點：Sanofi 介紹的重點主要集中在以 microRNA 為標的的 siRNA 藥物治療，miRNA 是一類 Non-coding 的短鏈雙股 RNA，長度約 22nt，目前已知的有超過 2000 種，其機制是透過與目標 mRNA 的 3'UTR 區域結合，並透過酵素的協同作用抑制基因的表現，特別的是一個 miRNA 可能同時能調節很多不同的 mRNAs，而一個 mRNA 也可能同時受多種不同的 miRNA 所調控，因此其基因調控機制並非傳統上了解的一對一抑制作用，而是類似網路(networks)的複雜關聯性調控。由於 miRNA 的領域還在快速發展中，因此以 miRNA 作為標的的藥物設計也是一新穎尚未被大量開拓的市場。以目前發展中的 miRNA-21 抑制藥物具有治療急性腎損傷(Acute kidney injury，AKI)與慢性腎臟疾病（Chronic kidney disease，CKD）的潛力，在小鼠模式動物上已證實 Anti-miR-21 具有保護腎臟纖維化的效果。另外在亞伯氏症候群（Alport's syndrome，即進行性遺傳性腎炎耳聾）的模式小鼠(COL4a3-/-)上抑制 miRNA-21 也具有避免小鼠疾病進程的效果，目前該藥物已在 2015 年進入臨床試驗。最近 Sanofi 也發現 miRNA-21 在肝癌 (Hepatocellular carcinoma)上也扮演部分角色，因在肝癌病人身上發現 miRNA-21 會大量過表現，而會抑制一些細胞凋亡(apoptosis)相關路徑，在 in vitro 細胞實驗中發現 Anti-miR-21 可增加細胞

凋亡蛋白的活化，在腫瘤模式小鼠(Hep3B)上施用 Anti-miR-21 也具有抑制腫瘤生長的效果。這些結果顯示了以 miRNA 為標的的 siRNA 治療具有的多型性與潛力。





(七)、 會議議程表

会议议程

Day 1 Wednesday, November 09		
08:45-08:55	Opening	**Organizers**
08:55-09:00	Chair	**Mikiko SIOMI, PhD**
09:00-09:45	Keynote	**Ada YONATH, PhD,** Professor, Weizmann Institute of Science, Israel Nobel Prize in Chemistry 2009 **Title:** Combating resistance to antibacterial and anti-parasite ribosomal antibiotics?
09:45-10:15		**Chuan HE, PhD,** Professor, University of Chicago, USA **Title:** New sequencing technology to map DNA epigenetic modifications
10:15-10:45	**Tea Break**	
10:45-11:15		**Erik SONTHEIMER,** Professor, University of Massachusetts Medical School **Title:** Genetic Interference and Genome Editing by Neisseria meningitidis Cas9
11:15-11:45		**Jin-Soo KIM, PhD,** Director, Institute for Basic Science, South Korea **Title:** CRISPR RNA-guided Genome Editing in Human Stem Cells, Animals, and Plants
11:45-12:00	Technology	**TBD** **Title:**
12:00-13:30	**Lunch**	
13:30-13:35	Chair	**Muthiah MANOHARAN, PhD**
13:35-14:20	Keynote	**Howard CHANG, MD, PhD,** Professor, Stanford University, US **Title:** Genome Regulation by Long Noncoding RNAs
14:20-14:50		**Judy LIEBERMAN, MD, PhD,** Professor, Harvard Medical School, USA **Title:** The Silent Treatment: Targeted gene knockdown
14:50-15:20	**Tea Break**	
15:20-15:50		**Troels KOCH, PhD,** VP and Head of Research,Roche, Denmark / Switzerland **Title:** New perspectives in LNA therapeutics
15:50-16:20		**Jian-Sheng SUN, PhD, HDR,** Professor, Muséum National d'Histoire Naturelle, France **Title:** Signal interfering DNA (siDNA): from an original concept to a promising a first-in-class DNA repair inhibitor against advanced stage cancer in patients
16:20-16:50		**Mark EDBROOKE, PhD,** Director, AstraZeneca, UK **Title:** Therapeutic nucleic acids including antisense oligonucleotides – significant progress towards a viable drug platform for tackling intractable targets in oncology
17:00-17:30		**After-Hours Social**

Day 2 Thursday, November 10		
08:55 - 09:00	Chair	**Elizabeth TRAN, PhD**
09:00-09:45	Keynote	**Craig C. Mello, PhD,** Professor, University of Massachusetts, 2006 Nobel Prize Winner, USA **Title:** RNA-guided inheritance
09:45-10:15		**Mikiko SIOMI, PhD,** Professor, the University of Tokyo, Japan **Title:** PIWI-interacting RNAs in animals
10:15-10:45	**Tea Break**	
10:45-11:15		**Robert HOLT, PhD,** Professor, University of British Columbia, Canada **Title:** Towards personalized T cell receptor therapeutics: Interrogating the T cell repertoire
11:15-11:45		**Muthiah MANOHARAN, PhD,** Senior Vice President, Alnylam Pharmaceuticals, USA **Title:** RNAi Therapeutics in Human Disease using GalNAc-siRNA Conjugates: How sweet it is to work with sugars
11:45-12:00	Technology	**TBD** **Title:**
12:00-13:30	**Lunch**	
13:30-13:35	Chair	**Mark EDBROOKE, PhD**
13:35-14:20	Keynote	**Stanley CROOKE, MD, PhD,** Founder, CEO and Chairman of the Board Ionis Pharmaceuticals, USA **Title:** Antisense Technology: Past, Present, Future
14:20-14:50		**Yi-Tao YU, PhD,** Professor, University of Rochester, USA **Title:** RNA-guided RNA Modifications
14:50-15:20	**Tea Break**	
15:20-15:50		**Elizabeth TRAN, PhD,** Associate Professor,Purdue University, USA **Title:** Long Non-Coding RNAs Regulate Gene Expression Through Formation Of RNA-DNA Hybrids
15:50-16:20		**Jan Gorodkin, PhD,** Professor,University of Copenhagen, Denmark **Title:** Computational analysis of RNA structure and interactions in genomic sequence
16:20-16:50		**Ekkehard LEBERER, PhD,** Professor, Senior Director, Sanofi, Germany **Title:** MicroRNA therapeutics for targeting the pathways of human disease
16:50-17:00	Closing	**Craig C. Mello, PhD,** Professor, University of Massachusetts, 2006 Nobel Prize Winner, USA

(八)、 會場紀要

↑廣州核酸國際論壇註冊處

↑楊員於簽到處留影

↑諾貝爾化學獎得主 Ada 帶來對核醣體作用抗生素之抗藥耐受性的演講，揭示結構對於解決抗藥性的重要。

↑Chuan H. E.教授揭示 RNA 甲基化的生理意義與其研究新方向。

↑Erik Sontheimer 教授介紹了腦膜炎雙球菌的 CRISPR/Cas9 基因編輯系統新技術。

↑Kim 教授將基因編輯技術用於動植物的基因修改上，創造出不同以往的基因改良生物。

↑Chang 教授揭開 lncRNA 在 Xist 這種性染色體不活化機制中所扮演的角色。

↑Judy Lieberman 用最新技術使得 RNAi 進入細胞的過程可以被「看見」，有助於研究其進入細胞的詳細機制。

↑羅氏 Troels Koch 博士向我們介紹以 LNA 技術可謂 siRNA 治療領域帶來的新視野。

↑Jian-Sheng Sun 博士利用 DNA 修復機制創造出抗癌新方法—Dbait，令人驚艷其創意。

↑Mark Edbrooke 博士帶來 AstraZeneca 製藥在 siRNA 藥物上的最新發展與設計策略

↑諾貝爾生醫獎得主 Mello 博士揭示了利用 RNA 進行水平遺傳的另一種機制。

↑Mikiko Siomi 博士實驗室以動物研究與 PIWI 蛋白交互作用 RNA 序列。

↑Robert 教授從 T 細胞的多樣性開始，介紹不同 T 細胞在癌症治療中的角色，並預示開發以 T 細胞為標地的癌症治療方法之可能。

↑Muthiah Manoharan 博士為我們介紹下一代 LNA 治療藥物設計策略與目前成果。

↑Stanley Crooke 博士以 Ionis 公司令人振奮的 SMA 新藥使大家看到 siRNA 治療領域的新希望。

↑Yu 博士介紹了兩種特別的 RNA 化學修飾，以及其如何影響 RNA 在細胞中的生理功能。

↑Elizabeth Tran 博士透過酵母菌的研究揭露長鏈非編碼 RNA 在生物適應環境中的重要功能。

↑Jan Gorodkin 講解生物資訊領域如何分析基因組 RNA 的結構以及其交互作用。

↑Leberer 博士以 miRNA 為標地設計的 siRNA 藥物，並舉出以抑制 miRNA-21 的方法治療腎臟疾病與肝癌的可能性。

(九)、　本次大會於 105 年 11 月 10 日結束所有的演講，至此為本屆廣州核酸論壇學術研討會畫下句點。楊員於次日 105 年 11 月 11 日下午五點自廣州白雲國際機場回台灣桃園國際機場，結束參加第四屆廣州核酸論壇學術研討會全部行程。

三、心　得

本次同位素組研究助理楊浚泓赴中國大陸廣州參加第四屆廣州核酸國際論壇學術交流會，蒐集國際最新核酸藥物開發與其在診斷與治療領域上的發展新知與研究成果，與國際專家學者進行交流與討論，出國公差自 105 年 11 月 08 日至 11 月 11 日止共計 4 日。楊員應邀參加第四屆廣州核酸論壇學術交流會，會議共計兩個整天，由 18 位國際核酸研究專家學者與核酸藥物開發藥廠進行專題演講，全程參與蒐集核酸藥物的最近技術、方法及研究成果並與與會人員進行交流與討論。此行收穫學習成果豐碩，心得條列如下：

(一)、 本次核酸國際論壇於廣州羊城舉辦，總與會人數約達三百多人，邀請了來自麻州大學、以色列魏茨曼科學研究所、史丹佛大學、IONIS 製藥公司等產學單位的 18 位核酸研究領域優秀科學家出席大會並進行專題報告演講。藉由該會進行學術交流與學習，有助於提升國內核酸藥物研發與相關技術發展的效果，並能強化研究人員的本職學能。

(二)、 此次會議有多個國際藥廠的研發領導上台演說，包含羅氏、Ionis、AstraZeneca、Sanofi 與 Alnylam，每個藥廠都介紹其發展中的 siRNA 新藥，其中有許多都已進入臨床試驗中，從這些藥物的共性中可發現，siRNA 藥物當前遇到的最大問題仍是「輸送系統」，由於 siRNA 藥物的特性使得發展出具有抑制效果的 siRNA 序列並不困難，困難點在於如何使藥物更有效率的進入細胞中。而因為 siRNA 本身的性質使其容易進入腎臟與肝臟，所以大部分的藥物目前的標的都集中在與腎臟或肝臟相關的疾病上。有趣的是，許多藥廠都不約而同地採用了在 siRNA 藥物上加上醣質(GalNAc)配體的作法，使其進肝臟的效率更佳，這樣的做法可以大大減低 siRNA 藥物的劑量，也降低了「脫靶效應」造成副作用的可能性，Alnylam 目前進入臨床三期新藥雖是以脂質奈米顆粒(LNPs)進行輸送，但其他幾乎所有的新藥都是採用加入醣質配體的方式運送，只是修改 siRNA 本身之結構，可見其重要性與潛力。

(三)、 除了 siRNA 藥物外，其他利用核酸進行的治療策略也讓人驚嘆國際先進研究者的創意，如 Jian-Sheng Sun 博士能利用分子生物學課本上都提到過的 DNA 修復機制，合成研發出對抗癌細胞的雙股 DNA 誘餌，與大部分找出目標蛋白去抑制或活化的策略完全不同；此外，Robert 教授也從個案中特殊現象出發，靈活運用各種工具去探求癌症免疫治療的可能。更有許多與直接應用無關，但卻闡釋了 RNA 重要生理功能的基礎研究，都具有相當大的啟發性。本所主要研究方向雖以放射性藥物與分子影像為主，參與不同的研究領域也往往能激發不同的創意與想像，如要繼續跟上國際的研究發展腳步，則勢必需要廣泛涉獵不同的技術與知識才能開拓研發的空間。

四、建 議 事 項

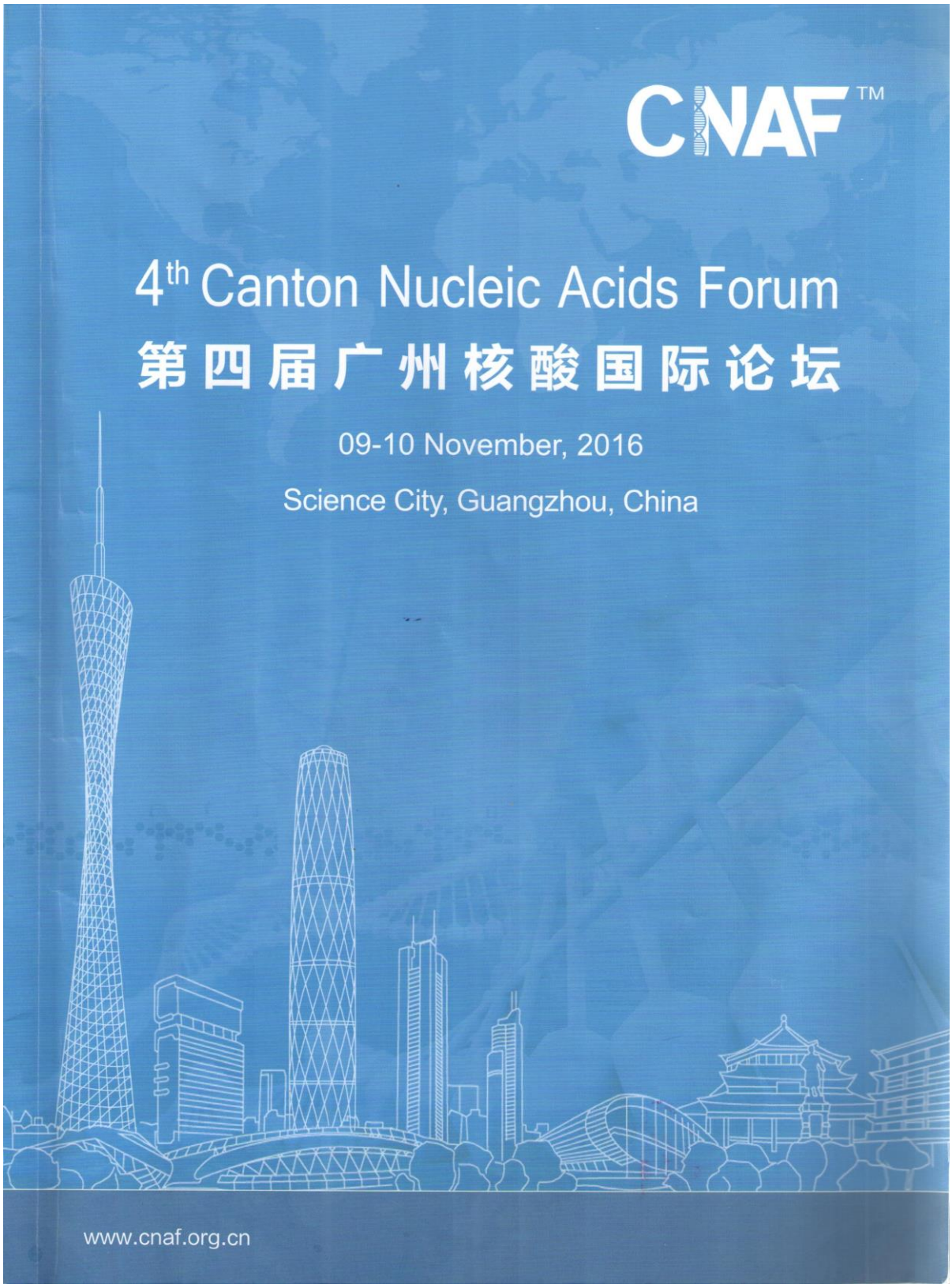
(一)、 **不局限於參加放射性藥物相關研討會**：本次參與的廣州核酸國際研討會並非專門探討本所同位素組「核醫藥物」專業的學術研討會，然而其特色在於以多位產學國際知名學者就當前最新的研究熱點「核酸藥物」的發展現況進行專題演說，相當具有學習拓展研究領域高度與廣度之功能。當前的核醫藥物發展設計也已日新月異，傳統上小分子研究領域已經不再專美於前，新興的胜肽、抗體等蛋白質領域已逐漸受到重視，因此在藥物開發的新興領域探求核醫藥物未來發展的可能性實為需要也是必要的選項。建議未來亦可持續派員參與會議，蒐集相關資訊作為本所後續研究之參考，另外諸如蛋白質藥物、免疫治療、細胞治療等領域亦可派員參加，使所內的研發能量更加充沛與寬廣，創造更多的可能性。

(二)、 **讓新領域與核醫藥物領域交流學習**：從本次研討會中可發現單一個核酸研究領域其複雜度與多樣性就非常的高，而不同領域專長的研究人員聚集總能激盪出不同的火花，本組作為核醫藥物研究的國家級機構徵集本領域優秀人才是為基本，但除此之外若有更多不同領域的人能來所發揮所長，不同領域間的激盪應更能有不同的想法與創意出現。建議未來在徵集如研發替代役人才時，亦能多考量不同相關領域的人才，或是派員前往不同領域的學研機構進行實習，確保技術的新穎性同時也激發不同以往的研究創意。

(三)、 **與其他研究機構(產學)建立技術合作**：核酸藥物的研發有其高度的專業性與技術門檻，會中各家藥廠難有一家能掌握所有最佳的技術，例如羅氏即利用另一家公司的 LNA 技術提高其藥物的穩定性，重新跨足核酸藥物領域，故常有策略合作聯盟的情況出現，建議若要跨足如核酸藥物或其他新領域前，多建立與其他具有專業技術的研究機構(包含產學)的溝通與合作，一方面可減低從頭學習技術的高門檻並減低成本，同時也是提供專業領域的相互學習，減少試誤期間的研發資源耗費。

五、附　錄

大會手冊內容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09:00-09:45, Wednesday, November 09

Ada YONATH, PhD

Professor, Weizmann Institute of Science, Israel
Nobel Prize in Chemistry 2009

Ada Yonath is focusing on protein biosynthesis, on antibiotics hampering it, on pathogenic parasites and on the origin of life. She graduated from the Hebrew University, Jerusalem, and postdocted at Carnegie-Mellon and MIT (USA). In the seventies she joined the Weizmann Institute and established the first structural-biology laboratory in Israel. During 1986-2004 she also headed Max-Planck-Research-Unit for Ribosome Structure in Hamburg. Among others, she is a member of US-National-Academy-of-Sciences; Israel Academy; German Science Academy (Leopoldina); the Pontificia Accademia-delle-Scienze (Vatican). She holds honorary doctorates from the universities of Oslo, NYU, Mount-Sinai, Oxford, Cambridge, Hamburg, Berlin-Technical, Patras, De-La-Salle, Xiamen, Lodz, Strasbiurg. Her awards include the Israel Prize; Louisa-Gross-Horwitz Prize;Linus-Pauling Gold Medal; Wolf-Prize; UNESCO/L'Oreal Award; Albert-Einstein-World-Award for Excellence; Nobel Prize for Chemistry.

09:45-10:15, Wednesday, November 09

Chuan HE, PhD

Professor, University of Chicago, USA
Howard Hughes Medical Institute

Chuan He is the John T. Wilson Distinguished Service Professor in the Department of Chemistry, Director of the Institute for Biophysical Dynamics at the University of Chicago, and an Investigator of the Howard Hughes Medical Institute. He is also a Cheung Kong Professor and Director of Synthetic Functional Biomolecules Center (SFBC) at Peking University in China. His recent research concerns reversible RNA and DNA methylation in biological regulation. Chuan He's laboratory has spearheaded development of enabling technologies to study the biology of 5-hydroxymethylcytosine (5hmC) in mammalian genomes. His laboratory also discovered the reversible methylation of N6-methyladenosine (m6A) in human messenger RNA (mRNA) in 2011.

10:45-11:15, Wednesday, November 09

Erik SONTHEIMER, PhD

Professor, RNA Therapeutics Institute
University of Massachusetts Medical School
Worcester, Massachusetts, USA

Erik Sontheimer is Professor in the RNA Therapeutics Institute (RTI) at the University of Massachusetts Medical School. He received his Ph.D. in 1992 from Yale, where he did his thesis work with Joan Steitz on pre-mRNA splicing mechanisms. He was then a Jane Coffin Childs Fund postdoctoral fellow with Joe Piccirilli at the University of Chicago. In 1999, Sontheimer joined the faculty at Northwestern, where he turned his attention to small RNA-based gene regulation in eukaryotes. In 2008 his laboratory also began working on genetic interference in bacteria. Among other advances, they provided the first demonstration that CRISPR RNAs (crRNAs) can target DNA, as well as the first explicit recognition of crRNA' s potential for gene targeting in eukaryotes, pointing the field down the path of RNA-guided genome engineering. He has received an NSF CAREER Award, a New Investigator Award from the Burroughs Wellcome Fund, and the Nestlé Award from the American Society for Microbiology, and he has also been elected to the American Academy of Microbiology. In 2014 he moved to the RTI, where he is continuing his research on the fundamental roles of RNA molecules, and on their uses in biomedical research and medicine. He is a co-founder and Scientific Advisory Board member of Intellia Therapeutics, which is developing Cas9-based genome editing for clinical applications.

11:15-11:45, Wednesday, November 09

Jin-Soo KIM, PhD

Professor, Seoul National University
Director ,Center for Genome Engineering,
Institute for Basic Science and Department of Chemistry, South Korea

- Scientific interests and expertise
  Genome engineering via programmable nucleases including the CRISPR-Cas system
  1) Genome editing in plants, animals, and cultured human cells including iPS/ES cells
  2) Engineered nuclease-mediated gene and cell therapy
  3) Functional genomics using genome-scale libraries of programmable nucleases

- Received degrees (including places and years)
  1987, BS, Dept. of Chemistry, Seoul National University
  1989, MS, Dept. of Chemistry, Seoul National University
  1994, PhD, Dept. of Biochemistry, University of Wisconsin-Madison

- Current position(s) and role(s) in affiliated organizations
  1994-1997, Research Associate, Howard Hughes Medical Institute/MIT
  1997-1999, Principal Investigator, Samsung Biomedical Research Institute
  1999-2005, CEO and CSO, ToolGen, Inc.
  2005-present, Assistant/Associate/Full Professor, Seoul National University
  2014-present, Director, Institute for Basic Science (IBS)
  Home pages: http://cge.ibs.re.kr/html/cge_en and http://gel.snu.ac.kr

13:35-14:20, Wednesday, November 09

Howard CHANG, MD, PhD

Professor, Stanford University, USA
Howard Hughes Medical Institute

Howard Y. Chang M.D., Ph.D. is Director of the Center for Personal Dynamic Regulomes and Professor of Dermatology at Stanford University School of Medicine. Chang earned a Ph.D. in Biology from MIT, M.D. from Harvard Medical School, and completed Dermatology residency and postdoctoral training at Stanford University. His research addresses how large sets of genes are turned on or off together, which is important in normal development, cancer, and aging. Chang discovered a new class of genes, termed long noncoding RNAs, can control gene activity throughout the genome, illuminating a new layer of biological regulation. He has invented new methods for defining the shapes of RNA and DNA genome-wide. The long term goal of his research is to decipher the regulatory information in the genome to benefit human health.

Dr. Chang' s honors include the Paul Marks Prize for Cancer Research, Judson Daland Prize of the American Philosophical Society, Howard Hughes Medical Institute Early Career Scientist, the Vilcek Prize for Creative Promise, Alfred Marchionini Research Prize, American Cancer Society Research Scholar Award, Damon Runyon Scholar Award, and elected membership to the American Society for Clinical Investigation. His work was honored by the journal Cell as a Landmark paper over the last 40 years and by Science as "Insight of the decade".

14:20-14:50, Wednesday, November 09

Judy LIEBERMAN, MD, PhD

Cellular and Molecular Medicine Program, Boston Children' s Hospital and Department of Pediatrics, Harvard Medical School, Boston MA USA

Judy Lieberman holds a Chair in Cellular and Molecular Medicine at Boston Children' s Hospital, is Professor of Pediatrics at Harvard Medical School and is Chair of the Executive Committee of Immunology at Harvard Medical School. She earned a Ph.D. in physics from Rockefeller University and worked as a theoretical physicist at the Institute for Advanced Study in Princeton and Fermilab, received an M.D. from Harvard and MIT, did a postdoctoral fellowship in immunology in the Eisen laboratory of the Cancer Center at MIT and worked as a hematologist/oncologist at Tufts Medical Center. She has received numerous awards for her research on AIDS vaccines, immunology and cancer. She is a member of the American Academy of Arts and Sciences.

The Lieberman laboratory has been in the forefront of developing RNAi-based therapeutics and using RNAi for genome-wide screening. They have developed strategies for cell-targeted RNAi to treat viral infection, immune disease and cancer. They also investigate the role of microRNAs in regulating cell differentiation and cancer. The Lieberman laboratory also studies cytotoxic T lymphocytes and their role in immune protection from infection and cancer. They study the molecular pathways used by killer lymphocytes to induce programmed cell death of both mammalian cells and microbes, especially those activated by cytotoxic granule proteases, called granzymes, and immune pore-forming proteins.

15:20-15:50, Wednesday, November 09

Troels KOCH, PhD

VP and Head of Research, RNA Therapeutics
Roche, Denmark / Switzerland

Dr. Troels Koch (TK) is Ph.D. in bio-organic chemistry and has worked in the area of nucleic acid chemistry and biology for more than 15 years. TK is co-founder of several Biotech companies of which Exiqon A/S and Santaris Pharma A/S are most commonly known. He is presently Vice President of Research & CTO in Santaris Pharma A/S with main responsibilities to further build on the fundamental understanding of the chemical and biological properties of LNA, refining the LNA antisense drug discovery process, and establishing a drug pipeline on RNA antagonists targeting both mRNA and microRNA. Collectively this work and associated IP has been a driver behind the four major partner deals that Santaris has entered over the past years. During his academic and biotech career TK has gained experience in managing R & D activities, intellectual property, quality systems, regulatory affairs, antisense drug substance/product manufacturing, and nucleic acid bio-organic chemistry. TK is the author of about 70 peer reviewed scientific papers and inventor of about 25 base patents. He is a frequently invited speaker at international conferences, and he has accepted more than 70 invitations in the past decade.

15:50-16:20, Wednesday, November 09

Jian-Sheng SUN, PhD, HDR

Professor, Muséum National d'Histoire Naturelle
MNHN-CNRS-INSERM, France

Born in Shanghai, after high school, he was sent to France by Chinese government to study theoretical physics. After M.S. degree, he served as assistant professor in the Department of Physics at Fudan University. Later on, he returned to Paris to study nucleic acids, was awarded Ph.D and Habilitation degrees in biophysics at Pierre & Marie Curie University. He also had an entrepreneurial training at HEC business school.

His research in nucleic acids (100+ peer-reviewed publications, 8 patents) led him to co-invent an original concept with Dr. Marie Dutreix at the Institut Curie – "the signal interfering DNA (siDNA)" which jams the recognition and signaling of double strand break (DSB) by using a short dsDNA mimicking a DSB. Acting agnostically at upstream, it can blind DSB repair signaling, thus inhibit all DSB repair pathways causing cancer cell death due to unrepaired DSB, while preserving normal cells.

In 2006, he co-founded DNA Therapeutics, served as Chairman & CEO, managed from scratch to clinical stage this virtually integrated biopharmaceutical company and executed from concept to clinic a 1st-in-class drug development with the help of the experts aggregating skills in early stage drug development, CMC, regulatory affairs and business development. After demonstrating good safety and significant anti-tumor activity of the 1st-in-class siDNA drug candidate in a phase I/IIa trial in patients with cutaneous metastatic melanoma (presented at the ASCO 2015), the Company was acquired in early 2016 by Onxeo – a public company specializing in the development of innovative oncology therapeutics. After closing, he is back to MNHN, focusing his research on the interplay between DNA damage, cancer and aging.

Prof. Sun received the physical chemistry 1991 award by French Chemical Society, the joint Grand Prize of Life Science 2006 by French Senate, INSERM-Transfert and ESSEC, the Award of Best Innovative Entrepreneur in Health 2008 by French Business Angels investing in health, the Next Gem award of best biotech at Biovision Investor Conference 2013.

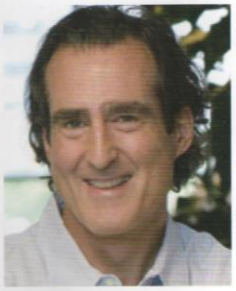
16:20-16:50, Wednesday, November 09

Mark EDBROOKE, PhD

Senior Principal Scientist, Oncology iMed, AstraZeneca, Cambridge, UK

Mark Edbrooke earned his PhD in molecular biology from the University of London. He ran a transnational Gene Interference functional genomics department at GSK that generated target identification and validation data for all therapeutic areas across the company (e.g. oncology, cardiovascular, respiratory, neurology and infectious diseases). He then founded and led a Discovery Performance Unit (DPU) within GSK focused on the development of therapeutic siRNAs and, laterly, on therapeutic antisense oligonucleotides. He recently joined AstraZeneca (AZ) and is involved in AZ' s alliances with Ionis Pharmaceuticals, Regulus Therapeutics, and Moderna Therapeutics.

09:00-09:45, Thursday, November 10



Craig MELLO, PhD

Professor, University of Massachusetts
Howard Hughes Medical Institute, USA
Nobel Prize in Physiology or Medicine (2006)

Dr. Mello's lab uses the nematode C. elegans as a model system to study embryogenesis and gene silencing. His collaborative work with Dr. Andrew Fire led to the discovery of RNA interference (RNAi), for which they shared the 2006 Nobel Prize in Physiology or Medicine. Together they showed that when C. elegans is exposed to double-stranded ribonucleic acid (dsRNA), a molecule that mimics a signature of viral infection, the worm mounts a sequence-specific silencing reaction that interferes with the expression of cognate cellular RNAs. Using readily produced short synthetic dsRNAs, researchers can now silence any gene in organisms as diverse as rice and humans. RNAi allows researchers to rapidly "knock out" the expression of specific genes and, thus, to define the biological functions of those genes. RNAi also provides a potential therapeutic avenue to silence genes that cause or contribute to diseases.

Dr. Mello received his BS degree in Biochemistry from Brown University in 1982, and PhD from Harvard University in 1990. From 1990 to 1994, he conducted postdoctoral research at the Fred Hutchinson Cancer Research Center in Seattle, WA. Now Dr. Mello is an Investigator of the Howard Hughes Medical Institute, the Blais University Chair in Molecular Medicine and Co-director of the RNA Therapeutics Institute at the University of Massachusetts Medical School.

Besides the Nobel Prize, Dr. Mello's work was recognized with numerous awards and honors, including the National Academy of Sciences Molecular Biology Award (2003), the Wiley Prize in Biomedical Sciences from Rockefeller University (2003), Brandeis University's Lewis S. Rosnstiel Award for Distinguished Work in Medical Research (2005), the Gairdner Foundation International Award (2005), the Massry Prize (2005), the Paul Ehrlich and Ludwig Darmstaedter Award (2006), the Dr. Paul Janssen Award for Biomedical Research (2006), the Hope Funds Award of Excellence in Basic Research (2008). He is a member of the National Academy of Sciences, the American Academy of Arts and Sciences, and the American Philosophical Society.

Additional information about Dr. Mello can be found in the following sites:
http://www.hhmi.org/scientists/craig-c-mello
http://profiles.umassmed.edu/profiles/ProfileDetails.aspx?From=SE&Person=1009
http://www.nobelprize.org/nobel_prizes/medicine/laureates/2006/mello-bio.html
http://en.wikipedia.org/wiki/Craig_Mello#Awards_and_honors

09:45-10:15, Thursday, November 10

Mikiko SIOMI, PhD

Professor, Department of Biological Sciences, Graduate School of Science, The University of Tokyo, Japan

Mikiko C. Siomi earned her Ph.D. in Agricultural Chemistry from Kyoto University, Japan in 1994, and then did post-doctoral studies with Prof. Gideon Dreyfuss, HHMI/University of Pennsylvania School of Medicine. Later, Dr. Siomi earned another Ph.D. in Medical Science from the University of Tokushima, Japan in 2003. Dr. Siomi started a joint laboratory with Prof. Haruhiko Siomi in the University of Tokushima, Japan in 1999 for elucidating the function of FMRP and the mechanism of RNAi using the Drosophila system. The laboratory discovered that Ago2 protein, the key player of RNAi, interacts with FMRP, an RNA-binding protein that is encoded by the fmr1 gene, the responsible gene for causing Fragile X Mental Retardation. Later, Dr. Siomi focused on elucidating how RNAi mechanistically occurs and the molecular mechanisms of piRNA biogenesis in the germlines. Dr. Siomi started her own laboratory at the University of Tokyo in 2012 (http://www-siomilab.biochem.s.u-tokyo.ac.jp/index.html). Dr. Siomi co-authored numerous research articles, reviews and book chapters, and currently serves as the president of the RNA Society of Japan and the vice-president of the Molecular Biology Society of Japan.

10:45-11:15, Thursday, November 10

Robert HOLT, PhD

Professor, University of British Columbia, Canada
Professor, Simon Fraser University, Canada
Scientist, British Columbia Cancer Agency, Canada

Rob Holt received his PhD in Pharmacology from the University of Alberta, Canada, in 1998. After a postdoctoral fellowship in molecular evolution at the State University of New York, Dr. Holt joined the company Celera Genomics in Rockville, Maryland where he served on Craig Venter's team as the Scientific Operations Manager for initial sequencing of the human genome. Since 2003 Dr. Holt has been a Senior Scientist at the British Columbia Cancer Agency (BCCA), where he is Co-director of the BCCA Immunotherapy Program and Co-director of the Genome Canada Science & Technology Innovation Centre. Dr. Holt is recognized for his leadership role in decoding some of the first model organism genomes and pathogen genomes and, more recently, for developing next-generation sequencing methods for interrogating the genetics of the adaptive immune system. He has served as a scientific advisor to the NIH Human Microbiome Project and discoveries by his research group have linked new infectious agents to cancer risk. His current research directions are focused on cancer genomics, T cell engineering, and immune interventions in cancer. He has published over 130 scientific papers that have received >49,000 citations.

11:15-11:45, Thursday, November 10

Muthiah MANOHARAN, PhD

Senior Vice President, Drug Discovery, Alnylam Pharmaceuticals, USA
Board Director, Oligonucleotide Therapeutics Society

Dr. Muthiah Manoharan serves as Senior Vice President of Innovation Chemistry at Alnylam Pharmaceuticals, Cambridge, Massachusetts, USA. Dr. Manoharan joined Alnylam in 2003. He built the chemistry group at Alnylam and pioneered the discovery of GalNAc conjugated siRNAs for RNA interference (RNAi) based human therapeutics. He was the former Executive Director of Medicinal Chemistry at Isis Pharmaceuticals, Inc., a leading biotechnology company focused on antisense oligonucleotide-based therapeutics where he had a12-year tenure. With a distinguished career as a world-leading nucleic acid and bioconjugate chemist, Dr. Manoharan is an author of nearly 200 publications and over 300 abstracts, as well as the inventor of over 200 issued U.S. patents. Prior to Isis Pharmaceuticals, He earned his Ph.D. in chemistry at the University of North Carolina-Chapel Hill and conducted post-doctoral work at Yale University and the University of Maryland. He was the recipient of the M. L. Wolfrom award of the ACS Carbohydrate Chemistry Division in 2007.

13:35-14:20, Thursday, November 10

Stanley CROOKE, MD, PhD

Founder, CEO and Chairman of the Board
Ionis Pharmaceuticals, USA

Dr. Crooke is one of the pioneers, most experienced scientists and knowledgeable experts in the oligonucleotide therapeutics field. He established and for more than 2 years supervised drug discovery and development platform, resulting in growing numbe (currently nearly 30) of therapeutic programs with diverse indications, includin cardiovascular and metabolic diseases, inflammation and cancer, severe and ra disorders. Many of the programs have been developed by leading biopharmaceutica companies, such as AstraZeneca, Biogen Idec, GlaxoSmithKline, Pfizer, Sanofi, Tev and advanced to phase 2 and phase 3 clinical trials. In January of 2013, an oligonucleotide inhibitor of apolipoprotein B-10 (Mipomersen, Kynamro), discovered and initially developed by Dr. Crooke' s team, was approved by the United States Foo and Drug Administration for treatment of familial hypercholesterolemia. Throughout all the years with Ionis Pharmaceutica Dr. Crooke also continued contributing to the basics of oligonucleotide science, authoring more than 500 research article and patents, and editing more than 20 books.

Dr. Crooke received his BS in Pharmacy from Butler University in 1966, PhD and MD at Baylor College of Medicine in 19 and 1974, correspondingly. Earlier in his career, Dr. Crooke helped create the anticancer program at Bristol-Myers (no Bristol-Myers Squibb), and then led Research and Development at SmithKline Beckman (now GlaxoSmithKline). In 1989, h co-founded Ionis Pharmaceuticals, where he now serves as Executive Chairman and Chief Executive Officer. Dr. Crook held professor positions at Baylor College of Medicine, University of Pennsylvania Medical School, University of Californ San Diego, and is currently a Member of the San Diego State University BioScience Center Scientific Advisory Board.

For his contribution to life sciences, Dr. Crooke received a number of awards and honors, including the Lifetime Achieveme Award from Scrip, the Director of the Year Award from the Corporate Directors Forum, the Distinguished Scientist Awar from the American Chemical Society, the Helix Award for the most important innovation in biotechnology by th Biotechnology Industry Organization, the Ernst and Young Entrepreneur of the Year Award, as well as Distinguishe Alumnus at Baylor College of Medicine and at Butler University. In 2006, Nature Publishing Group listed him as decade's on of the most remarkable and influential personalities in biotechnology.

Additional information about Dr. Crooke can be found in the following sites:
http://www.ionispharma.com/about/management/
http://ir.ionispharma.com/phoenix.zhtml?c=222170&p=irol-govBio&ID=189311

14:20-14:50, Thursday, November 10

Yi-Tao YU, PhD

Professor, University of Rochester School of Medicine and Dentistry, USA

Yi-Tao Yu received his PhD degree in Molecular Biology from Case Western Reserve University in 1994. He was awarded a post-doctoral fellowship from the Damon Runyon Cancer Research Foundation, and did his post-doctoral work (RNA biology) with Joan Steitz at Yale University (HHMI) from 1995 to 1999. He then joined the faculty of the Department of Biochemistry and Biophysics at the University of Rochester in late 1999. He is currently also a member of the Center for RNA Biology and Chair of the RNA Structure and Function Cluster at the University of Rochester. Dr. Yu' s research interests are in the areas of RNA modification, snRNP biogenesis and pre-mRNA splicing. Over the years, he has generated numerous publications and made significant contributions in these areas.

15:20-15:50, Thursday, November 10

Elizabeth TRAN, PhD

Associate Professor
Purdue University, USA

Elizabeth Tran earned her PhD in biochemistry at North Carolina State University where she developed an in vitro assembly and methylation system for trans acting box C/D snoRNAs. She then pursued postdoctoral training in the laboratory of Dr. Susan Wente at Vanderbilt University, where she identified the role of the RNA helicase Dbp5 in nuclear mRNA export. She joined the faculty at Purdue University in 2009, where she explores the biochemical mechanism and biological function of DEAD-box RNA helicases, a class of enzymes that are required for all aspects of RNA metabolism but whose in vivo roles are yet to be identified. Her laboratory is most well known for studies of the DEAD-box RNA helicase Dbp2 in S. *cerevisiae* and insights into the roles of long non-coding RNAs (lncRNAs) in gene expression. These insights span the fields of RNA biology, epigenetics, and metabolism. Moreover, the scientific community has highlighted her work for pivotal, paradigm shifting advances in lncRNA biology (Best of JBC 2012, Nature highlight, Science Signaling highlight). Her long-term goal is to understand the connection between RNA structure, gene regulation, and cellular adaptation in relationship to organismal survival and human pathology. In addition to research, Dr. Tran is a strong supporter of the international scientific community and mentoring the next generation of scientists. She is currently serving a two year term as a Director on the Board of the RNA Society, an international organization with ~1000 members worldwide.

15:50-16:20, Thursday, November 10

Jan GORODKIN, PhD

Professor, University of Copenhagen
Director, Center for Non-Coding RNA in Technology and Health, Denmark

Jan Gorodkin holds a MSc in physics from the Niels Bohr Institute and obtained his Ph.D in Bioinformatics from Center for Biological Sequence analysis at the Technical University, Denmark. He did his post docs at Aarhus University, Denmark and Washington University Medical School, St. Louis. He took up positions at the Royal Veterinary and Agricultural University (now University of Copenhagen), and is now professor and head of the bioinformatics group as well as director of Center for non-coding RNA in Technology and Health in the Department of Veterinary Clinical and Animal Sciences. His research interests span from RNA bioinformatics to animal and human genome analysis and his research group has been involved in developing numerous computational tools as well as applying them on genomic and transcription data.

16:20-16:50, Thursday, November 10

Ekkehard LEBERER, PhD, Professor of Biochemistry

Senior Director of R&D Alliance Management, Sanofi, Germany
Scientific Managing Director of COMPACT Consortium, Innovative Medicine Initiative Belgium

Dr. Leberer received his Ph.D. in Biology at the University of Konstanz, Germany (1986). He conducted post-doctoral training in molecular biology at the Banting and Best Institute of the University of Toronto, Canada, and then became a Professor of Biochemistry at the University of Konstanz, Germany (1992). He is currently responsible for R&D Alliance Management at Sanofi, and is the Scientific Managing Director of the Innovative Medicine Initiative COMPACT Consortium on the delivery of biopharmaceuticals across biological barriers and cellular membranes (www.compact-research.org).

Since joining Hoechst Marion Roussel in 1998, Dr. Leberer carried out various managing roles in this company, Sanofi predecessor companies and Sanofi itself, including responsibilities in functional genomics, biological sciences and external innovation for oligonucleotide-based therapeutics. He has also served as Head of Biotechnology Germany and a member of the Scientific Review Committee of Aventis Pharma Germany.

Prior to joining pharmaceutical industry, Dr. Leberer served as Senior Research Officer in genetics and genomics at the Biotechnology Research Institute, National Research Council of Canada, Montreal. His research has focused on the molecular mechanisms of signal transduction and the role of signalling molecules in human diseases. He is the principal discoverer of the p21 activated protein kinase (PAK) family of cell signalling proteins and of novel virulence-inducing genes in pathogenic fungi. He is co-author of more than 60 publications in prestigious peer-reviewed journals including Nature and Science.

Summary

During the past decade nucleic acids science through introduction of vast new classes of non-coding RNAs brought renewed interest and excitement towards the breadth of nucleic acids function in cells and their applications for diagnostics and therapeutics. The Canton Nucleic Acids Forum (CNAF) is a series of recurring conferences with the initial goal of exposing scientists in China to the latest developments and advances in nucleic acids research, with particular view of translating the new knowledge into practical applications.

Mission

The mission of the forum is to expose scientists in China to the frontiers of life sciences and biotechnology, expedite transformation of scientific development and bio-industrial advancement, promote integration of the quickly progressing and expanding Chinese and the established world scientific communities engaged in nucleic acids R&D, strengthen international cooperation and exchange of ideas.

Scientific Council

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Professor, University of Colorado, Boulder, Howard Hughes Medical Institute, USA
Member of the US National Academy of Sciences
Nobel Prize Winner in Chemistry (1989)

Craig C. MELLO, PhD
Professor, University of Massachusetts Medical School, Howard Hughes Medical Institute, USA
Member of the US National Academy of Sciences
Nobel Prize Winner in Physiology or Medicine (2006)

Directors

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Professor, Stanford University, Howard Hughes Medical Institute, USA

Runsheng CHEN, PhD
Professor, Institute of Biophysics, Chinese Academy of Sciences, China
Member of the Chinese Academy of Sciences

Carlo M. CROCE, MD
Distinguished University Professor and Chair, Ohio State University, USA
Member of US National Academy of Sciences, Foreign Member of the Italian National Academy of Sciences

Stanley T. CROOKE, MD, PhD
Chief Executive Officer and Chairman of the Board, Isis Pharmaceuticals, USA

Jennifer A. DOUDNA, PhD
Professor, University of California Berkeley, Howard Hughes Medical Institute, USA
Member of the US National Academy of Sciences

Mark EDBROOKE, PhD
Director, AstraZeneca, UK

(continued)

Scientific Council (continue)

Michael FAMULOK, PhD
Professor, Life and Medical Sciences Institute, University of Bonn, Germany
Member of the German National Academy of Sciences

Gregory J. HANNON, PhD
Professor, Group Leader, Cancer Research UK, University of Cambridge, UK
Howard Hughes Medical Institute, USA
Member of the US National Academy of Sciences

Ekkehard LEBERER, PhD
Professor, Senior Director, Alliance Management, Sanofi, France/Germany

David M.J. LILLEY, PhD
Professor, Director CRUK Nucleic Acids Structure Research Group, University of Dundee, UK
Fellow of the UK Royal Society

Muthiah (Mano) MANOHARAN, PhD
Senior Vice President, Drug Discovery, Alnylam Pharmaceuticals, USA
Board Director, Oligonucleotide Therapeutics Society

Aviv REGEV, PhD
Professor, Massachusetts Institute of Technology, Howard Hughes Medical Institute, USA

Cristina M. RONDINONE, PhD
Vice President, Head of Innovative Medicines Center of Excellence, AstraZeneca/MedImmune, USA

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Professor, Peking University School of Pharmaceutical Sciences, China
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Judy LIEBERMAN, MD, PhD
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Professor, Sungkyunkwan University, South Korea
Chief Executive Officer, OliX Pharmaceuticals

Henrik ØRUM, PhD
Head of RNA Therapeutics Research, Roche, Denmark

Nikolaus RAJEWSKY, PhD
Professor, Max Delbrück Center for Molecular Medicine, Germany

Laura SEPP-LORENZINO, PhD
Vice President, Alnylam Pharmaceuticals, USA

Harold P. SWERDLOW, PhD
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Matt WINKLER, PhD
Chairman of the Board and Chief Scientific Officer, Asuragen, USA