2015

Korea University Drug Discovery Symposium

Inception of a New Translational Approach for Successful Drug Discovery at KU

2015년 3월 31일 (화) 14:00 ~ 18:00

고려대학교 이공대캠퍼스 하나스퀘어 지하 1층 멀티미디어룸

주최 | 고려대학교 안암병원 임상시험센터 Korea University Anam Hospital Clinical Trial Center, 고려대학교 신약개발 연구발굴 추진단

후원 | KCGI 임상시험글로벌사업단 KOREA CLINICAL TRIALS GLOBAL INITIATIVE, KONECT 한국임상시험산업본부 Korea National Enterprise for Clinical Trials, KHIDI 한국보건산업진흥원, 보건복지부

>> 초청의 글

인류의 평균적인 수명은 지난 수십 년 전에 비해 놀랄 만큼 연장되었습니다. 가장 중요한 요인은 아마도 보건의식의 고양과 함께 혁신적인 질병 치료제들의 지속적인 개발일 것입니다.

이러한 평균수명의 연장에도 아직도 치명적인 질병의 치료제의 발견이나 삶의 질을 향상시킬 의약품들의 개발 요구는 점점 더 증대되어 가고 있습니다. 특히 항암치료의 새로운 트렌드에서 보듯이 환자 맞춤 의약품 개발 등 이전 패러다임과는 다른 관점에서의 의약개발도 요구되는 시점이기도 합니다.

이러한 사회 발전에 발 맞추어 본 고려대학교도 지난 수십 년간 의과대학을 중심으로 임상과 연구에서 국민건강 보호에 큰 기여를 해왔습니다. 동시에 기초과학–생명과학, 화학 그리고 약학–분야에서 새로운 질병 치료제의 개발 가능성을 내포한 연구결과들을 꾸준히 발표해 오고 있었습니다. 이제는 각자 독립적으로 진행되어오던 연구분야들을 통합된 목표아래 체계적으로 관리하고 발전시켜야 할 시점에 이르렀습니다.

이제 우리 고려대학교에서 수행중인 연구들의 위상을 한번 점검해 보려 합니다. 신약 개발 연구의 선두에 계신 네 분의 교내 연구자들의 강연을 통해 본교가 신약 개발에 어떻게 기여하고 있는지 또 앞으로 어떤 점을 보완해 완전한 시스템을 구성할 수 있을지 검증해보는 시간을 가지려 합니다. 동시에 신약개발에 있어 독보적인 성공사례를 보여주셨고 현재도 활발히 연구하시는 Inception Science의 Dr. Prasit 사장님을 모셔 연구단계의 업적들을 어떻게 임상에 진입시킬지 또는 그 이상의 과정으로 발전시키는 과정들에 대한 조언을 구하는 기회를 가집니다.

관련 업무 또는 연구에 종사하시는 모든 분을 초청합니다. 이 기회를 통해 고려대학교가 이 웅대한 계획에 어떻게 주도적인 역할을 하는지 인식하시는 기회가 되길 바랍니다.

고려대학교 이과대학 화학과
정 낙 철 교수

>> 인사글

임상시험의 목적은 혁신적인 치료법에 대한 안전성과 유효성을 확립하여 환자의 신약 접근을 가능케 하고자 하는 것입니다. 이러한 목적을 달성하기 위해 임상시험 환경이 최적화 될 때 임상시험은 발전하게 되고, 의학적, 산업적 가치는 더욱더 증대될 수 있으리라 믿습니다. 전 세계적으로 한국의 과학 수준과 신약개발 능력, 그리고 임상시험의 인프라는 이미 최고의 수준에 다다른 것으로 평가되고 있습니다. 정부도 신약개발과 임상시험의 미래성장동력으로서의 잠재력을 높이 평가하여 집중 투자를 계획하고 있습니다.

고려대학교 안암병원 임상시험센터에서는 이와 관련하여 아래와 같이 국내-외 관련 전문가 분들을 연자로 초청하여 [2015 Korea University Drug Discovery Symposium – Inception of a New Translational Approach for Successful Drug Discovery at KU]의 주제로 신약 연구개발 정보 교류의 장을 마련하고자 합니다.

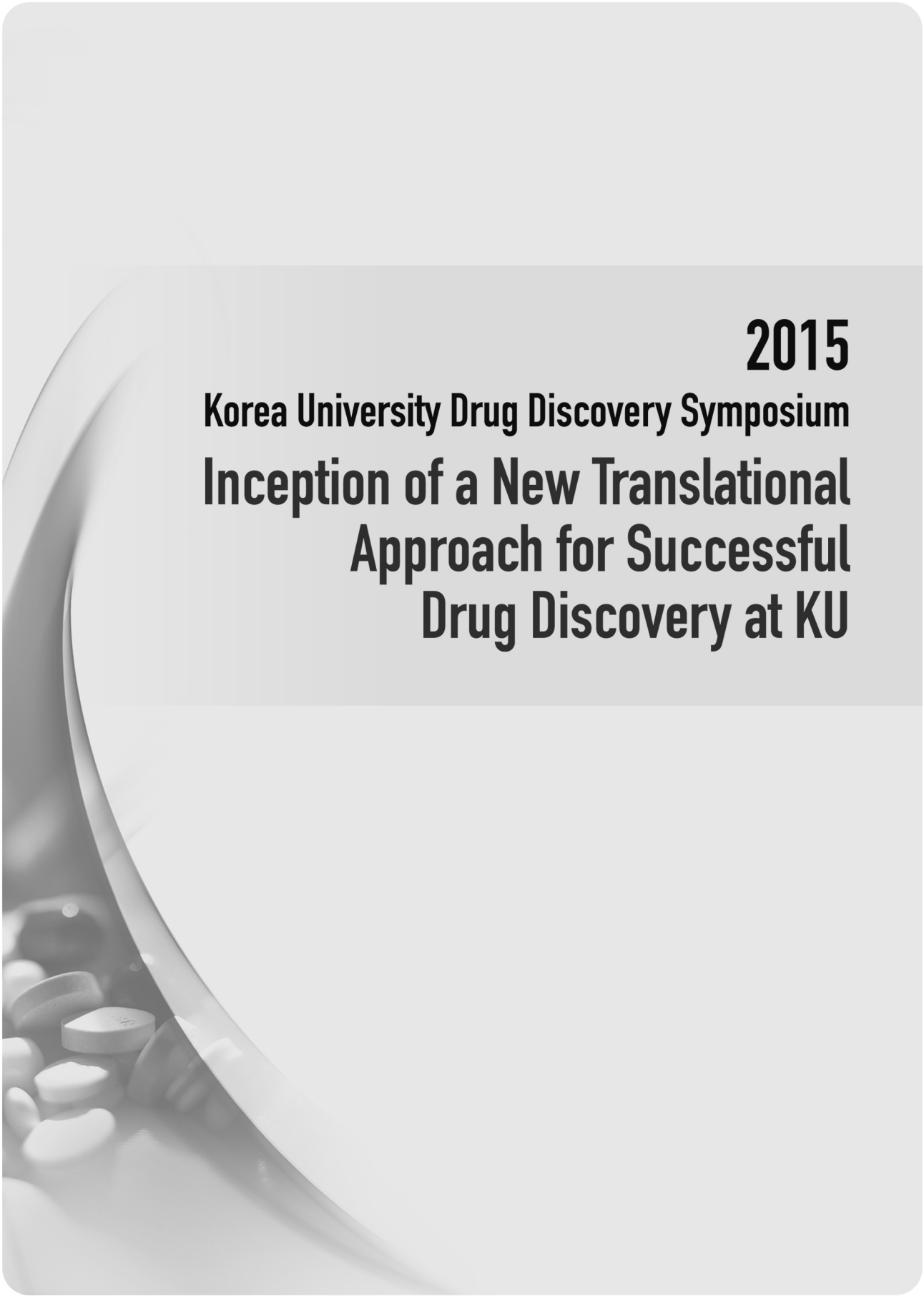
이번 심포지엄을 통해서 고려대학교 안암병원 임상시험센터와 고려대학교 신약연구발굴추진단 간의 소중한 정보 교류와 시너지 창출의 자리가 될 것을 기대하며 유익하고 활발한 토론장이 될 수 있도록 적극적인 참여를 부탁드립니다.

감사합니다.

2015년 03월
고려대학교 안암병원 임상시험센터장
김 열 홍 교수

>> PROGRAM

14:00–14:10	Opening Remark Professor Yeul Hong Kim, M. D., Ph. D. (Director of Korea University Anam Hospital Clinical Trial Center)	
14:10–14:50	Anti-BLT2 Compounds As Novel Therapeutic Agents for Steroid-resistant Severe Asthma or Severe Cancer Professor Jae-Hong Kim, Ph. D. (College of Life Sciences and Biotechnology, Korea University)	• 06
14:50–15:30	Extension of The Thrombolytic Time Window: A Therapeutic Strategy for Treatment of Cerebral Ischemic Stroke Professor Won-Ki Kim, Ph. D. (Director of Research Institute for Inflammation Control, Department of Neuroscience, College of Medicine, Korea University)	• 08
15:30–16:10	HCV Polymerase Inhibitors: Major Player for HCV Cure Professor Choung Un Kim, Ph. D. (Department of Chemistry, College of Science, Korea University, Vice President & CSO of Kainos Medicine)	• 10
16:10–16:30	*Coffee Break*	
16:30–17:10	Discovery of Novel Neuropeptides and Possible Use of Them in Human Diseases Professor Jae Young Seong, Ph. D. (Graduate School of Medicine, Korea University)	• 12
17:10–17:50	Drug Discovery: From Concept to Clinic Peppi Prasit, Ph. D. (CEO & CSO of Inception Sciences, CSO of Amira Pharmaceuticals)	• 14
17:50–18:00	Closing Remark Prof. Nakcheol Jeong, Ph. D. (Department of Chemistry, College of Science, Korea University)	



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>> Curriculum Vitae

Professor Jae-Hong Kim, Ph. D.

College of Life Sciences and Biotechnology, Korea University

E-mail: jhongkim@korea.ac.kr

Education

1991	Biochemistry, UMDNJ at Rutgers, Ph. D.
1983	Department of Biological Science & Engineering, KAIST, M. S.
1981	Department of Agricultural Chemistry, Korea University, B. S.

Professional Experiences

2003 – Present	Professor, Korea University
2001 – 2003	Associate Professor, Korea University
1999 – 2001	Associate Professor, Gwangju Institute of Science and Technology
1995 – 1999	Assistant Professor, Hallym University
1994 – 1995	Research Fellow, MGH, Harvard Medical School
1993 – 1994	Research Associate, Baylor College of Medicine, Cell Biology
1991 – 1993	Post-doc, Schering-Plough Res. Institute, Tumor Biology

Anti-BLT2 Compounds as Novel Therapeutic Agents for Steroid-resistant Severe Asthma or Severe Cancer

Jae-Hong Kim, Ph. D.
College of Life Sciences and Biotechnology, Korea University

BLT2 is a cell-surface G protein-coupled receptor (GPCR) for the inflammatory lipid mediators leukotriene B_4 (**LTB_4**), 12 (*S*)-hydroxy-5 (*Z*), 8 (*Z*), 10 (*E*), 14 (*Z*)-eicosatetraenoic acid (**12 (S)-HETE**), and 12 (*S*)-hydroxy-5 (*Z*), 8 (*E*), and 10 (*E*)-heptadecatrienoic acid (**12-HHT**). Our results demonstrate for the first time that BLT2 expression is highly up-regulated under severe inflammatory pathogenic conditions and this induced BLT2-linked inflammatory pathway greatly contributes to various inflammatory pathogenesis such as asthma and cancer. In particular, the generation of reactive oxygen species (ROS) via NADPH-oxidases (Nox) has been associated with BLT2-mediated pathogenesis. This knowledge offers new perspectives and targets for the development of novel anti-asthma or anti-cancer therapeutics.

Asthma is a chronic disease of the airways, which can vary from mild to very severe. Steroid-resistant severe asthma (SRSA) is characterized by difficulty to achieve disease control despite high-dose inhaled glucocorticoids plus long-acting β2-agonists (LABAs) or oral corticosteroids (OCSs). Over the past decades, the prevalence of SRSA has been estimated to be around 5% to 10% of the total asthmatic population. Although those patients represent a small number of all asthmatic patients, yet they present a significant clinical challenge because they remain symptomatic despite maximal doses of conventional therapy. Our recent results suggest that BLT2 is a critical regulator for the action/production of IL-33 and IL-13, two principle mediators of SRSA, pointing to BLT2 as a potential therapeutic target for SRSA as well as mild-to-moderate asthma.

In addition, our recent results suggest that BLT2 is a critical regulator for the progression of malignant cancers, pointing to BLT2 as a potential therapeutic target for severe cancers (e.g., chemoresistant & metastatic breast, metastatic bladder, chemo-resistant & metastatic ovarian, aggressive prostate cancers). As expected, BLT2 inhibitors (e.g., BLT2X-22 and BLTX-696 etc) developed by us show remarkable efficacy as therapeutic agents for those cancers in animal model. Together, we believe BLT2 inhibitors (e.g., BLT2X-22 and BLTX-696 etc) could be developed as a new anti-SRSA or anti-metastatic cancer agent.

>> Curriculum Vitae

Professor Won-ki Kim, Ph. D.

Department of Neuroscience, College of Medicine, Korea University

E-mail: wonki@korea.ac.kr

Education

1988	Department of Pharmacology & Therapeutics, SUNY at Buffalo, Ph. D.
1989	Department of Pharmacology, Seoul National University, M. S.
1985	College of Pharmacy, Seoul National University, B. S.

Professional Experiences

2013 – Present	Director, Institute for Inflammation Control, Korea University
2011 – 2013	Vice Dean, School of Pharmacy, Korea University
2009 – 2011	Director, Institute for Biomedical Research, Korea University
2007 – Present	Professor, Dept of Neuroscience, Korea University College of Medicine
2006 – 2007	Professor, Division of NanoSciences, Ewha Women's University
2004 – 2006	Director, Ewha Institute of Neuroscience, Ewha Women's University
2002 – 2004	Vice director, Ewha Institute of Neuroscience, Ewha Women's University
1999 – 2005	Chairman, Dept. of Pharmacology, Ewha Medical College
1997 – 2010	Vice director, Ewha Medical Research Center, Ewha Medical College
1995 – 2006	Professor, Dept. of Pharmacology, Ewha Medical College
1995 – 1995	Research Consultant, Children's Hospital, Harvard Medical School
1994 – 1995	Research Fellow, Children's Hospital, Harvard Medical School
1989 – 1994	Research Assistant, Dept. of Pharmacology, SUNY at Buffalo

Extension of The Thrombolytic Time Window: A Therapeutic Strategy for Treatment of Cerebral Ischemic Stroke

Won-Ki Kim, Ph. D.
Director of Research institute for Inflammation Control
Department of Neuroscience, College of Medicine, Korea University

Through excitotoxic, oxidative and inflammatory intertwining pathways, ischemic stroke causes irreparable cerebral injury which leads to disability and death worldwide. Although acute ischemic stroke causes 10-12% of all deaths in western countries as well as in Korea, advances in therapeutics and treatment are still in its infancy. Although tissue plasminogen activator (tPA) is currently approved by FDA for treatment of acute ischemic stroke, its clinical use is limited by narrow therapeutic time window; e.g., mostly up to ~3 h after the onset of ischemia. Limited use of tPA for post-ischemic treatment is related with its treatment time-dependent multiple cytotoxic mechanisms such as excitotoxicty, radicals formation, cerebral hemorrhage, and inflammatory action. Here, it can be seen that the multiple cytotoxic mechanisms responsible for severe adverse effect of delayed treatment of tPA are very similar to those involved in brain tissue damage during cerebral ischemic insult. Therefore, the combined use of a neuroprotective agent with tPA would be clinically beneficial to simultaneously reduce both tPA and ischemia-induced brain tissue damage. In the presentation, I will introduce several synthetic multi-target directed ligands (MTDLs) that extend the therapeutic time window of tPA by reducing the aforementioned adverse effects caused by delayed tPA treatment. For studies, filamentous as well as embolic ischemia models were employed. While early 3-h thrombolysis restored perfusion and reduced infarction, late 6-h tPA did not decrease infarction but instead worsened hemorrhagic conversion and mortality. MTDLs used in my studies reduced the aggravation of infarction, edema and neurobehavioral deficit caused by delayed tPA treatment. Moreover, MTDLs significantly attenuated delayed tPA treatment-worsened cerebral hemorrhage and mortality. Studies also revealed that the expression of matrix metalloproteases was associated with the reduction of cerebral hemorrhage and mortality. Thus, the combined use of a MTDL with tPA would be a therapeutic strategy to overcome the limitation of tPA therapy, reduce ischemic brain tissue damage and maximize clinical outcome.

>> Curriculum Vitae

Professor Choung Un Kim, Ph. D.

Distinguished Professor of Chemistry, College of Science, Korea University
Executive Vice President, Chief Scientific Officer, Kainos Medicine

E-mail: ckim@kainosmedicine.com

Education

1970	University of Oregon, Ph. D. in Organic Chemistry
1967	University of Tokyo, M. S. in Organic Chemistry
1965	University of Tokyo, B. S. in Pharmaceutical Sciences

Professional Experiences

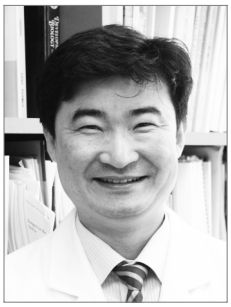
2012 – Present	Executive Vice President, Chief Scientific Officer, Kanos Medicine Distinguished Professor of Chemistry, College of Science, Korea University
1999 – 2012	Vice President, Chemistry, Gilead Sciences
1997 – 1999	Senior Director, Medicinal Chemistry, Gilead Sciences
1994 – 1997	Director, Medicinial Chemistry, Gilead Sciences
1991 – 1994	Senior Principal Scientist in Medicinal Chemistry, Bristol-Myers-Squibb
1984 – 1991	Research Fellow in Antiinfective Chemistry, Bristol-Myers-Squibb
1973 – 1984	Senior Research Chemist in Medicinal Chemical Research, Bristol Laboratories
1971 – 1973	Post-doc, Harvard University
1970 – 1971	Post-doc, University of Alberta

HCV Polymerase Inhibitors: Major Player for HCV Cure

Choung Un Kim, Ph. D.
College of Science, Korea University
Kainos Medicine

Recentry, Hepatitice C virus (HCV) treatment made remarkable progress as evidenced by high cure rate (>90%) by Sofosbuvir and Harvoni. The NS5B polymerase enzyme is essential for replication of the HCV virus. Active site nucleoside analogs mimic natural HCV RNA and terminate the chain elongation. Rationally designed C-nucleoside analog, GS-6620 is a potent HCV polymerase inhibitor with high plasma loading in dogs by oral dosing. This presentation will give the rational drug design of GS-6620 that was evaluated in Phase I.

>> Curriculum Vitae



Professor Jae Young Seong, Ph. D.

Graduate School of Medicine, Korea University

E-mail: jyseong@korea.ac.kr

Education

1996	Department of Molecular Biology, Seoul National University, Ph. D.
1992	Department of Molecular Biology, Seoul National University, M. S.
1990	Department of Zoology, Seoul National University, B. S.

Professional Experiences

2011 – Present	Professor, Graduate School of Medicine, Korea University
2008 – 2011	Associate Professor, Graduate School of Medicine, Korea University
2005 – 2008	Assistant Professor, Graduate School of Medicine, Korea University
2000 – 2000	Visiting professor, MRC Reproductive Biology Unit, Edinburgh, Scotland
2000 – 2005	Assistant Professor, Hormone Research Center, School of Biological Science and Technology, Chonnam National University
1997 – 1999	Post-doc, Division for Clinical & Experimental Endocrinology, University of Göttingen
1996 – 1997	Post-doc, Research Center for Cell Differentiation, Seoul National University

Discovery of Novel Neuropeptides and Possible Use of Them in Human Diseases

Jae Young Seong, Ph. D.
Graduate School of Medicine, Korea University

Neuropeptides and their G-protein-coupled receptors (GPCRs) have become diversified through evolutionary processes, such as gene/chromosome duplications and gene modification, generating families of related yet distinct peptides and receptors. Currently, the large accumulation of genome sequence information for various invertebrate and vertebrate species combined with recent advances in bioinformatic tools has allowed large-scale genome comparisons. Particularly, comparing entire genomes of evolutionarily distant taxa allows reconstructing the hypothetical chromosomes of vertebrate or chordate ancestor, facilitating the exploration of the origin and relationship of gene families of interest. Our lab has searched for the evolutionary lineages of neuropeptide and GPCR genes including novel neuropeptides and orphan GPCRs. Here, I will discuss discovery of novel neuropeptide genes and identification of their receptors using evolutionary genomics and possible use of these novel peptides in human diseases.

>> Curriculum Vitae

Peppi Prasit, Ph. D.

Chief Executive Officer/Chief Scientific Officer and Co-founder of Inception Sciences
Chief Scientific Officer and Co-founder of Amira Pharmaceuticals

E-mail: PPrasit@inceptionsci.com

Education

1982	Victoria University of Wellington, New Zealand, Ph. D. in Chemistry
1976	University College London, London University, B. S. in Chemistry

Professional Experiences

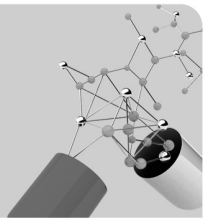
2011 – Present	CEO/CSO and Co-Founder of Inception Sciences
2005 – Present	Chief Scientific Officer and Co-Founder of Amira Pharmaceuticals
2000 – 2005	Head of Chemistry, Merck Research Labs
1996 – 2000	Senior Director, Medicinal Chemistry, Merck Research Labs
1994 – 1996	Director, Medicinal Chemistry, Merck Research Labs
1991 – 1994	Associate Director, Medicinal Chemistry, Merck Research Labs
1988 – 1991	Research Fellow, Merck Research Labs
1985 – 1988	Senior Research Chemist, Merck Frosst Canada
1982 – 1985	Post-doc, Princeton University

Drug Discovery: From Concept to Clinic

Peppi Prasit, Ph. D.
Inception Sciences, San Diego, CA 92121, USA

Drug discovery and development are the essential driving forces for drug therapy. It is an expensive, long and high-risk business taking 10−15 years and is associated with a high attrition rate. At the preclinical stage, drug discovery is an iterative process between chemistry, biology and drug metabolism, refining the molecular properties until a compound suitable for advancing to human is found. Typically, about one in a thousand synthesized compounds is ever selected for progression to the clinic and out of these approximately only 1 in 10 drugs that start the clinical phase will make it to the market.

The talk will focus a couple of successful examples, one in a large pharma setting and another in a startup biotech setting.



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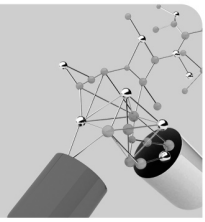

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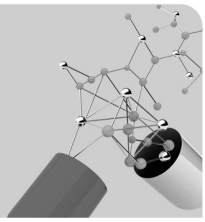

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