Contents

Mr. Pankaj R. Patel
Chairman and Managing Director
Zydus Cadila Healthcare Ltd.
Ahmedabad, India.

Message from Chairman and Managing Director

It is a matter of immense pleasure to welcome you to the second international symposium being held under the aegis of Ramanbhai Foundation and hosted by the Zydus Research Centre.

The Founder Chairman of Zydus Cadila, my father Late Mr. Ramanbhai Patel dedicated his entire lifetime to the quest for knowledge, as an academician, entrepreneur and a researcher. He realized quite early in his life that research and development would play a critical role in the growth of pharmaceutical industry. His vision about R&D in pharmaceutical industry was instrumental to transition of Cadila from a small family-owned business to an emerging global pharmaceutical company and aspiring to be a research-based global pharmaceutical company. The state-of-the-art Zydus Research Centre supports his quest for innovations and excellence in the field of research and spearheads the research initiatives of the group.

I am reminded of his saying "The challenge is to create a vision of the kind of Pharmaceutical Industry that the nation wants in 20 years of time.... To move beyond short-term thinking and the notion of incremental change. We must focus on fulfilling the unmet healthcare needs."

In 2003, we had organized the First International Symposium, a highly successful event that drew numerous compliments and praise from speakers and attendees. The second International Symposium would focus on emerging sciences of Genomics and Proteomics, which have the potential to extend and enhance the quality of human life. It is thus imperative to share the knowledge with the scientific communities across the globe specially, when India is going to honour Product Patent law. Through this symposium, the foundation aims to create a platform for establishing dialogue on scientific issues related to the use of Genomics and Proteomics in pharmaceutical research.

I would like to thank all the distinguished speakers who are going to share their knowledge and experiences and the delegates who have taken pain to travel from far and wide to attend the symposium.

I wish you all a very fruitful and rewarding experience and pleasant stay at Ahmedabad.

Ahmedabad

Date : 23rd January, 2005

Pankaj R. Patel

Dr. B. B. Lohray
President, Zydus Research Centre
Ahmedabad, India.

Message from President

It gives me immense pleasure to welcome you all to the Ramanbhai foundation (RBF) 2nd International Symposium. The biennial RBF symposia are dedicated to the memory of our visionary Founder Chairman, Late Shri Ramanbhai Patel, and aim to bridge the research endeavours taking place across the world, simultaneously creating a platform for sharing the knowledge. The focus of this symposium is on the impact of Genomics and Proteomics on current trends in Pharmaceutical sciences.

As you all know, nearly fifty years ago, James Watson and Francis Crick made the most important scientific breakthrough of the last millenium, when they discovered the structure of DNA, the genetic material present in all of us and other forms of life. Genes, about 30,000 of them in humans, which constitute the genetic material that we inherit from our parents, form the functional units of our genome, encoding instructions for making proteins, the functional units of the proteome. The proteins are responsible for all the biological processes that take place in the various cells of our bodies, ultimately determining our many genetically inherited traits such as, our hair and skin colour, height, weight, shape, immunity even our temperament etc. The above described nobel prize winning discovery sowed the seeds for what are today the frontier areas in biology - Genomics, the study of complex interactions of genes with each other and their environment, that makes us what we are and what we do, and Proteomics, the study of the entire proteome in the context of specific cells, tissues, and physiology.

This symposium brings together world leading scientists in proteomics and genomics from both academia and industry. These scientists have contributed immensely to improve our understanding of normal and abnormal physiology, identify new druggable targets, and using these discoveries to treat various diseases using old and new technologies. Proteomics and genomics are not just the buzz words of today. Instead, they are important areas of study where academia and pharmaceutical industry of India would have to invest in today to secure our future tomorrow. India has turned a new leaf in the history on January 1, 2005 by becoming fully patent compliant. Indian pharmaceutical industry would now have to compete with the rest of the world with only one weapon, i.e. Innovation. Therefore, I believe that this symposium is aptly timed to provide the Indian researcher a window to two new crucial tools that will certainly help us in becoming successful drug discoverers, developers, and pharmaceutical leaders of tomorrow in this new era.

As a representative of Zydus Research Center (ZRC) I urge you all to take maximum benefit from this opportunity. This symposium will provide you with a forum to make new friends, discuss new ideas, and sow the seeds for future mutually beneficial collaborations with ZRC and with each other.

I wish you all a very fruitful meeting at ZRC and an excellent stay at Ahmedabad.

Ahmedabad

Date: January 23, 2005

Dr. B. B. Lohray

Message from Chief Guest

प्रो० व. सु. राममूर्ति
सचिव
PROFESSOR V. S. RAMAMURTHY
SECRETARY

भारत सरकार
विज्ञान और प्रौद्योगिकी मंत्रालय
विज्ञान और प्रौद्योगिकी विभाग
टेक्नोलाजी भवन, नया महरौली मार्ग, नई दिल्ली-110 016

GOVERNMENT OF INDIA
MINISTRY OF SCIENCE & TECHNOLOGY
Department of Science & Technology
Technology Bhavan, New Mehrauli Road, New Delhi-110 016

January 19, 2005

MESSAGE

I am happy to know that the Ramanbhai Foundation 2nd International Symposium is being held at Zydus Research Centre, Cadila Healthcare Ltd., Ahmedabad during January 23-25, 2005. The theme "Current Trends in Pharmaceutical Sciences" with a special emphasis on the 'Role of Genomics and Proteomics in Pharmaceutical Research' is an appropriate for the present hour and I congratulate the organizers for choosing the same for this International Symposium. It is a befitting event to honour Late Mr. Ramanbhai Patel, the founder of Cadila who contributed to the growth of Indian Pharmaceutical Industry through such an International Symposium on an important area of modern biology and biotechnology.

I convey my greetings to the organizers and wish this Symposium a grand success.

[V.S. Ramamurthy]

Telegram : SCIENCTECH • Telephone : 6510068/6511439
Fax : 0091-11-6863847, 0091-11-6862418 • E-mail : dstsec@alpha.nic.in

About Ramanbhai Foundation

The Ramanbhai Foundation is dedicated to encourage learning and knowledge-sharing in the field of pharmaceutical research, education and healthcare. This mission is based on the philosophy of our late Founder Chairman, Mr. Ramanbhai B. Patel, who believed in the importance of research and enriching oneself through an ongoing quest for learning.

A first-generation entrepreneur, Mr. Ramanbhai Patel was one of the stalwarts of the Indian Pharmaceutical Industry.

Born at Kathor in South Gujarat on the 19th of August 1925, he began his career as an academician at the L. M. College of Pharmacy, one of the oldest pharmacy institutes in India. This short stint in academics formed a lasting imprint on his mind and the resolve to contribute to the cause of research and education. Mr. Ramanbhai Patel had published several outstanding research papers and took a keen interest in research and was actively involved in the research activities.

In 1952, Mr. Ramanbhai Patel turned a pharma entrepreneur. Armed with a sound business acumen, he laid a strong foundation for Cadila and contributed to the growth of the Indian Pharmaceutical Industry. Today, Zydus Cadila is amongst the top investors in research.

In recognition of his services, Mr. Ramanbhai Patel had been bestowed with several prestigious awards : President of India's Import Substitution Award in 1973, Prof. M.L. Shroff Memorial National Award in 1987, The Glory of India Award in 1991 at Washington, Grahak Suraksha Award in 1992, Acharya Prafulla Chandra Ray Memorial Gold Medal in 1993 and the Eminent Pharmacist Award in 1994, to name a few.

In a fitting tribute to his outstanding contributions to the growth of the pharma industry in India, he was conferred the Gujarat Businessman of the Year Award in the year 2000. He was also honoured by Express Pharma Pulse with the 'Lifetime Contribution Award' for his lasting contributions to the Indian pharma industry.

The Zydus Research Centre, a state-of-the-art facility which was set up during his lifetime, spearheads the research initiatives of the Zydus group and supports the quest for innovations and excellence in the field of research.

The Ramanbhai Foundation is also committed to a number of special initiatives in the field of education. The Zydus School for Excellence which was a dream nurtured by Mr. Ramanbhai Patel has been set up to provide a rich academic environment where children can seek creative expressions for their endeavours.

The Ramanbhai Patel-AMA Centre for Excellence in Education has also been set up to raise the bars of excellence in the field of education through progressive learning programmes for academicians, knowledge sharing forums and by studying successful models of education and creating a platform for sharing these experiences. The centre inaugurated by Hon'ble President of India, Dr.A.P.J. Abdul Kalam in May 2002, organises open house programmes and memorial lectures in the field of education. Eminent personalities such Dr. Abid Hussain, Justice (Retd.) P.N. Bhagwati and Dr. Karan Singh have delivered the memorial lectures at the Centre. The teachers contribution to the child's world of learning is also honoured every year with the Shreshtha Shikshak Award.

The Ramanbhai Foundation International Symposium is the second in the series of events devoted to the discussion on the 'Recent Trends in Pharmaceuticals Sciences'. Through the symposium, the Foundation aims to bridge the research endeavours taking place across the world and create a platform for knowledge sharing.

About Zydus Cadila

Zydus Cadila, one of the India's leading healthcare groups provides total healthcare solutions in the filed of healthcare ranging from formulations, active pharmaceutical ingredients, biologicals, diagnostics, herbals, animal healthcare to cosmetics. Headquartered in Ahmedabad, the group is spearheaded by Chairman and Managing Director, Mr. Pankaj R. Patel.

Established in 1952, as Cadila Laboratories, the group's association with the industry spans over five decades. The company, founded by the Late Mr. Ramanbhai B. Patel, grew to become the third largest Indian pharmaceutical company in the early 1990s. In 1995, the group restructures its operations and emerged with a new identity under the aegis of the Zydus group.

The key to the group's success has been in its ability to accelerate growth, globalise business operations and lead in a highly competitive environment. The new product launches coupled with therapy management and brand management skills have helped sharpen Zydus Cadila's competitive edge in the Indian pharmaceutical industry. The group's strategic focus has been on fast growing therapeutic segments such as cardiovascular, gastrointestinals, pain management, preventives, anti-infectives, CNS, respiratory and women's healthcare. Zydus Cadila also has an extensive marketing network with one of the strongest distribution networks in the industry.

Successfully globalising operations, Zydus today has set up a base in the highly regulated markets of Europe and USA. With an aim to be one of the top ten global generics company by 2010, the group has already launched generics in France, one of Europe's fastest growing generics market. The group also plans to extend its base to the other European markets of Italy, Spain and Germany. To cater to the demand of Formulation generics and APIs in the USA, the group has set up two subsidiaries Zydus Pharmaceuticals (USA) Inc., and Zydus Healthcare (USA) LLC. In the Latin American market, the company has set up base in Brazil with Zydus Healthcare Brasil Limitada.

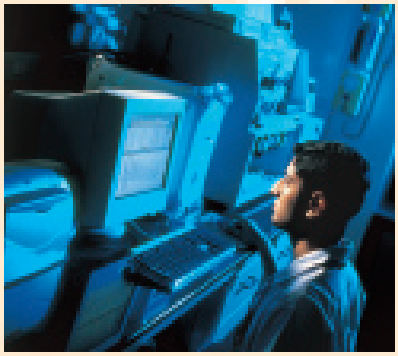
Successful operations in the domestic and international market and strengths in research are backed by a strong infrastructure network. The group has right state-of-the-art vertically integrated manufacturing facilities spread across 3 states.

The formulation facilities at Ahmedabad are spread over 1,40,000 square metres and is perhaps one of the largest of its kind at a single location in Asia. This plant has received approvals from some of the world's leading regulatory authorities such as the USFDA, MHRA of U.K., MCC of South Africa, ANVISA of Brazil, BFAD of Philippines, besides regulatory bodies of several other countries.

To successfully address the challenges of the post 2005 era, Zydus Cadila has a team of 500 professionals engaged in research. The Zydus Research Centre has a dedicated team of 170 research scientists working in the frontier areas of New Chemical Entities, New Drug Deliver Systems and Biotechnology.

By leveraging existing strengths and building on new competencies, the group aims to be one of the top global generic company with a strong R&D pipeline and sales in excess of $ 1 billion by 2010 and a global research driven company by 2020.

In its pursuit of these goals the group is supported by a team of 6000 people, comprising professionals, research scientists, medical advisors and workers. Poised for a higher growth and more success in the coming years, Zydus Cadila draws confidence from its proven track record which both prescribes and projects a vibrant and soundly based future.



About Zydus Research Centre (ZRC)

Zydus Research Centre is the research arm of the Zydus Group, one of India's frontline healthcare conglomerates. Founded in January 2000 at Ahmedabad in Western India, this state-of-the-art research center sprawls over 2,60,000 sq ft, in a serene locale. The Centre is equipped with sophisticated equipment and infrastructure, necessary to carry out research in modern drug discovery and development and is recognized by the Department of Science and Industrial Research (DSIR), Government of India. Here, two hundred scientists conduct seminal research in diverse disciplines including Medicinal Chemistry, Biotechnology, Bio-Informatics, Genomics, Molecular & Cellular Biology, Pharmacology & Toxicology, Microbiology, Analytical Research, CMC Research, Clinical Research, and Novel Drug Delivery Research.

Zydus Research Center is driven by a vision of "emerging as the most admired pharmaceutical research center, through meaningful inventions and path-breaking innovations in Life Science making a perceptible difference in human lives". Its mission is to utilize science to alleviate human suffering, in all possible ways, using all possible means.

The focus of the drug discovery programme at ZRC is to design New Molecular Entities (NMEs) based on defined targets for therapeutic uses. The main therapeutic areas of interest are metabolic disorders including dyslipidemia, hypercholesteremia, diabetes and obesity. Significant research is also conducted in the area of inflammation (arthritis and pain).

In the New Millennium, as Biotechnology emerges as a vital component of modern medical science, Zydus Research Centre has built excellent capabilities to carry out cloning, fermentation and purification of recombinant proteins, vaccines and antibodies.

In the area of novel formulation development ZRC aims to build new drug delivery platform technologies to support & enable the development of novel formulations.

ZRC has complete infrastructure & facilities to take novel molecules/biologicals/formulations from concept to clinical evaluation stage in healthy human volunteers.

The research activities in the areas of Pharmacology, Toxicology, DM-PK, Analytical Research, Clinical Research and CMC Research are monitored by an independent Quality Assurance Department so as to ensure compliance to GLP, GCP and cGMP specifications.

A number of patents have been filed from ZRC in India, US and other PCT countries. Several high quality research articles have been published in reputed International Journals.

At ZRC research is being initiated towards unraveling new frontiers in the relationship that exists between human genes, chromosomes and diseases. Future research efforts in this area will probe the cause of several diseases based on genetic disorders or defects.

People are our Strength - we believe in teamwork and groom scientists to take up newer challenges and responsibilities. As a part of a growing organization that continuously seeks to attain and maintain the competitive edge through innovation, we accord a high value to diversity of thoughts, which is critical for arriving at the most innovative solutions to several problems and challenges confronting the human healthcare.

For more detail about Zydus Research Centre, please visit our website : www.zyduscadila.com

Ramanbhai Foundation 2nd International Symposium

Programme Schedule

Day 1 : Sunday : 23rd January, 2005

8.00 - 8.45 hr	Registration	
8.45 - 9.00 hr	Inauguration	
9.00 - 10.00 hr	Welcome Address	: Dr. B. B. Lohray, President, Zydus Research Centre
	Introduction to the Symposium	: Mr. Pankaj R. Patel, CMD, Zydus Cadila
	Inaugural address	: Chief-Guest Prof. V. S. Ramamurthy Secretary to Government of India Department of Science and Technology
10.00 - 10.30 hr	TEA BREAK	
Session I		
	Chairpersons: Dr. J. S. Yadav and Dr. Volker Figala	
10.30 - 11.30 hr	Key Note Address (PL-1): Gene Therapy: Ups and Downs Prof. Inder M. Verma Professor, Laboratory of Genetics, The Salk Institute, La Jolla, California, USA	
11.30 - 12.15 hr	Invited Lecture (IL - 1): From Genome to Therapy Dr. Dalia Cohen, Vice President and Global Head of Functional Genomics, Novartis Pharmaceuticals, USA	
12.15 - 13.00 hr	Invited Lecture (IL -2):From genome to systems to targets: the path with yeast Dr. Steve Oliver, Professor of Genomics, Faculty of Life Sciences, University of Manchester, United Kingdom	
13.00 - 14.00 hr	LUNCH BREAK	
Session II		
	Chairpersons : Dr. Balu Balasubramanium and Dr. Samir Brahmachari	
14.00 - 14.45 hr	IL-3: Coordinating roles of PPARs in energy homeostasis and tissue repair Dr. Walter Wahli, Professor and Director, Center for Integrative Genomics, University of Lausanne, Switzerland	
14.45 - 15.30 hr	IL-4: Steroid hormone receptors in gene regulations Dr. Shigeaki Kato, Professor, Institute of Molecular and Cellular Biosciences, University of Tokyo, Japan	
15.30 - 17.00 hr	TEA BREAK and POSTER SESSION	
Session III		
	Chairpersons: Dr. Elisabeth Hervier	
17.00 - 17.45 hrs	IL - 5 : Peptides in Oncology / Endocrinology Prof. Dr. Juergen Engel, Chairman and Managing Director, Zentaris GmbH, Germany	
19.00 hr onwards	DINNER AND CULTURAL PROGRAMME	

Day 2 : Monday : 24th January, 2005

Session IV		
	Chairpersons: Prof. K. N. Ganesh and Prof. H. L. Bhalla	
08.30 - 09.30 hrs	Key Note Address (PL - 2): Intrinsically Unfolded Proteins: What is their Possible Biological Role? Prof. Joel L. Sussman, The Morton and Gladys Pickman Professor of Structural Biology Weizmann Institute of Science, Israel	
09.30 - 10.15 hrs	IL - 6: Peptide Toxin from Indian Cone Snails : Revisiting the Chemistry & Biology of Natural Products Prof. P. Balaram, Molecular Biophysics Unit, Indian Institute of Science, India	
10.15 - 10.45 hrs	TEA BREAK	
Session V		
	Chairpersons: Dr. M. Venkateshwarlu and Dr. Bansi Lal	
10.45 - 11.30 hrs	IL - 7: Channelling mechanism as revealed from the crystal structure of a fatty acid β-oxidation multienzyme complex	

	Prof. Kosuke Morikawa, Director, Biomolecular Engineering Research Institute, Osaka, Japan
11.30 - 12.15 hrs	IL - 8: The Application of Proteomics Technologies in Pharmaceutical Industry Dr. Hanno Langen, Head of Proteomics Initiative, Roche Center for Medical Genomics, Hoffmann-La Roche, Switzerland
12.15 - 13.00 hrs	IL - 9: Compartive proteomics in-slico for drug target indentification Prof. Samir K. Brahmachari, Director, Institute of Genomics & Integrative Biology, India
13.00 - 13.45 hrs	IL - 10: Application of an Integrated Biological and Chemical Genomics Platform for Drug Profiling and the Identification and Validation of Drug Targets Deepika Madan, Director of Automation, ALTANA Research Institute, USA
13.45 - 15.30 hrs	LUNCH AND POSTERS
15.30 - 18.00 hrs	Visit to Zydus Facilities/Ahmedabad City Tour
19.00 hrs onwards	Cultural program of Zydus Research Centre and dinner

Day 3 : Tuesday : 25th January, 2005

Session VI

	Chairpersons: Dr. M. K. Sahib and Prof. Bharath Chattoo
09.00 - 10.00 hrs	Key Note Address (PL - 3): Proteomics Approaches to Diagnosis and Therapy of Cancers Gilbert S. Omenn, Executive Vice President for Medical Affairs, CEO for University of Michigan Health System, Professor of Internal Medicine, Professor of Human Genetics, University of Michigan, USA
10.00 - 10.45 hrs	IL - 11: Improving target and compound quality. The application of genomic technologies to drug discovery and development Dr. Mark Cockett, Vice-President, Applied Genomics, Bristol-Myers Squibb, USA
10.45 - 11.15 hrs	TEA BREAK

Session VII

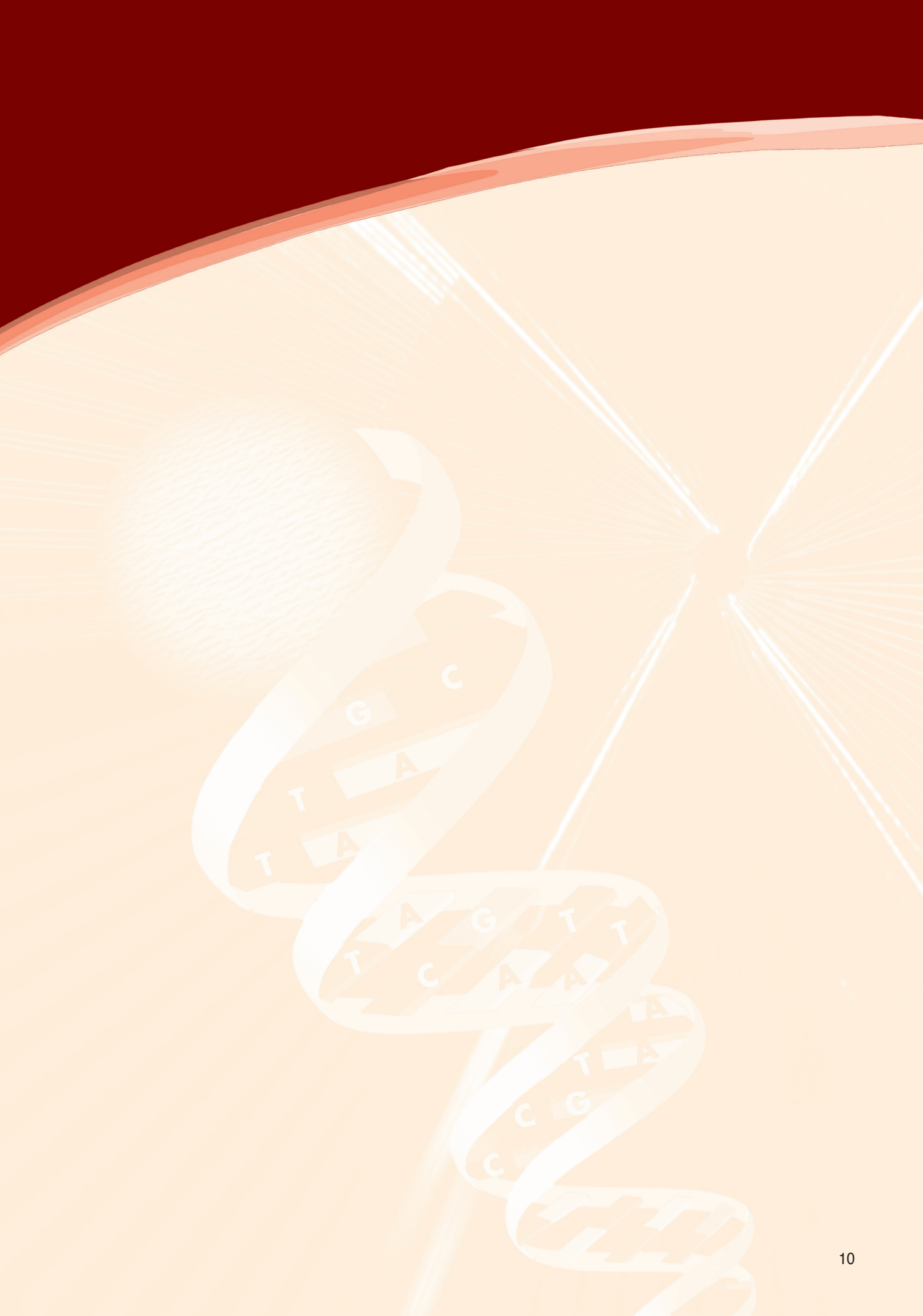
	Chairpersons: Mr. Ashwini Kumar and Dr. S. Nath
11.15 - 12.00 hrs	IL - 12: Production of a Allelic Series of the Mouse Dishevelled 2 Gene: Determination of Developmental Pathways and Mechanisms Important for Neural Tube Closure Dr. Wynshaw Boris, Professor, Departments of Pediatrics and Medicine, Director, Center for Human Genetics and Genomics, Chief, Division of Genetics, Department of Pediatrics, Univ of California, San Diego, USA
12.00 - 12.45 hrs	IL - 13: Genetics on Embryonic Stem cells; closing the gap between yeast and mouse Dr. Andras Nagy, Professor, Department of Medical Genetics & Microbiology, University of Toronto, Canada
12.45 - 13.30 hrs	IL - 14: Design and Application of Synthetic Antibodies Dr. Sachdev Sidhu, Senior Scientist, Department of Protein Engineering, Genentech, USA
13.30 - 14.30 hrs	LUNCH

Session VIII

	Chairpersons: Dr. Steve Hawkins and Dr John Wotherspoon
14.30 - 15.15 hrs	IL - 15: Conformationally-constrained Oxetane Modified Antisense Oligonucleotides Function Efficiently as Novel Gene Silencing Molecules Dr. Jyoti Chattopadhyaya, Professor & Chairman, Department of Bioorganic Chemistry, Uppsala University, Sweden
15.15 - 16.00 hrs	IL - 16: Nucleic Acid Based Therapeutics for Treating Human Malignancies Dr Alan M. Gewirtz, Doris Duke Distinguished Clinical Professor, Medicine and Pathology. Leader, Stem Cell Biology & Therapeutics Program, University of Pennsylvania School of Medicine, USA
16.00 to 16.30 hrs	TEA BREAK

Session IX

	Chairpersons: Prof. Harish Padh and Dr. Sunil Patel
16.30 - 17.15 hrs	IL - 17: Pharmacogenetic aspects of the metabolic syndrome components hypertension, diabetes, and obesity Prof. G Neil Thomas, Research Assistant Professor, Department of Community Medicine, University of Hong Kong
17.15 - 18.00 hrs	IL - 18: Identifying and validating biomarkers that bridge the preclinical and clinical Dr Pauline Gee, Vice-President, Predictive Biology, MDS Pharma, UK
18.00 - 19.00 hrs	**Panel Discussion & Closing Ceremony** Mr. Pankaj R. Patel, Dr. B. B. Lohray, Mr. Ashwini Kumar, Mr. Hari Mundra, Elisabeth Hervier, Dr. Jyoti Chattopadhyaya, Mr. Ramesh Srinivasan and Dr. M. K. Sahib



Session I

Introduction to the Chairpersons

Dr. J. S. Yadav,
Director
Indian Institute of Chemical Technology

Dr. J. S. Yadav has been associated with IICT, Hyderabad, India since 1986 and currently he is the director of this premier institute. After obtaining his Ph.D. from M.S. University, Baroda he did his Postdoctoral research work at Rice University, Houston, USA and Wisconsin University, USA. He was also a scientist at NCL, Pune. He is a recipient of several awards such as Vigyan Gaurav Samman Award, Uttar Pradesh; Vigyan Ratna Award, Uttar Pradesh, Andhra Pradesh Scientist Award; CRSI Silver Medal; Prof. S. Swaminathan Commemorative Lecture Award; Ranbaxy Research Award in Pharmaceutical Sciences;Shanti Swarup Bhatnagar Award in Chemical Sciences etc. He is a fellow of INSA and FNA. He has published over 450 Research Papers in peer reviewed journals; co-author of 4 books and reviews.

Dr. Volker Figala,
Managing Director
Altana Pharma, India

Dr. Figala obtained his Master degree in Chemistry from the University of Munich in 1970. He joined in the research group of Prof. Dr. Gompper at the University of Munich for carrying out his Ph.D work in organic chemistry. After his Ph.D he joined Byk Gulden in 1974. Dr. Figala continued to give his best at Byk Gulden. He has developed a X-ray contrast agent, Osbil, which is in production since 1976. He was involved in the synthesis of Antiphlogistics. The product Eltenac was licensed to Schering Plough and is marketed in the veterinary market. He has also contributed in the field of selective Antimuscarinics. A product Telenzepine has proceeded to Phase III clinical trials. Dr. Figala's group was also one of the first to elucidate the mechanism of action of irreversible proton pump inhibitors. He has been the co-inventor of Pantoprazole. Since 1989 he has been heading the Group for Respiratory Diseases and is spearheading in the development of Phosphodiesterase Inhibitors. In 1991 he became the Director of Chemical Research and was honored as Honorary Professor at the University of Constance. He was Vice President of pharmaceutical development of ALTANA Pharma, Germany. Since 2004 he is serving as Managing Director, ALTANA Pharma Pvt. Ltd India.

Speaker's profile

Prof. Inder M. Verma
Laboratory of Genetics, The Salk Institute, La Jolla, CA 92037, USA.

Professor Inder Verma is associated with The Salk Institute, La Jolla, California since 1974. He is currently a Professor in Laboratory of Genetics at Salk Institute and also an Adjunct Professor in Department of Biology, University of California, San Diego. He is a recepient of innumerable awards such as - Fellow of American Academy of Arts and Sciences; Member of Institute of Medicine of The National Academy of Sciences (USA); Associate Member of European Molecular Biology Organization (EMBO); Member of The National Academy of Science (USA); Fellow of American Academy of Microbiology; Member of The Third World Academy of Sciences; Charaka Award of The Association of Indians in America; Annual Award for 1993 from Thrombosis Research Institute, London,; NIH Outstanding Investigator Award; Medal for Outstanding Scientist of North American Scientists of Indian Origin.

Born in Punjab, India, he did his M.Sc. from Lucknow University, India and Ph.D. Weissman Institute of Science, Israel. He worked with Dr. D. Baltimore at Massachusetts Institute of Technology, Cambridge, MA. as a postdoctoral fellow.

He is on the Editorial Board of the Proceedings of the National Academy of Sciences (USA). He is the Editor-in-Chief, Molecular Therapy (Journal of the American Society for Gene Therapy). Since 1983 he is the Coordinator of the Scientific Advisory Committee established by the Prime Minister of India for the Department of Biotechnology

He is the member, Scientific Advisory Board and Board of Directors of Ceregene, Inc., Xenogen, Jubilant Biosys, Ltd., Agensys, Santa Monica, CA, Cell Genesys, Inc., Foster City, CA. He is also a Member, Board of Trustees, The Salk Institute. In the year 2000-2 he was the President of American Society of Gene Therapy.

He is currently a member of several Review Committees such as Fred Hutchinson Cancer Research Center, Scientific Advisory Board, Cleveland Clinic Foundation, External Advisory Board, Wellcome Trust Fellowship Review Committee, Damon Runyon Scholar Award Committee, General Motors Sloan Selection Committee.

Professor Verma has over 200 scientific publications in prestigious peer-reviewed journals. He is a well known authority in the field of Viral Gene Therapy.

For Notes :

Topic

Gene Therapy: Ups and Downs

Inder M. Verma
Laboratory of Genetics The Salk Institute, La Jolla, CA 92037, USA.

At the beginning of the third millennium, man has an opportunity to fulfill the cherished goal of improving the lot of humankind. Newer modalities of medicine are being practiced and daily new breakthroughs are being reported. I would like to talk about gene therapy, a form of molecular medicine, which will have a major impact on human health. At present, gene therapy is being contemplated for both genetic and acquired diseases. These include hemophilia, cystic fibrosis, diabetes, cancer, Parkinson's, Alzheimer's, etc. In the former case, a wide variety of somatic tissues are being explored for the introduction of foreign genes with a view towards gene therapy. A prime requirement for successful gene therapy is the sustained expression of the therapeutic gene without any adverse effect on the recipient. A highly desirable delivery vehicle will be the one that can be generated at high amounts, integrate in non-dividing cells and have little or no associated immune problems. We have recently generated vectors based on the AIDS virus that have the ability to introduce genes into both dividing and non-dividing cells. The vectors (lentiviral) also have a very expanded host range and can introduce genes in a variety of cells. We have recently generated third generation of lentiviral packaging constructs that contain only the gag/pol, VSV G envelope and the sin vector. Thus our current lentiviral vectors are devoid of six viral genes and therefore we consider them to be safe vectors. Using third generation lentiviral vectors we can introduce genes directly into brain, liver, muscle, hematopoietic stem cells, and more recently retina and a number of tumor cells. Our data shows that lentiviral vectors can not only efficiently deliver genes, but also have long term sustained production of the foreign protein. We have not observed any untoward immunological consequences due to the vector. My talk will discuss in detail the use of vectors for a wide variety of genetic and acquired diseases. Additionally I will discuss the use of lentiviral vectors for transgenesis, and uses in studying complex biological systems. I will also discuss the social and ethical implications of genetic approaches to human health.

For Notes :

Speaker's profile

Dr. Dalia Cohen
Vice President and Global Head,
Functional Genomics
Novartis Institute for Biomedical Research, Inc.

Dalia Cohen is the Global Head of Functional Genomics at the Novartis Institutes for BioMedical Research. In this post, Dalia directs global research teams, consisting of scientists employing functional genomics approaches, with laboratories in the United States and Switzerland. In addition, Dalia runs a laboratory which initiated the Histone Deacetylase Inhibitor program, presently in Phase I trials.

Dalia has 18 years of research experience in the pharmaceutical industry, starting her career in 1986 at the Albert Einstein College of Medicine (Bronx, NY). Since 1992, Dalia has been an integral part of the research being conducted at Novartis Pharmaceuticals (formerly Sandoz). Dalia holds positions on 10 boards and committees, including the Board of Directors for the SNP Consortium and the Novartis Pharma Research Board.

Since 1995, Dalia has held teaching positions in the Department of Molecular Genetics & Microbiology at UMDNJ-Robert Wood Johnson Medical School. Dalia's credits include numerous invited worldwide speaking engagements, over 60 published scientific articles, and nine patents. Her honors include Outstanding Service by Volunteer Faculty from the UMDNJ-Robert Wood Johnson Medical School and a Camp David Visiting Scholar in International Health award.

In 1984, Dalia received her Ph.D. in cell biology from the Faculty of Medicine Technion, Israel Institution of Technology.

For Notes :

Topic

From Genome to Therapy

Dr. Dalia Cohen
Vice President and Global Head, Functional Genomics
Novartis Institute for Biomedical Research, Inc.

The recently completed human genome sequence is yielding a plethora of potential new targets for intervention by novel therapeutic agents in a variety of diseases. These therapeutic agents will be developed against targets identified through a better understanding of the function of the genes and proteins involved in disease initiation and progression. In order to effectively and competitively exploit the genome data, an industrialized multidisciplinary and process-driven approach was instituted for drug target identification and validation. This allows the generation of a multidimensional profile of potential and promising targets for drug development.

For Notes :

Speaker's profile

Dr. Steve Oliver
Faculty of Life Sciences,
The University of Manchester
Manchester, UK

Stephen Oliver is Professor of Genomics in the Faculty of Life Sciences at the University of Manchester. He gained his BSc degree in Microbiology from the University of Bristol in 1971, winning the Max Russ/ Anna Mayr-Harting Prize for Bacteriology, and then gained a PhD from the National Institute for Medical Research (Mill Hill) in 1974. Following a post-doctoral period at the University of California at Irvine, Dr. Oliver became Lecturer in Microbiology at the University of Kent at Canterbury in 1977. He moved to UMIST in 1981, becoming Professor of Biotechnology there in 1987, and finally accepting his present position in 1999.

Professor Oliver's research involves both experimental and bioinformatics approaches to functional genomics, mainly using the yeast *Saccharomyces cerevisiae* as his experimental system. Stephen Oliver led the European team that sequenced the first chromosome, from any organism, yeast chromosome III. He continued to play a major role in the Yeast Genome Sequencing Project, and went on to become Scientific Coordinator of EUROFAN, which pioneered a wide range of approaches to the systematic analysis of gene function, using S. *cerevisiae*. His current work involves studies at the levels of genome, transcriptome, proteome, and metabolome, as well as the development of bioinformatics tools to integrate data from all of these types of analysis.

Stephen Oliver is the Editor-in-Chief of two journals - *Yeast* and *Comparative & Functional Genomics*. He is a member of EMBO, an Honorary member of the Hungarian Academy of Sciences, a Fellow of the American Academy of Microbiology, and a Fellow of the Academy of Medical Sciences. He was the Cape Lecturer at McGill University in 1996, and Pirie Lecturer at IACR, Rothamsted in 1997. Prof. Oliver was the Kathleen Barton-Wright Memorial Lecturer of the Institute of Biology & Society for General Microbiology in 1996, and won the AstraZeneca Award of the Biochemical Society in 2001.

He also has many publications in peer reviewed journals

For Notes :

Topic

From Genomes to Systems and Targets: The Path with Yeast

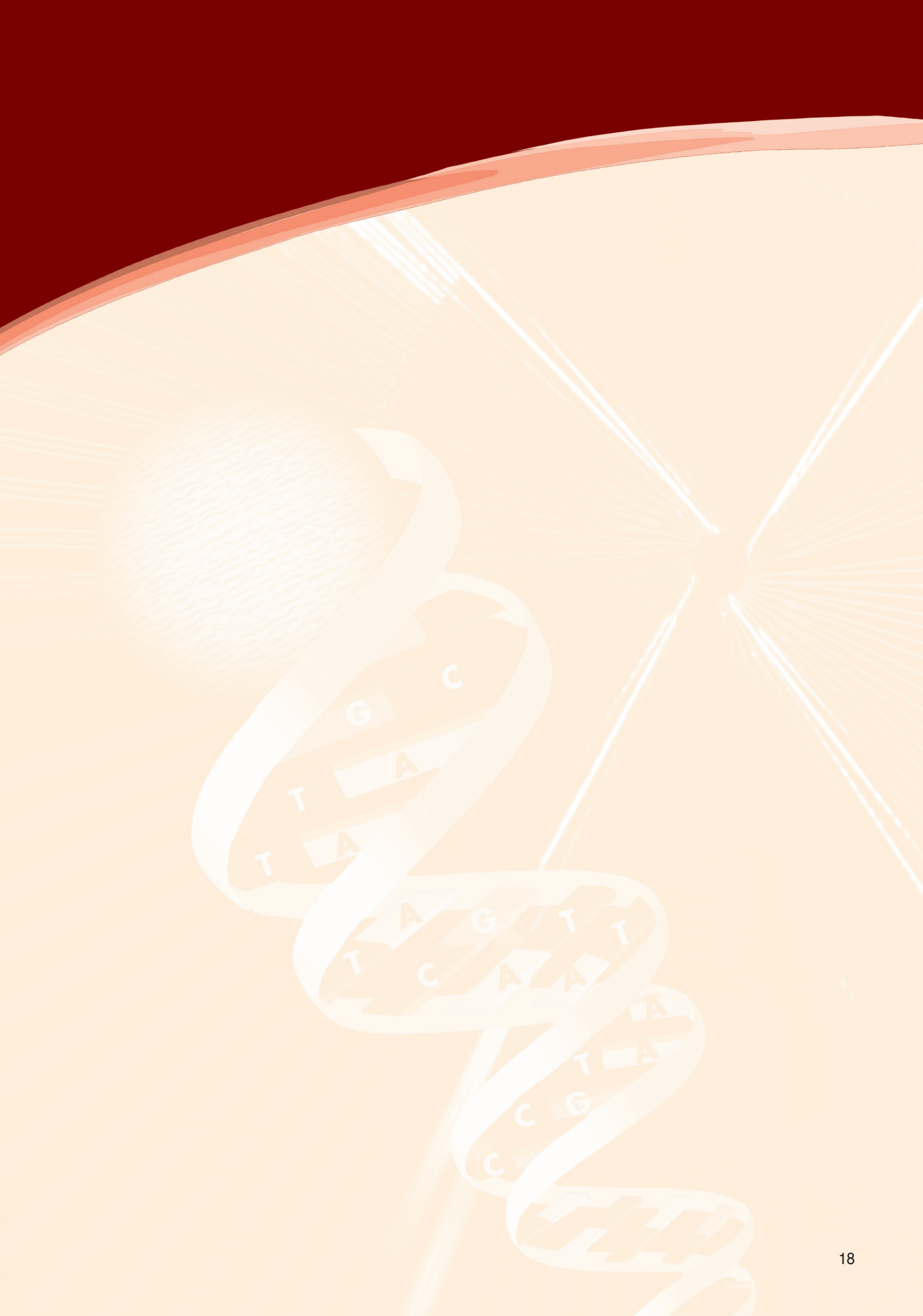
Steve Oliver
Faculty of Life Sciences, The University of Manchester, Manchester M13 90PT, UK

Post-genomic biology aims to reverse the reductionist trend that has dominated the life sciences for the last 50 years, and adopt a more holistic or integrative approach to the study of cells and organisms. Systems Biology is central to the post-genomic agenda and there are plans to construct complete mathematical models of unicellular organisms, with talk of the 'virtual *E. coli*', the '*in silico* yeast' etc. In truth, such grand syntheses are a long way off - not least because much of the quantitative data that will be required, if such models are to have predictive value and explanatory power, simply does not exist. Therefore, we will have to approach such comprehensive models in an incremental fashion, first constructing models of smaller sub-systems (e.g. energy generation, cell division etc.) and then integrating these component modules into a single construct, representing the entire cell.

The problem, then, is to ensure that the modules can be joined up in a seamless manner to make a complete working model of a living cell that makes experimentally testable predictions and can be used to explain empirical data. There is a general awareness of this problem and there is much debate about the relative merits of 'bottom-up' and 'top-down' approaches in Systems Biology. In fact, both will be needed - but foregoing discussion demonstrates that the 'top-down' approach faces the larger conceptual problems.

It is difficult to construct an overarching framework for a model of, say, a yeast cell when one has no idea what the final model will look like. We need to build a very coarse-grained model of the yeast cell based on our current knowledge. This is dangerous since our current knowledge is very incomplete, with much relevant data being unavailable at present. Therefore, while a coarse-grained model is desirable, it would be best to get the yeast cell to construct it for us, rather than make an imperfect attempt ourselves. How might this be achieved? First, we need a general mathematical framework in which to build the coarse-grained model. We have chosen to use the formalism of Metabolic Control Analysis, which was developed in part as a shorthand way of modelling biochemical genetic systems and metabolism, but is more widely applicable since, in effect, it represents a sensitivity analysis of the degree of control that different components of a system have over the system as a whole. As such, it seems eminently suitable for our purposes. What we now need to do is to identify those components of the system that exert the greatest degree of control over the pathways in which they participate (or which they regulate). Moreover, it is these system components that should represent the most favourable drug targets since even if their function is merely compromised, rather than completely negated, it will have a profound effect on growth and survival. I will describe the sorts of experiments that might be used for such an approach to Systems Biology and Target Identification.

For Notes :



Session II

Introduction to the Chairperson

Dr. Samir Brahmachari
Director, IGIB

Dr. Samir K. Brahmachari completed Ph.D. in Molecular Biophysics. He is presently the Director of Institute of Genomics & Integrative Biology (IGIB), Delhi under the Council of Scientific and Industrial Research, India. Earlier he was a Professor of Molecular Biophysics and Genetic Engineering at Indian Institute of Science, Bangalore.

He heads the Functional Genomics Unit at IGIB. He has demonstrated the structural flexibility of DNA and the role of repetitive sequences in DNA transactions much before the discovery of repeats association with genetic disorders. His work on the structural flexibility of telomeric repeat sequences is one of his well-cited contributions. He has made major contribution in molecular analysis of genetic disorders associated with trinucleotide amplification and repetitive sequence instability. Using a combination of structural biology, computational genomics and population-based polymorphism scanning he and his group have provided a novel structural frame work for understanding the etiology of several neurological disorders. One of the outcomes of these efforts has been the demonstration that loss of triplet repeat interruption as the primary step in ataxia SCA 2 which is followed by repeat expansion. Dr. Brahmachari and his group also identified a susceptibility locus on chromosome 22 using a novel positional candidate gene approach for schizophrenia and bipolar disorder patients in the Indian population and have for the first time identified a nonsense mutation in synaptogyrin I gene, a component for presynaptic pathway in schizophrenia patients. His group has developed novel *in Silico* bioinformatics tools to identify functional signature of hypothetical proteins and novel drug targets

He got many prestigious National and International Awards for his contributions in Science. He is a Fellow of Indian National Science Academy and Indian Academy of Science. He was elected a member of the Human Genome Organization in 1991 and to the HUGO Council in 2004; member of various Committees, Govt. of India; member, expert group on Human Rights and Biotechnology, United Nations and member of various International Committees. He has been the recipient of FICCI Award (1998-99) in recognition of individual initiative in Life Sciences including agriculture; Ranbaxy Research Award for The Year 2001 in the field of "Medical Sciences" among many others. He has also been involved in issues relating to Genomics research, ethics and Human Rights. As a member of the steering committee of the International Human Rights Commission he has contributed to the formulation of the draft guidelines in terms of benefit sharing by the populations that are the part of the research endeavor as resources of genetic material and addressed issues of unethical exploitation of genetic resources of the Third world. He has contributed significantly in promoting industry-academia interactions through novel program of knowledge partnerships.

Speaker's profile

Dr. Walter Wahli
Professor and Director,
Center for Integrative Genomics,
University of Lausanne, Switzerland

Walter Wahli received his PhD in Bern in 1977. He carried out a postdoctoral fellowship with Dr. Igor Dawid at the Department of Embryology, Carnegie Institution of Washington in Baltimore. He then was at the Department of Biochemistry of the National Cancer Institute, NIH, in Bethesda, as visiting fellow and visiting associate. He moved to Lausanne in 1980, where he was appointed Professor of biology and Director of the Institute of animal biology of the University. He was Vice-rector for Research and Postgraduate Education of the University between 1999 and 2003. In 2003, he became Director of the Center for Integrative Genomics and in 2004 he was elected President of the Biology and Medicine Division of the Swiss National Science Foundation.

The Otto Naegeli Award 2002 and the European Lipid Science Award 2002 have honored the work of Walter Wahli who has discovered novel nuclear hormone receptors, has identified specific ligands for these receptors, and has demonstrated the central physiological significance of these regulatory proteins in metabolism, inflammation, and wound healing.

Dr. Wahli has published many publications in well respected and peer viewed journals and earned a respectable position in exploring mechanism of different diseases related to nuclear receptors.

For Notes :

Topic

Coordinated roles of PPARs in energy homeostasis and tissue repair

Walter Wahli
Center for Integrative Genomics, NCCR Frontiers in Genetics,
University of Lausanne, Switzerland

Investigating metabolism by unveiling the functions of the nuclear receptors peroxisome proliferator-activated receptors (PPARs) has been very rewarding. Initially crucial roles were determined for PPARalpha in fatty oxidation and for PPARgamma in adipocyte differentiation and lipid storage. More recently, the uncovering of the molecular bases of the functional links between glucose, lipid, and protein metabolism, under the important but nonexclusive control of PPARalpha and PPARgamma, has been an important step ahead. In addition, in the last couple of years evidence has been provided for an important role of PPARbeta (delta) in energy homeostasis. Inevitably, such important actors of metabolic and energy homeostasis are implicated in the physiopathology of complex metabolic disorders, such as those constituting the metabolic syndrome, resulting in atherosclerosis and cardiovascular diseases.

The inability of chronic wounds to heal is a major health problem and will increase in magnitude as the population ages. Healing of cutaneous wounds, which is crucial for survival after an injury, proceeds via a well-tuned pattern of events including inflammation, re-epithelialisation, and matrix and tissue remodelling. These events are regulated spatio-temporally by a variety of growth factors and cytokines. The inflammation that immediately follows injury increases the expression of PPARbeta (delta) and triggers the production of endogenous PPARbeta ligands. These events result in increased resistance of the keratinocytes to the apoptotic signals released during wounding, allowing faster re-epithelialisation. Thus, current understanding of the roles of PPARbeta (delta) in different cell types implicated in tissue repair has revealed an intriguing intercellular cross-talk that coordinates, spatially and temporally, inflammation, keratinocyte survival, proliferation and migration, which are all essential for efficient wound repair. These novel insights into the orchestrating roles of PPARbeta (delta) during wound healing may be helpful in the development of drugs for acute and chronic wound disorders.

For Notes :

Speaker's profile

Dr. Shigeaki Kato
Professor
Institute of Molecular and Cellular biosciences,
University of Tokyo, Japan

Dr. Shigeaki Kato is Professor at Institute of Molecular and Cellular Biosciences, University of Tokyo, Japan. After obtaining his Ph.D. at University of Tokyo, Bunkyo-ku, Tokyo he was associated with Tokyo university of Agriculture, Setagaya-ku, Tokyo in various positions. He is a recipient of several awards such as Young Investigator Award: Japan Society for Biosciences, Biotechnology, and Agrochemistry, Young Investigator Award :Japan Society for Vitaminology, IBCI outstanding investigator award, Gold medal, Yomiuri award,The Fuller Albright Award, Award: Japan Society for Vitaminology, International Prize 2000: Austrian Bone and Mineral Research, Special Award: Japan Society for Bone and Mineral Research. He has published several papers in peer reviewed journals.

For Notes :

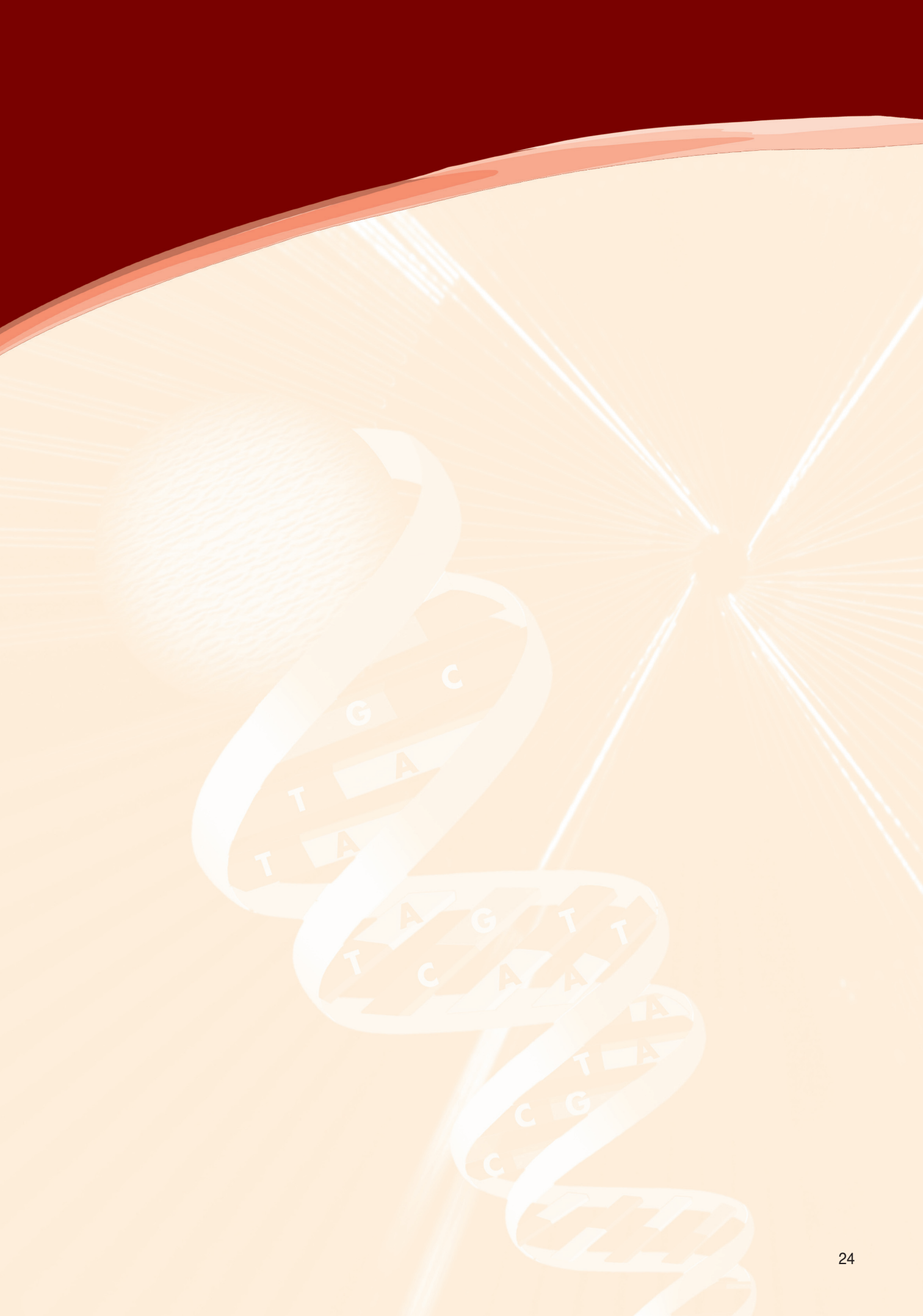
Topic

Steroid hormone receptors in gene regulations

Dr. Shigeaki Kato
Professor
Institute of Molecular and Cellular biosciences,
University of Tokyo, Japan

Fat-soluble factors like steroid/thyroid hormones and vitamin A/D serve as ligands for nuclear receptors. Nuclear receptors form a nuclear receptor gene superfamily, acting as ligand-inducible transcriptional factors. During the ligand-induced transactivation of most nuclear receptors, ligand-dependent recruitments of nuclear coregulator complexes are prerequisite. These complexes compromise histone-modifying enzymes and chromatin remodeling activity, and functionally associate with signal inducers to constitute signaling cross-talks. Recent progress mainly with findings in our laboratory will be overviewed.

For Notes :



Session III

Introduction to the Chairperson

Dr. Elisabeth Hervier
President, ZyFrance

Dr. Elisabeth Hervier is a Ph.D. from University of Paris and is an expert in International regulatory affairs and biotechnologies regulations. She was a founder of International Drug Development (IDD) in 1980, which she managed for 20 years. She was also a founder of International Drug Licensing (IDL) in 1985 and she is a member of Chamber of Trade and Industry. Since October 2003 she is President of Zydus France (French subsidiary of Zydus Cadila).

Speaker's profile

Prof. Dr. Juergen Engel
Chairman and Managing Director
Zentaris GmbH, Germany
Executive Vice President, Gobal Research & Development, Chief Operating Officer and Member of the Board of Director, Æterna Zentaris Inc., Quebec/Canada

Before spinning out Zentaris GmbH in the beginning of 2001 Dr. Juergen Engel was in-charge of all research and development activities of ASTA Medica AG, supervising more than 700 scientists and clinical professionnals.

Dr. Engel holds a doctorate in organic chemistry and doctorate habil. in pharmacy. He is full adjunct professor at University of Regensburg and also honorary professor at the Technical University in Dresden. In 1995, he received the Galenus-von-Pergamon prize for having developed miltefosine as a new class of anti-tumor agents. Dr. Engel is the author of more than 200 scietific articles, various books and filed more than 100 patent applications.

He was Chairman of the Board of the section Medicinal Chemistry of the German Chemical Society from 1997-2002 and is elected Member of the Scientific Advisory Board of the Biocenter of University of Wuerzburg.

Since January 05, 2005 he has management responsibility for the new Æterna Zentaris subsidiary Echelon Biosciences Inc. in Salt Lake City / US.

For Notes :

Topic

Peptides in Oncology / Endocrinology

Prof. Dr. Juergen Engel
Chairman and Managing Director
Zentaris GmbH, Germany

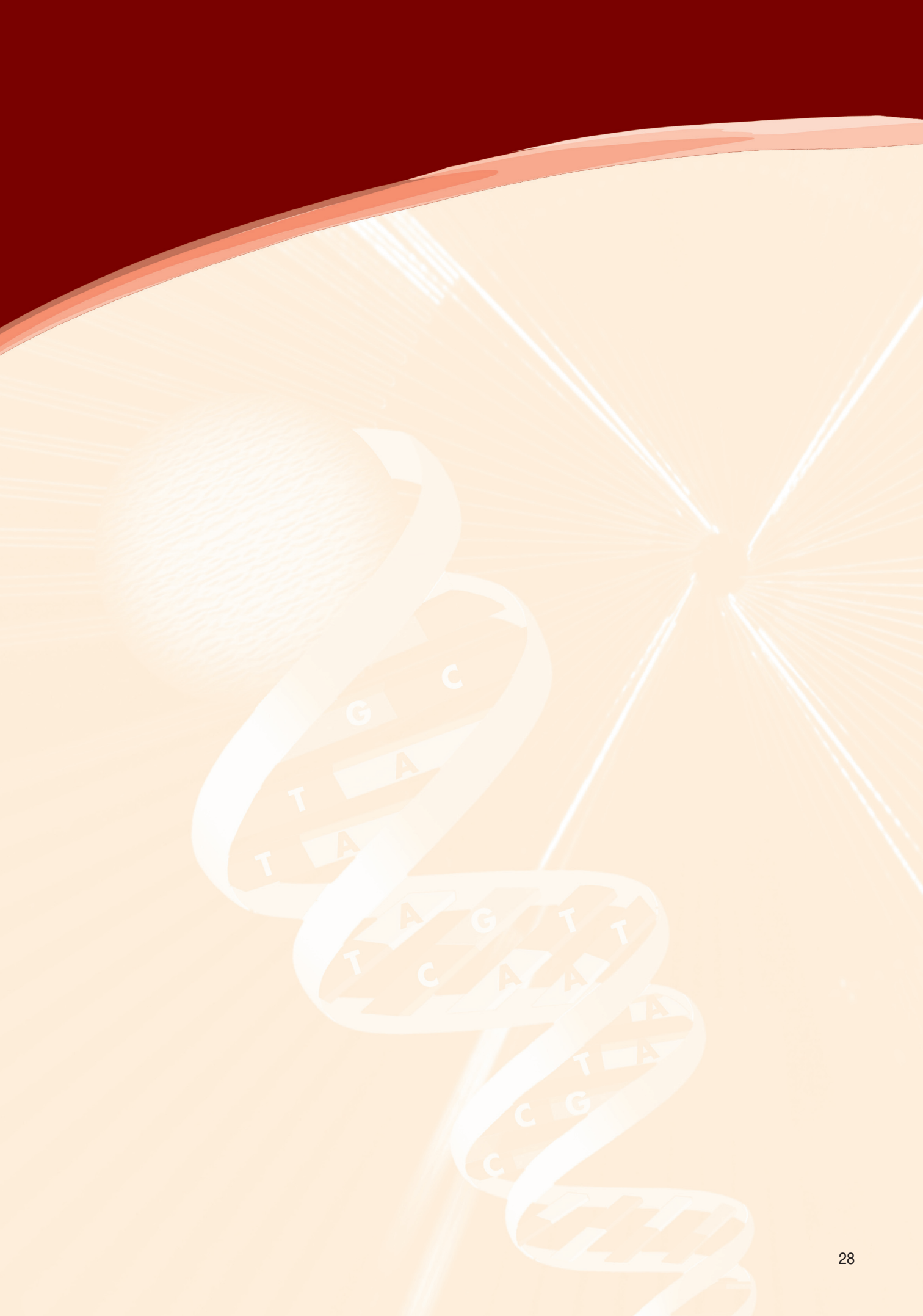
Peptides are well established in the therapy of various diseases in oncology and endocrinology.

LHRH agonists such as Leuprorelin, Goserelin and Triptorelin are worldwide approved and widely used for treatment of prostate cancer and various gynecological diseases. Somatostatin analogs like Octreotide and Vapreotide are on the market in indications like acromegely, carcinoid tumors and VIPomas.

The presentation will focus on LHRH antagonists, their therapeutic advantages and the clinical results achieved so far in indications like in-vitro fertilization, uterus myoma, endometriosis, benign prostatic hyperplasia, prostate and ovarian cancer.

Furthermore the importance of patient convenient sustained drug delivery formulations will be addressed and the status of the development of orally active LHRH antagonists reviewed. In addition a new drug targeting concept based on the expression of LHRH receptors at cancer cell membrans will be described.

For Notes :



Session IV

Introduction to the Chairpersons

Prof. K N Ganesh, Ph.D.
National Chemical Laboratory, Pune, India

Dr. K. N.Ganesh is currently Scientist – G and head of Organic Chemistry Division, NCL, Pune. He obtained his Ph.D. from Cambridge University in 1980 and is a recipient of a number of awards and honors such as Fellow, Indian Academy of Sciences, Bangalore; Fellow, The National Academy of Sciences, Allahabad; CSIR Bhatnagar Award in Chemical Sciences; Fellow, Indian National Science Academy, Delhi etc. He has published about 140 research papers and is a member of several professional bodies and committees. He has made immense contributions in the area of DNA therapeutics, in particular in the design of therapeutic agents based on chemically modified DNA, PNA, etc.

Prof. H. L. Bhalla

Prof. H.L. Bhalla, B. Pharm., M. Pharm., Ph.D. (Tech.), is senior most professor of Pharmaceutics & Pharmaceutical Technology in India. He is currently Advisor SciTech Centre, President, CRS-Indian Chapter, Emeritus Professor and Founder Director, B.V. Patel Pharmaceutical Education Research & Development Centre. He has over 100 research publications in National & International journals and guided 16 Ph.D. and over 30 M. Pharm. Scholars. He has coordinated many workshops/seminars as well as national and international conferences to promote Pharmaceutical Sciences and technology and interaction between industry and academic institutions.

Prof. Bhalla has been member of advisory boards of many journals in India and abroad. He was elected as President, Indian Pharmaceutical Congress Association (IPCA) for 1993 and President, Indian Local Chapter of Controlled Release Society in 1995. He is recently nominated to the Council of FAPA College of Pharmacy, Bangkok (Thailand); and European Association of Pharmaceutical Technology, Germany and Scientific Advisory Board of the 3rd World Congress on Emulsion, France. He is recipient of several Awards.

His services in social fields were recognized as Best President by Lions Club of India and Special Executive Magistrate for 2 years by State Government of Maharashtra in early 1980's. He is permanent invitee to the meetings of many trusts and associations.

Speaker's profile

Prof. Joel L. Sussman
The Morton and Gladys Pickman Professor of Structural Biology
Weizmann Institute of Science, Israel

Prof. Joel L. Sussman obtained his Ph.D. from MIT in Biophysics. He is associated with Weizmann Institute of Science, Israel since 1976. Currently he is incumbent of the Morton and Gladys Pickman Chair in Structural Biology. He has held several positions such as Head of Protein Data Bank, Brookhaven National Laboratory, Upton, NY; Professor, Dept of Structural Biology, Weizmann Institute; John von Neumann Visiting Professor in Residence - Rutgers Univ; Head, Kimmelman Center for Biomolecular Structure & Assembly, WIS; Head, Dept of Structural Chemistry, Weizmann Institute; Associate Prof., Dept of Structural Chemistry, Weizmann Institute. He is a recipient of several honors and awards such as Elected Member of European Molecular Biology Organization (EMBO); Bergmann Prize - Outstanding Research in Chemistry in Israel; Member of the Scientific Advisory Board for the EC-BIOXHIT Project; Director, Israel Structural Proteomics Center; Member of The European Synchrotron Radiation Facility SAC Committee; Chairman, Israel Council of Higher Education Bioinformatics Committee; Member of the NIH Task Force & Council on Structural Genomics Initiative; Chairman, Israel National Committee for Crystallography; Member of the Swiss Institute of Bioinformatics SAC Committee. He has vast teaching experience and has published a number of scientific papers in peer reviewed journals.

For Notes :

Intrinsically Unfolded Proteins: What is their Possible Biological Role?

Professor Joel L. Sussman
Dept. of Structural Biology and the Israel Structural Proteomics Center (ISPC)
Weizmann Institute of Science, Rehovot 76100 Israel

Studies during the last decade have identified a family of neural cell adhesion proteins, which are single-pass transmembrane proteins, with substantial sequence similarity to cholinesterases (ChEs). The regions of sequence similarity correspond to only part of their complete sequences, thus establishing the ChE domain as a modular domain incorporated into different proteins, i.e. cholinesterase-like adhesion molecules (CLAMs)[1-3]. CLAMs, however, devoid of catalytic activity, since they lack residues crucial for catalysis. They appear to play a key role in the earliest stages of the development of the CNS and mutations, in the ChE domain of one of them, i.e. neuroligin, has been associated with autism[4,5].

The cytoplasmic domains of CLAMs bear no sequence homology to any known protein, and physicochemical studies show that they are 'intrinsically disordered'[6,7] when expressed in E. coli[3]. It has been estimated that a large percentage of cellular proteins exist in this disordered state6; e.g., in eukaryotic cells, the estimated range is 36-63%. Using an extension of the algorithm described by Uversky and coworkers[7], we have developed a web-based tool, FoldIndex© (see http://bioportal.weizmann.ac.il/fldbin/findex)[8], which has proven useful in predicting regions of a new protein sequence that are likely to be disordered. We have applied FoldIndex© to examine the CLAMs family as well as cholinesterase molecules. These 'in silico' studies will be compared with our recent solution studies on CLAMs and their adhesion partners

References:

This work was supported by The Israel Ministry of Science and Technology (MOST) infrastructure grant for the Israel Structural Proteomics Center; by The European Commission Fifth Framework "Quality of Life and Management of Living Resources" 'SPINE' (Structural Proteomics in Europe) Project; Grant number: QLG2-CT-2002-00988; and by a grant from the Divadol Foundation (Rehovot, Israel).

1. Botti, S.A., Felder, C.E., Sussman, J.L. & Silman, I., Protein Eng 11, 415-420 (1998).
2. Felder, C.E., Botti, S.A., Lifson, S., Silman, I. & Sussman, J.L., J Molec Graphics & Modelling 15, 318-327 (1997).
3. Zeev-Ben-Mordehai, T., Rydberg, E.H., Solomon, A., Toker, L., Botti, S., Auld, V.J., Silman, I. & Sussman, J.L., Proteins 53, 758-767 (2003).
4. Laumonnier, F. et al. & Briault, S., Am J Hum Genet 74, 552-557 (2004).
5. Jamain, S. et al. Bourgeron, T., Nature Genet 34, 27-29 (2003).
6. Dunker, A.K., Brown, C.J., Lawson, J.D., Iakoucheva, L.M. & Obradovic, Z., Biochemistry 41, 6573-6582 (2002).
7. Uversky, V.N., Gillespie, J.R. & Fink, A.L., Proteins 41, 415-427 (2000).
8. Prilusky, J., Felder, C.E., Zeev-Ben-Mordehai, T., Rydberg, E., Man, O., Beckmann, J.S., Silman, I. & Sussman, J.L., Bioinformatics (submitted) (2004).

For Notes :

Session V

Introduction to the Chairpersons

Dr. M. Venkateshwarlu
Dy. DCGI, India

Dr. M. Venkateshwarlu obtained his Ph.D. from Andhra University. He has been associated with Drug Control Department since 1974 and currently he is Deputy Drugs Controller, India. His has contributed immensely in the implementation of GMP guidelines and DMF requirements for API's in India and bringing it at par with various international laws. He has played a major role in detection of spurious and counterfeit drugs in last 25 years. He was nominated as an expert at ICH Expert Working Group on GMP for API's. He has received the Best Drug Control Officers Award in 2001 and Eminent Pharmacists Award in 2001.

Dr. Bansilal

Dr. Bansilal hails from Kashmir. He obtained his Ph.D degree from Lucknow University while working in CDRI, Lucknow under the supervision of Dr. Nityanand. He was post-doctoral research associate at Stevens Institute of Technology, New Jersey; post-doctoral researc fellow at Indiana University at Bloomington Indiana and at Rice University, Houston Texas, USA. He joined Hoechst Research Center as a research scientist in 1975 in chemistry department and became the Head in 1986. In 1997, he became the Vice President & Head of Research, Hoechst Marion Roussel Ltd. He has 30 years of rich experience in New Drug Discovery and since 1999 he is President and Head of Research, Quest Institute of Life Sciences, Nicholas Piramal India. Two drugs from his research team has reached the market namely - Trequinsin a vasodialator and Buquiterine which is an antiallergic & bronchodilator. Yet another drug Flavopiridol is in late Phase II clinical trials for cancer. He has published 50 papers in national and international journals and holds 45 patents. He is a member of several professional bodies.

Speaker's profile

Prof. Kosuke Morikawa
Director, Biomolecular Engineering Research Institute
Osaka, Japan

Prof. Kosuke Morikawa is Director of Biomolecular Engineering Research Institute, Osaka, Japan. He obtained his B.S.; M.S. and Ph.D. degrees form Faculty of Pharmaceutical Sciences, the University of Tokyo, Japan. He has worked at Aarhus University, Denmark and MRC Laboratory of Molecular Biology, England. He has been associated with Biomolecular Engineering Research Institute, Osaka, Japan since 1986. His Research Interest are focussed on Structural Biology and X-ray crystallography. He has published research articles in several peer-reviewed journals.

For Notes :

Channelling mechanism as revealed from the crystal structure of a fatty acid ß-oxidation multienzyme complex

Kosuke Morikawa
BERI, Suita. Osaka 565-0874, Japan

The atomic view of the active site coupling termed channelling is a major subject in molecular biology. Fatty acid metabolism, linked to energy storage and human obesity, frequently involves multifunctional enzyme complexes, which catalyze sequential reactions through this efficient mechanism. We have determined two distinct crystal structures of the bacterial multienzyme complex that catalyzes the last three sequential reactions in the fatty acid ß-oxidation cycle. The a2ß2heterotetrameric protein shows the uneven ring architecture, which undergoes striking alterations in the positional relationships among the three reaction centers, coupled with the binding of substrate analogues. This domain rearrangement is closely connected to the deformation of an α-helical linker, which is conserved in multienzymes and interacts with substrate analogues. The versatile architecture of the complex, with its functionally profound domain and subunit movements, suggests how the individual catalytic components orchestrate the channelling mechanism of fatty acid ß-oxidation. This channelling mechanism could be applied to other ß-oxidation multienzymes, as revealed from the homology model of the human mitochondrial trifunctional enzyme (TFE) complex homologous to bacterial enzymes.

For Notes :

Speaker's profile

Dr. Hanno Langen
Head of Proteomics Initiative, Roche Center for Medical Genomics,
Hoffmann-La Roche, Switzerland

Dr. Hanno Langen is a biochemist by training. He studied at the University of Zürich in Switzerland. In 1989 after his PhD thesis he moved to the Rockefeller University, where he worked on site directed mutagenesis in the group of Prof. Bruce Merrifield. After his postdoctoral training, he joined the protein analysis group at Hoffmann-La Roche in Switzerland. Since 1997 he is heading the Proteomics group in Basel. Since 2001 he is responsible for the proteomics initiative at Roche with groups in the diagnostic and pharma division of Roche with about 50 people working in this area. Dr. Langen has published more than 50 papers in this area. He has also a teaching position for proteomics at the University of Bern. He is one of the founding council members of the Human Proteome Organization.

For Notes :

Topic

The Application of Proteomics Technologies in Pharmaceutical Industry

Dr. Hanno Langen
Head of Proteomics Initiative, Roche Center for Medical Genomics, Hoffmann-La Roche, Switzerland

Information is not only stored in genes but modulated by differently expressed proteins and their modifications. The protein profile present at a given time in a biological system will be different once the shift from the "healthy " to the "diseased" state occurs. Tracing such "Disease-specific proteins" (DSPs) with analytical approaches summarized under "proteomics" is a promising way to arrive at the needed diagnostic tools and will help to understand the molecular mechanisms of disease.

Our proteomics approach makes use of subcellular fractionation and the removal of abundant proteins prior to separation techniques like 2D-gel electrophoresis. We separate several hundred proteins in one gel, followed by mass spectrometry for the rapid identification of these proteins. Many steps in the process are completely automated like the robotic gel processing and mass spectrometry. With our high throughput system we can produce several thousand peptide fingerprints per day.

Several examples of the application of proteomics in pharmaceutical industry from early target identification to applications in biomarker programs in clinical trials will be shown.

For Notes :

Speaker's profile

Prof. Samir K. Brahmachari
Director
Institute of Genomics & Integrative Biology, India

Dr. Samir K. Brahmachari completed Ph.D. in Molecular Biophysics. He is presently the Director of Institute of Genomics & Integrative Biology (IGIB), Delhi under the Council of Scientific and Industrial Research, India. Earlier he was a Professor of Molecular Biophysics and Genetic Engineering at Indian Institute of Science, Bangalore.

He heads the Functional Genomics Unit at IGIB. He has demonstrated the structural flexibility of DNA and the role of repetitive sequences in DNA transactions much before the discovery of repeats association with genetic disorders. His work on the structural flexibility of telomeric repeat sequences is one of his well-cited contributions. He has made major contribution in molecular analysis of genetic disorders associated with trinucleotide amplification and repetitive sequence instability. Using a combination of structural biology, computational genomics and population-based polymorphism scanning he and his group have provided a novel structural frame work for understanding the etiology of several neurological disorders. One of the outcomes of these efforts has been the demonstration that loss of triplet repeat interruption as the primary step in ataxia SCA 2 which is followed by repeat expansion. Dr. Brahmachari and his group also identified a susceptibility locus on chromosome 22 using a novel positional candidate gene approach for schizophrenia and bipolar disorder patients in the Indian population and have for the first time identified a nonsense mutation in synaptogyrin I gene, a component for presynaptic pathway in schizophrenia patients. His group has developed novel *in Silico* bioinformatics tools to identify functional signature of hypothetical proteins and novel drug targets

He got many prestigious National and International Awards for his contributions in Science. He is a Fellow of Indian National Science Academy and Indian Academy of Science. He was elected a member of the Human Genome Organization in 1991 and to the HUGO Council in 2004; member of various Committees, Govt. of India; member, expert group on Human Rights and Biotechnology, United Nations and member of various International Committees. He has been the recipient of FICCI Award (1998-99) in recognition of individual initiative in Life Sciences including agriculture; Ranbaxy Research Award for The Year 2001 in the field of "Medical Sciences" among many others. He has also been involved in issues relating to Genomics research, ethics and Human Rights. As a member of the steering committee of the International Human Rights Commission he has contributed to the formulation of the draft guidelines in terms of benefit sharing by the populations that are the part of the research endeavor as resources of genetic material and addressed issues of unethical exploitation of genetic resources of the Third world. He has contributed significantly in promoting industry-academia interactions through novel program of knowledge partnerships.

For Notes :

Topic

Comparative Proteomics *in silico* for Drug Target Identification

Samir K. Brahmachari, Tulika Prakash, Dipayan Dasgupta, C. Ramakrishnan, Debasis Dash
G.N.Ramachandran Knowledge Centre for Genome Informatics, Institute of Genomics and Integrative Biology, CSIR, Mall Road, Delhi, India.

We have developed a novel in silico approach, Peptide Library based Homology Search Tool (PLHOST), to compare proteomes of multiple genomes. Using this approach, we have identified a large number of invariant signature (IS) peptides in several pathogenic as well as non-pathogenic bacteria. These peptides are observed in functionally similar proteins. A detailed analysis of these invariant peptides indicated that these sequences are not only functionally important, but are also very critical for the structure of the protein. Hence, these invariant peptides act as important functional signatures and/or structural determinants of the proteins. Also, it has been observed that these IS peptides harbor functionally critical residues, since mutations in these peptides either lead to complete or partial loss of activity of the respective protein. In this talk, the possibility of identification of proteins harboring important SD peptides as novel antibacterial drug targets will be discussed.

For Notes :

Speaker's profile

Deepika Madan
Director - Automation
ALTANA Research Institute, USA

Deepika Madan is the Director of Automation at the ALTANA Research Institute since August 2002. In this capacity, she oversees the Automation department, which is responsible for developing and establishing automation solutions for target discovery and validation.

Previously, Deepika was at Genome Therapeutics Corporation where she acquired extensive experience in software development and genomics automation for high throughput operations. As a member of the GTC Sequencing Center, she contributed to the Human Genome Project.

Deepika received a B.Sc. and an M.Sc. in Physics from the University of Delhi & M.Sc. in Biophysics from Brandeis University in Waltham, Massachusetts.

For Notes :

Topic

Application of an Integrated Biological and Chemical Genomics Platform for Drug Profiling and the Identification and Validation of Drug Targets

Deepika Madan
Director - Automation
ALTANA Research Institute

The ALTANA Research Institute (ARI) is the US research division of ALTANA Pharma AG. ARI has been built over the past 2.5 years in Boston/Waltham (MA). The establishment of the institute was accelerated through collaboration with GPC-Biotech. ARI functions within the R & D organization of ALTANA Pharma. The research focus at ARI is on the application of innovative technologies that support the company's drug discovery efforts for treatment of inflammation/respiratory disorders, gastrointestinal disease and cancer. ARI's integrated genomics and proteomics technology platform is strengthened by underlying state-of-the-art IT/bioinformatics and automation components. Scientists at ARI are decoding complex molecular and cellular mechanisms associated with disease, for development of novel and safe drugs in ALTANA Pharma's core therapeutic areas. The approach uses (i) focused gene libraries (e.g. kinases, phosphodiesterases, others), (ii) focused functional gene screening campaigns for identification and validation of drug targets and (iii) the mapping of such targets into protein interaction pathways linked to disease. Chemogenomics applications complement target driven research, integrating target identification and validation with early and late stage compound profiling.

For Notes :

Session VI

Introduction to the Chairpersons

Dr. M. K. Sahib
Director - Genomics & Biotechnology
Wockhardt

Dr. M. K. Sahib has been associated with Wockhardt Reseach Centre since 1991. He has contributed immensely to the growth of Biotechnology in India and the recognition of Wockhardt as a Biotech company. He is responsible for successful development of several Recombinant therapeutic proteins, and Biopesticides. He obtained his Ph.D. from CDRI, Lucknow and did his post-doctoral research at Harvard Medical School, Boston. He was a visiting Scientist at NIH, Bethesda, Maryland, USA; National Institute of Medical Research Mill Hill, London, UK, Institute Pasteur, Paris France and INSERM, France. He was associated with CDRI, Lucknow during 1971 - 91 at various levels. He has several publications in peer reviewed journals.

Prof. Bharat Chattoo

Bharat Chattoo is a senior professor with the Department of Microbiology and Biotechnology Centre, M.S. University of Baroda. He has been the Head of the Department of Microbiology, M.S. University of Baroda, (1996-2001) and has been a professor since 1986. He is the Coordinator of Biotechnology Teaching Programme and the Director of Centre for Genome Research at M.S. University and is the founder Vice Chancellor of the Shri Mata Vaishno Devi University, Jammu.

He received his Ph.D. from the University of Delhi, in the field of Microbial Genetics. Subsequently, he worked at the University of Rochester Medical Centre in the area of yeast molecular genetics. He has been a Visiting Scientist/Professor, at the Weizmann Institute of Science, Israel, National Institute of Bioscience and Human Technology, Tsukuba, Japan, Rice Genome Programme, Tsukuba, Japan and United States Department of Agriculture, Beltsville, Maryland.

Dr. Chattoo is a fellow of the Indian National Science Academy. He is a member of the Gujarat Biotechnology Council. He received the national technology award for transfer of technology to industry. He has published extensively in the area of microbial and molecular genetics and genome analysis. His current interests are in the functional genomics of fungal pathogens, genomics and proteomics approaches to the study of host-pathogen interactions and in bioprocess development.

Speaker's profile

Gilbert S. Omenn, M.D., Ph.D.
Executive Vice President for Medical Affairs
CEO for University of Michigan Health System
Professor of Internal Medicine, Professor of Human Genetics, University of Michigan, USA

Dr. Gilbert Omenn is Professor of Internal Medicine, Human Genetics, and Public Health at the University of Michigan. He served as Executive Vice President for Medical Affairs and as Chief Executive Officer of the University of Michigan Health System from 1997 to 2002. He was formerly Dean of the School of Public Health, and Professor of Medicine and Environmental Health, University of Washington, Seattle. His research interests include cancer proteomics, chemoprevention of cancers, public health genetics, science-based risk analysis, and health policy. He was principal investigator of the beta-Carotene and Retinol Efficacy Trial (CARET) of preventive agents against lung cancer and heart disease; director of the Center for Health Promotion in Older Adults; and creator of a university-wide initiative on Public Health Genetics in Ethical, Legal, and Policy Context while at the University of Washington and Fred Hutchinson Cancer Research Center. He served as Associate Director, Office of Science and Technology Policy, and Associate Director, Office of Management and Budget, in the Executive Office of the President in the Carter Administration. He is a longtime director of Amgen Inc. and of Rohm & Haas Company. He is a member of the Council and leader of the Plasma Proteome Project for the international Human Proteome Organization (HUPO). In 2004 he became president-elect of the American Association for the Advancement of Science (AAAS).

Omenn is the author of 390 research papers and scientific reviews and author/editor of 17 books. He is a member of the Institute of Medicine of the National Academy of Sciences, the American Academy of Arts and Sciences, the Association of American Physicians, and the American College of Physicians. He chaired the presidential/congressional Commission on Risk Assessment and Risk Management ("Omenn Commission"), served on the National Commission on the Environment, and chaired the NAS/NRC/IOM Committee on Science, Engineering and Public Policy.

He is active in cultural and educational organizations. He is a good musician and a tennis player. Omenn received his B.A. from Princeton, the M.D., magna cum laude, from Harvard Medical School, and a Ph.D. in genetics from the University of Washington.

For Notes :

Topic

Proteomics Approaches To Diagnosis And Therapy Of Cancers.

Gilbert S.Omenn
University of Michigan, Ann Arbor, MI, USA.

Proteomics can generate important applications for cancer research and cancer care by (1) profiling tumor specimens for diagnosis and stratification of patients; (2) profiling tumor specimens for prognosis with particular therapies; (3) discovering and validating circulating serum or plasma proteins as biomarkers for early diagnosis; (4) applying such biomarkers to monitoring of patients for response to treatment and recurrence of tumors. Proteins are much closer to the pathophysiologic changes and molecular targets for drugs than are mRNAs; changes in mRNAs and corresponding proteins often are not highly correlated. Rapidly emerging advances in the fractionation of complex protein mixtures, in the identification of peptides and proteins with mass spectrometry, and in the quality of curated databases of proteins will accelerate these developments. Three-dimensional fractionation of proteins, Cy-dye and isobaric tagging of proteins for differential quantitative analyses of specimens, direct MS on tissue sections, and construction of a knowledge base of circulating proteins from the HUPO Plasma Proteome Project will be highlighted in this presentation.

For Notes :

Speaker's profile

Dr. Mark Cockett
Vice-President, Applied Genomics
Bristol-Myers Squibb, USA

Mark Cockett is currently the Vice President of the Applied Genomics department at Bristol-Myers Squibb Pharmaceutical Research Institute.

Mark joined BMS in January 2000 and is responsible for functional genomics and bioinformatics applied to pre-clinical research and development at BMS. His group has strategic alliances with the Whitehead Institute, Exelixis, Lexicon, Athersys, and Pharmagene, and is a centralized resource supporting all therapeutic areas at BMS.

Before joining Bristol-Myers Squibb, Mark worked for 7 years in the Neuroscience group at Wyeth, ultimately as Director, molecular & cell biology and for 10 years in the biotech industry for Celltech PLC, where he worked on mammalian gene expression technology and in oncology. Whilst at Celltech he obtained his Ph.D. in collaboration with the Strangeway Research Laboratory, Cambridge, UK working on the involvement of matrix metalloproteinases in tumour cell invasion.

Mark has published over 40 peer reviewed articles in the field of recombinant gene expression in mammalian cells, the biochemistry and function of several matrix metalloproteinase enzymes and their role in disease, and more recently in the field of heterotrimeric G protein signaling, and Genomics in the pharmaceutical industry.

For Notes :

Topic

Improving target and compound quality. The application of genomic technologies to drug discovery and development

Mark I. Cockett
Vice President, Applied Genomics. Bristol-Myers Squibb Company.

The two key decisions made in pharmaceutical research today are selecting the right target to develop a drug against, and selecting the right compound to bring forward for development. Today's genomic information and technologies provides us with a multitude of data and capabilities that if applied systematically to all pipeline programs can enhance decision making for these two important selections.

A rigorous application of target validation technologies to all pipeline programs ensures that the best decisions are made in target selection and that targets validity is continually challenged as new tools and information become available. This leads to more informed decision making on the biology surrounding programs in our pipeline.

Similarly, use of genomic technologies as broad genome-wide biosensors for drug effects on cellular and *in vivo* systems can help us weed out bad compounds earlier by measuring the extent of on- and off-target activities. This allows us to: ensure follow-on compounds offer significant improvements over existing treatments or gold standards; it enables us to identify our most selective leads, picking up off-target activities that would not readily be apparent by other means; and can even help us differentiate our products by providing mechanistic insights behind improved clinical observations.

This presentation will illustrate by example how genomic technologies are being applied at BMS to improve both target and compound selection.

For Notes :

Session VII

Introduction to the Chairpersons

Mr. Ashwini Kumar
Drug Controller General, India

Dr. S. Nath
Associate Professor
IIT, New Delhi

Dr. S. Nath is associated with Department of Biochemical Engineering and Biotechnology at IIT, New Delhi. He obtained his M.S. and M.A. from Princeton University, Princeton, USA; did his Doctoral and Postdoctoral research at National Research Institute of Biotechnology (GBF) / Technical University Braunschweig, Germany. He was a visiting scientist at MIT, Cambridge, USA. He is a recipient of several awards such as Swarnajayanti Research Project under the Swarnajayanti Fellowships; Amar Dye-Chem Award for Excellence in R&D, SGSITS Award for Best Research Work by Young Teachers, Indian Society for Technical Education, All-India Council for Technical Education Career Award for Young Teachers. He has published a number of papers in peer reviewed journals and edited two books.

Speaker's profile

Dr. Tony Wynshaw-Boris
Professor, Departments of Pediatrics and Medicine
Director, Center for Human Genetics and Genomics
Chief, Division of Genetics, Department of Pediatrics, Univ of California, San Diego, USA

Dr. Tony Wynshaw-Boris is a Professor, Departments of Pediatrics and Medicine and also the Director, Center for Human Genetics and Genomics and Chief of Division of Genetics, Department of Pediatrics. He obtained his Ph.D. and M.D. from Case Western Reserve University, Cleveland, OH. He completed his Residency in pediatrics from Rainbow Babies and Children's Hospital, Cleveland, OH and Clinical Fellowship in Genetics from The Children's Hospital, Boston, MA

He was a Howard Hughes Medical Institute Physician Research Fellow during 1991-94. He was Head of Mouse Models Unit, Genetic Disease Research Branch, NHGRI, NIH during 1994-99 and since 1999 he is associated with UCSD.

He is a member of the Editorial Boards of Journal of Biological Chemistry, Human Molecular Genetics, Neurogenetics, BioMedCentral, Core Reviewer in Genetics. He has published a number of papers in peer reviewed journals and has contributed significantly in the area of transgenic animals.

For Notes :

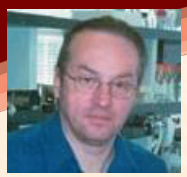
Production of a Allelic Series of the Mouse *Dishevelled 2* Gene: Determination of Developmental Pathways and Mechanisms Important for Neural Tube Closure

Jianbo Wang[1], Ping Chen[2] and Anthony Wynshaw-Boris[1]
1. School of Medicine, UCSD, La Jolla, CA, USA 92093-0627
2. Emory Univ. School of Medicine, Atlanta, GA, USA 30322

Dishevelled (DSH in *Drosophila* and Dvl in mammals) is known to mediate both the canonical Wnt signaling pathway and the planar cell polarity (PCP) pathway in fly and convergent extension (c/e) morphogenetic movement in *Xenopus*. Our previous gene-targeting analyses indicated that the three mouse *Dvl* genes, *Dvl1*, *2* and *3*, share redundant functions during neural tube closure. Among the three *Dvl* genes, *Dvl2* appears to be most crucial and sufficient by itself to mediate neural tube closure, while *Dvl1* and *Dvl3* become indispensable when *Dvl2* is completely missing. To define the molecular pathway mediated by Dvl during mammalian neurulation, a *Dvl2* allelic series has been constructed through BAC (bacterial artificial chromosome) recombineering and transgenesis. We found that wild-type *Dvl2* BAC could fully rescue *Dvl1*$^{-/-}$; *Dvl2*$^{-/-}$ mutants. However, introducing a single point mutation identical to the fly *dsh1* allele or a deletion of the C-terminal DEP domain (DEP), which were shown to specifically abolish the PCP pathway but leave the Wnt signaling intact in fly, completely disrupted the ability for the *Dvl2* BAC to rescue *Dvl1*$^{-/-}$; *Dvl2*$^{-/-}$ mutants. IOn-frame GFP tagging in the *Dvl2* BAC transgenes allowed us to follow Dvl2 localization. Interestingly, during neurulation, the Dvl2-GFP transgenic protein was found to localize primarily at the plasma membrane, a prerequisite for its involvement in the PCP pathway and c/e. Similar to fly and frog DSH proteins, the C-terminal DEP domain is required for Dvl2-GFP to localize to the plasma membrane. We suggest that neural tube closure in mammals involves a c/e-like morphogenesis process controlled by Dvl through a homologous pathway that define planar cell polarity in fly, and demonstrates the value of using BAC recombineering to define developmental pathways and mechanisms *in vivo*.

For Notes :

Speaker's profile



Dr. Andras Nagy
Professor
Department of Medical Genetics & Microbiology
University of Toronto, Canada

Dr. Andras Nagy is a Senior Investigator of Development and Fetal Health and Professor, Department of Medical Genetics and Microbiology University of Toronto. In 1974 Dr. Nagy completed his B.A. (M.A.) in Mathematics and in 1979 completed his Ph.D. in Genetics both at Lorand Eötvös University Budapest. Dr. Nagy currently holds the Canadian Institute of Health Records Senior Scientist Award 2002-2007. In partnership with Bristol-Myers Squibb he also was awarded the Medical Research Council of Canada/ Pharmaceutical Manufacturers Association of Canada Scientist award 1996-2001.

The Nagy laboratory is interested in using mouse genetics to study mammalian development and to apply this knowledge to human disease. Dr. Nagy is also developing new, powerful tools for genetic approaches and phenotype analysis for these ongoing studies. Another main activity of the Nagy lab is connected to mammalian genomic imprinting

For Notes :

Topic

Genetics on Embryonic Stem cells; closing the gap between yeast and mouse

Dr. Andras Nagy
Mount Sinai Hospital, Samuel Lunenfeld Research Institute, Toronto, Canada

Although over 20 years have passed since the establishment of the first mouse Embryonic Stem (ES) cells, it is clear that their genetic potential has not yet been fully exploited. These remarkable cells keep amazing us by constantly revealing new secrets and surprises.

Novel ES cell lines have emerged which display an exceptionally high developmental potential.

A new recombinase - phiC31 - has joined the classical Cre-loxP system, providing nearly unlimited possibilities of targeted genetic manipulations.

New ways have been discovered to induce chromosome specific loss of heterozygosity in vitro by either high concentration G418 selection, or by Cre mediated mitotic recombination events.

Chemically induced large-scale mutagenesis has become a reality also in cultured ES cells.

A steadily growing number of in vitro differentiation assays allows us to study gene function in specific lineages and very early embryonic development.

In this presentation, these new developments will be illustrated by our novel gain- and loss-of-function genetic screens. The unique nature of the screens were designed in an effort of minimizing the costly and time intensive animal breeding component of the genetic approaches in the mouse.

For Notes :

Speaker's pro-file

Dr. Sachdev Sidhu
Senior Scientist
Department of Protein Engineering, Genentech, USA

Dr. Sachdev Sidhu's research interests are focussed on studying the relationships between protein structure and function, using phage display in conjunction with high-throughput screening and sequencing. Currently, he is studying several important biological systems using various display libraries, including antibodies, peptides and cytokines. After his Ph.D. from Simon Fraser University in Biochemistry he has been associated with Genentech since 1997.

For Notes :

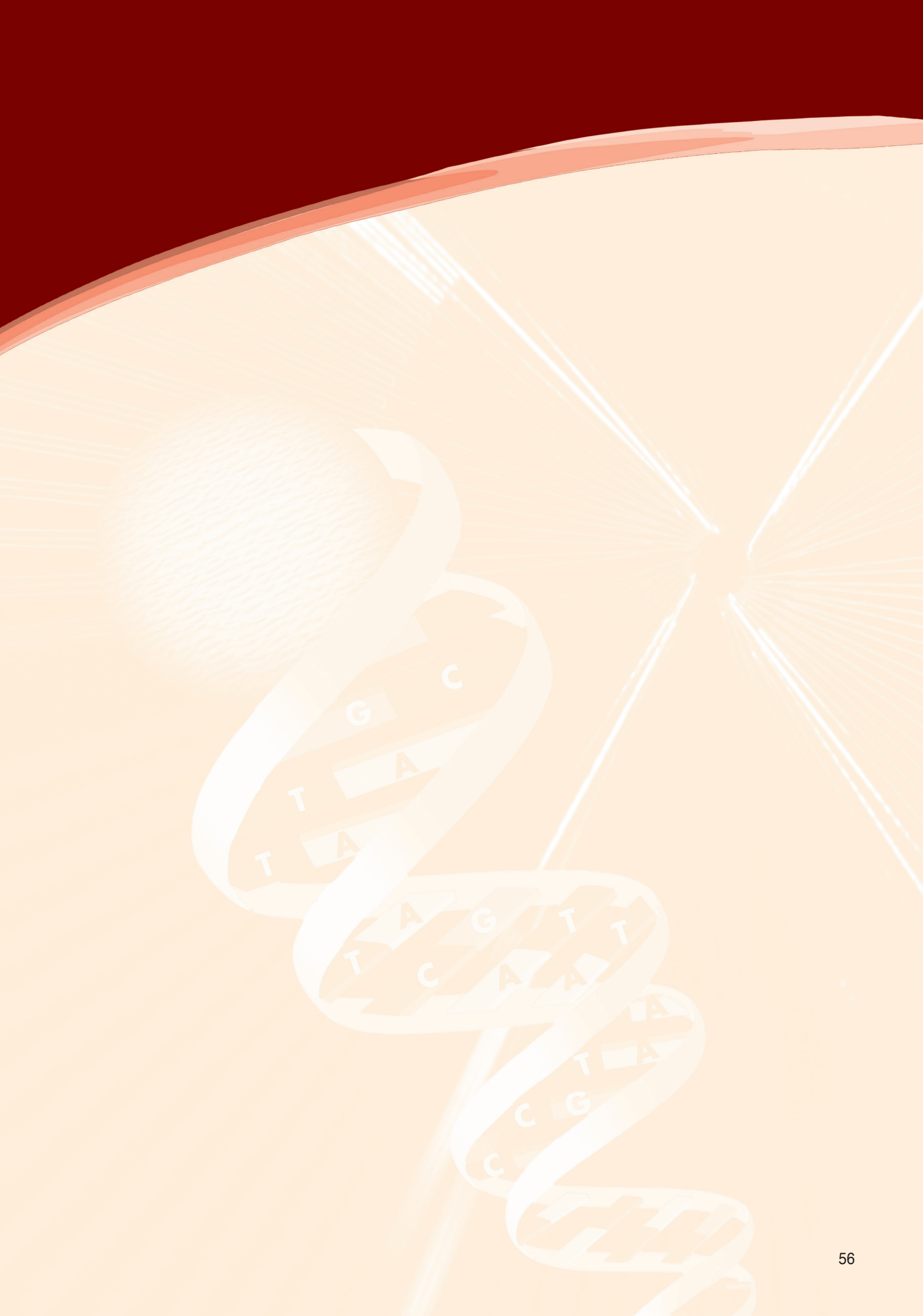
Topic

Design and Application of Synthetic Antibodies

Sachdev S. Sidhu, PhD
Senior Scientist
Genentech Inc.

We have developed phage-displayed antibody libraries with completely synthetic complementarity determining regions. We have explored basic principles of antigen recognition with libraries containing extremely limited chemical diversity. In addition, we have derived highly potent antagonists and agonists of important biological processes. These libraries should be highly valuable for the generation of antibody reagents and therapeutics.

For Notes :



Session VIII

Chairpersons

Dr. Steve Hawkins
European Array Systems Product Line Leader, PerkinElmer Life and Analytical Science

Dr. John Wotherspoon
BD Biosciences

Dr John Wotherspoon is a Ph.D from University of Sydney. He is preseb=ntly associated with Becton Dickinson, USA as a Management executive. He is a recognised technical expert with over 20 years experience in functional cell biology assessed through Flow Cytometry, Monoclonal Antibody technology. He has broad experience in technical training, and is a consultant and supervisor for academic research programs.

Speaker's pro-file

Dr. Jyoti Chattopadhyaya
Professor & Chairman
Department of Bioorganic Chemistry, Uppsala University, Sweden

Prof. J. Chattopadhyaya is working on the interface of Biology and Chemistry. He has held several important positions with University of Uppsala, Sweden since 1979 and is presently Chairman and Professor in Department of Bioorganic Chemistry. He obtained his Ph.D. from National Chemical Laboratory, Poona, India and then did his Postdoctoral Research (1974 - ´79) on Nucleoside & Nucleotide Chemistry at Dept. of Chemistry, King´s College, University of London, London U.K and D.Sc [Docent in Bioorganic Chemistry (1982, Uppsala University). He is a recipient of several awards such as *Norblad-Ekstrand Gold Medal* (1993) by Swedish Chemical Society in March; *Humboldt Research Prize* (1995) from Alexander von Humboldt Stiftung, Germany; *Philip-Morris award* (2002), USA for contribution in the development of RNA chemistry. He has published a number of papers in peer reviewed journals.

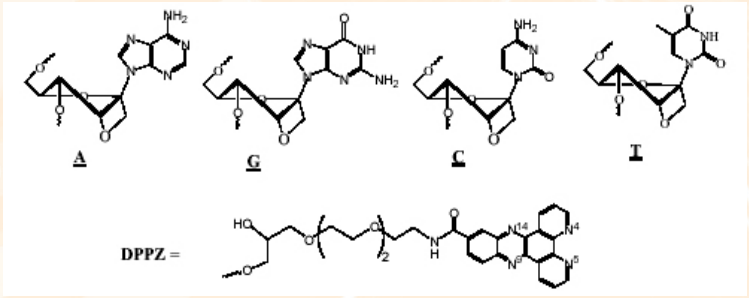
For Notes :

Topic

Conformationally-constrained Oxetane Modified Antisense Oligonucleotides Function Efficiently as Novel Gene Silencing Molecules

Jyoti Chattopadhyaya
Department of Bioorganic Chemistry, Box 581, Biomedical Center,
University of Uppsala, S-75123, Uppsala, Sweden.

Incorporation of novel conformationally constrained oxetane (OXE) nucleosides [oxetane, 1-(1',3'-Oanhydro- ß-D-psicofuranosyl nucleosides)] (Figure 1)[1-3,5] into antisense (AS) oligodeoxyribonucleotides (ODN) improves the gene silencing efficiency4 of these molecules. This is because of the fact that (1) the OXE modified nucleosides provide nuclease protection to natural backbone ODN, (2) they can impart thermodynamic stability (Tm) very similar to those of the corresponding native AS-ODN/RNA hybrids, and most importantly (3) they also very efficiently accelerate RNaseH mediated catalytic cleavage of the target RNA. These conclusions are based on our experiments (in collaboration with Prof Alan Gewirtz, see ref 4) in living cells by directly comparing the ability of OXE and PS ODN to target and effectively down-regulation the proto-oncogene c-myb mRNA in the K562 human leukemia cells[4]. It was observed[4] that Myb mRNA and protein levels were equally diminished by OXE and PS ODN, but the latter were delivered to cells with~6x greater efficiency suggesting that OXE modified ODN were more potent on a molar basis as efficient gene silencing agents. The chemistry, enzymology and the use of these OXE modified ODN-RNA hybrids will be discussed.



References

(1) (a) Pradeepkumar, P. I.; Zamaratski. E.; Foldesi A.; Chattopadhyaya J. *Tetrahedron Lett.* **2000**, *41*, 8601. (b) Pradeepkumar, P. I.; Zamaratski E.; Foldesi A.; Chattopadhyaya J. *J. Chem. Soc., Perkin Trans. 2* **2001**, 402. (c) Pradeepkumar, P. I.; Chattopadhyaya J. *J. Chem. Soc., Perkin Trans. 2* **2001**, 2074. (d) Boon, E. M.; Barton, J. K.; Pradeepkumar, P.I.; Isaksson, J.; Petit, C.; Chattopadhyaya, J. *Angew. Chem. Int. Ed.* **2002**, *41*, 3402.

(2) Amirkhanov, N.V.; Pradeepkumar, P.I.; Chattopadhyaya, J. *J. Chem. Soc., Perkin Trans. 2* **2002**, 976. (b) Zamaratski, E.; Ossipov, D.; Pradeepkumar, P. I.; Amirkhanov, N.V.; Chattopadhyaya, J. *Tetrahedron* **2001**, *57*, 593.

(3) Pradeepkumar, P.I.; Amirkhanov, N.V.; Chattopadhyaya, J. *Org. Biomol. Chem.* **2003**, *1*, 81.

(4) Opalinska, J. B.; Kalota, A; Rodriquez, L.; Henningson, H.; Gifford, L. K.; Lu, P; Jen, K-Y.; Paradeepkumar, P. I.; Barman, J.; Kim, T. K.; Swider, C.; Chattopadhyaya, J.; Gewirtz, A.M. *Nucleic Acids Research* **32** (19), 5791-5799 (2004).

(5) P.I. Pradeepkumar, P. Cheruku, O. Plashkevych, P. Acharya, S. Gohil and J. Chattopadhyaya, *J. Am. Chem. Soc.* **126**, 11484-11499 (2004)

For Notes :

Speaker's pro-file

Dr Alan M. Gewirtz
Doris Duke Distinguished Clinical Professor, Medicine and Pathology.
Leader, Stem Cell Biology & Therapeutics Program, University of Pennsylvania School of Medicine, USA

Dr Alan M. Gewirtz is Doris Duke Distinguished Clinical Professor, Medicine and Pathology, and is Leader, Stem Cell Biology & Therapeutics Program, University of Pennsylvania School of Medicine, USA. He obtained his M.D. from State University of New York, Buffalo, N.Y. During 1983 to 1990 he has held several important positions in Temple University School of Medicine. Since 1990 he is in University of Pennsylvania School of Medicine. He is on the editorial board of Journal of Clinical Oncology; Nucleic Acids Research; Oligonucleotides; Stem Cells and several reputed journals. He is a recipient of several awards and honors such as Doris Duke Distinguished Clinical Scientist Award; William Osler Award for Patient Oriented Research (University of Pennsylvania); Chair & Member- Biological & Targeted Therapies, ASCO Annual Meeting; Associate Team Leader, Hematology, Immunology, and Microbiology, National Space Biomedical Research Institute; Publications Committee- American Association for Cancer Research and Board of Directors- Leukemia and Lymphoma Society. He has published more than 100 research papers in prestigious peer reviewed journals.

For Notes :

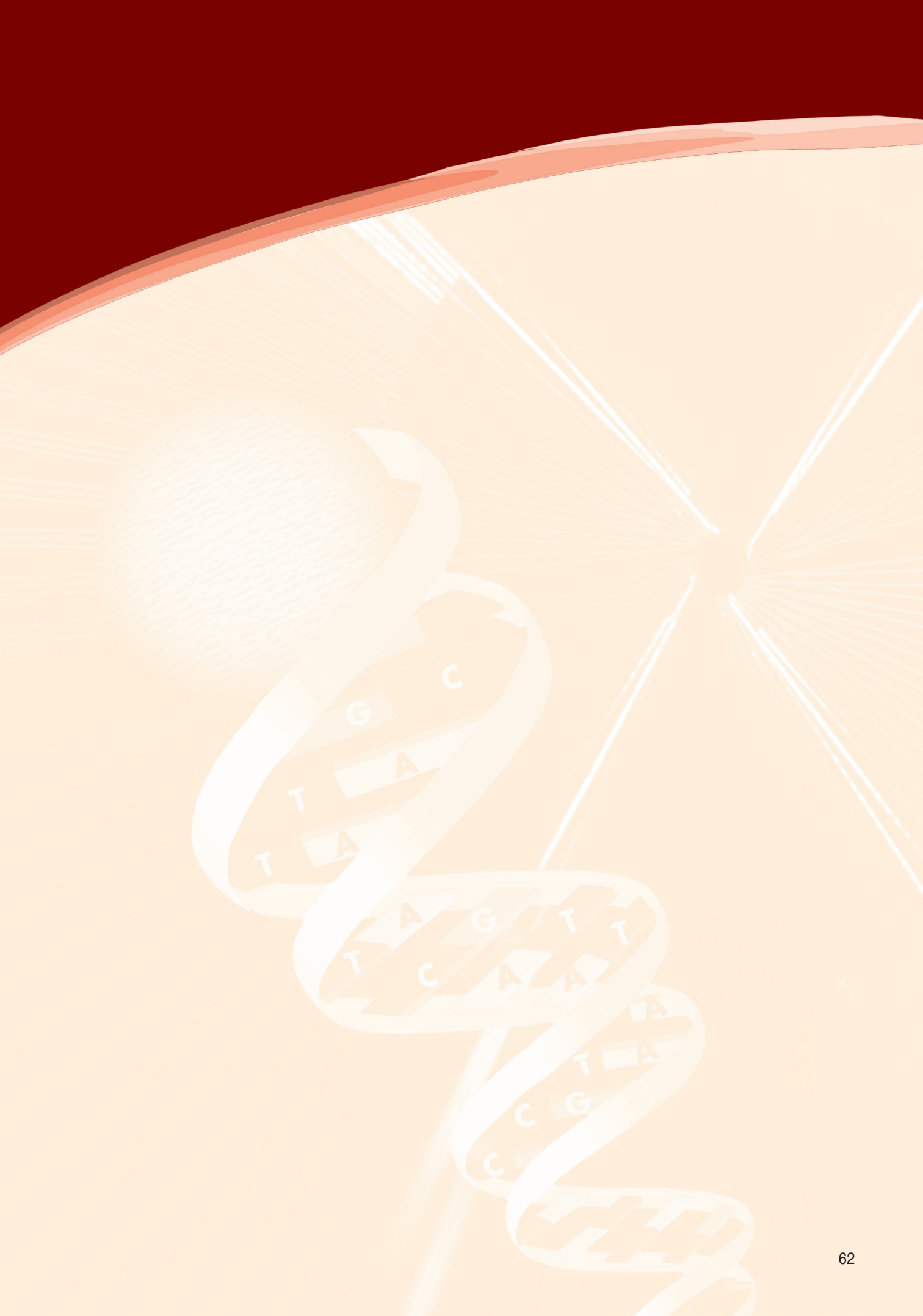
Topic

Nucleic Acid Based Therapeutics for Treating Human Malignancies

Dr Alan M. Gewirtz
Doris Duke Distinguished Clinical Professor, Medicine and Pathology.
Leader, Stem Cell Biology & Therapeutics Program, University of Pennsylvania School of Medicine, USA

The sequencing of the human genome, combined with the elucidation of many molecular and biochemical pathways important in pathogenesis of human disease, has provided unprecedented opportunities for the development of new therapeutics. While small molecule drugs, and antibodies targeted to disease causing proteins have caused much excitement, molecules targeted to the messenger RNAs that encode these proteins are also under development. The types of molecules being studied are increasingly varied, and include antisense oligonucleotides and short interfering RNAs (siRNA). This presentation will review different strategies for modulating gene expression, discuss recent clinical results, and ways to further improve the development of RNA targeting drugs.

For Notes :



Session IX

Introduction to the Chairpersons

Prof. Harish Padh
PERD Centre

Dr. Harish Padh is currently Director of B.V. Patel PERD Centre, Ahmedabad. He obtained his Ph.D. from University of Delhi in 1978 and he did his postdoctoral research and held academic positions at St. Jude's Children Research Hospital, Memphis, TN; Temple University, Health Sciences Centre, Phildelphia and University of Chicago at Department of Biochemistry and Molecular Biology; and North Western University at Centre for Biotechnology, IL. He was a Professor at M.S. University, Baroda during 1996-2001. He is an advisor to the Government of Gujarat on Pharmaceutical and Biotechnology matters. He has published a number of research papers in peer reveiwed journals.

Dr. Sunil Patel
Acclerys

Dr. Sunil Patel is associated with Acclerys, Cambridge, UK as Strategic Accounts Scientific Manager. He has over 10 years experience and expertise in drug design and synthesis, protein modelling and simulations and bioinformatics. Past experience includes NMR protein structure determination, hardware design in combining NMR and Ultrasound as a technique for modification of NMR relaxation times and design and development of electric fields in NMR magnets for measuring the effects of liquid crystal orientations in the presence of combined electric and magnetic fields.

Speaker's pro-file

Dr. G Neil Thomas
Research Assistant Professor
Department of Community Medicine, University of Hong Kong.

Dr. G Neil Thomas did his D.Phil. in Medical Sciences from Division of Clinical Pharmacology, Department of Medicine and Therapeutics, The Chinese University of Hong Kong. He has held academic appointments with Department of Community Medicine, University of Hong Kong, Hong Kong; Department of Public Health and Epidemiology, University of Birmingham, Edgbaston, Birmingham, UK.; Research Assistant Professor. Department of Community Medicine, The University of Hong Kong, HK; Dept of Medicine and Therapeutics, Chinese University of Hong Kong. and Department of Microbiology, Chinese University of Hong Kong, HK. His research interests are focussed on molecular epidemiology and biochemical investigation of the pathogenesis of the metabolic syndrome disease clustering of Type 2 diabetes, obesity, hypertension and dyslipidaemia; and treatment of this disease cluster using pharmacological agents and lifestyle modifications, such as increasing physical activity. He has a number of publications in peer reviewed journals and is a member of the editorial boards of Current Pharmacogenomics, and Current Diabetes Reviews.

For Notes :

Topic

Pharmacogenetic aspects of the metabolic syndrome components hypertension, diabetes, and obesity

Dr. G Neil Thomas
Research Assistant Professor
Department of Community Medicine, University of Hong Kong.

The prevalence of components of the metabolic syndrome is generally increasing in both developed and developing countries, in part through lifestyle changes and population ageing. Increases in these conditions promote morbidity and mortality associated with a range of cardiovascular diseases and a number of cancers.

Each of these components has been shown to have a genetic component, with heritability ranging from 13-81%. The genetic profile of the individual determines their potential risk of developing the disease and the environmental exposure determines whether this potential is realised. Genetic analyses have determined a number of monogenetic forms of these conditions, which exhibit clear Mendelian inheritance, although in most patients the condition is a result of multiple interacting genes. It is also important to remember that each of these components, such as hypertension is an umbrella term for a cluster of numerous polygenic disorders presenting with a similar phenotype, such as elevated blood pressure. Identification of subgroups that constitute this group through phenotypic and genotypic markers will help elucidate pathogenic mechanisms and allow the institution of preventative measures and targeted drug interventions, which may lead to improved treatment control.

Obesity

Studies of Mendelian traits in mice have led to the identification of several homologous mutations in humans, such as mutations in the mouse ob/ob gene which caused obesity led to the identification of leptin. Leptin is an adipocyte derived circulatory hormone that reflects the body fat content and acts on hypothalamus to control appetite and energy expenditure. A few individuals have been identified with monogenetic leptin deficiencies. Two cousins from Pakistan have been identified with a frame shift mutation in the leptin gene which led to severe obesity. Treatment of these patients with recombinant leptin led to marked sustained weight loss by reducing hyperphagia and increasing the level of physical activity. In contrast patients with the mouse db/db homologue in the leptin receptor had a similar severe obese phenotype, yet had elevated leptin levels, but no downstream signal transduction. In addition to helping clarify the role of leptin in the regulation of obesity, important points in the in-

For Notes :

vestigation of the genetics of obesity can be drawn from studies of these monogenetic disorders. These cases of leptin deficiency and resistance are likely to represent extremes in leptin metabolism and in a similar manner to insulin in diabetes the degree of production and resistance are likely to cover a wide spectrum. These highlight the problems of categorising patients based on phenotype, where in these cases it is clear that the pathogenic mechanisms of the obesity differ.

Diabetes

Although many possible candidate genes have been proposed for the development of diabetes, little is known regarding the potential of polymorphisms within these genes to influence treatment. As with obesity, much of our understanding in this regard has come from monogenetic causes, such as the autosomal dominant Maturity onset diabetes of the young (MODY). MODY accounts for less than 5% of Type 2 diabetes and has been related to mutations in several nuclear transcription factors. Mutations in the Hepatocyte Nuclear Factor-1α (HNF-1α) in patients with MODY result in impaired β-cell function. Compared to patients with Type 2 diabetes, those with MODY HNF-1α mutations have a nearly 4 fold stronger sensitivity in glucose levels to the sulphonylurea, gliclazide. These findings highlight the importance of accurate characterisation of the condition that is being treated if treatment is to be effective.

Hypertension

Rare (<1%) monogenetic causes of hypertension have been identified, with elevations in blood pressure generally resulting from an over production or increased activity of mineralocorticoids leading to excessive sodium retention. This suggests that low sodium diets may delay the onset of symptoms. In patients with primary hypertension, which affects between 10 and 30% of adult populations, blood pressure reduction in response to a single antihypertensive agent is in the order of 10%. Interestingly, in those cases with a monogenetic aetiology treatment can result in 30-40% reductions in blood pressure, such as with spironolactone in the treatment of Apparent Mineralocorticoid Excess. These features may be extrapolated to patients with primary hypertension of whom 50% have elevated blood pressure even after the initiation of treatment, and suggests if hypertension can be better characterised into a number of discrete conditions and specific treatment applied we may be able to significantly improve the efficacy of existing agents.

For polygenic primary hypertension, data are increasing on mutations that influence blood pressure and its treatment. For example with the dopamine D2 receptor TaqI polymorphism, the A2 homozygotes had 6 and 4 mm Hg higher systolic and diastolic blood pressures than the A1 homozygotes. Intervention studies suggest that antihypertensive therapies can lower diastolic blood pressure by 5-6 mm Hg, similar to the difference between homozygous subjects. These falls were associated with significant

For Notes :

reductions in vascular disease (eg 35-40% less stroke, 20-25% less CHD). If these findings are confirmed, the extrapolation of these findings to the population indicates how important individual genes may be in determining mean blood pressure levels.

Complexity

The findings relating to the blood pressure association with the dopamine D2 receptor were only present in normoglycaemic subjects and not those with hyperglycaemia. Furthermore, in both groups the A1 allele was associated with increasing obesity, which is a strong predictor of blood pressure. Therefore both alleles may contribute directly or indirectly to blood pressure, but through different mechanisms. It was lucky that the contribution to obesity through the A1 allele did not mask the proposed direct effect of the A2 allele on blood pressure. These data support differences in the pathogenesis of hypertension in those with and without diabetes. For instance, interventional and epidemiology studies suggest that diabetes is a sodium replete disease which responds to a greater extent to treatment with calcium channel blockers compared to those targeting the renin-angiotensin system, which are more effective in non-diabetics.

Non-pathogenic genetic influences on treatment

Genes which influence the pharmacokinetic and pharmacodynamic drug profile will influence treatment efficacy and the development of adverse side effects. The most clearly defined action has been reported with the drug metabolising enzymes. For example, the cytochrome P450 (CYP) gene CYP2D6, which metabolises a quarter of all drugs, including β-blockers, contains over 50 reported alleles, with over 20 being shown to significantly alter substrate metabolism. Therefore, even as our understanding of the genetic contributors to disease unfolds, such polymorphisms influencing drug metabolism, although not involved in the pathogenesis of the disease condition, are likely to remain the major genetic markers influencing drug response.

In summary, our knowledge of the genetic components contributing to the pathogenesis of the metabolic syndrome is continuously increasingly. Such genetic makers may also influence treatment responses, as in the monogenetic examples of hypertension and obesity, as well as potential adverse drug reactions. To date, polymorphisms of drug metabolising enzymes, due to their significant influence on a wide range of pharmaceuticals are likely to be of most widespread interest in the pharmacogenetics of the metabolic syndrome and other disease conditions.

For Notes :

Speaker's pro-file

Dr Pauline Gee
Vice-President, Predictive Biology
MDS Pharma, UK

Dr Pauline Gee is currently associated with MDS Pharma Services as Vice President, Predictive Biology. She is Responsible for implementing predictive strategies into drug discovery & development. She was Vice President, Toxicogenomics and Acting Vice President, Business Development at Discovery Partners International, Inc. (DPII). She was associated with Xenometrix, Inc since 1994 and during 1999-2001 she was the President & Chief Executive Officer of this company before it got merged with DPII. Her research contributions led to development of over 12 products and services to commercialization and was granted gene expression profiling patents. Assays developed in R&D became commercial kits and services that monitor the cells' response(s) to chemicals and other agents of commercial interest and provide unique biological information to complement chemical, physical, physiological and toxicological properties. She has developed and patented a set of 30 Salmonella strains that quantify and identify the mutagenic potential of chemicals and other test agents now a Xenometrix assay that is automated for robust high throughput-screening of chemicals and drug candidates. Interestingly she has found for the first time that differentiated neuronal cells repaired their DNA albeit slowly. She obtained her Ph.D. from Simon Fraser University, Canada and was also associated with Bruce N. Ames as Medical Research Council Fellow, Department of Biochemistry at University of California at Berkeley. She has published a number of papers in peer reviewed journals.

For Notes :

Topic

Identifying and validating biomarkers that bridge the preclinical and clinical

Dr Pauline Gee
Vice-President, Predictive Biology
MDS Pharma, UK

I propose to present our work on identifying and validating biomarkers that bridge the preclinical and clinical. MDS Pharma Services has put into place a strategic alliance with a chemogenomics company, Iconix Pharmaceuticals who has mined clusters of genes in rats that are robust and predictive of many phenotypic expressions that encompass animal behavior to clinical chemistry to histopathology. We are using this information from these genes clusters, or signatures to guide our biomarkers efforts within MDS Proteomics in our quest.

For Notes :

Scientific Poster Presenta-

PS-01. Structural basis for substrate channelling mechanism of a fatty acid β-oxidation multienzyme complex

Momoyo Ishikawa, Daisuke Tsuchiya, Takuji Oyama, Yasuo Tsunaka, Kosuke Morikawa
Biomolecular Engineering Research Institute, Japan

Many enzymes are organized into multienzyme complex to catalyze sequential reactions termed the channelling mechanism. The purpose of our structural study is to elucidate this mechanism at the atomic level, focusing the fatty acid β-oxidation multienzyme complex from *Pseudomonas fragi*. Fatty acid metabolism, linked to energy storage and human obesity, frequently involves multifunctional enzyme complexes. We have determined two distinct crystal structures of the bacterial multienzyme complex that catalyzes the last three sequential reactions in the fatty acid β-oxidation cycle. The $\alpha_2\beta_2$ heterotetrameric structure shows the uneven ring architecture, where all the catalytic centers of 2-enoyl-CoA hydratase (ECH), L-3-hydroxyacyl-CoA dehydrogenase (HACD) and 3-ketoacyl-CoA thiolase (KACT) face a large inner solvent region. The substrate, anchored through the 3'-phosphate ADP moiety, allows the fatty acid tail to pivot from the ECH to HACD active sites, and finally to the KACT active site. Coupling with striking domain rearrangements, the incorporation of the tail into the KACT cavity and the relocation of 3'-phosphate ADP bring the reactive C2-C3 bond to the correct position for cleavage. The α-helical linker specific for the multienzyme contributes to the pivoting center formation and the substrate transfer through its deformation. The versatile architecture of the complex, with its functionally profound domain and subunit movements, suggests how the individual catalytic components orchestrate the channelling mechanism of fatty acid β-oxidation. This channelling mechanism could be applied to other β-oxidation multienzymes, as revealed from the homology model of the human mitochondrial trifunctional enzyme (TFE) complex.

PS-02. Somatostatin analogues: Radiolabeling and bio-evaluation for potential radiopharmaceuticals

Aruna Korde, Usha Pandey, Archana Mukherjee, #H.D. Sarma, Sharmila Banerjee and Meera Venkatesh
Radiopharmaceuticals Division, #Radiation Biology and Health Sciences Division, Bhabha Atomic Research Centre, Mumbai, India-400 085.

Peptide receptors are newer molecular targets for cancer diagnosis and therapy due to their over-expression in malignant neoplasm. Somatostatin is one such regulatory peptide and metabolically stable synthetic somatostatin analogues are most extensively studied for clinical application for receptor imaging (sst-PRI) and peptide receptor radiotherapy (sst-PRRT) with various chelators and radionuclides. The availability of multiple isotopes of iodine with suitable radionuclide properties for diagnosis (123I) and therapy (125/131I) makes iodine one of the attractive isotopes for such studies. Here we describe radioiodinations and bioevaluation studies of two sst analogues namely Lantreotide [_-Naphthyl-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH2] and DOTA-TATE [DOTA-Tyr3- Octreotate].

The radioiodination (with 125I) of both the analogues were carried out using chloramineT as an oxidizing agent at molar ratios of 20:1. The radioiodination yields were between 80 to 90% as determined by paper electrophoresis. The radiolabelled products were purified using sep-pak and characterized using HPLC. The products obtained showed >95% radiochemical purity and good serum stability. The pharmacokinetic studies of radioiodinated products were carried out in swiss mice by injecting 37KBq/animal. Animals were sacrificed at 3h and 24h post injection. 125I DOTA-TATE showed better pharmacokinetics pattern with rapid clearance. Both the products showed significant tumor uptake (~3% injected dose/gm of tumor tissue at 3h.p.i.) in sst receptor expressing melanoma in C57BL/6 mice. These studies can be extrapolated for development of a 123I based SST-PRI radiopharmaceutical for malignancy diagnosis

PS-03. Molecular analysis of Wilson's Disease (WD): Detection of mutations in the ATP7B gene in the Indian population

Nirzari Parikh, Aabha Nagral and Firuza Parikh
Jaslok Hospital and Research Centre, Mumbai, India

Wilson's disease (WD) is an autosomal recessive disorder of copper metabolism, characterized by excessive accumulation of copper in the liver, central nervous system, kidneys, eyes, and several other organs. Recent data suggests the prevalence of the disorder to be about one in thirty thousand people worldwide. The gene responsible for WD is known as ATP7B, located on chromosome 13q14.3, and codes for a copper-transporting P-type ATPase. The disease is caused by alterations in the ATP7B gene. Our study aims to screen the ATP7B gene for mutations and hotspots in the gene associated with the Indian WD patients. We have currently screened exons 2, 8, 14 and 16, reported as having some predominant mutations. Mutations in the exons were detected by direct sequencing of PCR product using the ABI 3100 Genetic Analyzer. A total of thirty-six patients (female/male: 14/22) were tested. Twenty mutations were observed in exons 2 and 14, with eighteen mutations identified in exon 2 and two mutations in exon 14. The mutations identified included eleven missense, six silent and three frameshift mutations. Nineteen mutations are novel, while only one other mutation, 3182 G>A, has been reported earlier, which shows a frequency of 13.8 in our patient population. In addition to these mutations, two polymorphisms, both of which are novel, have been observed. Both these polymorphisms have been identified in exon 2. These novel mutations may be responsible for altered WD gene expression.

Key words: ATP7B gene; Wilson's Disease; novel mutation

PS-04. Association of Single Nucleotide Polymorphism in the Renin Gene and Essential Hypertension

Aparna Bhanushali, V.T. Shah and Firuza Parikh
Dept. of Molecular Medicine and Biology, Jaslok Hospital and Research Centre, Mumbai, India

Hypertension (htn) is an important risk factor for the development of Cardiovascular Diseases (CVD). It is noteworthy that CVDs occur in Indians, about 10-15 years earlier than in the West. The current concept that besides environment, the genetic variation of an individual, defined as Single nucleotide polymorphisms(SNPs), may contribute to susceptibility to the disease, response to drug, and prognosis, has initiated the discipline of Pharmacogenomics. The Renin-Angiotensin System has been implicated in hypertension. We have initiated a study in Indian hypertensives to examine blocks of SNPs in the Renin-Angiotensin system. Hypertensive patients (63) and normal individuals (67) have been analysed. The renin-angiotensin system genes ACE, AGT, AGTR1 and REN have been initiated for SNP analysis in haplotype blocks (5 -10 SNPs/gene), with a total of 24 SNPs. Initial study was done with a single polymorphism in the Renin gene at the polymorphic site A4280C. The methodology involves direct sequencing of the PCR products on the ABI 3100 Genetic Analyzer. Our results indicate a higher frequency of the allele C in htn patients. A report in an American study indicated that ren A4280C did not constitute a part of the haplotype block in the renin gene which is overtransmitted to the affected offspring however with the Indian population the studies conducted so far indicate that ren A4280C may have a role to play in the pathophysiology of the disease.

PS-05. Prevalence and genotyping of HBV and HCV in hepatitis and HCCs

Naina Rane, Nirzari Parikh, Samir Shah, Firuza Parikh
Jaslok Hospital and Research Centre, Mumbai, India

HBV/HCV are etiological agents of acute and chronic liver disease including cirrhosis and hepatocellular carcinoma. In developing countries, the estimated percentage of liver cancers attributable to HBV infection is 59%, and HCV infection is 26%. It is estimated that currently there are more than 350 million carriers worldwide. HBV/HCV genotypes have been associated with the clinical features of the infection including severity, prognosis and response to the treatment regimen. In our study, we have standardized in-house PCR methodology for detection of HBV/HCV and genotyping of HBV/HCV. The HBV detection used PCR amplification of Pre'S' and Core regions. HCV was detected by preparation of cDNA, PCR amplification of the Core region. HBV/HCV genotypes were confirmed by direct sequencing of PCR products, Pre'S' and Core region in case of HBV and Core region in case of HCV, using the ABI 3100 Genetic Analyzer. The referral samples for our study were mainly of patients having elevated SGPT/SGOT and alkaline phosphatase levels, which are indicative of hepatic dysfunction. 25% of these samples were HBV positive while 12% of these samples were HCV positive. Our results on genotyping of HBV positive samples, indicated maximal presence of single infections with D genotype at 82% and genotype A at 18%. A small number of HCV positive samples have been genotyped and primarily HCV genotype 1a and 3 have been observed.

PS-06. Dialkyl Bromomethylfumarate: Useful Synthon in Natural Product Synthesis

Md. Merajuddin Baag, Sanjib Gogoi and Narshinha P. Argade*
Division of Organic Chemistry (Synthesis), National Chemical Laboratory, Pune 411 008, India argade@dalton.ncl.res.in

Utilities of dialkyl bromomethylfumarate as a synthon in designing of several bioactive natural products will be presented. Some of the target molecules on which work is under progress starting with dialkyl bromomethylfumarate are telfairic anhydride, graphenone, maleic anhydride segment of tautomycin, (+)-*erythro*-roccellic acid, etc.

PS-07. Identification of extracallular protein of *Mycobacterium tuberculosis* for immunodiagnosis of active tuberculosis infection

Dileep Tiwari[1,2], R.P.Tiwari[1], S.K.Singh[1], Anju Katyal[2], Ramesh Chandra[1,2], and P.S. Bisen[1]
[1]Department of Biotechnology, J.C. Bose Institute of Life Sciences, Bundelkhand University, Jhansi, India. [2]Dr. B.R. Ambedker Centre for Biomedical Research, University of Delhi, Delhi, India

Tuberculosis (TB) remains major global health problem. Human TB is the most frequent case of death from a single infectious agents being responsible for eight millions new cases and two millions deaths annually. We immunocharacterized the extra-cellular proteins of *Mycobacterium tuberculosis* for their serodiagnostic value. We cultured *M. tuberculosis* H_{37}Rv in Souton's medium and isolated the extra-cellular proteins employing an ion-exchange column chromatography. Five extra-cellular proteins were purified and characterized. The apparent molecular mass of these proteins were determined to be 10 kDa, 28 kDa, 30 kDa, 45 kDa, and 65 kDa. The serological potency of these proteins were analyzed by the detection of the respective antibodies present in a pool of the tuberculosis patients employing western blot and ELISA methods. Four of five proteins that, 10KDa, 30 kDa, 45 kDa and 65 kDa were found highly sensitive and specific for pulmonary, extra-pulmonary and latent tuberculosis. This finding may be further explored for the diagnostic marker of *M. tuberculosis*.

PS-08. Extraction, purification, and inhibitory effect determination of alpha - amylase inhibitor from wheat (Triticum aestivum var zarrin) against human salivary and bacillus subtilis alpha amylase

R.Heidari, M.Heidarizadeh
Biology Department, science faculty, urmia university, urmia,Iran

The relative inefficacy of alpha-amylase inhibitors in affecting human digestion of starch has been highlighted by recent scientific and public controversy over the commercial sales of so-called starch-blockers or slimming pills. These formulations, which were derived frome powdered kidney beans, were claimed to cause weight loss .alpha amylase and its inhibitors are drug-design targets for the development of compounds for treatment of diabetes Obesity and Hyperlipaemia .

Plant alpha-amylase inhibitors show great potential as biotechnological tools to engineer resistance of crop plants against Pests. They are also drug-design targets for treatment of diabetes and digestion disorderes. these inhibitors also known as sensitizing agents contain major allergenscausing baker asthma disease in human. the numerous form of alpha -amylase inhibitors were reported .in this study alpha-amylase inhibitor was extracted from Iranian wheat cultivar (Triticum aestivum v zarrin), precipitated and purified by anion exchange fast protein liquid chromatography .electrophoresis of purified protein showed 0.66 relative mobility .total hydrolytic activity of human salivary and bacillus subtilis alpha -amylase were inhibited 97% and 89.97% respectively by collected purified alpha- amylase inhibitor

Key words: alpha-amylase inhibitor, wheat, ion exchange chromatography, human salivary

PS-09. Synthesis of some novel triazolo thienopyrimidines as possible antibacterial agents

M.Raghu Prasad, Prasanth John, Shilpa Kulkarni
PES College Of Pharmacy, Hanumanthanagar, Bangalore-50

Several pharmacological activities like mitotic, hypotensive, CNS stimulant, antiinflammatory, analgesic, antipyretic, antiasthmatic and antibacterial activities has been attributed to condensed triazoles. Based on these observations it has been proposed to synthesize some novel triazolothienopyrimidines as possible antibacterial agents.

Herewith we are reporting the syntheses of some novel 5-substituted 1,2,4-triazolo[4,3-c] 8,9,10,11,12-pentahydro cyclohepta / 8,9,10trihydro cyclopenta[b]thieno[3,2-e] pyrimidin-3-thiones(4a -4h) as antibacterial agents.

Ortho amino ester of thiophenes (1) has been prepared by using Dean Stark Apparatus. Compound 1 was irradiated with various aryl and alkyl nitriles under strongly basic conditions using microwave oven to produce 2 substituted thieno[2,3-d]pyrimidin-4[3*H*]ones (2a-2h), a novel route hitherto unreported in the literature. Compounds 2a-2h was converted to 2-substituted 4-chloro thieno[2,3-d]pyrimidines using oxalyl chloride. This method, using oxalyl chloride for chlorination of thienopyrimidines is a novel method that not only gave better yields but also provided a simple work up procedures when compared with other conventional chlorinating agents like $POCl_3$, PCl_5 etc. The chloro derivatives, without further purification, were hydrazinated to yield 2-substituted 4-hydrazino thieno[2,3-d] pyrimidines(3a-3h). These compounds were cyclized with carbon disulphide to give the title compounds (4a - 4h) in quantitative yields. All the synthesized compounds were characterized by IR, UV, NMR and Mass Spectroscopy and analyzed by elemental analysis.

The title compounds were screened for antibacterial activity by Kirby Bauer's method using ampicillin as the standard against various gram positive and gram negative bacteria. All the compounds showed antibacterial activity.

PS-10. Prevention of *Pseudomonas aeruginosa* biofilm using castor oil

Vishnu Agarwal, Priyanka Lal, Vikas Pruthi
Molecular Microbiology lab., Deptt. of Biotechnology, IIT Roorkee, Roorkee-247667

Pseudomonas aeruginosa is considered among the leading pathogen associated with nosocomial bacteremia, exacerbations of cystic fibrosis, malignant external otitis and contact lenses keratitis. This organism becomes more problematic when it aggregates to form biofilm. Scanning electron microscopy of our investigation showed that biofilm associated cells of *P. aeruginosa* can be differentiated from their suspended counterparts by generation of an extracellular polymer substance (EPS) matrix. Infact, these biofilm associated cells could be considered as micro ecosystem in which these cells efficiently cooperate in order to protect themselves against environmental stresses and to facilitate more efficient nutrient uptake. Biofilm formation pattern of *P. aeruginosa* was studied at different time intervals showed that maximum biofilm formation take place after 36 h at 30˚C using MTP assay. The amount of crystal violet bound to the biofilm in the microtiter plate was quantified via solubilization of crystal violet in dimethyl sulfoxide (DMSO) and subsequently measuring the absorbance at 560nm. In our attempt to prevent biofilm formation castor oil, which is readily available, relatively inexpensive and environmentally benign, obtained from a naturally occurring renewable source was used. The crude dehydrated viscous yellow color liquid of unsaturated fatty acid from castor oil was coated on microtitre plate. It was observed that coating prevents >72% adherence of *P. aeruginosa* to microtitre plate when tested using MTP assay.

PS-11. Synthesis of Some Biologically Active Triazolothiadiazines Containing Halogen and Arylfuran Moieties

B. Shivarama Holla*, K. Narayana Poojary, B. Sooryanarayana Rao, D. Jagadeesh Prasad, M. S. Karthikeyan and Boja Poojary
[a]Department of Post-Graduate Studies and Research in Chemistry, Mangalore University, Mangalagangothri,-574 199, Karnataka State, India.

Triazolothiadiazines exhibit wide spectrum of biological activities such as anti-bacterial, antifungal, antiparasitic, antiinflammatory, anthelmintic and anticancer activity. Aryl furan-2-carboxaldehyde derivatives have been reported to possess wide spectrum of biological activities. It has been reported that the incorporation of fluorine atom can alter the course of reaction as well as augment the activities of the compounds. In the light of such observations and in continuation of our search for bio-active triazolo-thiadiazines, we undertook the synthesis of some newer congeners of triazolo-thiadiazines with various active moieties in a single molecular framework. Some of the selected compounds were screened for their antibacterial and anticancer activities. Results of such studies are described in this paper.

The reaction of various 3-substituted-4-amino-5-mercapto-1,2,4-triazoles (1) with 1-(2,4-dichloro-5-fluorophenyl-3-arylfuryl-2-bromo-2-propen-1-ones (**2**) in the presence of potassium hydroxide gave 3-substituted-6-(2,4-dichloro-5-fluoro-phenyl)-7-arylfurfurylidene-1,2,4- triazolo[3,4-b]-1,3,4-thiadiazines (**3**) in good yields. The title compounds were also synthesized by an alternate route. 3-Substituted-4-amino-5-mercapto-1,2,4-triazoles (**1**) were first condensed with 2,4-dichloro-5-fluoro-phenacyl bromide (**5**) in the presence of anhydrous sodium

acetate in absolute ethanol to yield 3-substituted-6-(2,4-dichloro-5-fluorophenyl)-7H-1,2,4-triazolo[3,4-b]-1-,3,4-thiadiazines (**5**). These compounds were then condensed with arylfurfurals in the presence of piperidine and absolute ethanol to afford the title compounds (**3**). The newly synthesized compounds displayed promising antibacterial and anticancer activities.

PS-12. Database Challenges in the Integration of Post Genomic Data Sets

Rakesh Nagarajan[1], Mushtaq Ahmed[2] and Aditya Phatak[2]
1. Washington University School of Medicine, Department of Pathology & Immunology, Saint Louis, MO, 63110, USA.
2. Persistent Systems Private Limited, Bhageerath, 402, Senapati Bapat Road, Pune 411016, India

The post genomic technologies like proteomics, microarray and sequencing present exciting and difficult data management and integration issues. Current research efforts in the field of biomedicine heavily depend upon integrated storage, querying, analysis, and visualization of functional genomic research data sets along with the annotations and clinicopathology information. Such large scale experimental analyses are essential to decipher and detect the pathophysiological processes occurring in most human diseases (diagnostics) so that they may be effectively treated (thearaputics). In this poster we discuss the data management and integration challenges of post genomics data and present the data warehousing based solution that we have employed at Washington University School of Medicine in St Louis. We also describe the tools we have developed to store, query, analyze, and visualize these data sets together.

PS-13. Synthesis of some novel potential analgesic and anti-inflammatory agents

J. Saravanan, Kavitha PN, S. Mohan
PES College Of Pharmacy, Hanumanthanagar, Bangalore-50

An ecofriendly synthesis of 3-substituted amino 2-mercapto-5,6,7,8-tetrahydro(1)benzothieno (2,3-*d*) pyrimidine-4 (3*H*)-one was carried out.

Condensed quinazolines like thiadiazoloquinazolines & the corresponding bioisostere thiadiazolothienopyrimidines were found to be biologically active molecules,2-substituted 1,3,4-thiadiazolo (2,3-b) quinazolin-4-one was reported to possess activity from our laboratories. Therefore it was thought of interest to utilize the concept of bioisosterism of the synthesis of 3-substituted amino 2-mercapto-5, 6,7,8-tetrahydro (1) benzo thieno (2,3-d) pyrimidine-4 (3H)-one for activity.

The dithiocarbamate derivative was obtained from 2-amino 3-carbethoxy thiophene in dimethylsulphoxide along with dropwise addition of carbon-di sulphide & sodium hydroxide alternatively at room temperature. The stirring was continued for half an hour, then dimethylsulphate was added dropwise at 0-5^{0}C and stirring was continued further for 3 more hours. The solid thus obtained was poured into ice-water mixture, filtered, dried and crystallized from ethanol. The 3-substituted amino 2-mercapto-5, 6,7,8-tetrahydro (1) benzothieno (2,3-d) pyrimidine -4(3H)-one was synthesized by refluxing the latter with hydrazine hydrate (99%)and isopropyl alcohol.

Finally, the compound was condensed with different substituted arylaldehydes to yield ten new compounds. The synthesized new compounds were characterized by preliminary lab techniques like melting point, TLC & by I.R, NMR spectra. The synthesized compounds will be subjected to analgesic & anti-inflammatory screening.

PS-14. Synthesis,Characterization and Biological activity of some novel potential analgesic and anti-inflammatory agents

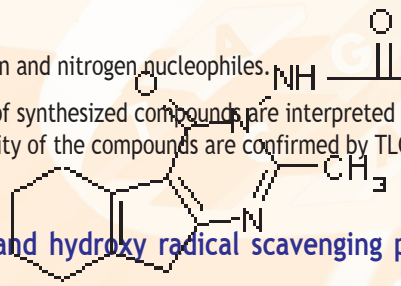
J. Saravanan, Vijayanthimala.P, S. Mohan
PES College Of Pharmacy, Hanumanthanagar, Bangalore-50

The present study is concentrated on the synthesis of substituted thienopyrimidines. As these medicinal agents have become very promising by possessing a variety of pharmacological activities like antibacterial,antifungal, analgesic anti-inflammatory and antitumor activities.

The starting material 2-amino-3-carbethoxy-4,5,6,7-tetrahydro benzo(b) thiophene-compound (I) is synthesized by K.Gewald synthesis.The compound (I) is subjected to acetylation using acetic anhydride to yield-compound(II).The acetylated product obtained is cyclised using hydrazine hydrate leading to formation of 3-amino-2-methyl-6,7,8,9-tetrahydro-3H-benzo(b)thieno pyrimidin-4-one-compound (III)

i)A mixture of **(III)** and substituted aryl acid chlorides yielded a series of 3-substituted-2-methyl-6,7,8,9-tetrahydro-3H-benzo(b)thieno pyrimidin-4-ones.III (a-j)

ii) The compound **(III)** is treated with chloroacetyl chloride to yield the compound(IV) is obtained.A mixture of compound **(IV)** and oxygen and nitrogen nucleophiles yielded a series of 3-substituted -2-methyl-6,7,8,9-tetrahydro-3H-benzo(b) thieno pyrimidin-4-ones- IV (a-e).



Where X= oxygen and nitrogen nucleophiles.

The structures of synthesized compounds are interpreted using spectra obtained from I.R,NMR & MS.The homogeneity and purity of the compounds are confirmed by TLC.

PS-15. Superoxide and hydroxy radical scavenging properties of Pippali *(Piper longum Linn.)* and Kababchini *(Piper cubeba Linn.)* extracts

J.Kanungo, J.Sen, G.B.N.Chainy and B.P.Shaw*
Dept of Zoology, Ulkal University, Bhubaneswar-7, Orissa, India
*Institute of Life Sciences, Nalco Square, Bhubaneswar-751023

Pippali and Kababchini are dried fruits of *Piper longum Linn.* and *Piper cubeba Linn.* Respectively. Both are ex-

tensively used in Indian traditional medicine for the cure of cough, bronchitis and asthama. Since reactive oxygen species are supposed to be the root cause of many diseases and all diseases in general leads to oxidative stress condition, superoxide and hydroxyl radical scavenging properties of Pippali and Kababchini were investigated under *in vitro* system. Superoxide scavenging activity was monitored by determining the percentage of inhibition of formation of this species from hydroxylamine by photoreduction of riboflavin. Hydroxyl radical formation and its scavenging was monitored by determining the level of degradation of deoxyribose sugar. The results of the present study indicated that aqueous as well as ethanolic extracts of Pippali and Kababchini can significantly scavenge superoxide. However, the alcoholic extract is more effective. The aqueous extract of Pippali fail to scavenge hydroxyl radical, but that of Kababchini did show potentiality of scavenging this reactive oxygen species. Identification of the bioactive molecule(s)/compound(s) responsible for the antioxidant properties of the extract is in progress.

PS-16. CYP3A4 phenotypes and genotypes in North Indians

Naushad Rais[1], Yogesh K Chawla[2] and Krishan K Kohli [1]
Department of Biochemistry[1] and Hepatology[2], Postgraduate Institute Of Medical Education And Research, Chandigarh, UT-160 012.

Cytochrome P4503A (CYP3A) is the most abundant subfamily in liver and intestine and its members metabolize more than 50 % clinically used drugs. Caucasians and Orientals demonstrate large interindividual variation in the activity of CYP3A. This may be due to genetic and environmental factors. CYP3A phenotyping is performed by measuring the metabolic ratio of cortisol (CS), nifedipine, midazolam and erythromycin. These experiments have not established the presence of CYP3A genetic polymorphism in different ethnic groups. Since no data on CYP3A4 phenotypes and genotypes was available in North Indians, the present research was undertaken. Morning spot urine samples were collected from 280 healthy North Indians. CS and 6b-OH-CS were extracted and quantified by HPLC. Urinary 6b-OH-CS/CS ratios ranged from 1.1-401.9 (64 ± 61.4). North Indians demonstrated unimodal distribution with respect to urinary 6b-OH-CS/CS ratios. On the basis of CYP3A phenotypes, the subjects were divided into low CYP3A, intermediate CYP3A and high CYP3A activity groups consisting of 75, 130, 75 subjects, respectively. These groups demonstrated 1.1 to 26.9 (16 ± 6.7), 27 to 77.5 (46.0 ± 15) and 79.6 to 401.2 (143.3 ± 69.0) ratios of 6b-OH-CS/CS, respectively. In the low CYP3A activity group 25, 17, 26, 22, 21 and 15 subjects were genotyped for *CYP3A4* 1B, *2, *4, *5, *6* and **10* alleles. In the intermediate CYP3A activity group 37, 34, 12 and 40 subjects were genotyped for *CYP3A4*1B, *4, *5,* and **6* alleles. In the high activity group 33, 19, 34, 17, 27 and 19 subjects were genotyped for *CYP3A4*1B, *2, *4, *5, *6* and **10* alleles. Only two heterozygotes with genotype *CYP3A4*1/*1B* were found in the high CYP3A activity group. None of the other *CYP3A4* variant genotypes were found in any of the subjects studied. This is the first investigation establishing CYP3A phenotypes and demonstrating the absence of common *CYP3A4* genotypes in North Indians.

PS-17. Development of a Secretory Vector for Dictyostelium: An Alternative System for Heterologous Recombinant Protein Production.

Bhavesh Vats and Harish Padh
B. V. Patel PERD Centre, Ahmedabad. perd@perdcentre.com

With the enormous data being harnessed by genomics and proteomics, the role of proteins as targets for curing diseases is escalating day by day but the importance of proteins as therapeutics is known for the past 15-20 years.

These therapeutics are produced as recombinant proteins in heterologous systems. Some of these proteins are structurally simple enough to be produced in prokaryotic systems but many of them require modifications like N- and O- glycosylations for which eukaryotes like yeast, Pischia pastoris and mammalian cell lines are proficient though none of these systems is complete. Other than the proper synthesis of protein, its purification has always been a major quandary.

Dictyostelium discoideum is a eukaryote capable of synthesizing proteins with post translational modifications like N- and O- glycosylations. By means of expression vectors, many recombinant proteins have been synthesized ascertaining its role for production of recombinant proteins.

We have modified an existing expression vector of D. discoideum by adding two sequences: a) Secretory sequence, b) Purification tag; enabling the system to secrete the recombinant protein into the growth medium and easing the downstream processing. The modified vector was analyzed using Green Fluorescent Protein as a reporter gene. The stable integration of the transgene confirmed by specific primer PCR analysis of the genomic DNA, proper transcription ascertained by RT-PCR analysis of the total RNA and the protein analyzed by fluorescence assay. We have been able to establish significant expression of the protein in the media whereas no fluorescence was observed in the cells. Further work is in progress to enhance the protein production.

We acknowledge CSIR and Industries Comissionerate, Govt. of Gujarat for the financial assistance and UGC for research fellowship.

PS-18. Oxazolidinones as Antimicrobial Agents: A Molecular Modeling Study.

Brijesh Kumar Srivastava, Neha Gandhi, V.B.Lohray
Zydus Research Centre, Ahmedabad.

The Oxazolidinones not only represent a new structural class of antibiotics, but they also have a unique mechanism of action. En route to novel oxazolidinones with an expanded antibacterial spectrum and improved potency, we have analyzed two oxazolidine-2-thiones, thio-analogs of linezolid for their antibacterial activities. Unlike oxazolidinones, the thio-analog in which carbonyl oxygen of the oxazolidinone ring was replaced by sulfur, did not inhibit the growth of Gram positive bacteria. A molecular modeling study has been carried out to aid the understanding of this unexpected finding.

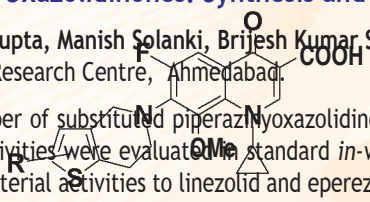
PS-19. Synthesis and evaluation of antibacterial activity of novel quinolone derivatives.

Bhupendra Mishra, Rina Soni, Brijesh Kumar Srivastava, Purvi Pandya, V.B.Lohray
Zydus Research Centre, Ahmedabad.

A number of 7-substituted fluoro-quinolone derivatives have been synthesized and their antibacterial activities were evaluated in standard *in-vitro* MIC assay method. Some of the compounds showed comparable activities to Gatifloxacin and remarkable activities against Gram +ve organism. A SAR has been carried out to get a potent quinolone derivative.

PS-20. Novel Oxazolidinones: Synthesis and SAR

Sunil Gupta, Manish Solanki, Brijesh Kumar Srivastava, Purvi Pandya, V.B.Lohray
Zydus Research Centre, Ahmedabad.



A number of substituted piperazinyoxazolidinone derivatives 5-11 have been synthesized and their antibacterial activities were evaluated in standard *in-vitro* MIC assay method. Most of the compounds showed superior antibacterial activities to linezolid and eperezolid. A SAR has been carried out to get a potent derivative.

PS-21. Synthesis and Antibacterial activity of novel 4-N- substituted aryl pent-2-ene-1, 4-dione derivatives of piperazinyloxazolidinones.

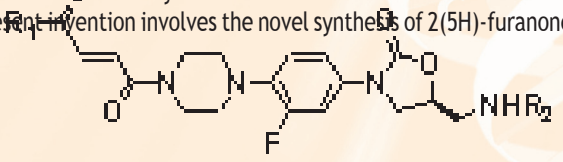
Vijay Takale, Prashant B. Kapadnis, Brijesh Kumar Srivastava, Purvi Pandya, V.B.Lohray
Zydus Research Centre, Ahmedabad.

A number of oxazolidinones having substitution on distant nitrogen atom of piperazine ring in piperazinyloxazolidinone were synthesized and evaluated for their antibacterial activity. Most of the compounds showed superior antibacterial *in-vitro* MIC values than linezolid and eperezolid.

PS-22. Novel Synthesis of 2(5H)-furanone.

A. D. Argade; P. S. Thombare and V. B. Lohray
Zydus Research Centre, Ahmedabad

2(5H)-Furanone skeleton is found in a number of active drug molecules and one of these is rofecoxib which is a COX-2 inhibitor. Recently rofecoxib has been withdrawn from the market due to its cardiovascular side effects. The present invention involves the novel synthesis of 2(5H)-furanone and particularly rofecoxib by novel methods.



The invention exploited the Wittig-Horner reaction to get cyclised furanone derivative.

PS-23. New drug targets for Type II Diabetes.

Bahekar R.H., Lohray V.B., Jadav P., Prajapati V and Sarkar S.S
Zydus Research Centre, Ahmedabad.

Type II diabetes accounts for 90-95% of all the diabetes. Current therapy for type II diabetes includes use of drugs like Sulfonylureas, which increase insulin release from pancreatic islets, PPAR_ agonist, which enhance insulin action, metformin, which acts to reduce hepatic glucose production and insulin itself, which suppresses glucose production and augments glucose utilization. Most of these current therapeutic approaches were largely developed in the absence of defined molecular targets.

However, these therapies have limited efficacy, less tolerability and significant mechanism-based side effects, such as hypoglycemia and weight gain. Thus, newer approaches are desperately needed, particularly emphasis should be placed on finding and using mechanisms that are dependent on physiological responses, such as glucose mediated insulin release. Within the past few years, our understanding of biochemical pathways related to the development of metabolic syndrome has expanded. As a result, several mechanistic categories (new targets) for new therapeutic approaches have evolved, which in near future is likely to yield wider array of potential approaches for the therapeutic intervention of typeIIdiabetes.

PS-24. Synthesis of Peptides by Solid Phase Peptide Synthesis Approach (SPPS)

Bahekar R.H., Gupta A., Patel D. and Lohray V.B.
Zydus Research Centre, Ahmedabad.

In the recent years, enormous therapeutic potential of peptide and protein drugs have been realized as a result, several synthetic peptide and protein drugs are available in the market for the treatment of various diseases. Similarly, the endogenous peptide and proteins were found to be useful to understand the pathophysiology of various disease conditions. With the advancement in solid phase peptide synthesis (SPPS), today, synthesis of various peptides has become possible.

In this project, Using Fmoc-Based SPPS approach, around 10 different peptides with acids sequence ranging from 10 - 40 residues were successfully synthesized. The coupling and deprotection of amino acids were monitored by Ninhydrin test. After the assembly of desired sequence, peptide chain was separated (cleaved) from solid support using suitable cleavage

PS-25. Novel Pyrrole Containing Hypoglycemic and Hypotriglyceridemic Compounds

Saurin Raval, Preeti Raval, Sujay Basu, Atul Godha, Jayendra Patel, Vidya Lohray, Mukul Jain, Archana Patel
Zydus Research Centre, Ahmedabad

Several substituted a-alkoxy phenyl propionic acids were synthesized and their hypotriglyceridemic properties were evaluated in Swiss Albino mice. Some of the compounds showed excellent triglyceride and cholesterol lowering

properties even a dose of 1 mg/kg dose. 2,5-Substitued pyrrole containing heterocycles were among the most potent alkoxy propionic acid class of compounds. These compounds also showed excellent anti-diabetic activities in animal model.

PS-26. A novel HPLC method development for enantiomeric separation of levetiracetam and its key intermediate to make very rapid and economical method.

Prakash M. Davadra, Shailesh M. Buha, Himanshu Vachhani, Srinivas Kone.
Zydus Research Centre, Ahmedabad.

The aim of this study to develop a very rapid and economical HPLC method for the determination of undesired enantiomer of levetiracetam and its key intermediate. Levetiracetam is an anticonvulsant. It has one chiral carbon atom and its S-isomer is active. We have developed reverse phase HPLC method to assess the chiral purity of levetiracetam and key its intermediate- *2-(2-Oxo-pyrrolidin-1-yl)-butyric acid*.

PS-27. Chiral chromatographic method development for enantiomer separation of duloxetine hydrochloride in bulk drug and tablet

Prakash M. Davadra, K. M. Rana, Snehal Patel, Srinivas Kone.
Zydus Research Centre, Ahmedabad.

Duloxetine is an antidepressant drug. It has one chiral carbon atom and its S-isomer is desired. Reverse phase HPLC method was developed for estimating enantiomeric impurity of duloxetine hydrochloride in bulk drug and tablet by using chiral stationary phase.

PS-28. Quantification of Clopidogrel bisulfate form-II contamination in Clopidogrel bisulfate form-I by X-ray powder diffraction

Hemant Gadpe, Amrita Srivastava, Rohit Mudgal and Manish Srivastava,
Zydus Research Centre, Ahmedabad.

Polymorphism specifying the diversity of nature is widely observed in pharmaceutical compounds. Differences in their physico-chemical and mechanical properties led to the emergence of characterization based stringent quality control measures of these altered solid-state forms, in active pharmaceutical ingredients (APIs) and drug products, both during filing of New Drug Applications (NDAs) and Abbreviated New Drug Applications (ANDAs). The lower energy form, though the most stable and preferred form for the final dosage form, exhibits lower solubility and dissolution profiles, an issue especially important for the biopharmaceutics classification system (BCS) class II and IV drugs. Additional complexities can arise due to the differences in flow proper-ties, compactability, water uptake behavior, crystal morphology and hence processability of different forms. The sudden appearance or disappearance of a crystalline form can threaten process development, and can lead to serious pharmaceutical consequences if the transformation occurs during the manufacturing or storage of the dosage form. Therefore, qualitative and quantitative analyses of polymorphs must be incorporated early on in the drug development stage, both in the API manufacturing and the formulation stage.

This study deals with characterization and quantification of form II in form I of Clopidogrel bisulphate (CLP), a selective and irreversible inhibitor of ADP-induced platelet aggregation. Thermal (DSC, TGA), crystallographic (XRD) and spectroscopic (FTIR) methods were used for characterization. A XRD method was successfully devel-

oped for the quantification of form II in form I. The analytical method was validated by verifying its performance characteristics and its ability to meet the requirements for its intended analytical application. The performance characteristics were expressed in terms of analytical variables including the parameters Specificity, Precision, System suitability, Linearity, Limit of Quantification and Accuracy (recovery).

PS-29. pka Determination of an organic compound by UV Spectrophotometry.

Malini Sharma, Jigar Gajjar, Rahul Pathak and Manish Srivastava.
Zydus Research Centre, Ahmedabad.

The pKa or dissociation constant is a measure of strength of an acid or a base. The pKa is a useful parameter for understanding the behavior of drug molecules. Different ionic species of a molecule differ in their physical, chemical and biological properties and so, it is important to be able to predict which ionic form of the molecule is present on the site of action.

In cases of poor solubility or small sample amount, pKa values are best determined by UV spectroscopy. The method simply relies on the change in UV spectra at different pH values since the electronic transitions are known to be pH dependent.

PS-30. A rapid reverse phase chiral HPLC method for Linezolid.

Prerana Sharma, Asha Thulaseedharan , Srinivas Kone
Zydus Research Center, Ahmedabad.

A fast, reliable and rapid reverse phase chiral HPLC method was developed for determination and confirmation of enantiomeric purity with good resolution. A baseline separation of linezolid was achieved on a 5µm reverse phase alpha 1 acid glycoprotein (chiral AGP 150*4.6 mm column) at 225nm. Mobile phase comprised of 25 mM di-sodium hydrogen ortho phosphate buffer (pH 6.9) with flow rate of 0.5 ml/min.

This method gave good resolution between two enantiomers. The retention time of two enantiomers(R and S) were at 5.4 min. and 6.3 min. respectively.

PS-31. Enantiomeric separation of Tadalafil by RP-HPLC using alpha 1 acid glycoprotein as a chiral stationary phase.

Prerana Sharma, Asha Thulaseedharan, Srinivas Kone
Zydus Research Center, Ahmedabad.

Tadalafil is a drug for the treatment of erectile dysinfection in men. Tadalafil is having two chiral centers and out of the four isomers *RR -isomer* is the desired one. A new precise, well resolved chiral method was developed for separating the two enantiomers of Tadalafil by using alpha 1 acid glycoprotien as a stationary phase.

PS-32. Validation of LC-MS Electrospray Ionization method for quantitation of haloperidol in human plasma and its application to bioequivalence study

Sapna Gupta, Harilal Patel, Manish Jain, D.P.Shrivastava, Meghna Vyas
Zydus Research Center, Ahmedabad.

In the present investigation, a sensitive LC/MS – electrospray ionisation mass spectrometric method has been de-

veloped for the quantitation of Haloperidol – an antipsychotic drug, in human plasma. The method was developed with the objective of accurately measuring the concentration of Haloperidol in the plasma of human subjects enrolled in the bioequivalence study of Haloperidol (5 mg) tablets of M/S Cadila Healthcare Ltd India *versus* 5 mg Haloperidol tablets of Geneva Pharma USA. The sample purification and pre-concentration was performed by liquid – liquid extraction (LLE) using Duloxetine as internal standard. The chromatographic separation was achieved using an isocratic mobile phase containing 1.0 mM ammonium acetate pH 3.0 and Acetonitrile (70:30,v/v) flowing through Xterra MS C18 100 X 2.1 mm, 3.5 µm analytical column, at a flow rate of 0.2 ml/min. The lower limit of quantitation (LLOQ) of 70.0 pg/ml was achieved using mass spectrometric detection in positive mode. The ion signals of m/z 375.9 and 297.9 were measured for Haloperidol and internal standard respectively .An exhaustive pre-study method validation was performed in accordance with USFDA guidelines. The standard curves were linear in the concentration range of 70.0 pg/ml to 14.0 µg/ml with a correlation coefficient better than 0.996. The method was successfully applied to the bioequivalence study of Haloperidol in healthy human male volunteers.

PS-33. Measurement of drug protein binding by using immobilized human serum albumin liquid chromatography- UV spectrometry

Dr. Sonu Singh & Jitendra Mehta
Zydus research centre, Ahmedabad.

Many methodologies have been investigated for quantitative determination of drug-protein binding. Among those, equilibrium dialysis and ultrafiltration followed by HPLC analysis have been conventionally and most commonly used. These conventional methods suffer from relatively long analysis time, the need of additional analytical step to determine the actual final drug concentration, non-specific binding of drugs on to the membrane, which makes them not very applicable to highly protein bound drugs.

Compared to conventional methods, chromatography based method is intrinsically simpler and faster in terms of sample preparation and analysis. In this method column capacity factor (k') is used to evaluate the protein binding strength of the drug.

Newly developed HPLC-UV based (HSA) method was used for drug-protein binding study of UV active compounds. Results from methodology were compared with literature data for each analyzed drug and good agreement was observed. Compounds not suitable for Ultrafiltration were also successfully analyzed by this method.

PS-34. Validation of HPLC method for the estimation of carboxylic acid metabolite of clopidogrel in rat plasma and its application for comparative pharmacokinetics of clopidogrel bisulphite (Form-1 and Form-2) in male wistar rats.

Kuldeep Sharma, Ram Mohan, Deepak Barot, Jayesh Maradiya, Ramesh Padodara and Sonu S. Singh
Zydus Research Center, Ahmedabad.

Clopidogrel is an anti-platelet drug, which inhibits the ability of platelets to clump together and form a blood clot. It selectively inhibits the binding of adenosine-diphosphate (ADP- mediated activation of GPIIb-IIa complex, thereby inhibiting platelet aggregation [1]. Clopidogrel is similar to Ticlopidine in chemical structure but un-

like Ticlopidine it is devoid of the side effects of serious reduction of white cells. Long term prophylactic use of Clopidogrel has been reported [1] to be beneficial in prevention of ischemic stroke, myocardial infarction and vascular death in patients. Clopidogrel is a prodrug, which is inactive in-vitro and hepatic biotransformation via cytochrome P450 pathway, primarily by CYP3A4 and CYP3A5 [2]; is essential for its in-vivo antiplatelet activity. The active metabolite [3] a thiol compound is formed by the oxidation of Clopidogrel to 2-oxo Clopidogrel and subsequent hydrolysis. The active metabolite is highly labile and remains un-detected in plasma. It was isolated *in-vitro* from human microsomes and structure elucidation [3] was performed on stabilized acrylonitrile derivative.

Since, neither the parent drug nor the active metabolite could be detected in plasma, a novel HPLC method was developed for estimating the inactive carboxylic acid metabolite of Clopidogrel which is the most abundant species circulating in blood. Earlier a GC-MS [4] method had been reported. The new HPLC method was developed with the objective of assessing the pharmacokinetic parameters of different salts of Clopidogrel. The present method was sensitive enough to quantify the acid metabolite in rat plasma. The lower limit of Quantitation was 125 ng/ml. The method was validated in accordance with USFDA guidelines [5]. The method was successfully applied to two different salt forms of Clopidogrel: Clopidogrel bisulphite (Form-1) and Clopidogrel bisulphite (Form-2). Clopidogrel bisulphite (Form-1) was found to be more bioavialable than Clopidogrel bisulphite (Form-2).

PS-35. Modified push-pull osmotic system for simultaneous delivery of theophylline and salbutamol

D. Prabakaran[*] and Suresh P. Vyas[**]
[*]Zydus Research Centre, Ahemdabad.

[**]Drug Delivery Research Laboratory, Department of Pharmaceutical Sciences, Dr. Harisingh Gour University, Sagar, India.

Simple controlled porosity osmotic pump contained both drugs (in freely soluble form) did not provide satisfactory extended release of theophylline. A modified two-layered, push-pull osmotic system was developed by using the basic designs of various oral osmotic pumps, such as controlled porosity osmotic pump (CPOP), elementary osmotic pump (EOP) and push-pull osmotic pump (PPOP). Granulation, compression, coating, scanning electron microscopy studies and in vitro release studies were conducted. Formulations were initially developed for theophylline and the release was optimized by using two different soluble forms of theophylline with varying amount of hydrophilic polymer mixture in upper layer and polyethylene oxide (expandable hydrogel) in lower layer. Further, the release of salbutamol sulphate was optimized by keeping the drug in upper or lower layer or both layers. The modified push-pull osmotic system could be effective in the multi-drug therapy of asthma by delivering both drugs simultaneously at a controlled manner. The prototype design of the system could be applied for other combination of drugs (one water slightly soluble or insoluble drug and another freely water soluble drug) used for cardiovascular diseases, diabetes, etc.

PS-36. A Novel Approach In Receptor Mediated Targeting Using Lipobeads In The Treatment Of *Helicobacer pylori* Infections.

R.B. Umamaheshwari[*] and N.K. Jain[**]
*Zydus research centre, Ahmedabad
**Pharmaceutics Research Laboratory, Department of Pharmaceutical sciences, Dr. Hari Singh Gour University, Sagar, Madhya Pradesh, India.

H. pylori is a gram-negative bacterium that is associated with the gastric inflammation, peptic ulcer, gastric cancer

and is a risk factor for non-Hodgkin's lymphomas of the stomach. An understanding of the strategies by which *H. pylori* persists in the gastric epithelium and the mechanisms underlying the host responses induced is thus of crucial importance to better understanding the pathogenesis of *H. pylori* infections. Adherence is important for entry of organisms into epithelial cells. Phosphatidyl ethanolamine (PE) is a predominant lipid in the antrum of the human stomach and functions as a receptor for *H. pylori* adhesion. On the basis of the above facts, antiadhesion drug delivery system based on PE has been developed as a receptor mediated drug delivery system for use in blocking adhesion of *Helicobacter*.

PS-37. Evaluation of Strategies for the Formulation of Protein Coated Gold Microparticles

K.V. Rudresha Prasad, and Paul Laidler*
Zydus Research Centre, Ahmedabad, India
*Powdermed Limited, 4 Robert Robinson Avenue, The Oxford Science Park, Oxford, United Kingdom.

It has been hypothesised that the delivery of protein coated gold to both intra- and extracellular compartments of the viable epidermis may be able to induce both cellular and humoral immune responses. Delivery of gold particles coated with protein antigens (Hep B and flu nucleoprotein) to the viable epidermal cells using PowderJect technology has been previously demonstrated to elicit both antibody and CTL responses. Little work was performed to either enhance efficacy and stability of the formulations used in the studies or to optimise the processes for their manufacture. Therefore the need to assess alternative approaches for the fabrication of protein coated gold particles was identified.

Different coating or precipitation methodologies were evaluated to produce improved protein coated gold microparticles formulations with respect to titratability of antigen loading and uniformity and consistency of coating for needle-free edpidermal vaccine delivery application.

PS-38. Efficacy and Toxicity Profile of Linezolid.

Patel P.P., Joshi G.S., Sanjaya R.J., Jain M.R., Valani D.T.
Zydus Research Centre, Ahmedabad.

LINEZOLID is a synthetic antibacterial agent of Oxazolidinones class having good clinical utility in the treatment of various infections caused by Gram positive aerobic bacteria. The *in vitro* efficacy was evaluated against Gram positive and Gram negative aerobic bacterial strains as per NCCLS standards and a 28 days oral toxicity was assessed in Witstar rat for hematological, biochemical and histopathological alteration at 2, 5 and 10 times higher than maximum human therapeutic dose on body weight basis.

Linezolid was found to be effective antibacterial agent on various Gram positive bacterial strains including drug resistance strains *viz.*, MRSA, VRE and PRSP. There was significant reduction in haematological parameters like RBCs, Haemoglobin and Haematocrits in the high dose (85.7 mg/kg) female groups only. There was no significant toxicological effects on biochemical and histopathological parameters in linezolid treated wistar rats.

PS-39. Synthesis and Hypolipidemic Activity of Oxazole Containing Aralkyl Derivatives.

Hari Kishore Pingali, Pankaj Makadia, Saurin Raval, Pandurang Zaware, Pravin Patil, Jayendra Patel, Chetan

Puri, Vidya Bhushan Lohray, Mukul.R.Jain.
Zydus Research Centre, Ahmedabad.

2-Ethoxy-3-[4-(5-methyl-2-aryl-oxazol-4-ylalkoxy)-phenyl]-propanoic acids are known to possess excellent hypolipidemic and antihyperglycemic activities. Although extensive work has been done on the phenyl propanoic acid class of compounds, the corresponding alcohols, amines, ethers and similar other functionalised derivatives have not received much attention. We have synthesised several oxazole containing aralkyl derivatives of general formula (I) and studied their hypolipidemic activities in relevant animal models. Several compounds showed very good triglyceride lowering activity.

PS-40. Toxicoproteomic Analysis of Acetaminophen Dosed Rat Livers

Madhurarekha Ch*, Ravikumar K*, Sasidhar V*, Sunil Kumar K. B#, Rajasekhar B*[1]
*Proteomics Division, Discovery Research, Dr. Reddy's Laboratories Ltd., Miyapur, Hyderabad, India. 500049
Preclinical Safety Evaluation, Dr. Reddy's Laboratories Ltd., Miyapur, Hyderabad, India. 500049

A major challenge for the toxicologists is to understand the mechanism of chemical toxicity, which is essential for cross species and dose extrapolations. Standard mechanistic studies in animals to examine the toxic and pathological changes associated with the chemical exposure have often been limited to single end point or pathways. Toxicoproteomics represents a potential aid to the toxicologist to understand the multiple pathways involved in the mechanism of toxicity and also determine the biomarkers that are predictive of the toxicological response. We performed an acute toxicity study in Wistar rats with the prototype liver toxin, acetaminophen (APAP) to determine the effects on protein profile in the liver and its correlation with the plasma biochemical markers for liver injury. Three groups (five rats/group) of animals were treated orally with vehicle (control), nontoxic and toxic doses of APAP. The proteins isolated from the livers were separated by 2-DE and analyzed by MALDI TOF. The differential proteins in the gels were analyzed by BIORAD's PDQuest software and identified by feeding the peptide mass fingerprint data to various public domains like Mascot and MS-Fit. Many of the liver drug metabolizing and detoxifying enzymes like Glutathione S transferase, Glutathione peroxidase, Selenium binding protein, Aldehyde dehydrogenase and some of the CYP enzymes are up-regulated in toxic conditions and the liver damage markers like aspartate amino transferase (AST) and alanine amino transferase (ALT) are depleted in toxic conditions. These and several other proteins were identified as a first step to develop an in-house rodent liver toxicoproteomics database.

All are equal contributors.
[1] Corresponding author

DRL publication No. 471

PS-41. Pharmacogenomics of Hypertension -Shift from "One Size Fits All" to Personalized therapy: Study in Indian Population

Chandan Kumar, Prabal Chattopadhyay, and Sumera N. Hasham_____
Genomics Group, Discovery Research, Dr Reddy's Laboratories Ltd., Bollaram Road, Miyapur, Hyderabad-500049

Pharmacogenomics, the study of correlating the genetic profile with an individual's drug response, is being applied to shift from "one size fits all" drug regimen to personalized drug therapy. As a preliminary step towards this goal, in the present study, pharmacogenomics of antihypertensive drug therapy in Indian population was undertaken. The Renin-angiotensin-aldosterone system (RAAS) is one of the key regulators of blood pressure and pharmacological agents modulating the RAAS pathway are highly successful in the treatment of hypertension. Though multiple drugs targeting different gene products are efficient in controlling hypertension, the choice of initial antihypertensive drug is still largely empirical. Known polymorphisms in majority of these genes: Angiotensinogen [M235T, T174M, and G(-6)A], Angiotensin II Type Receptor I [A1166C], B1 Adrenergic Receptor [R389G] and [S49G] were investigated to test the hypothesis of association of these genetic variants with hypertension and drug response in Indian population. Genetic profile was obtained for both normo and hypertensive individuals at these loci using a combination of RFLP-PCR and automated DNA sequencing. Allele frequencies were calculated and an association with hypertension was tested using the c2 _analysis. The population profiled in the present study was found to be in Hardy-Weinberg equilibrium. Preliminary analysis indicates that the variant alleles at most of these loci are predominantly present in hypertensive individuals profiled in the present study, indicating a possible association with hypertension. These studies when completed will help us to tailor the antihypertensive therapy based on the genetic profile of an individual.

* DRL Publication No. 394-A

PS-42. Variability in Paroxetine Pharmacokinetics in Indian population: Possibility of phenotype-genotype correlation

Neelam Chauhan, Shubha Rani and Harish Padh
B. V. Patel PERD Centre, Thaltej-Gandhinagar Highway, Thaltej, Ahmedabad-380054. E-mail:perd@perdcentre.com

It is well known that Cytochrome P450 (CYP) is principal catalyst involved in the disposition of drugs and other xenobiotics. This group of compounds is extremely widespread in nature, occurring in all living organisms. Of all CYP enzymes, highly genetically polymorphic enzyme *debrisoquine-4-hydroxylase*, or CYP2D6, is involved in the oxidative metabolism of more than 40 widely prescribed drugs. More than 50 different CYP2D6 alleles have so far been identified. This enzyme has a wide range of activity within human population with inter-individual rate of metabolism differing more than 10,000 folds. Due to its highly genetically polymorphic characteristics, high inter-individual variations in pharmacokinetics (PK) of drug metabolized by this enzyme are observed. This variation poses a challenge for safety and efficacy in humans.

Paroxetine, an antidepressant, is also metabolized by the enzyme CYP2D6. Considerable inter-individual variability in pharmacokinetics is reported in the literature for Caucasian, Oriental and African population. Hence this study was aimed to investigate the variability in paroxetine pharmacokinetics in healthy Indian males. Data showed 20-fold difference in maximum plasma concentration (C_{max}) and 100-fold difference in area under the

curve (AUC). This prompted us to investigate the genotype of the individuals and examine if any correlation exists between the genotype and phenotype (PK profile) of an individual. Researchers have already suggested to adjust the dose based on the therapeutic response. Hence it will be of great importance if a correlation exists between the genotype and phenotype of an individual that may lead to individualized drug therapy prior to the drug administration. Consequently it will prevent adverse drug reaction / therapeutic failure.

Acknowledgement: We would like to acknowledge the clinical group to conduct the pharmaokinetic study and the Industrial Commissionerate grant for funding the research.

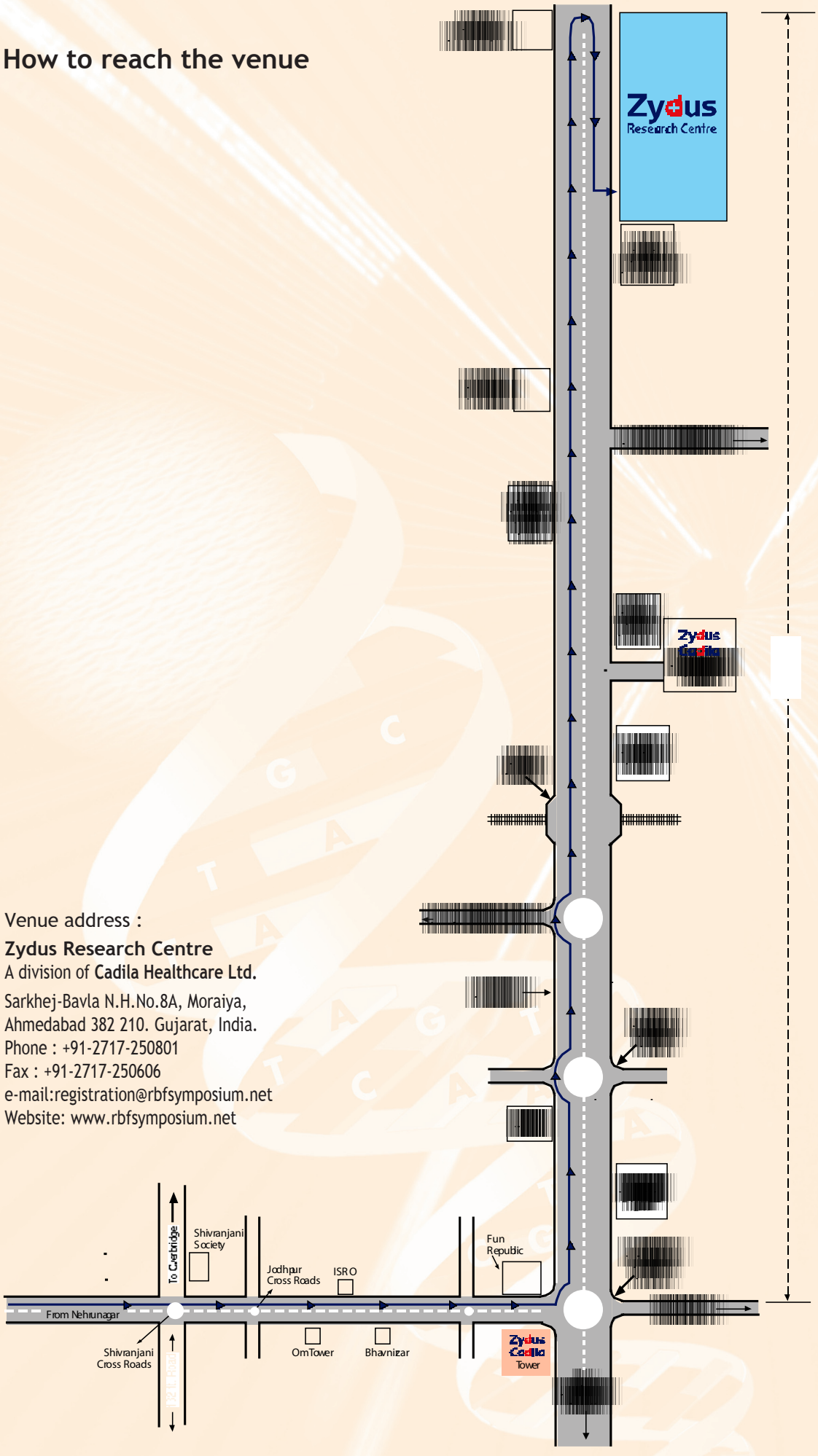
PS-43. Development of Immunoassays for detection of FSH, LH, E1G and PdG in Urine

Nisha Sadhwani, Toral Shah, Dipen Soni, Gaurav Mehta, Sanjay Singh, Sanjeev Kumar
Zydus Research Center, Ahmedabad.

Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH) are glycoprotein hormones whereas Estrone Glucuronide (E1G) and Pregnane diol Glucuronide (PdG) are metabolites of steroid homones estradiol and progesterone respectively. Measurement of FSH is a valuable tool for evaluating pituitary-hypothalamic mediated gonadal function and LH indicates occurrence of ovulation. Estimation of E1G helps in assessment of follicular function and PdG for the detection of fertility. The poster details the development of ELISA for the detection of these analytes from the urine. FSH and LH are detected by sandwich ELISA whereas E1G and PdG are detected by competitive ELISA. Urine integrates the episodic secretion of these hormones over a defined period of time. Using urine specimen for long term endocrinological studies precludes the need for repeated venipuncture, increases compliance and volunteer availability. Urine samples of all the three phases of one menstrual cycle were run for detection of levels of all the four analytes in all the four kits. A bell shape curve for FSH was found starting in the follicular phase and ending in the ovulatory phase. A sharp peak for LH was found in the ovulatory phase. Concentrations of PdG rised rapidly following ovulation and decreased before the onset of next cycle. Rise in levels of E1G was found in follicular phase as well as luteal phase.

Author Index

How to reach the venue



Venue address :

Zydus Research Centre
A division of **Cadila Healthcare Ltd.**
Sarkhej-Bavla N.H.No.8A, Moraiya,
Ahmedabad 382 210. Gujarat, India.
Phone : +91-2717-250801
Fax : +91-2717-250606
e-mail:registration@rbfsymposium.net
Website: www.rbfsymposium.net