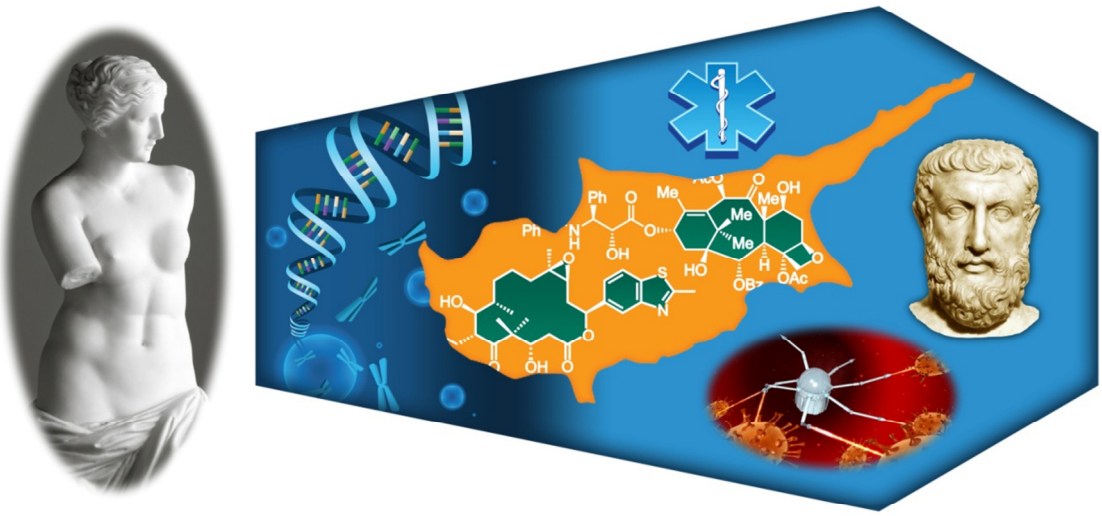
COST Conference | Personalised Medicine: Better Healthcare for the Future

17 to 22 June 2012, Larnaca, Cyprus

Booklet of Abstracts



Foreword

Personalized medicine, a discipline enabled by genetic, biopharma, diagnostic, and information and communications (ICT) technologies attempts to tailor disease treatment to individual patients. Personalized medicine is rapidly emerging as a state-of-the-art approach to diagnostics and therapeutics and is beginning to revolutionize our health care system, promising better medicine for all.

COST – European Cooperation in Science and Technology – opened up the field of personalized medicine in 1986 when, as part of the Biomedicine and Molecular Biosciences Domain, it sanctioned a research network (aka COST Action) to recruit trial subjects based on differences in metabolic capacity (COST Action B1, 1986). Since then, progress in technology, along with a growing understanding of individual susceptibility to disease and treatment effects, has led to new concepts in translational science such as the Virtual Patient Model. These developments are transforming the way we think about health and disease.

Interdisciplinary methods are facilitating the creation of integrated data sets that incorporate biological, chemical, and clinical observations through the use of sophisticated software and hardware. Mathematics, physics, and chemistry are all employed in all aspects of ICT, including gathering data, simulating biological processes, and visualizing the system as a whole.

Despite the advances, considerable challenges remain in realizing the full potential of personalized medicine, including creating a greater awareness among global stakeholders. Initiatives in Europe, including the UK's Stratified Medicine Innovation Platform, Sweden's Biobank Program, BIOMEDREG in the Czech Republic, and the Munich Biotech Cluster in Germany, are working toward this goal, but the efforts are still modest. Our conference aims to highlight the current activities, along with future possibilities, to a broader audience. Overcoming identified obstacles to making personalized medicine more available for patients requires a focus on basic, translational, and regulatory science, especially in the areas of ethical, legal, and social issues. Improvement in patient care must remain a priority throughout the collection and use of information on an individual patient's genome and its downstream products including transcriptomes, proteomes, and metabolomes. This will require a significant exploration of strategic relationships between all interested parties with proposals for further interdisciplinary collaborations involving mathematics, physics, chemistry, and ICT.

Connecting high-quality trans-disciplinary scientists through programs such as COST can support capacity building and increase the impact of personalized medicine research on regulatory bodies, decision makers, pharmaceutical companies, and payers. Such collaborations could enable breakthrough scientific developments, lead to new concepts and products, and contribute to Europe's strength in research and innovation, while reforming the health care system. With this vision in mind, the Chairs of the COST Domains of ICT, Biomedicine and Chemistry used their privileged positions to gather their corresponding scientific communities together with science policy makers (António Correia de Campos MEP – European Parliament, Irene Norstedt – European Commission, Stavros Malas – Minister of Health of Cyprus) and patients' associations (Mary Baker – former President of European Parkinson Disease Association) for the upcoming conference. We believe the three domains have succeeded in putting together the necessary stakeholders to prepare the ground for significant advancement in science and technology, and for critical influence on science policy. The success in attracting such a significant and diverse cadre of policy makers, patients, and top scientists is the full justification for another conference on personalized medicine. The conference will take place from June 17 to 22, 2012 at Golden Bay Beach Hotel in Larnaca, Cyprus (http://www.cost.eu/events/pemed). This event will be not only published in proceedings but will also be featured on YouTube.

Soulla Louca

COST DC Information and Communications Technologies

Roland Pochet

COST DC Biomedicine and Molecular Biosciences

Dieter Schinzer

COST DC Chemistry and Molecular Sciences and Technology

Programme

Day 0 | Sunday 17 June 2012

14:00 – 18:00	Arrival at Larnaca airport
16:30 – 19:30	Registration at the COST desk
19:30 – 22:00	Welcome cocktail and dinner

Day 1 | Monday 18 June 2012

08:30 – 09:00	Registration at the COST desk (latecomers)	
09:00 – 09:50	**Conference Opening**	
09:00 – 09:05	**Soulla Louca** *(5')*	Conference Chair / Chair of the COST Domain Committee for Information and Communication Technologies (ICT) / Associate Professor, University of Nicosia, CY
09:05 – 09:10	**Vassilios Tsakalos** *(5')*	Director General, Research Promotion Foundation, CY
09:10 – 09:25	**Stavros Malas** *(15')*	Minister of Health, CY
09:25 – 09:40	**António Correia de Campos** *(15')*	MEP and Science and Technology Options Assessment (STOA) Panel chair, European Parliament
09:40 – 09:50	**Primož Pristovšek** *(10')*	Vice-President, COST Committee of Senior Officials
09:50 – 10:20	Coffee break	
10:20 – 12:40	**Session 1: Research Challenges and Future Strategies**	
	Chair: António Correia de Campos	MEP and Science and Technology Options Assessment (STOA) Panel chair, European Parliament
10:20 - 10:40	**Morag Park** *(20')*	Scientific Director, Institute of Cancer Research, Canadian Institutes of Health Research, CA Personalised Medicine Research and Canada
10:40 – 11:20	**Irene Norstedt** *(30'+10')*	Deputy Head of Unit, Unit F.5: Personalised medicine, Directorate F – Health, DG Research and Innovation, European Commission Personalised Medicine Research at European level
11:20 – 12:00	**Mary Baker** *(30'+10')*	President, European Brain Council, UK Perception of what personalised medicine is as seen by patient organisations
12:00 – 12:40	**Jacques Haiech** *(30'+10')*	Professor, University of Strasbourg, FR Education and Personalised Medicine: The challenge
12:40 – 14:00	Lunch	
14:00 – 16:00	**Session 2: Empowering the Patients**	
	Chair: Roland Pochet	Conference Vice-Chair / Chair of the COST Domain Committee for Biomedicine and Molecular Biosciences (BMBS) / Professor, Université libre de Bruxelles, BE
14:00 – 14:40	**Michael Strupp** *(30'+10')*	Professor, Ludwig-Maximilians-University Munich, DE How to improve the diagnosis and treatment of patients with vertigo and dizziness: The German Vertigo Center

14:40 – 15:20	**Jonathan Knowles** *(30'+10')*	Professor, Ecole Polytechnique Fédérale de Lausanne (EPFL), CH / Institute for Molecular Medicine Finland (FIMM), FI The Molecular Personalization of Medicine: Future vision or immediate necessity?
15:20 – 16:00	**Adriano Henney** *(30'+10')*	Program Director, German Virtual Liver Network Lecture title TBA
16:00 – 16:30	Coffee break	

16:30 – 17:45 **Roundtable Discussion with Stakeholders**

Chair: Constantinos N Phellas	Vice Rector for Faculty & Research, President of the Cyprus Sociological Association, CY
Aleksandar Dimovski	Dean, University St Cyril and Methodius, F.Y. Republic of Macedonia
Jacques Haiech	Professor, University of Strasbourg, FR
Jonathan Knowles	Professor, Ecole Polytechnique Fédérale de Lausanne (EPFL), CH / Institute for Molecular Medicine Finland (FIMM), FI
K.C. Nicolaou	Chairman of the Department of Chemistry, The Scripps Research Institute, US
Irene Norstedt	Deputy Head of Unit, Unit F.5: Personalised medicine, Directorate F – Health, DG Research and Innovation, European Commission
Michael Strupp	Professor, Ludwig-Maximilians-University Munich, DE
Albrecht von Müller	Director, Parmenides Foundation, DE

17:45 – 19:45 **Poster Session**

Co-Chair: Roland Pochet	Professor, Université libre de Bruxelles, BE
Co-Chair: Mira Marcus-Kalish	Director for International Research, Tel Aviv University, IL

20:00 – 22:00 Dinner and poster prize award

Day 2 | Tuesday 19 June 2012

09:00 – 12:50 **Session 3: ICT in action in Personalised Medicine**

	Chair: Soulla Louca	Associate Professor, University of Nicosia, CY
09:00 – 09:40	**Richard Frackowiak** *(30'+10')*	Head of the Department of Clinical Neurosciences, Le Centre hospitalier universitaire vaudois (CHUV), CH Lecture title TBA
09:40 – 10:20	**Hans Lehrach** *(30'+10')*	Director, Max Planck Institute for Molecular Genetics, DE The future of medicine
10:20 – 11:00	**María Berdasco** *(30'+10')*	Associate Researcher, Bellvitge Biomedical Research Institute (IDIBELL), ES Cancer Epigenetics
11:00 – 11:30	Coffee break	
11:30 – 12:00	**Christos A. Nicolaou** *(20'+10')*	Principal Research Scientist, Global Scientific Informatics, Eli Lilly and Company, US Evolving Approaches to Drug Selectivity and Designed Polypharmacology

12:00 – 12:30	**Cristiana Pavlidou** *(20'+10')*	GOLDEN HELIX Institute of Biomedical Research, GR Development of centralized National Genetics databases and their implications for personalized medicine
12:30 – 12:50	**Christos Kannas** *(15'+5')*	Special Scientist, University of Cyprus, CY Towards a modular Web-based Workflow environment for enabling large scale Virtual Screening in Cancer Chemoprevention Research
13:00 – 14:30	Lunch	
14:30 – 18:20	**Session 4: Natural Products as a Source for New Drugs**	
	Chair: Dieter Schinzer	Conference Vice-Chair / Chair of the COST Domain Committee for Chemistry and Molecular Sciences and Technologies / Professor, Otto-von-Guericke University Magdeburg, DE
14:30 – 15:30	**Maurizio Botta** *(45'+15')*	Professor, University of Siena, IT Three different approaches to target the T315I mutation: ATP-competitive, ATP-non-competitive and 14-3-3 inhibitors
15:30 – 16:30	**Jef De Brabander** *(45'+15')*	Professor, UT Southwestern Medical Center, US Natural Products: An Opportunity for Discovery
16:30 – 17:00	Coffee break	
17:00 – 17:20	**Andrea Danani** *(15'+5')*	Professor, University of Applied Sciences of Southern Switzerland, CH System Information Therapy and Personalized Medicine
17:20 – 17:40	**Yannis Missirlis** *(15'+5')*	Professor, University of Patras, GR All the appropriate signals are necessary for engineering proper tissues
17:40 – 18:00	**Andreani Odysseos** *(15'+5')*	Director of Biomedical Research, EPOS-Iasis, R&D, CY γ-Tocotrienol, a nutrient-derived natural product, induces differential modulation of the therapeutic efficacy of anti-EGFR Tyrosine Kinase Inhibitors
18:00 – 18:20	**Harald Schmidt** *(15'+5')*	Professor, Maastricht University, NL Personalised cardiovascular medicine: From antioxidants to validated molecular sources and targets of oxidative stress
19:00 – 21:00	Dinner	
21:00 -	**Evening lecture: K.C. Nicolaou**	Chairman of the Department of Chemistry, The Scripps Research Institute, US Molecules that Changed the World

Day 3 | Wednesday 20 June 2012

09:00 – 15:30	**Session 5: Constellation Thinking in the Diagnosis and Therapy**	
	Chair: Srecko Gajovic	Editor-in-Chief Croatian Medical Journal / University of Zagreb, HR
09:00 – 09:40	**Stephane Berghmans** *(30'+10')*	Head of Unit , European Medical Research Councils (EMRC), European Science Foundation, FR Personalised Medicine for the European citizen - an ESF Forward Look
09:40 – 10:20	**Anne Bruinvels** *(30'+10')*	CEO, Elixior Ltd, UK Personalised Medicine: The Future is Now
10:20 – 11:00	**Ursula Gundert-Remy** *(30'+10')*	Federal Institute for Risk Assessment, DE The choice of the right drug and the choice of the right dose

11:00 – 11:30	Coffee break	
11:30 – 12:10	**Barbara Prainsack** *(30'+10')*	Professor, Brunel University London, UK Personalised Medicine and the Citizen: A Participatory Turn in Health?
12:10 – 13:10	**Albrecht von Müller** *(45+15')*	Director, Parmenides Foundation, DE Constellatory diagnostics
13:10 – 14:30	Lunch	
14:30 – 14:50	**Maria Laura Bolognesi** *(15'+5')*	Associate Professor, University of Bologna, IT Styrylquinolines as amyloid chemical probes and theranostics in Alzheimer's and prion diseases
14:50 – 15:10	**Darko Bosnakovski** *(15'+5')*	Assistant Professor, University "Goce Delcev" Stip, former Yugoslav Republic of Macedonia Gene corrected FSHD-IPS cells, once step closer to cell therapy for Facioscapulohumeral muscular dystrophy
15:10 – 15:30	**Marija Krstic-Demonacos** *(15'+5')*	Lecturer, University of Manchester, UK Dynamic Modelling for Personalised Cancer Care
16:00 – 19:00	Excursion / Beach volleyball	
19:30 – 22:00	Dinner at Ouzeri Tavern	

Day 4 | Thursday 21 June 2012

09:00 – 13:10	**Session 6: Personalised health**	
	Chair: Dina Simunic	University of Zagreb, HR
09:00 – 09:40	**Davor Milicic** *(30'+10')*	University of Zagreb, HR Lecture title TBA
09:40 – 10:20	**Kamran Sayrafian** *(30'+10')*	National Institute of Standards and Technology (NIST), US Personalised Health: An ICT Perspective
10:20 – 11:00	**Dina Simunic** *(30'+10')*	University of Zagreb, HR Wireless in-body positioning methods for personalized medicine
11:00 – 11:30	Coffee break	
11:30 – 12:00	**Paul Mitcheson** *(20'+10')*	Senior Lecturer, Imperial College London, UK Energy harvesting in health care applications
12:00 – 12:30	**Emmanuel Mikros** *(20'+10')*	University of Athens, GR Metabonomics: A new tool in diagnosis and personalised medicine
12:30 – 12:50	**Saulius Klimasauskas** *(15'+5')*	Head of Department, Insitute of Biotechnology, Vilnius University, LT Chemo-enzymatic approaches to genome-wide profiling of cytosine modifications
12:50 – 13:10	**Alain van Gool** *(15'+5')*	Coordinator for Personalised Medicine, Netherlands Organization for Applied Scientific Research (TNO), NL Towards Personalised Medicine in Metabolic Disease
13:10 – 14:30	Lunch	
14:30 – 18:00	**Session 7: New Targets and Inhibitors Based on Epigenetics**	
	Chair: Dieter Schinzer	Professor, Otto-von-Guericke University Magdeburg, DE
14:30 – 15:30	**Wim Vanden Berghe**	Professor, University of Antwerp

	(45'+15')	Epigenomic profiling of phytochemical effects in cancer-inflammation and cardiovascular disease: challenges & pitfalls
15:30 – 16:30	**Arasu Ganesan** *(45'+15')*	Professor, University of East Anglia, UK Natural Products and Epigenetic Drugs
16:30 – 17:00	Coffee break	
17:00 – 18:00	**Manfred Jung** *(45'+15')*	Professor, University of Freiburg, DE Epigenetics and available epigenetic drugs: An overview
18:00 – 18:30	**Closing session: Conference wrap-up**	
	Chair : Mira Marcus-Kalish	Director for International Research, Tel Aviv University, IL
	Soulla Louca	Conference Chair / Chair of the COST Domain Committee for Information and Communication Technologies (ICT) / Associate Professor, University of Nicosia, CY
	Roland Pochet	Conference Vice-Chair / Chair of the COST Domain Committee for Biomedicine and Molecular Biosciences (BMBS) / Professor, Université libre de Bruxelles, BE
	Dieter Schinzer	Conference Vice-Chair / Chair of the COST Domain Committee for Chemistry and Molecular Sciences and Technologies / Professor, Otto-von-Guericke University Magdeburg, DE
20:00 – 23:00	Conference dinner	

Day 5 | Friday 22 June 2012

08:00 – 10:00	Breakfast and departure

Invited Speakers, Roundtable Participants, Session Chairs and Organising Committee Members

Dr Mary Baker

Position President

Organisation European Brain Council

Town Woking

Country United Kingdom

E-mail bobandmary@btinternet.com

Biography Mary Baker, MBE, is President of the European Brain Council, immediate past President of the European Federation of Neurological Associations, Consultant to the World Health Organisation (WHO) and Chair of the Working Group on Parkinson's Disease formed by the WHO in May 1997.

In 2008 the Council of Europe re-appointed Mary for a second term until March 2012 as one of the patient representatives to serve on the Management Board of the European Medicines Agency (EMA), and in the same year she was appointed to the IMI JU Scientific Committee. In 2007 Mary was appointed to the Council of the Association of the British Pharmaceutical Industry (ABPI) and also a Member of the ABPI Code of Practice. Other significant appointments include Director at Large for the World Stroke Association, former patient editor of the British Medical Journal (BMJ).

In June 2011 Mary joined the Ethical Issues sub committee of the Faculty of Pharmaceutical Medicines for a period of three years and in July 2011 was invited to become a member of the Network of Global Agenda Councils for a term of one year. In 2009 Mary received the prestigious British Neuroscience Association Award for Outstanding Contribution to British Neuroscience and for Public Service.

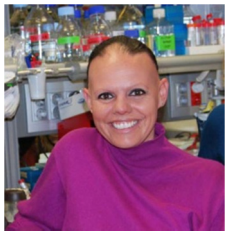
Mary is a Patron of the European Parkinson's Disease Association (EPDA) and the former past President of EPDA, a position to which she was elected in 1992 when the EPDA was first formed. Mary retired as Chief Executive of the Parkinson's Disease Society of the United Kingdom in 2001 where she had worked for 18 years.

Abstract **Perception of what personalised medicine is as seen by patient organisations**

Personalised Medicines – Society's Perspective

Today clinicians diagnose and treat based on symptoms and a subjective interpretation of symptoms. In the future, the clinicians will diagnose and treat based on biology and select medication based on an objective evaluation of the benefit/risk for the individual patient.

This is an exciting step forward but will be very dependent upon the ability to communicate to general society the understanding of benefit/risk. We should build the doctor/patient relationship in order that decisions can be taken jointly by the patient and the clinician, thereby increasing the responsibility of society in its management of health.



Dr María Berdasco

Position Senior Researcher

Organisation Bellvitge Biomedical Research Institute (IDIBELL)

Department Cancer Epigenetics and Biology Program (PEBC)

Town L'Hospitalet de Llobregat- Barcelona

Country Spain

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Biography Dr María Berdasco (Luarca, Asturias, Spain, 1978) is a senior researcher in the Cancer Epigenetics and Biology Program (PEBC) at IDIBELL (Barcelona, Spain) and has been trained on epigenetics during the last decade. She graduated in Molecular Biology with Honors from the Universidad de Oviedo in 2001, where she also obtained her Ph.D degree specializing in plant epigenetics in 2005. Her stay at the Spanish National Cancer Research Center (CNIO, Madrid) during four years (2004-2008) and the actually position at PEBC-IDIBELL allows her to work with the state-of-the-art technology in the field of Epigenetics. Furthermore, she is involved in the coordination of international research consortia of several European projects, covering funding schemes from the Cooperation Scheme in FP6 and FP7 to COST actions as well as various other privately funded endeavors and Spanish Programs (FIS). She is also a member of the Ethical Committee of the IDIBELL. Her current research is devoted to the establishment of the epigenome maps of normal and transformed cells, the study of the interactions between epigenetic modifications and non-coding RNAs, and the development of new epigenetic drugs for cancer therapy.

Abstract **Cancer Epigenetics**

Initially, cancer was thought to be solely a consequence of genetic changes in key tumor-suppressor genes and oncogenes that regulate cell proliferation, DNA repair, cell differentiation, and other homeostatic functions. However, recent research suggests that these alterations could also be due to epigenetic disruption. The study of epigenetic mechanisms in cancer, such as DNA methylation, histone modification, nucleosome positioning and micro-RNA expression, has provided extensive information about the mechanisms that contribute to the neoplastic phenotype through the regulation of expression of genes critical to transformation pathways. Regarding DNA methylation, the low level of CpG methylation in tumors compared with that in their normal-tissue counterparts and the hypermethylation of the CpG islands in the promoter regions of tumor-suppressor are accepted as being a common feature of human cancer. Due to the complexity of permutations and combinations, less is known about the patterns of histone modification disruption in human tumors. Results have shown that the CpG promoter hypermethylation event in tumor-suppressor genes in cancer cells is associated with a particular combination of histone markers and the opposite of that observed in normal cells. Aberrations in the epigenetic profiles, with respect to DNA methylation and histone modifications, could also be a consequence of genetic disruption of the epigenetic machinery, such as disruption of the histone methyltransferase NSD1 in neuroblastomas or mutations in the histone deacetylase HDAC2 in colon cancer. The deregulation of miRNA expression has also been linked to tumor progression. Changes in miRNA expression in cancer can be achieved through various mechanisms, including impairment of miRNA processing machinery, such as the recently identified mutations of TRBP2 (an essential functional partner of the DICER1 complex) in sporadic and hereditary carcinomas with microsatellite instability or by CpG hypermethylation of miRNas with tumor-suppressor properties. The possibility of “resetting” the abnormal cancer epigenome by applying pharmacologic or genetic strategies will be also discussed.

Dr Stephane Berghmans

Position Head of Unit

Organisation European Science Foundation

Department European Medical Research Councils

Town Strasbourg

Country France

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Biography Stephane Berghmans is a Doctor in Veterinary Medicine who obtained his Ph.D. studying

epigenetic mechanisms of inheritance and developing expertise in genetics and molecular biology at the University of Liege (Belgium). He then became a postdoctoral fellow at Harvard Medical School in Prof. Thomas Look's laboratory, Dana Farber Cancer Institute, where he established zebrafish as a model organism to study cancer. Seeing the opportunity for a more direct application of zebrafish in drug discovery, he moved to the biotech sector and joined DanioLabs (Cambridge, UK) in 2004 where he headed development, implementation and automation of zebrafish drug discovery and liability assays for early in vivo compound screening. He moved to Portland (Oregon, USA) in 2008 where he joined Znomics as Director of Biology, installing new research teams and facilities. Rich from a strategic experience in the private sector and interested in science policy, he joined the European Science Foundation in June 2009 as Head of the Biomedical Sciences Unit. In this position he manages the secretariat general for the European Medical Research Councils (EMRC) with activities spanning from science management to scientific networks and a very strong emphasis on science policy and strategy.

Abstract **Personalised Medicine for the European citizen - an ESF Forward Look**

In recognizing the importance of Personalised Medicine the European Medical Research Councils (EMRC) commissioned a Forward Look to gain insight into the needs for research programmes and infrastructures, policy and education. Forward Looks are foresight exercises that enable Europe's scientific community, in interaction with policy makers, to develop medium- to long-term views and analyses of future research developments with the aim of defining research agendas at national and European level. The challenges ahead are significant, and it is becoming clear that biological systems operate in a far more complex way that we might have previously thought. Nevertheless this approach is starting to yield results and it is predicted that these technologies will generate innovative therapies, limit adverse effects of treatments, increase the quality of clinical care, create an optimal fit between a patient and a treatment, and decrease the costs of healthcare. But Personalised Medicine will have a broader impact on society as increased transparency of individual biological inequalities will affect basic issues such as risk, responsibility, and solidarity, raising complex social and ethical questions. For these reasons the Forward Look is a collaborative effort between all Standing Committees under the auspices of the European Science Foundation (ESF): Life, Earth & Environmental Sciences (LESC); Humanities (SCH); Social Sciences (SCSS); and Physics & Engineering (PESC). The overall aim of this Forward Look is to analyse in a systematic way the complex and constantly moving field of personalised medicine to provide timely policy advice that will help prepare Europe for the likely changes in how society deals with health and disease. The final stakeholder conference will have taken place in April 2012 to finalise and prioritise recommendations to be published in a final report with a launch in summer 2012.

Prof. Maurizio Botta

Position Professor

Organisation University of Siena

Department Dipartimento Farmaco Chimico Tecnologico

Town Siena

Country Italy

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Biography Prof. Maurizio Botta, PhD (U.N.B. – Canada) is full Professor of Medicinal Chemistry at the Faculty of Pharmacy, University of Siena, from November 1st 2009 is Dean of the same Faculty of Pharmacy and, from January 1st 2008, Adjunct Professor in Temple University's College of Science and Technology, in the Department of Biology, Philadelphia (USA). From November 2002 to October 2008 has been Head of the Dipartimento Farmaco Chimico Tecnologico of the University of Siena.

EU expert for reviewing projects belonging to the TMR research program, for the Mid-Term review of the approved TMR projects. He is Executive Guest Editor of "Current

Pharmaceutical Design" in the field of Anti-Angiogenesis Agents, EU expert in the panel "Quality of Life" for reviewing projects belonging to the "Life sciences, genomics and biotechnology for health" research program. Projects reviewer for Italian and Slovenian Research Projects, for the Austrian Research Fund (Wissenschaftsfonds-FWF), for the Cancer Research UK Programme and actually for "Fondazione Roma", for the French National Research Agency and for Italian Ministery for the Economic Development. He is Member of the Editorial Board for "ChemMedChem" (Wiley), from January 2008 Member of the Editorial Advisory Board for "Journal of Medicinal Chemistry" and from January 2010 Member of the Editorial Advisory Board for "Medicinal Chemistry Letters" (ACS).

He is member of the "Società Chimica Italiana" from 1976, member of the American Chemical Society from 1984 and of the QSAR Society from 1997 and, from 1998 to 2004, he was member of the "Direttivo della Divisione di Chimica Farmaceutica della Società Chimica Italiana". He was Chairman of 18 scientific schools and meetings, among which Schools of Synthetic Methodologies in Medicinal Chemistry of SCI and European Workshops in Drug Design and in Drug Synthesis, of European COST Meetings, of the "Twelfth FeCheM – conference on Heterocycles in Bio-Organic Chemistry", "ACS EFMC Frontiers in CNS & Oncology Medicinal Chemistry", "1st iDDi Workshopon Neglected and Orphan Diseases" held at University of Siena; he was co-Chairman at the Conference "3rd IUPAC-2002 International Symposium on the Chemistry of Natural Products", Firenze. Since 1998, he has contributed to the organization of more than 80 scientific seminars at the Dipartimento Farmaco Chimico Tecnologico of Siena University.

He carries out reviewing activity for well know journals in organic and medicinal chemistry, received five Merck Research Laboratories Awards "Academic Development Program in Chemistry" (1996, 1997, 1998, 2001, and 2002).

Since 1988, Prof. Botta is the owner of research funds granted by University, MIUR, CNR, EU, and Pharmaceutical Companies. Professor Botta is the author of more than 350 papers, 9 publications on volumes, 14 patents and more than 150 proceedings at congresses.

His main research areas include chemical studies on beta-lactam antibiotics; total synthesis and structure determination of biologically active natural products; synthesis of pyrimidine derivatives as antiviral and antitumor agents.

The following methodologies have been used in such studies: classical methodologies for organic synthesis, methodologies for the solid phase synthesis of small molecules, use of enzymes, microwave and parallel synthesis; structural studies of biological macromolecules (enzymes, receptors, growth factors), studies about structure-function relationship of lypases, molecular modeling application on medicinal subjects; Virtual Library Design.

Abstract **Three different approaches to target the T315I mutation: ATP-competitive, ATP-non-competitive and 14-3-3 inhibitors**

A serious problem in the treatment of Chronic Myeloid Leukemia (CML) is represented by the development of resistance to Imatinib (IM, Gleevec®), which is currently used in frontline therapy. The insurgence of drug-resistance, especially in the advanced phases of the disease, can be caused by both Bcr-Abl-dependent mechanisms (e.g. mutation in the kinase domain of the enzyme, Bcr-Abl gene amplification) and Bcr-Abl-independent mechanisms (e.g. Src family kinase activation). As a consequence, there is a growing interest in developing novel TK inhibitors able to target IM-resistant forms of CML, especially the T315I mutant. The application of molecular modeling and combinatorial techniques led our Research Group to the identification of three different families of compounds active on three different targets: 1) The ATP binding site of the Bcr-Abl T315I mutant[1]; 2) the myristate binding pocket of Bcr-Abl[2] and 3) the 14-3-3 σ protein.[3] While coumpounds active on the first two targets represent valuable inhibitor of IM-resistant Bcr-Abl-dependent forms of leukemia, 14-3-3 σ inhibitors could allow to overcome Bcr-Abl-dependent and -independent form of resistance targeting an alternative pathway involved in the regulation of the causative events of CML. The successful application of these three approaches for the inhibition of the T315I Bcr-Abl mutant will be discussed.

Santucci, M. A.; Corradi, V.; Mancini, M.; Manetti, F.; Radi, M.; Schenone, S.; Botta, M. "C-6 Unsubstituted Pyrazolo[3,4-d]Pyrimidines are Dual Src/Abl Inhibitors Effective Against Imatinib Mesylate-Resistant Chronic Myeloid Leukemia, Including that Arising from T315I Mutation." ChemMedChem 2009, 4, 118-126.

Radi, M.; Crespan, E.; Falchi, F.; Bernardo, V.; Zanoli, S.; Manetti, F.; Schenone, S.; Maga, G.; Botta, M. "Design and synthesis of new thiadiazoles and thiazoles targeting the Bcr-Abl T315I mutant: from docking false-positive to ATP non-competitive inhibitors" ChemMedChem 2010, 5, 1226-1231. b) Crespan, E.; Radi, M.; Zanoli, S.; Schenone, S.; Botta, M.; Maga, G. "Dual SRC and ABL inhibitors target wild type ABL and the ABLT315I imatinib-resistant mutant with different mechanisms" Bioorg. Med. Chem. 2010, 18, 3999-4008.

Corradi V, Mancini M, Manetti F, Petta S, Santucci MA, Botta M. "Identification of the first non-peptidic small

molecule inhibitor of the c-Abl/14-3-3 protein-protein interactions able to drive sensitive and Imatinib-resistant leukemia cells to apoptosis." Bioorg. Med. Chem. Lett. 2010, 20, 6133-6137.

Dr Anne Bruinvels

Position CEO

Organisation Elixior Ltd

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Country United Kingdom

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Biography Anne Bruinvels is heading Elixior, an advisory company focused on the development and growth of innovative personalized medicine businesses. Also, she recently founded Px HealthCare, a company aiming to provide online and mobile personalized healthcare support to people with (or at risk of) chronic diseases.

Previously, Anne established Curidium, a personalized medicine company focused on identifying companion diagnostics and therapeutics to treat patients with central nervous system disorders more effectively. She started Curidium's business activities in 2001 and raised several rounds of angel funding before taking the company public on the AIM of the London Stock Exchange in 2006. Anne was Curidium's CEO until late 2007, when she took on the role of Chief Scientific Officer. In March 2009, Curidium was sold to Avacta Group plc., UK-based diagnostic services provider.

Prior to founding Curidium, Anne was Scientific Director, Business Development at Pharmagene (now Asterand), where she contributed to the growth of the organisation from private start-up to publicly listed biotechnology company. Previously, she has led research groups, as Head of Neurogenetics, SmithKline Beecham Pharmaceuticals (now GlaxoSmithkline) and as Head of Neuroanatomy and co-leader of global schizophrenia research at Wyeth. Anne was awarded a PhD scholarship at Sandoz Pharma (now Novartis) and obtained her PhD (neuroscience) from Utrecht University (the Netherlands). She was presented with the London Biotechnology Network "Young Entrepreneur of the Year Award" in 2003.

Abstract **Personalized Medicine: The Future is Now**

Ask a physician what is personalized medicine and he or she will most likely answer: "That's the medicine I practice each day." Physicians will always try to give each patient the treatment that is best for them. However, given that personalized medicine takes into account genetic and biological patient information to select the most appropriate treatment regimen for a patient, only a handful of personalized drug therapies have recently come on to the market.

This talk will outline the hurdles that personalized medicine needs to overcome, including scientific, development, regulatory and reimbursement issues, as well as the grand medical possibilities that may lay ahead of us. Oncology, being the therapeutic area most advanced in applying personalized medicine, will be exemplified. Furthermore, the role of the empowered patient in making personalized healthcare a reality will be discussed.

Prof. Jef De Brabander

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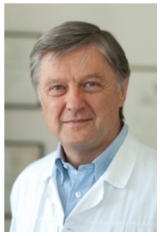
Biography Jef K. De Brabander is a native of Belgium where he pursued his undergraduate and graduate studies at the University of Ghent (with Prof. M. Vandewalle, Ph.D. 1993). Following postdoctoral studies with the late Wolfgang Oppolzer at the University of Geneva (94-95) and Paul Wender at Stanford University as a NATO and Fulbright-Hays fellow (95-96), he began his independent career as a junior faculty member at the University of Geneva. In 1998, he was recruited to the Department of Biochemistry at the University of Texas Southwestern Medical Center at Dallas, where he was promoted to Full Professor in 2007 and appointed Co-Director of the “Chemistry and Cancer Scientific Program” of the Simmons Comprehensive Cancer Center. He was an Alfred P. Sloan Foundation Fellow (2001-03), received the “Journal Award” from the editorial boards of Synlett and Synthesis (2006) and an Academic Development Award from the Chemistry Council of Merck Research Laboratories (2004-08), and is serving on the Scientific Advisory Board of Reata Pharmaceuticals, a company he co-founded. Jef was a chartered member of the National Institutes of Health Study Section (2007-2011), the Chair of the 51st Gordon Research Conference on Natural Products (Tilton, New Hampshire, July 2010) and the ESF-COST conference on Natural Products Chemistry, Biology and Medicine III (Maratea, Italy, September 2010).

Abstract **Natural Products: An Opportunity for Discovery**

Our laboratory focuses on the synthesis of complex molecular architectures. Synthetic targets include both designed and naturally occurring substances with novel structural features and interesting biological function. To facilitate the execution of efficient and practical syntheses, we also develop novel methodology towards functionality found in complex natural products. Taking advantage of the multi-disciplinary research environment at UT Southwestern, we integrate our synthetic program with molecular pharmacology, biochemistry, and cancer biology. Our group also collaborates on various biomedical research projects including the discovery of novel small-molecule activators of programmed cell death (apoptosis), orexin receptor agonists for the treatment of narcolepsy, and antitumor agents that target the tumor micro-environment.



Prof. Richard Frackowiak

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Biography Richard Frackowiak is Professor and head of the Department of Clinical Neurosciences at the Université de Lausanne (UNIL) and its Centre Hospitalier Universitaire Vaudois (CHUV). He is a co-director of the proposed EU Human Brain Project.

Formerly Foundation Professor of Cognitive Neurology at University College London (UCL),

Director of the Department of Cognitive Studies (DEC) at the Ecole Normale Supérieure in Paris, Wellcome Trust Principal Clinical Research Fellow and Vice-Provost of UCL and Dean-Director of its Institute of Neurology. He founded the Wellcome Department of Imaging Neuroscience in 1994.

Professor Frackowiak has an MA and MD from Cambridge (Peterhouse), a DSc from London University, an honorary medical doctorate from Liege University and an honorary professorship from UCL. A Fellow of the Academies of Medical Sciences of the UK, France and Belgium, he is a member of the Academia Europaea and a foreign associate of the Institute of Medicine of the American Academies. He has served as president of the British Neuroscience Association and the European Brain and Behaviour Society.

He is scientific advisor to the Director-General of INSERM. He has held prestigious visiting professorships, a chaire d'excellence from the Agence Nationale de Recherche, editorships and international society roles worldwide. He has always shown a commitment to Europe and had many advisory positions in the context of FP5 through to the present, including chairmanship of the European Research Council (ERC) starting grants committee in Life Sciences.

His interest is in human brain structure and function relationships in health and disease. He has recently moved to a more translational strategy in research by using novel image classification techniques. His scientific output is highly cited with an h-index of 144. He has won the Ipsen, Wilhelm Feldberg and Klaus Joachim Zulch prizes.

Abstract **From group to individual studies with imaging – examples from dementia**

We now know that a single gene mutation may present with multiple phenotypes, and vice versa, that a range of genetic abnormalities may cause a single phenotype. As a result, our traditional approach to determining disease nosology – eliciting symptoms and signs, creating clusters of like individuals and then defining a disease on those criteria - though it has served medicine and therapeutics well in the last century and a half, is now outdated. Under that traditional model, the collection of data is subjective, depending as it does on patient-doctor interactions, and that may be why it has not generated fundamental breakthroughs in our understanding of the pathophysiology of psychiatric and neurological diseases.

What lies ahead? It is time to radically overhaul our epistemological approach to brain disease. We now know a great deal about brain structure and function. From genes, through functional protein expression, to cerebral networks and functionally specialised areas defined via physiological cell recording and microanatomy, we have accumulated a mass of knowledge about the brain that defies easy interpretation. Advances in information technologies, from supercomputers to distributed and interactive databases, now make integration of very large and diverse datasets and advanced data-led analysis possible.

The application of modern computerized automated techniques for analyzing structural and functional brain images are leading to real advances in the application of advanced neuroimaging to clinical practice in ways undreamed of only a short time ago. One major advance is the development of image classification techniques that put diagnosis of the individual at the centre of the enterprise. Another is the application of data-mining techniques to help classify patients according to disease mechanisms rather than simple phenomenology. Finally multi-modal and multi-modal imaging approaches are leading to a redefinition of the dementias in terms of brain system diseases. These ideas will be illustrated with reference to the human dementias. These will serve as exemplars of the new nosology, which will be brought about by new mathematics, high performance computing and by federation of existing and future clinical and neuroscientific data.

Prof. A. Ganesan

Position Professor

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Biography Prof. Ganesan obtained a BSc (Hons) in Chemistry at the National University of Singapore (1986). He did his PhD in synthetic methodology and total synthesis under the supervision of Clayton Heathcock at the University of California-Berkeley (1992) followed by a postdoctoral stint with Gregory Verdine at Harvard University. In 1993, he joined the Institute of Molecular and Cell Biology in Singapore as a Senior Research Chemist at the Centre for Natural Product Research and in 1996 became Principal Investigator of the Institute's Medicinal and Combinatorial Chemistry group. In 1999 he joined the University of Southampton as a Reader in the Combinatorial Chemistry Centre for Excellence. In 2011 he became the Chair of Chemical Biology at UEA's School of Pharmacy.

Abstract **Natural Products and Epigenetic Drugs**

Historically, natural products have been an important source of drugs either as crude extracts or in purified form. Nevertheless, the screening of natural products has been downsized in the pharmaceutical industry. The presentation will discuss the unique chemical space occupied by natural products compared to synthetic compounds and their favourable physicochemical properties. Examples will be provided of natural product inhibitors of epigenetic enzymes and SAR studies by total synthesis.

Prof. Ursula Gundert-Remy

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Biography Prof. Ursula Gundert-Remy has studied human medicine. After her doctorate she underwent postdoctoral training in pharmacology and toxicology as well as in internal medicine. At the academic level she progressed by becoming the "habilitation". After finishing training, she became the head of the medical reviewers in the former Federal Health Office in Berlin, Germany, for 9 years. Thereafter she returned to academia and became full professor and chair holder in Clinical Pharmacology at Goettingen University, Germany. The last 12 years before her retirement, Prof. Gundert-Remy was the chair of the Department of Safety of Substances and Products at the Federal Institute for Risk Assessment. Prof. Gundert-Remy is now Guest Professor at Charité, the Medical Faculty in Berlin, Germany and Guest Scientist in the Federal Institute for Risk Assessment.

Prof. Gundert-Remy was continuously working in the field of pharmaco-/toxicokinetics and -dynamics using different approaches, among them modelling to enable prediction of effects and to elucidate mechanisms.

Abstract **The choice of the right drug and the choice of the right dose**

The diagnosis of a disease has been based on typical signs and symptoms and on typical clinical findings. However, many diseases are rather heterogeneous concerning the underlying cause and hence, the disease progression and the selection of the appropriate treatment should be tailored according to the subtype present in a particular patient. Subtypes of a disease have been identified on clinical findings. However, identification of the molecular disease mechanisms allows specific subtyping and provides a handle for predicting the course of the disease and the appropriate therapeutic choice. Examples are given in cardiology by subtype-specific treatment for the three most common LQT syndromes, and in oncology by the selection of the treatment regimen in breast cancer and in leukaemias.

Even with the right drug treatment the response intensity may vary individually. Genotype specific drug responses have been described as early as 1976 and the first COST Action in Biomedicine (COST B1) was devoted to the question how to identify subjects with genetically impaired drug metabolism. Several important and often used drugs such as antidepressants, clopidogrel, platelet aggregation inhibitors and also Warfarin, an

anticlotting agent are metabolized by enzymes which show genetic variants which are functionally important.

Genetic variants are not only known for CYP enzymes but also for enzymes mediating conjugation reactions and for transporters. Thus, the kinetics of the drug and its clearance depend on the activity of the genetically determined enzyme expression. Thus, the right dose for the individual patient of these drugs depends on his/her genetic makeup.

It is clear that the next generation of doctors will increasingly rely on pharmacogenetics to guide therapy.

Prof. Jacques Haiech

Position Professor

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Biography Prof. Jacques Haiech graduated in Mathematics from Orsay University, France and has obtained his PhD in Biochemistry in Montpellier with research in the fields of Calcium signaling. After a post-doctoral appointment at National Cancer Institute (NIH, Bethesda), Jacques has been recruited at CNRS (Centre national de la recherche scientifique, France). He headed the department of biochemistry and pharmacology and then moved to Marseilles in 1987. He was also visiting professor at the Vanderbilt University and then at the Northwestern University (Chicago, Michigan). He became full professor at the university of Marseille-Luminy in 1991 and moved to Strasbourg university in 1987 where he developed the first academic screening platform and headed a research institute until 2005 (Biotecthnology and Therapeutic Innovations).

He has been the executive director of the French genomic program at the ministry of research (1999-2003). He is now vice-president of the scientific council of ARIIS (the Alliance for research and innovation of health industries) in France and scientific deputy in the new French evaluation agency (AERES).

Jacques has published more than 150 papers in peer-reviews journals that have received more than 6000 citations.

He has developed several training programs in synthetic biology in Strasbourg and Paris for students in pharmacy and in school of engineers.

Abstract **Education and Personalized Medicine: The Challenge**

In this presentation, we will describe a general frame in order to anticipate the evolution of life sciences from a descriptive science to a predictive science with the emergence of systems biology and synthetic biology.

We will open a debate on the impact of such new paradigms on health research and discovery (from new therapeutic innovations to personalized medicine) and the consequences on the education of health professionals.

Ongoing pilots of innovative training programs in France will be described in order to benchmark with other pedagogical initiatives in Europe.

Dr Adriano Henney

Position Director

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Biography Dr Henney obtained a PhD in Medicine and has 23 years' research experience in cardiovascular disease in laboratories in London, Cambridge and Oxford. His interests have focused predominantly on atherosclerosis, with studies ranging from pathology, through molecular and cellular biology to molecular genetics. In 1997, he was recruited by Zeneca Pharmaceuticals from a Senior Fellowship position leading his own molecular genetics group in Oxford, to lead the exploration of new therapeutic approaches in atherosclerosis, specifically focusing on his research interests in vascular biology. Following the merger with Astra, Dr Henney moved within the newly formed company, AstraZeneca, to a position of Global Programme Manager responsible for prototyping strategic improvements to the company's approaches to pharmaceutical target identification, and the reduction of attrition in early development. This involved directing activities both across research sites and across functional project teams in the US, Sweden and the UK. The work undertaken in this Programme resulted in the creation in July 2003 of an entirely new multidisciplinary department that focused on pathway mapping, modelling and simulation. With personnel based in the UK and US, and global project interactions across all therapy areas, the work of this department supported drug projects across Research and Development. Under his leadership, the department evolved to establish the practice of Systems Biology that, together with strong relationships with key academic centres and biotechs, prototyped the application of mechanistic disease modelling approaches to the discovery of innovative new medicines. Since leaving AstraZeneca in 2009, Dr Henney has continued his interest in Systems Biology through his company, Obsidian Biomedical Consulting Ltd., helping academics to work more closely with industry. In April 2010, Dr Henney was invited to direct a, new major German national initiative in Systems Biology: the Virtual Liver Network.

Prof. Manfred Jung

Position Full Professor

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Biography Manfred Jung (1966) was educated at the Universities of Marburg, Ottawa and Münster (Ph.D. with Prof. Dr. Wolfang Hanefeld, postdoctoral studies with Prof. Dr. Tony Durst, habilitation association with Prof. Dr. Bernard Unterhalt). He is currently Professor for Pharmaceutical Chemistry at the University of Freiburg. He has published over 100 papers, holds two patents and has received the joint Medicinal Chemistry Award of the Medicinal Chemistry groups of the German Pharmaceutical Society and German Chemical Society.

His research focus is Chemical Epigenetics. The group is active in the synthesis of inhibitors of epigenetically active enzymes, both as biological tools and potential drugs. Another strong methodological focus is the development of screening assays for enzymes and their application in the search for new epigenetic modulators.

Abstract Epigenetics is defined as heritable changes in the phenotype without changes in the genetic code. The development of a complex organism requires that only a selected number of genes from the whole genome is expressed according to the cell type. The maintenance of such expression profiles upon cell division is governed by epigenetic processes such as DNA methylation and histone modifications. If we study these mechanisms we may understand their role in human disease and find new ways for treatment and stratification of patients in personalized medicine. This lecture will provide an overview of epigenetics and available epigenetic drugs. The work of our group both in the direction of drug discovery but also in the use of assays for detecting the activity of epigenetic enzymes in cells and patient samples will be presented.

Prof. Jonathan Knowles

Position Professor

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Biography Dr. Knowles was Head of Group Research and Member of the Executive Committee at Roche up to the end of 2009. He was a member of the Genentech Board for the last 12 years and a member of the Chugai Board for seven years. Dr. Knowles was also the chairman of the Corporate Governance Committee of Genentech. Prior to this he served as Director of the Glaxo Institute in Geneva for 10 years and as head of European Research for Glaxo Wellcome.

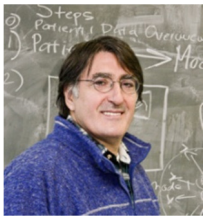
Jonathan Knowles holds a Distinguished Professorship in Personalized medicine at FIMM (Institute for Molecular Medicine Finland) at the University of Helsinki, was recently appointed Professor of Translational Medicine at EPFL in Switzerland, and has been appointed to a Visiting chair at the University of Oxford. In addition, he is a Member of the European Molecular Biology Organization and a Visiting Fellow of Pembroke College Cambridge. In 2011, Jonathan Knowles was appointed as a Trustee of Cancer Research UK, one of the world's leading Cancer Research Organisations.

Abstract **The Molecular Personalization of Medicine: Future vision or immediate necessity?**

The application of molecular "omics" to address medical questions has dramatically increased in recent years and is revolutionizing our understanding of the molecular pathology and interrelationships between different human conditions. Despite this, the number of new therapies made available each year is in relative decline and clinical practice is slow in adopting the new molecular diagnostics.

There is a growing need to reclassify human disease through new more specific molecular criteria to allow the creation of new treatments and therapies. Equally, there is a critical need to apply today's knowledge especially in the treatment of cancer patients.

The molecular personalization of Medicine is thus an immediate necessity for both basic research into disease mechanisms and for the treatment of patients today. The rational for these statements will be provided and strategies for rapid and transformational implementation will be outlined.



Prof. Hans Lehrach

Position Director

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Biography Hans Lehrach is one of Germany's foremost molecular biologists. He obtained his Ph.D. at the Max Planck Institute for Experimental Medicine and the MPI for Biophysical Chemistry in 1974. He moved on to Harvard University, Boston (1974-1978) for a postdoc and then became group leader at EMBL, Heidelberg (1978-1987). At the Imperial Cancer Research Fund, London (1987-1994) he was head of the Genome Analysis Department. He then returned to Germany to become Director at the MPI for Molecular Genetics (since 1994).

His scientific achievements are many. Highlights include his key involvement in several genome sequencing projects, such as the human, rat, and Schizosaccharomyces. His group was part of the team which identified the Huntington's disease gene. Dr. Lehrach also performed key work on technologies such as protein microarrays, protein interactome analysis, yeast artificial chromosomes and RNAseq.

Dr. Lehrach has co-founded several biotechnology companies such as Sequana Therapeutics, GPC Biotech, Scienion, Prot@gen, PSF Biotech, Atlas Biolabs, and Alacris Theranostics.

Abstract **The Future of Medicine**

The solution of many medically important problems depends primarily on being able to predict the behaviour of complex networks (e.g. the biological networks acting within a tumor, but also in the other tissues of the patient) under complex disturbances (e.g. a particular therapy). Decades of molecular cancer research, but also the recent genome revolution, have however still not been able to provide this urgently needed power to predict.

We are currently sequencing the genome and transcriptome of the tumor and the genome of the patient for individual cancer patients, as the basis of a 'virtual patient' models, which can then be used to predict effect and side effects of specific therapies on the individual patient (www.treat1000.org). In addition, we have proposed IT Future of Medicine (ITFoM), www.ITFoM.eu), with the goal to develop integrated molecular/physiological/anatomical models of every individual in the health care system, on the basis of –omics (genomics, epigenomics, transcriptomics, proteomics, metabolomics, metagenomics etc), imaging and sensor data, as the basis of a new, data rich, computation based individualised medicine of the future.

Prof. Soulla Louca

Position Associate Professor

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Biography Soulla Louca received her Ph.D. in Computer Science in 1994 from Illinois Institute of Technology in Chicago. Prior to that, she had received a B.A in Computer Science and Mathematics and a M.Sc. in Computer Science from Kalamazoo College and Western Michigan University respectively. She has participated and coordinated numerous projects including National Science Foundation (NSF-USA), Research Promotion Foundation (RPF-Cyprus) and European; has served as a reviewer for various international conferences/journals as well as an ICT expert for the European Commission. Her research interests include socio-economic aspects of Green ICT, e-learning, social integration and digital divide, and e-business Since June 2008; she is the Chair of the Domain Committee for Information Communication Technologies for COST. Dr Louca is an Associate Professor at the University of Nicosia in the Department of Management and Management Information Systems.

Abstract **Why another Conference on Personalised Medicine?**

The major obstacles for making personalized medicine available to patients requires basic, translational, and also regulatory science, especially in the areas of ethical, legal and social issues. The vision of a good healthcare system in which the patient care is consistently augmented through the use of information on the individual patient's genomes and their downstream products requires the exploration of strategic relationships among all interesting parties and constellation thinking for proposing new ways in the diagnosis and therapy of diseases integrated with a planned trans-disciplinary scientific approach involving various disciplines such as life sciences, mathematics, physics, chemistry and ICT. Connecting high-quality trans-disciplinary scientists through programs such as COST can support capacity building, and increase the impact of personalized medicine research on regulatory bodies, decision makers, pharmaceutical, insurance companies and the paying public. Such group efforts could enable breakthrough scientific developments leading to new concepts and products and thereby contribute to the strengthening of Europe's research and innovation capacity while reforming the healthcare system.

Dr Mira Marcus-Kalish

Position Director, International Research

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Biography Dr. Mira Marcus-Kalish is currently a Senior Research Fellow at ICTAF – Interdisciplinary Center for Technological Analysis and Forecasting, and the director for international research affairs at Tel Aviv University. Her main areas of interest are mathematical modelling, data Analysis, converging technologies and data mining (mainly a targeted rule discovery tool for Bio-Medicine). Recent projects focused on personalized skin treatments, rehabilitation of the discrete sensory motor learning function, cerebellar motor learning, protein- protein interactions, drug toxicity analysis, learning machine systems, smart sensors for tackling oil spill, multilevel multisource data mining applied to neurology, etc.

Mira Marcus-Kalish holds a Ph.D in operations research from the Technion, Haifa, where she developed a computerized E.C.G. diagnosis system. She did her post doctorate training at Harvard University, at the MBCRR laboratory (Molecular Biology Computer Research and Resource) and the Dana Farber Cancer Institute. Her B.Sc. is in Statistics and Biology from the Hebrew University in Jerusalem.

Coming back to Israel, she joined the Tel-Aviv University Business School, focusing on Medical informatics and management, than moved to the Weizmann Institute working with Prof. Ephraim Katzir mainly on protein interactions. She was involved at the private business enterprise and served as the scientific advisor and later as the head of the Enterprise Marketing Department in IBM Israel. Dr. Kalish is involved in many EU framework projects: ReNaChip, SkinTreat, EpoCan, HBR, etc and was the joint research

work package leader in the Nano2Life NoE (Network of Excellence).

Abstract **Simultaneous Systematic Analysis approach, an essential enabler to preventive, predictive and personalized medicine.**

The revolutionary trends in scientific health care research have provided new and profound insights into the human body functioning in its surroundings enabling various degrees of sensitivity.

The goal is to enable the “whole approach” - a simultaneous systematic analysis providing the broad insight on various phenomena and disease through identifying all relevant factors at the micro as well as macro environment. The simultaneous sharing and converged research of the body physical mechanisms combined with mental, cultural, community and environmental factors are the enabler for reliable and responsible personalized medicine.

This approach will require the endeavour of interdisciplinary research, new philosophical approach as well as new innovative analysis tools specially developed to utilize all acquired knowledge translated into the optimum practice of preventive, predictive and personalized medicine.

The coupling of computer sciences, complexity theory, non linear dynamics and logic theory lead the development of learning machines revealing the underlying rules in specific phenomena and various disease that improves it accuracy and prediction tools while usage.

These tools are crucial for medical research and especially for clinical trials, enabling the analysis of small and well defined groups towards responsible treatment.

Our patented Data Mining rule discovery tool is just one example, specially developed to relate to the individual within the natural and artificial surroundings as one complex functioning system. The tool enables multilevel, multisource data analysis (images, numeric, signals, categorical, descriptive data, etc) while relating to the whole data set as is – no normalization, manipulation or data neglected. Further more the tool minimizes over-fitting and identifies the unexpected rules and cases which are crucial for reliable clinical trials. It was already applied successfully to autoimmune diseases, degenerative diseases, structural biology, drug development, personalized skin treatment, neuronal biomarkers, etc.

It is time to shift the paradigm in research and development, join all forces – knowledge, information and tools to enable the new era of healthcare treatment for the well being of all

Prof. Emmanuel Mikros

Position Professor

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Biography Emmanuel Mikros, Chemist, Ph.D. is Professor in Pharmaceutical Chemistry University of Athens. He obtained his Ph.D in Chemistry from Universite Paris-Sud (Paris XI) in 1988 and then he joined University of Athens. Research Fellow at the Institut für Chemie Medizinische Universität zu Lübeck, Germany, with Prof. T. Peters at 1996 and at the Laboratoire Ingenierie Moleculaire, INRA, Centre de Recherches de Nantes, France with Dr. S. Perez (1993 and 1994). He was awarded the DAAD (Germany, 1996) and Marie Curie (European 1994) Fellowships. He is an author of 70 peer reviewed scientific publications (1000 citations, h-factor 18). He has participated in over 20 research and educational projects funded by National and EU organisms, the most recent are : FP7-Research Potential-2007, FP7-PEOPLE-Industry-Academia Partnerships And Pathways-2008 Marie Curie Actions, FP7- Knowledge Based Bio-Economy-2009-3-1-04 He is member of several national and international scientific societies (EFMC, ACS) and vice president of Hellenic Society of Medicinal Chemistry. Invited speeker in more than 20 international meetings, he has also participated in the organising committee of 4 international and national scientific congresses. Prof. Mikros leads a research group focused on NMR spectroscopy, NMR based Metabonomics Structure elucidation of

biomolecules, natural products and drugs, as well as Molecular Modeling docking-scoring calculations, in silico screening and Structure Activity Relationships. The group is currently involved in several metabonomic projects in collaboration with internal and external partners covering areas like characterisation of metabolic responses to chemical exposure hepatotoxicity, cardiotoxicity), disease diagnosis (inborn error of metabolism, cancer), sports biochemistry and plant metabolic profiling. Important experience has been also gained through the systematic study of receptors like Kinases (CDKs, GSK3, DYRK, CK1), Nuclear Receptors (ERα, ERβ, AR) and membrane transporters, concerning their interaction with small molecules using Molecular Modeling calculations. Specific docking calculation protocols and scoring functions have been established and used in order to design new molecules with desired biological activity. Supervisor of 4 Ph.D. theses. He set up and he is responsible of the NMR facility of the Faculty of Pharmacy University of Athens.

Abstract Metabonomics represents a holistic, hypothesis-free, approach to the study of metabolic responses to various stimuli through powerful data acquisition and advanced data processing techniques. This approach aims to the highthroughput analysis of the metabolic profiles of biofluids, tissues, extracts etc taking advantage of the degree of inherent biochemical similarities between samples.

NMR spectroscopy and/or MS have been utilized as main analytical platforms in Metabonomics studies. The application of NMR and MS to biological materials allows the simultaneous detection, identification, and quantitation of a variety of low-molecular-weight metabolites from a range of intermediate metabolic pathways. This is possible in combination with the newly emerging methods for automated data reduction and pattern recognition techniques (multivariate chemometric analysis) leading to the efficient exploitation of complex spectral profiles.

Metabolic profiling and understanding metabolic fluctuations could be translated into clinical tool with applications in personalized medicine. In this aspect administration of drugs should be adjusted to achieve maximum effectiveness and avoid side effects which may be different for each organization. One of the approaches is the understanding of genetic differences between individuals and the correlation with the response to drug therapies both in the therapeutic effect and to the side effects, known as pharmacogenomics. The relationships between the individual genomic and phenotypic variation in response to drug treatment have not yet fully understood, and it is unlikely that genetic information is not able to guide personalized drug therapy. The metabolic phenotype or metabotype provides a holistic approach to the biological system being the product of genetic and environmental contributions (diet, lifestyle, intestinal flora, etc.), ie a particular set different for each body. Very recently, an alternative approach to understanding the variability of responses to pharmacotherapy has been developed, called Pharmacometabonmics. The new approach can be used to predict the metabolism, toxicity and general organization of a response to medication based solely on analysis and modeling of metabolic profiles before treatment (Clayton TA, et al. Nature 440, 1073-1077, 2006).

Dr Paul Mitcheson

Position Senior Lecturer (Associate Professor)

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Biography Paul. D Mitcheson received the M.Eng. degree in electrical and electronic engineering and the Ph.D. degree from Imperial College London, U.K., in 2001 and 2005 respectively. He became a lecturer (Assistant Professor) at Imperial College in 2006 and is currently a senior lecturer (Associate Professor) in the Control and Power Research Group, Electrical and Electronic Engineering Department and Imperial College London. He has research interests in energy harvesting devices, in particular the power processing requirements for harvester powered systems and devices powered from human body motion.

Abstract **Energy harvesting in health care applications**

The supply of power to worn or body-implanted medical devices remains a barrier to their ease of use and their uptake. In this talk I will discuss the possibilities for powering devices from the human body, including movement, thermal and RF energy harvesters. The issue of wireless powering of devices using near field inductive coupling and acoustic coupling will also be covered. Experimental details of prototype power sources targeted to human body worn applications will be discussed.

Dr Christos A. Nicolaou

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Abstract **Evolving Approaches to Drug Selectivity and Designed Polypharmacology**

Modern drug discovery focuses for the most part on the identification of 'magic bullets', i.e. perfect drugs that cure a disease in the general population with no, or very low, danger of side effects. The specific aim of the drug discovery process is to identify molecules that selectively bind and interact with a specific biological receptor implicated in the outbreak of a disease, and cause certain desired behaviour. In addition, a drug must also exhibit satisfactory pharmacokinetics and toxicity properties to ensure that it moves appropriately in the living organism to be treated, reaches the region of the target without causing side effects and binds selectively to the pharmaceutical target.

The drugs currently available to patients are a testimony to the success of this paradigm. However, the decreasing numbers of new drugs approved as well as a number of drug recalls are an indication to the paradigm's limitations. Numerous recent advances in our understanding of human biology and disease occurrence pave the way for a new, complementary approach that takes into account pharmaceutical target relations to design more selective drugs and drugs which exhibit appropriate polypharmacology. This presentation will initially review the steps of the modern drug discovery process and elaborate on some of its challenges. The advances in the new field of pharmacogenomics will be described and a brief overview of new strategies for designing drugs with increased selectivity will be provided. The later section of the presentation will focus on the potential for multi-target drugs and the evolving drug discovery paradigm of designed polypharmacology.

Prof. K.C. Nicolaou

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Biography K.C. Nicolaou was born on July 5, 1946 in Cyprus. In 1964, he emigrated from Cyprus to England. His studies in chemistry were completed at the University of London (B.Sc., 1969, Bedford College, First Class Honors; Ph.D. 1972, University College, with Profs. F.

Sondheimer and P.J. Garratt). In 1972, he moved to the USA and completed postdoctoral appointments at Columbia University (1972–1973, Prof. T.J. Katz) and Harvard University (1973–1976, Prof. E.J. Corey), after which he joined the faculty at the University of Pennsylvania, and rose to the rank of Rhodes-Thompson Professor. In 1989, he accepted joint appointments at the University of California, San Diego, where he is Distinguished Professor of Chemistry, and The Scripps Research Institute, where he is the department chairman and holds the Darlene Shiley Chair in Chemistry and Aline. W. and L. S. Skaggs Professorship in Chemical Biology.

For his scientific work, Professor Nicolaou has received numerous awards and honors, including the ACS Linus Pauling Medal (1996), RSC Centenary Medal (2000–2001), Tetrahedron Prize for Creativity in Organic Chemistry (2002), ACS A. C. Cope Award (2005), and Benjamin Franklin Medal in Chemistry (2011).

Nicolaou is a Fellow of the American Academy of Arts and Sciences (1993), Member of the National Academy of Sciences (USA, 1996), Foreign Member of the Academy of Athens (Greece, 2001), Member of the German Academy of Sciences Leopoldina (2009), and Member of the American Philosophical Society (2011), and holds 10 honorary degrees from universities around the world.

He is the author or co-author of over 735 scientific articles, reviews, and book chapters, 66 patents, and 5 books, including the popular Classics in Total Synthesis (Vols. 1–III) series with Wiley-VCH, and Molecules That Changed the World, co-authored with Tamsyn Montagnon (2008, Wiley-VCH). His dedication to chemical education is evidenced by his training of more than 400 graduate students and postdoctoral fellows.

Abstract **Molecules that Changed the World**

This lecture, based on the recent book by Nicolaou and Montagnon[1], will expound on our learned knowledge of some of Nature's most intriguing molecules and the ability of Man to discover, synthesize, modify and use them to our advantage in what was not formerly envisioned. Through the development of the theme, it is hoped that one will also discover just how profound the impact of chemistry is in our lives. The lecture will also explore some of the most exciting frontiers in modern science and medicine, and the opportunities they present to young students for future careers. Illustrated in a colorful style, this presentation will aim to provide insights about the role of chemistry in society in general and how chemical synthesis, the art and science of constructing natural and designed molecules, in particular, shaped and continues to shape our world. Indeed, the lecture will touch upon fascinating tales about molecules and their presence in, among many items, high tech materials, foods, vitamins, nutritional supplements, and above all, medicines. The history of total synthesis, the flagship of chemical synthesis, as unraveled within the scope of this lecture will hopefully serve to underscore how admirably chemical synthesis enabled and facilitated world-shaping innovations in medicine since its inception in 1828 by Friedrich Wöhler.

1 Molecules That Changed The World, by K.C. Nicolaou and T. Montagnon, Wiley-VCH, 2008.

Ms Irene Norstedt

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Biography Irene Norstedt has been working with various aspects of European Life Sciences research at the European Commission since 1996. She is currently Deputy Head of Unit for the Personalised Medicine Unit in the Health Research Directorate in DG Research and Innovation. Before that she was one of the key drivers for setting up the Innovative

Medicines Initiative (IMI), a public private partnership between the EC and the Pharmaceutical industry. Previous responsibilities at the EC have primarily focussed on Small and Medium size Enterprises and industry aspects of biotechnology and health research at European level. Before starting her job in Brussels she worked for Biscoe AB in Uppsala, Sweden. There she had several positions including Business Development for the Drug Discovery and Food Analysis areas and Technical Services Manager. She has also worked as Assistant Technical Attaché at the Swedish Embassy in London.

Abstract **Personalised Medicine Research at European level**

Personalized medicine is a novel approach to healthcare based on a better molecular understanding of health and disease. Some personalized medicine approaches have begun to show results but much research is still needed to progress the area.

The European Commission (EC) has allocated some €900 million to personalized medicine, enabling research over the latest 5-year period via the Health Theme of the Seventh EU Framework Programme for Research and Technological Development (FP7).

To gain a better understanding of key research needs in the area, the Personalised Medicine Unit of the ECs Health Research Directorate organized several workshops and a large-scale conference during the period between 2010–2011.

The key research challenges identified can be grouped around four main themes:

Breaking barriers and speaking the same language: facilitating interaction between different disciplines from basic to clinical research by creating appropriate interfaces for collaboration and discussion among stakeholders.

Generating knowledge and developing the right tools: adapting research tools to clinical use by developing common standards for data collection and linking clinical data with molecular profiles, for example, translating 'omics research into clinical application.

Translation to medical applications: finding new approaches for identification, qualification and clinical validation of all types of biomarkers; improving the use of biomarkers for better use of existing therapies and adaptive clinical trial methodologies.

Economic aspects: proving the economic viability and positive patient benefits of personalized medicine and developing methodologies for health technology assessments and for comparative cost–effectiveness studies on personalized medicine approaches.

The EC will continue to invest in research fostering the development of personalized medicine approaches, both through its current FP7 Health Research Theme in 2012 and 2013 as well as in its next funding program for research and innovation – Horizon 2020.

Dr Morag Park

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Biography Dr. Morag Park received her PhD in 1983 at Glasgow University, Scotland. For her postdoctoral studies she joined the lab of Dr. George Vande Woude at the National Institute of Cancer, US where she identified the Met receptor tyrosine kinase. She joined McGill University in 1988 where she is now a Professor in the Departments of Oncology, Biochemistry and Medicine. In addition, she holds the Diane and Sal Guerrera Chair in Cancer Genetics. Dr. Park is currently the Scientific Director of the CIHR Institute of Cancer Research. She has also served as Director of the McGill Molecular Oncology Group and joint head of the Cancer Axis at the McGill University Health Centre, and as a member of the Fonds de la Recherche en Santé du Québec, Réseau Cancer. She has a long standing

interest in the molecular mechanisms of cancer. Dr. Park has published over 100 papers in peer-reviewed journals. She is recognized for her work on the Met receptor tyrosine kinase and signaling pathways that regulate cell migration and invasion in cancer. A major thrust of her work now focuses on human breast cancer and the importance of the tumour microenvironment to the outcome of this disease. Her work has been recognized with numerous awards including becoming a Fellow of the Royal Society of Canada

Abstract **Personalised Medicine Research and Canada**

The overall goal of the Canadian Institutes of Health Research Personalised Medicine Signature Initiative is to support translational research for the effective prevention, diagnosis, and treatment of complex diseases with the ultimate goal of stratifying patients based on their susceptibility to a disease or their response to a specific treatment; and to promote health services research to effectively integrate such innovations into policy and practice for the benefit of Canadians.

Dr Cristiana Pavlidou

Position Collaborator

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Biography Dr. Christiana Pavlidou has completed her Bachelor Degree in Dietology and Applied Dietetics , receiving the tiltle of Dott.ssa (Dr) as Nutritionist-Dietitian in 1998 concluding her thesis on the role of the Nutritional Counselling in Cystic Fibrosis Pediatric patients. Between 1998 and 1999 she was involved in one of the first research projects in the supplementation of EPA/DHA in Cystic Fibrosis Pediatric Patients in the Pediatric Clinic of the University of Naples Federico II. In 2001 she received her MSc in Clinical Nutrition from the University of Surrey (Roehampton, London, UK) concluding a thesis project on the prevalence of body image dissatisfaction and eating disturbances among sports and non-sports students. In addition, she completed the 2 parts in order to obtain an online diploma on the promotion of Science and Technology from the University of Ca' Foscari, Venice Italy.

She is now in the process of completing her PhD at the University of Patras, Greece on nutrigenomics with Dr. George Patrinos.

She works as a freelance dietitian-nutritionist in a seaside suburb in Palaio Faliro in Athens, Greece and as a collaborator of the children's private hospital 'IASO Paidon' in Marousi, Athens involved in the nutritional counseling and support of pediatric patients.

In the previous years, she has collaborated with a private clinic in Athens and has previously worked (2004-2008) in the biscuit Industry Papadopoulou as a nutritionist consultant involved in marketing and R&D projects. Between 2008- 2011 she was the Scientific Director of Paideiatrofi by Epode programme for childhood obesity prevention currently running in Greece and also the Scientific Director of Nostus Communications and Events. During 2008-2010 she worked as a nutrition/dietetics professor in the IEK private schools for Chef (Le Monde) and Dietitians (Ippokrateios in 2010 only).

She is a collaborator of the Golden Helix Institute of Biomedical Research (www.goldenhelix.org) involved in various research projects.

She has presented many of the projects involved in many world and regional congresses and she holds scientific publications.

Abstract **Development of centralized National Genetics databases and their implications for personalized medicine**

National/Ethnic Mutation databases (NEMDBs) are increasingly becoming important tools for the documentation of genomic variations in various populations around the globe and as

such they assume an important role in the provision of genetic services. Presently, the adoption of NEMDBs is not uniform and varies among different populations and national healthcare systems. Also, development of these NEMDBs should conform to certain guidelines and recommendations that would assist genetic variation data capture in developing countries to ensure a comprehensive worldwide data collection and better provision of healthcare services. We have previously reported the development of the ETHNOS software, on which several NEMDBs have been developed [Patrinos et al., Hum Mutat, 2005; van Baal et al., Hum Genomics, 2010], which has contributed not only to the establishment of similar databases for different populations but also to database content uniformity, as more than half of the available NEMDBs are based on this software. The NEMDB notion has also been further expanded, yielding either a worldwide central repository for allele frequency data or a data warehouse of anonymous individual-level genetic data. One such worldwide central allele frequency repository, where frequency of genetic variants that relate to a phenotypic alteration, namely inherited disease or variable drug response, will be deposited is FINDbase (www.findbase.org; 12) has already been established along these lines and documents a substantial amount of genetic data and allele frequencies of pathogenic mutations [van Baal et al., Nucleic Acids Res, 2007; Georgitsi et al., Nucleic Acids Res, 2011] and pharmacogenetically relevant SNPs [Georgitsi et al., Pharmacogenomics, 2011]. Apart from this application, collection of clinical genetic information on patients with particular genetic diseases, the investigation of a family's clinical history and genotype-phenotype correlations are also of utmost importance. The first efforts in that direction have begun to make an appearance. In particular, a prototype software, allowing an individual’s genetic profile to be stored has been developed (Gkantouna, Tzimas, Patrinos, unpublished), so that this information can only be retrieved by the patient and his/her physician. Such database, currently under development, would allow patients to securely store all his or her genetic information and related phenotype, hence contributing decisively to customized medical treatment, better diagnosis of hereditary diseases of patients, unambiguous personal identification. Also, having data in a structured format, the end-user can now easily statistically analyse them and draw useful conclusions.

Prof. Roland Pochet

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Biography Roland Pochet was born in Brussels. He studied Chemistry, did a PhD in Biochemistry at Université Libre de Bruxelles (ULB), a postdoctorate as EMBO fellow at the Hebrew University of Jerusalem (Dpt of Experimental Medicine). He spent 6 months at Vanderbilt University (Nashville) as NATO fellow. He is Professor of cell biology at the Faculty of Medicine ULB, General secretary of the Belgian Brain Council, chair of the Biomedicine and Molecular Biosciences Domain Committee of COST and member of EDAB (European DANA Alliance for the Brain). He is head of the ALS (Amyotrophic Lateral Sclerosis) unit at the Histology, Neuroanatomy and Neuropathology laboratory (ULB) and focuse his research on cell transplantation of stem cells in an ALS animal model.

Prof. Barbara Prainsack

Position Professor of Sociology and Politics of Bioscience

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Biography Barbara Prainsack was awarded her PhD in Political Science at the University of Vienna, Austria, where she worked and published on issues of governmentality. She is now Professor of Sociology and Politics of Bioscience at the Centre for Biomedicine & Society (CBAS), Dept. of Sociology and Communications, Brunel University. She has published widely on the societal, ethical, and regulatory dimensions of biomedicine and bioscience (genetic and genomic science and technologies in particular). She is a member of the Austrian National Bioethics Commission, and co-chair of the Scientific Committee of the ESF's Forward Look on Personalised Medicine. From January to July 2011, she was AHRC/ESRC Fellow for the project 'Solidarity as a Core Value in Bioethics' at the Nuffield Council on Bioethics in London, UK.

Abstract **Personalised Medicine and the Citizen: A Participatory Turn in Health?**

Recently, a lot of attention has been paid to the topic of patient and citizen empowerment in the health domain. But what citizen empowerment in health and medicine mean in practical terms, and how does it impact on how healthcare is organised, delivered, accessed, "consumed", evaluated, and financed? What does it mean for the context of Personalised Medicine specifically, with its inherent focus on rendering prevention, diagnosis, treatment, and monitoring more "tailored" to individuals? Moreover, now that we are seeing citizens organising their own trials, publishing papers, and crowd-sourcing treatment decisions to wider audiences instead of turning to traditional experts, has citizen empowerment perhaps already transcended the concepts and issues dominating our debates? Finally, does citizen empowerment in the health domain catalyse the development of Personalised Medicine, or is it in any way detrimental to the endeavour?

Dr Kamran Sayrafian

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Biography Dr. Kamran Sayrafian is a program manager at the Information Technology Laboratory of the National Institute of Standards and Technology (NIST) located in Gaithersburg, Maryland. He leads several strategic projects that are focused on Pervasive healthcare technologies. NIST is actively pursuing the standards and measurement research necessary to achieve the goal of improving healthcare delivery through information technology. Dr. Sayrafian is an actively with several standard organization committees such

as IEEE802.15.6 international standardization on medical body area networks and ASTM 2761. Prior to joining NIST, he was the cofounder of Zagros Networks, Inc. a fabless semiconductor company based in Rockville, Maryland where he served as President and senior member of the architecture team. He is the co-inventor/inventor of four U.S. patents. He has served as invited member of technical program committee and co-chair of many international conferences and workshops. His research interests include medical body area networks, mobile sensor networks and interference analysis/coexistence. He has published over 70 conference and journal papers, and book chapters in these areas. He was the recipient of the IEEE PIMRC 2009 & SENSORCOMM 2011 best paper awards. Dr. Sayrafian holds Ph.D., M.S. and B.S. degrees in Electrical & Computer Engineering from University of Maryland, Villanova University and Sharif University of Technology, respectively. He is a senior member of IEEE and an adjunct faculty of the University of Maryland.

Abstract **Personalised Health: An ICT Perspective**

Recent advances in miniature-sized microelectronics have created the opportunity to build ultra-small devices that can be implanted inside the human body. Adding communication capability to the limited computational power of such devices would allow the possibility of performing more complex functions by connecting multiple devices to each other or to external IT infrastructure. These radio-enabled medical devices can be used to continuously gather and process a variety of important health and/or physiological data wirelessly. They offer a revolutionary set of applications such as smart pills for precision drug delivery, intelligent endoscope capsules, and eye pressure sensing systems. The trend to create networking capability among many tiny devices is also expected to continue to molecular-sized sensors/actuators (i.e. nano-networking). In this presentation, an ICT perspective on challenges facing this trend is briefly discussed.

Prof. Dieter Schinzer

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Biography Professor Schinzer holds a degree in Chemistry from the University of Marburg and obtained his doctoral degree from the University of Bonn. Since 1998 he has been teaching Chemistry at the University of Magdeburg in Germany and between 2002 and 2005 he was the dean of the Faculty of Process and Systems Engineering. Professor Schinzer is the chair of the CMST domain at COST and is also CEO of MOLISA GmbH since 2002.

Prof. Dina Simunic

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Biography Dr. Dina Šimunić is a full professor at University of Zagreb, Faculty of Electrical Engineering and Computing in Zagreb, Croatia. She graduated in 1995 from University of Technology in Graz, Austria. In 1997 she was a visiting professor in ”Wandel & Goltermann Research Laboratory" in Germany, as well as in "Motorola Inc", Florida Corporate Electromagnetics Laboratory, USA, where she worked on measurement techniques, later on applied in IEEE Standard. In 2003 she was a collaborator of USA FDA on scientific project of medical interference. Dr. Simunic is a IEEE Senior Member, and acts as a reviewer of IEEE Transactions on Microwave Theory and Techniques and on Biomedical Engineering and Bioelectromagnetics, journal JOSE and as a reviewer of many papers on various scientific conferences (e.g., IEEE on Electromagnetic Compatibility). She was a reviewer of Belgian and Dutch Government scientific projects, of the EU FP programs, as well as of COST-ICT and COST-TDP actions. She was acting as a main organizer of the data base in World Health Organization, for the service of International EMF Project from 2000 to 2009. From 1997 to 2000 she acted as a vice-chair of COST 244: “Biomedical Effects of Electromagnetic Fields”. From 2001 to 2004 she served as vice chair of Croatian Council of Telecommunications. In 2006 she is elected the first time and re-confirmed in 2010 as vice-chair of COST Domain Committee on Information and Communication Technologies (ICT). She is one of the proposers as well as a member of COST Trans-domain Committee. She is organizer of many workshops, symposia and round tables, as well as of special sessions. She has held numerous invited lectures, among others at ETH Zuerich, Switzerland in 1996 and US Air Force, Brooks, USA in 1997). She is author or co-author of approximately 100 publications in various journals and books, as well as her student text for wireless communications, entitled: “Microwave Communications Basics”. She is co-editor of the book “Towards Green ICT”, published in 2010. She is also editor-in-chief of the “Journal of Green Engineering”. Her research work comprises electromagnetic fields dosimetry, wireless communications theory and its various applications (e.g., in intelligent transport systems, body area networks, crisis management, security, green communications). She serves as Chair of the “Standards in Telecommunications” at Croatian Standardization Institute.

Prof. Michael Strupp

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Biography Michael Strupp is Professor of Neurology and Clinical Neurophysiology at the University of Munich and Deputy Speaker of the new Integrated Center for Research and Treatment of Vertigo, Balance and Ocular Motor Disorders at the University of Munich. He studied medicine at the Technical University of Aachen, where he did his MD in the field of cardiophysiology. He then spent time doing basic neuroscience research involving patch-clamp recordings with axons, muscle cells, glial cells and vestibular hair cells. Prof. Strupp’s particular area of interest is the pharmacotherapy of vestibular and ocular motor disorders. He is currently Editor-in-Chief of Frontiers in Neuro-otology and Join-Chief-Editor of the Journal of Neurology. He has received many clinical and scientific awards, including a “best teacher” award from the German Neurological Society, and has been a visiting professor at the University of Graz and the University of Prague. He is the author of more than 200 peer-reviewed papers and four books on vertigo, dizziness and ocular motor

disorders. He lives in Munich with his wife and four children.

Prof. Wim Vanden Berghe

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Biography Epigenomic profiling of phytochemical effects in cancer-inflammation and cardiovascular disease: challenges & pitfalls

Abstract **Epigenomic profiling of phytochemical effects in cancer-inflammation and cardiovascular disease: challenges & pitfalls**

Cancer and cardiovascular diseases remain one of the leading causes of death in Western society. Recently, epigenetic changes in DNA methylation patterns at CpG sites (epimutations) or deregulated chromatin states of genes and noncoding RNAs emerged as major governing factors in lifestyle diseases such as, cancer, obesity, diabetes and cardiovascular disease. Furthermore, various environmental factors such as nutrition, behavior, stress, and toxins remodel our epigenomes lifelong in a beneficial or detrimental way. Since epigenetic marks (epimutations) are reversible in contrast to genetic defects, various phytochemicals (soy, genistein, resveratrol, catechin, curcumin, cocoa flavanols) are currently evaluated for their ability to reverse adverse epigenetic marks in various diseased cell types (cancer cell, immune cell, endothelial cell). Although phytochemicals present in fruit and vegetables may help to protect against various inflammatory disease conditions, few protective effects have been firmly established, presumably because of inappropriate timing or dosing of diet exposure or due to confounding factors such as smoking and alcohol. We have applied genomewide MBD2-capture sequencing, Illumina 450K CpG array, restriction enzyme methylation profiling, chromatin accessibility assays, cofactor profiling and CpG pyrosequencing in cancer cells or blood samples exposed to physiological concentrations of phytochemicals in cell culture or in diet interventions studies. Correlation of methylome profiles with gene expression data reveal complex epigenetic control mechanisms which may attenuate or interfere with disease progression. Challenges and pitfalls will be discussed of different platforms with respect to data analysis, normalization, interpretation and biological significance.

Mr Albrecht von Müller

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Biography Albrecht von Müller is director of the Parmenides Center for the Study of Thinking. He

teaches philosophy at the Ludwig Maximilians University of Munich (LMU) and theory of thinking in an international master`s program on advanced complexity management, organized by SISSA (International School for Advanced Studies, Trieste). His two main fields of research are the concept of time and the phenomenon of thinking. In addition, Mr von Müller is interested also in the practical application of the findings. He developed a visual reasoning language for supporting complex strategic reasoning and decision making. He served as scientific adviser to several governments, international institutions and large companies. Mr Von Müller is an external member of two multi-disciplinary research centers at the University of Munich, the Human Science Center and the Munich Center for Neuroscience, he is member of the Board of Trustees of the Max Planck Institutes of Neurobiology and Biochemistry, and he is co-editor of the Springer book series “On Thinking”.

Abstract **Constellatory diagnostics**

Constellatory diagnostics (CD) is a novel approach to support complex medical thinking and decision making. Its main task is to make sure that the best available knowledge is effortlessly available in all diagnostic situations. The MD just needs to represent the constellation of symptoms with a few finger strokes on a tablet. The methodological core of CD is that it doesn’t just aggregate individual symptoms but allows interpreting them in their specific constellation. By this, CD supports MDs in the way outstanding experts in this field do think. In basic research on advanced human cognition a fundamental complementarity between two basic modes of thinking has been found. One is the well-known, Boolean-type of rational concatenation of mental content. The other is the constellatory unfolding of meaning. Usually circumscribed by notions like “intuition”, “gut feeling” or “expert judgment”, it is far from “irrational”, it just follows a very different type of logic. The three basic principles of the logic of constellations are: (1) the mutual semantic unfolding of the involved components, (2) the emergence of an overarching meaning, and (3) the re-interpretation of the initial components in the light of the emergent overarching meaning. In evolutionary terms, constellatory logic might to be an exaptation of Gestalt perception, re-utilized in the domain of advanced conceptual thinking. Cognitive breakthroughs, from science to diagnostics, are characterized by an effortless interplay between the two basic modes of thinking. CD is the first practical application supporting both modes of thinking, and their effortless interplay. In parallel, CD makes sure that all residual risks and rare eventualities are taken into account. An optional by-product is a documentation that (a) minimizes the administrative burden of MDs, that (b) provides a high resolution record, e.g. for purposes of a patient transfer, and that (c) can prove comprehensive lege artis procedures.

Short Talk Presenters

Prof. Maria Laura Bolognesi

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Abstract **Styrylquinolines as amyloid chemical probes and theranostics in Alzheimer's and prion diseases**

Alzheimer's and prion diseases etiological mechanisms have been linked to a conformational change of normally expressed proteins that leads to the aggregation and abnormal deposition of protease-resistant and insoluble isoforms, namely amyloid-beta (Aβ) and prion protein scrapie (PrPSc). As the fibrillar aggregates of both these proteins are toxic to neurons, it has long been hypothesized that fibrils cause the underlying neurodegeneration. Thus, the amyloid plaques have been historically considered the neuropathological hallmark of these diseases determined at autopsy and, more recently, the classical biomarker for diagnostic purposes. In a personalized medicine perspective, a molecular biomarker can be utilized in the diagnosis, but also in staging and monitoring of therapy. On these basis, we explored the possibility of devising imaging probes to image the amyloid deposition in vivo and potentially provide treatment strategies against both maladies. To this aim, we focused on styryl derivatives, because several styryl compounds have been employed to detect Aβ plaques and have been successfully tested against PrPSc. Since the quinoline fragment is contained in many anti-prion compounds, we proposed to generate a library of styrylquinoline derivatives, to detect, and potentially inhibit fibrillar aggregates. The synthesis of the designed derivatives was achieved via a vinylogous variation of the Povarov reaction. They exhibited a promising activity against prion replication in ScGT1 cells and, importantly, showed no appreciable cytotoxicity. We also studied their activity as inhibitors of Aβ and PrPSc aggregation in vitro. To corroborate the possibility of employing them in vivo, we tested their ability to cross the BBB and investigated their native fluorescence in a variety of polar and non-polar environments to model their interaction with proteins, and provide the information required for their possible use as theranostic agents.

Prof. Darko Bosnakovski

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Abstract **Gene corrected FSHD-IPS cells, once step closer to cell therapy for Facioscapulohumeral muscular dystrophy**

Human induced pluripotent stem (IPS) cells overcome several disadvantages of human embryonic stem cells, including host specificity and ethical issues. These cells can be generating from different cell types of each donor making them suitable tool for autologous cell therapy and tissue engineering. Furthermore, iPS cells generated from patients with genetical disorders capture the disease genotype in the cell. These cells are good model for studying pathology of the diseases and testing different therapies. One approach is cell therapy by using specific cell types from genetically corrected IPS cells

Facioscapulohumeral muscular dystrophy (FSHD), one of the most common inherited myopathies, is caused by a contraction within a subtelomeric array of D4Z4 repeats 4q35.2. It is characterized by uneven and progressive weakness and atrophy of facial, shoulder and upper arm muscle.

To develop cell based study model for FSHD and relevant source for cell therapy we generated IPS cells from FSHD myoblasts and myoblasts from healthy donors. To induce myogenic differentiation FSHD-IPS cells were transduced with Myf5, one of the key myogenic transcriptional factors. Under certain conditions Myf5 modified cells differentiated in myoblasts and fused to form myotubes. DUX4 expression was detected in all stages of IPS myogenic differentiation, pluripotent, mesenchymal and myogenic stage. By this, we established relevant diseases model to study FSHD. However, to overcome the issues of comparison of IPS clones from different donors and variations acquired prior reprogramming, and in same time to generate adequate cells for tissue engendering, we genetically corrected FSHD-IP cells by removing 4qA161 allele. We targeted FSHD-iPS cells with a linear targeting vector bearing a single homology arm of 500 bp followed by the neo cassette and human artificial telomeric repeats (T2AG3), using zinc finger nucleases. Expression analyses reveled that corrected FSHD-IPS clones do not express DUX4.

Prof. Andrea Danani

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Abstract

System Information Therapy and Personalized Medicine

Living organisms can nowadays be viewed as dynamic processes sustained by a ceaseless flows of matter, energy and information within so-called morphogenetic fields. Life is a far from equilibrium process and the process aimed to keep stability through dynamic changes has been recently defined as allostasis. Allostatic load is referred to the total amount of stress the whole system has to cope to maintain allostasis and leads to a decrease of health potential toward pathogenesis. Allostasis and allostatic load are in a dynamic relationship as an expression of the flow of informations due to adaptive dynamics and health and disease can be viewed as an expression of this dynamics. Information flows in biological system can be studied either by a chemical and molecular description either by an electromagnetic signals emission. It has been established, in the last decays, that electromagnetic signals are endogenously generated at different level in many cell components and supposed to play an active role in synchronizing either inner cell function at microscopic level either systemic adaptive response of organs, apparatus and whole organism. In this framework all the adaptive response both at microscopic and macroscopic level, either local or holistic, could be identified by their specific electromagnetic signals emission. Each specific adaptive reaction, being unique for any person at any time, will have his own specific and personal electromagnetic signature. System Information Therapy (SIT) is a developing clinical methodology employing medical devices working by a combination of endogenous and external electromagnetic signals with the aim of restoring the self regulation and self regeneration capability of the human being. This process has been clarified at the microscopic level with evidence of repatterning of cell membrane components or at epigenetic level with evidence of selective mRNA expression induction. At macroscopic level the self regulation effect has been, for instance, demonstrated in postural repatterning with evidence of disappearance of fluctuating asymmetry or in pain management . SIT is a new effective and efficient tool in personalized medicine allowing to cure each person by his own specific dysfunctional or pathological electromagnetic signals at local or systemic level. Moreover SIT is also a suitable tool in preventive medicine allowing to manage allostatic load in order to keep allostasis and coping efficiently with everyday stress of life.

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Abstract

Towards a modular Web-based Workflow environment for enabling large scale Virtual Screening in Cancer Chemoprevention Research

The vision of the GRANATUM project is to bridge the information, knowledge and collaboration gap among biomedical researchers in Europe and beyond, ensuring that the biomedical scientific community has homogenized access to the globally available information and data resources needed to perform complex cancer chemoprevention experiments and conduct studies on large scale datasets. This way, GRANATUM will facilitate the social sharing and collective analysis of biomedical experts' knowledge and experience, as well as the joint conceptualization and design of scalable chemoprevention models and simulators, towards the enablement of collaborative biomedical research activities beyond geographical barriers, helping researchers in this highly multidisciplinary field to manage the complex tasks involved in carrying out collaborative research.

Within the scope of the GRANATUM project we have the task to implement a Web-based Virtual Screening Tool. It will provide the researchers with a set of In-Silico Tools and Models that will be used to create Virtual Screening Workflows aimed for the use in Cancer Chemoprevention Research. The Virtual Screening Tool will facilitate the use of In-Silico Tools from the Drug Discovery process and custom made Predictive Models based on the research on Cancer Chemoprevention. The researchers will be able to create Virtual Screening Workflows and Predictive Models. The GRANATUM platform will provide its users the functionality to share the Workflows and Predictive Models created, among them. The GRANATUM platform will facilitate mechanisms to retrieve information from various recourses in the Cloud and semantically interlink them to create a knowledge base for Cancer Chemoprevention. The results from the Virtual Screening Workflows will be used to update this knowledge base.

As a proof of concept initially we will provide In-Silico Tools and Models to support research for cancer chemopreventive agents based on the human proteins ER-Alpha, ER-Beta and DNMT.

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Abstract

Chemo-enzymatic approaches to genome-wide profiling of cytosine modifications

Enzymatic methylation of cytosine at the 5 position in DNA serves as a key epigenetic regulatory mechanism in higher eukaryotes including humans. Aberrant DNA methylation correlates with a number of pediatric syndromes and cancer, or predisposes individuals to various other diseases. This reaction is carried out by methyltransferase enzymes (MTases) which catalyze the transfer of a methyl group from the ubiquitous cofactor S-adenosyl-L-methionine (AdoMet). Recently, the sixth component of vertebrate DNA, 5-

hydroxymethylcytosine (hmC), has been identified in genomic DNA from the brain and neuronal cells [1], which is likely involved in yet unknown epigenetic mechanisms. However, most existing methods used to query the modification status of CG sites in DNA are not suitable for analysis of hmC, which hampers studies of these new phenomena. To this end, we redesigned the methyltransferase reaction for covalent attachment of larger chemical moieties to DNA by rational engineering of the catalytic center and employing synthetic AdoMet analogs with extended propargylic sidechains [2], and employed atypical reactions of the cytosine-5 MTases with non-cofactor-like compounds that permit exchange and labeling of 5-hydroxymethyl groups in DNA [3,4]. Based on these chemo-enzymatic reactions we developed analytical tools permitting covalent derivatization, biotin labeling and affinity capture of DNA fractions containing different modified cytosines (hydroxymethylated and unmethylated CpG sites) and have adapted them for genome-wide mapping of the cytosine modifications using DNA microarrays.

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Abstract **All the appropriate signals are necessary for engineering proper tissues**

The highly interdisciplinary area of tissue engineering, by its nature, involves several fields of research from basic materials development to stem cell handling to clinical applications.

While the need for quick applications is driven by necessity we are still far away from understanding how the hybrid system of material scaffolds-cells-biomolecules operates optimally either in-vitro (in a bioreactor) or in-vivo.

In our effort to monitor some basic responses of particular cells to specific environments we have developed a bioreactor able to supply a multitude of mechanical cues, singly or in combination to endothelial cells.

In this presentation we will provide evidence of the importance of substrate stretching and frequency of stretching, of the shear rate of the flowing feeding medium on top of the cells, and of a simulated microgravity environment, especially by combining all these signals to the morphological adaptation of the cells and the rearrangement of its cytoskeletal proteins for each particular adaptation.

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Abstract **γ-Tocotrienol, a nutrient-derived natural product, induces differential modulation of the therapeutic efficacy of anti-EGFR Tyrosine Kinase Inhibitors**

The Tyrosine-Kinase Receptor (TRK) family of proto-oncogenes, epitomized by the Epidermal Growth Factor Receptor (EGFR), provide a well-established system of cancer biomarkers. Mutations within parallel or cross-sectioning signaling pathways confer resistance to anti-EGFR therapies. Dissecting molecular cascades and inter-molecular interactions in these pathways is therefore essential to overcome resistance and optimize anti-EGFR therapeutic interventions. γ-Tocotrienol is a minimally toxic poly(oxo)phenolic derivative of the vitamin E family with potent signal-modulating properties in colon and prostate cancer carcinogenesis.

Herein we provide strong evidence that γ-Tocotrienol differentially modulates the efficacy of EGFR Tyrosine Kinase Inhibitors (TKI) in colon cancer models with diverse EGFR expression levels and discloses intermediate molecular markers of response interacting within the EGFR cascade. γ-Tocotrienol-modulated protein phosphorylation showed significant overlap with TKI -modulated protein phosphorylation. Combined with TKI in TKI-non-responding cells, γ-Tocotrienol elicited novel hits representing kinases associated with the EGFR cascade for the first time and representing potential new intracellular targets. These findings are further supported by our temporal pharmacoprotemics studies where γ-Tocotrienol exhibited strong caspase-independent pro-apoptotic activity in EGFR overexpressing cell lines, cross-sectioning the EGFR axis and maintaining a dynamic interplay between tyrosine phosphorylation and nitrosylation, underlying these signaling events.

In order to further reveal the molecular basis of synergistic or antagonistic outcome of combinatorial signals elicited by combinations of biopharmaceuticals, Bioluminescence/Fluorescence Resonance Energy Transfer (BRET/FRET) systems, constituting powerful tools in the assessment of efficacy of candidate molecular leads have been developed. Application of BRET/FRET assays has enabled the monitoring of inter-molecular interactions between established and newly identified target proteins, in live- cell settings. FRET signals induced by fluorescently labeled γ-Tocotrienol suggested that EGFR may also serve as a candidate target of this agent.

Conclusively, these findings provide substantial evidence for the potential role of γ-Tocotrienol, a minimally toxic natural agent, in enhancing sensitivity and overcoming resistance to anti-EGFR therapies and are, therefore, expected to further enable patient stratification for combined therapies in the clinical setting.

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Abstract

Personalised cardiovascular medicine: From antioxidants to validated molecular sources and targets of oxidative stress

Rationale

Oxidative stress has been postulated for many years as a major cause and driver of vascular disease states such as coronary artery disease, peripheral artery disease, and stroke. However, all therapeutic applications have focused on antioxidants with little or no success and no clinical implications. Here we show that identifying and specifically targeting the molecular sources of vascular oxidative stress and its target proteins is much more promising and provides specific, biomarker-assisted therapeutic avenues. One of the major functional targets of oxidative stress is the nitric oxide-cyclic GMP signalling pathway (NO-cGMP). Relevant sources include the innate immune response enzyme, gp91phox, a NADPH oxidase, now termed NOX2. Related NOX2-like enzymes are expressed on many surface cells (endothelium, epithelium) as an extended innate immune or stress response system.

Methods & Results

NOX deficient mice were subjected to ischemia, ischemia-reperfusion and metabolic stress models. NOX1 promotes atherosclerosis and is associated with an hypertensive phenotype. NOX4 is upregulated in ischemia-reperfusion and causes neurodegeneration after stroke.

Impaired NO-cGMP signalling is found in heart failure and coronary artery disease and can be targeted in stroke, hypertension and diabetes. eNOS recoupling appears to be efficient in peripheral artery disease. Biomarkers indicate both oxidative stress as well dysfunctional NO-cGMP signalling.

Conclusion

These data suggest that oxidative stress can be efficiently targeted using inhibitors of NOX or activators/stimulators of cGMP formation.

Clinical Relevance

Together with recent genetic evidence, the NO-cGMP pathway in conjunction with NOX-derived oxidative stress appears to be the first mechanism-based cardiovascular therapy.

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Abstract

Towards Personalized Medicine in Metabolic Disease

The field of oncology has paved the way in the use of biomarkers in translational and personalized medicine, enabling the selection of most responsive patients for specific treatments. Most successful examples are those where disease can be linked to a single genetic driver and drugs are used to shut down an overactivated pathway. A challenge appears however when these lessons-learned are to be applied to complex chronic diseases as metabolic syndrome. The progression from a healthy state to obesity, diabetes and ultimately to diabetes complications, including cardiovascular events, nephropathy and brain disorders to name a few, is based on a gradual disturbance of multiple equilibria. Influencing one equilibrium using specific nutrition or drugs affects other pathways in this complex system, resulting in seemingly positive effects on short-term but deleterious effects in seemingly non-related diseases on long-term. Key to successful treatment in metabolic disease is the use of system biology, not only to elucidate key disease mechanisms and identify key biomarkers, but also to use panels of such biomarkers to monitor the effect of interventions on the human system as a whole, and timely adjust when needed. Opportunities to implement such approach in health care through public private partnerships will be discussed.

Poster Presenters

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Abstract

Linked2Safety - A next generation, secure linked data medical information space for semantically-interconnecting electronic health records and clinical trials systems advancing patients safety in clinical research

Linked2Safety is an FP7 project funded by the European Commission under the area of ICT for health. The vision of the project is to advance clinical practice and accelerate medical research, by providing pharmaceutical companies, healthcare professionals and patients with an innovative semantic interoperability framework facilitating the efficient and homogenized access to distributed Electronic Health Records (EHRs). Even though EHRs contain an increasing wealth of medical information, the European healthcare information space is fragmented due to the lack of legal and technical standards, cost effective platforms, and sustainable business models. The Linked2Safety project aims to build the next-generation, semantically-interlinked, secure medical and clinical information space in the enlarged Europe. This will allow dynamically discovering, fruitfully combining and easily accessing medical resources and information contained in spatially distributed EHRs. Moreover it will leverage the reuse of EHRs in clinical research, towards the early detection of potential patient safety issues, based on the genetic data analysis and the extraction of the bio-markers associated with an identified type of an adverse event. It also aims to support sound decision making, towards the effective organization and execution of clinical trials, allowing health carers and medical scientists to easily submit their own query and get homogenized access to high-quality medical data.

Linked2Safety will allow the analysis of all the available data of the subjects, such as genetic, environmental and their medical history during a clinical trial, leading to the identification of the phenotype and genotype factors that are associated with specific adverse events and thus early detection of potential patients' safety issues. It will also enable subject selection for clinical trials through the seamless and standardized linking with heterogeneous EHR repositories, providing advice on the best design of clinical studies. Finally it aims to develop proof-of-concept pilot clinical trials design studies to validate and evaluate the Linked2Safety results. The University of Cyprus is responsible for the creation of the Linked2Safety Data Analysis Space. This includes the design and development of data mining techniques on genotypic and phenotypic data for single hypothesis testing and the identification of bio-markers associated to adverse events. All of the knowledge created by this system will be extracted, so that it can be used for future data sets and for an adverse events early detection mechanism.

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Abstract

Self-assembled Peptide and Protein Nanostructures in Diagnosisrelevance

Biological compounds able to organize into nanostructures such as self-assembled peptides, proteins or amphiphile compounds play an active role in the development of electrochemical sensors and electronic sensing devices (Field effect transistors, FETs) used for the detection

of compounds of biomedical importance.

Structures such as nanopores, nanowires or nanotubes can be synthesized using proteins, self-assembling aromatic peptides or viruses as building blocks. These nanostructures can be utilized as sensors to get information regarding the concentration, structure and dynamics of a single molecule that is translocated inside a channel protein as in a protein nanopore-based sensor.

Using manipulation techniques such as dielectrophoresis, self-assembling peptide nanotubes can be immobilized on top of metal microelectrodes in order to characterize their electrical properties. These non-conductive nanostructures can then be modified on its surface using antibodies or enzymes to fabricate very sensitive devices such as FETs for the detection of compounds of biomedical relevance (viruses, glucose, metals, neurotransmitters, etc) through impedance changes.

Electrochemical biosensors can be developed by immobilizing these biological nanostructures by physical adsorption or by trapping those using polymers on the surface of metal transducers. In this case the concentration of compounds is monitored through changes in the current which is proportional to the changes in analyte concentration. In this situation the nanostructures increase the surface area of the metal transducer.

In this work the different building blocks used for the synthesis of these biological structures will be discussed as well as their electrical and structural properties that make them suitable for the development of sensing devices. Additionally, the techniques for their controlled immobilization and functionalization will be presented.

Finally a review of the different sensing devices will be listed discussing its advantages and challenges when compared with sensing devices developed using nanomaterials traditionally used such as carbon nanotubes or silicon nanowires.

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Abstract

Antioxidant natural compounds transermal delivery and hypoglicamic effect - personalized approach

Personalized approach is extremely important for the treatment of diabetes mellitus. Non-enzymatic, free radical-mediated oxidation of biological molecules, membranes and tissues is present in a variety of pathological events, including diabetes mellitus. Hyperglycaemia appears to play a major role in free radical production .

The skin, as the outermost barrier of the body, comes in direct contact with many environmental factors. Substances with antioxidant properties could inhibit or significantly delay the above mentioned phenomena. Topical application of antioxidants may result in a sustained antioxidant capacity of the skin, possibly due to antioxidant synergisms. Another advantage of the skin is that it can be used to possibly deliver the antioxidant agent for obtaining systematic effects.

The isolation of polyphenols from plants grown in Georgia and their phytochemical investigation have been done by the Laboratory of Polyphenols of Institute of Pharmacochemistry. The high antioxidant activity of polyphenols: Robinin, Astragalegoside, Isoastragalegoside, Kaemferol; Rutin, Anthocyanes, Sums: Geranium pussilum and Geranium robertianum, has been determined by different methods. Their anti-inflammatory and antidiabetic activities by topical application have been examined on albino hairless mice SKH-1. The studes have been done in collaboration with Schools of Pharmacy and Medicine of the University of Athens. The in vitro release of active natural compounds from formulations was examined with the membrane diffusion method.

The studies have been done considering pharmacogenetic and pharmacogenomic factors. Antidiabetic activity by topical application has been studied on mice. Insulin has been measured at the end of experiment in plasma samples by using DRG ultrasensitive mouse

ELISA Insulin enzymeimmunoassay. According the results of clinical studies developed semisolid formulation and due to antidiabetic activity of the selected compound by topical application we consider the further studies of this natural product as a personalized medicine against diabetis and its complications.

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Abstract

Combined high resolution and functional CT imaging in an asthma mouse model, utilizing synchrotron radiation

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Background: Asthma is a common growing disease affecting over 300 million people worldwide. Therefore, development of novel therapies are of great demand which will be normally evaluated in preclinical asthma mouse models. Asthma is characterized by inflammation and air hyper responsiveness accompanied with airway wall thickening. To assess these alterations in the lungs of such mouse models, imaging methods with superior spatial resolution need to be applied. These methods are by definition limited in terms of sensitivity which hampers the detection of inflammation at the same time.

Method & Findings: We developed a novel approach to expand the high resolution microCT imaging technique with a functional aspect by utilizing barium labeled macrophages. Immortalized alveolar macrophages were kept in culture, labeled with clinical used barium containing contrast agent for 24h intra tracheal administered (6 Mio cells each) in asthma as well as in control mice. Mice were sacrificed 24h later and analyzed with phase contrast microCT at the SYRMEP beamline of the Elettra synchrotron (Trieste, Italy). A single distance phase retrieval algorithm was applied to retrieve phase information of the scanned lung regions. The reconstructed data showed the effectiveness of the technique to differentiate barium from lung tissue. Compared to control and blank samples, in asthmatic mice not only a higher barium content has been found, also increased soft tissue volume, reduced air volume and shrunken air pathways are demonstrated.

Discussion: Phase contrast enables delineation of the airways in great detail and allows therefore the analysis of weak alterations in their pathology. Decoupling phase and absorption effects mixed in the acquired data was achieved by utilizing a novel phase retrieval algorithm, enabling bio-distribution analysis of the macrophages. A great difference between the concentrations of labeled macrophages in the lungs of asthma animals compared to the controls was found. We therefore believe, that for the first time a functional as well as high resolution microCT imaging approach in an inflammatory lung disease model has been established with is of great potential for clinical applications in the near future at our opinion.

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Abstract

Methods of individualising treatments for patients with chronic conditions

Background

For long term conditions, treatment regimes can be complex, time consuming, and have serious adverse effects. Patients have various concerns and priorities surrounding treatment(s). Healthcare providers use various methods to prescribe treatments based on individual factors; however, there is little guidance to support healthcare providers and patients to achieve individualised treatments.

We aimed to:

(i) Clarify what individualisation means in the context of chronic disease

(ii) Explore the methods/techniques that are used to individualise treatments.

Method

A review of the literature was conducted. The Cochrane Central Register of Controlled Trials, EMBASE, CINAHL, MEDLINE, and PsychInfo were searched for papers published between 1990 and 2011. To supplement the literature review a qualitative exploration of healthcare providers' understanding of individualisation, and methods used to individualise treatments was conducted. Ten healthcare providers were interviewed. Data were analysed using thematic analysis.

Results

The interview study revealed that healthcare providers were often uncertain about what individualisation meant. Definitions included: doing what the patient wants; doing what (the healthcare provider thought) was best for the patient; not following guidelines; trading off risks and benefits; and treating medical versus social problems.

The literature review revealed a number of methods used by healthcare providers to individualise treatments. These methods were broadly categorised as methods used to: make initial diagnoses / treatment decisions; review patients' treatments; involve the patient and incorporate patient preferences in treatment decisions; and support patients outside the consultation.

Conclusions

Further research is needed to refine the concept of individualisation; develop a comprehensive list of techniques used by healthcare providers to support patients in achieving individualised treatments; and develop a tool kit for supporting individualised treatments. This could be practically useful in clinical practice in supporting patients and healthcare providers achieve individualised treatments, as well as advancing our understanding of individualisation.

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Abstract **Apoptosis-Modulating Action of the New Extract from Far-Eastern Holothurians**

Anticancer effects of most drugs are related to their apoptosis-inducing capacities. However, chemotherapy usually has numerous side-effects. Recently, some extracts from marine invertebrates, holothurian Cucumaria frondosa including, were suggested for treatment of several types of cancer. The extracts damaged cancer cells via apoptosis without manifest toxic side-effects. The content of the main apoptosis-inducing substances, triterpenoid glycosides, in tissues of Far-Eastern holothurians Eupectacta fraudatrix is significantly higher than that in C. frondosa. The object of the current work was research on apoptosis-modulating effects of the extract from Far-Eastern holothurians and the studies on safe using of the extract. It was shown that at doses more than 1000-fold lower than LD50, the extract given once a day for three days decreased levels of both apoptosis and nitrotetrazolium blue at the reversed dose-dependent manner in mice peritoneal macrophages. Additionally, it decreased activities of antioxidant enzymes catalase and glutathione reductase in direct dose-dependent manner. Obviously, the high antiradical activity of the extract induced “energy-conserving” conditions of the work of the antioxidant system in the normal cells. Nevertheless, the lowest of the doses studied significantly increased apoptosis in macrophages treated with stress-agent (bacteria) compared to the action of bacteria. On the contrary, the highest dose decreased the apoptosis in bacteria-treated cells. Research on the mechanisms of action of the extract on model system (phagocytes of holothurian E. fraudatrix) revealed that they were similar to those for dexamethasone. Apparently, the extract and dexamethasone competed in binding to cell surface receptors. One-year lasting supervision of mices after one-month treatment with the extract showed no changes in blood and liver biochemical and immunological markers. Taken together with data on possibilities of artificial cultivation of E. fraudatrix, the extract can be considered to be promising novel therapeutic agent for different types of cancer, sarcoma including.

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Abstract **Self-assembling synthetic lipids comprising privileged pharmaceutical structures**

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We have designed and synthesised amphiphilic lipids possessing several activities important to medicine chemistry. 1,4-Dihydropyridine (1,4-DHP) derivatives possess, depending on substituents, several pharmacological activities, e.g., anti-hypertensive, anti-anginal, memory enhancing, neiroprotective, anti-Alzheimer, anti-diabetic, anti-cancer, anti-oxidant, anti-mutagenic, growth stimulant and geroprotective [1,2].

It is possible to obtain compounds possessing selective activity or multifunctional molecules for polypharmacology. Self-assembling lipid type 1,4-DHP derivatives form nanoaggregates and possess gene transfection properties [3] and antiradical activity as well.

Unsubstituted in position 4 dialkyl-1,4-DHP-dicarboxylates are antioxidants and antiradical compounds. 4-Aryl-1,4-DHPs have low antiradical activity, but insertion of strong electron-withdrawing substituents (pyridinium, substituted pyridinium) in 2- and 6-methyl groups of 1,4-DHPs leads to active antiradical compounds.

So, it is shown that self-assembling lipids, gene delivery agents, in case of insertion of privileged 1,4-DHP moiety obtain novel - antiradical activity.

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Z. Hyvonen, A. Plotniece, I. Reine et. al. Novel cationic amphiphilic 1,4-dihydropyridine derivatives for DNA delivery. Biochem. Biophys. Acta. vol. 1509, 451- 466, 2000.

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Abstract

Personalised E-health care for patients with chronic somatic diseases

Chronic somatic conditions, such as rheumatoid arthritis, psoriasis, diabetes or multiple sclerosis, result in severe physical symptoms and psychological adjustment problems in about 30-40% of the patients. Previous research has shown that these physical and psychological adjustment problems can be effectively treated by personalised self-management care approaches for patients at risk for long-term adjustment problems.

The Internet has become a main medium for the delivery of computer-tailored self management interventions for patients with chronic somatic conditions. The greater flexibility, the fulltime accessibility, the potential high reach and the possible higher cost-effectiveness make the Internet an attractive channel for delivery self-management interventions.

Based on effective face-to-face treatments, a personalized E-health application for tailored self-management for patients with chronic somatic conditions has been developed in close cooperation with patient organizations. After screening of patients' risk profiles, tailored treatment modules are chosen, focusing on individualized programs for coping with pain, itch, fatigue, negative mood, or social relationships. During the E-health program, patients have weekly mail contact with the therapist with daily home-work assignements that are indivdualy tailored to the specific problems.

Results indicate that applying personalized E-health to risk groups of patients is feasible and patients perceive more advantages than disadvantages for E-health treatments in comparison with face-to-face treatments. Reviews on the effectiveness of the E-health self-management treatments in patients further suggest beneficial effects for physical and psychological functioning comparable to face-to-face treatments.

Tailored E-health self-management programs for patients with chronic somatic diseases seems to promising to offer personalized E-health care in an (cost)effective and userfriendly way.

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Abstract

Challenges and Opportunities in Ambient Assisted Living

The creation of new devices and frameworks for provision of Ambient Assisted Living (AAL) promises to revolutionize the manner at which Health Systems have addressed health service for its citizens.

Yet, despite the age of the telemedicine concept, the scope and degree of implementation of such platforms is far from ideal, thus failing to bring the much needed advantages.

In this short presentation, the challenges facing AAL will be addressed, from the point of view of its main stakeholders. New opportunities for AAL will also be discussed, primarily focusing on those resulting from the interaction of different areas, such as mass-media, computer science and telecommunications, and wearable medical devices.

The main conclusions will be drawn, from different points of view, further contributing to a wide-picture of the current standpoint of AAL.

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Abstract **Monte Carlo simulation for personalized laser treatment of inflammatory process**

Underlying mechanisms of low power laser irradiation beneficial effects in treatment of chronic inflammatory conditions are yet far from being explained, as there are many aspects of photon propagation in anisotropic media. Aims of present studies were to disclose characteristics of laser light penetration in live tissues and to reveal processes involved in cellular effects of soft laser irradiation at power densities comparable to those achievable in in vivo irradiated living tissues. We measured the diffuse reflectance in the area of inflammation of laser treated patients and used Monte Carlo simulations in order to obtain characteristic parameters of absorption and scattering phenomena and to compute the absorbed radiation dose at cellular level. Thus we can project the personalized treatment total dose and irradiation regime calculated for target tissue following Monte Carlo simulations.

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Abstract **Millimeter Wave Induced Suppression of Sarcoma Growth in Mice**

Unlike now widely applied traditional methods treatment of tumors by means of ionizing radiation (gamma therapy, proton therapy) and the chemotherapy, the considered method of MM-therapy is non- ionizing and non- invasive and hence is completely deprived of any harmful side effects. The present study was undertaken to investigate whether low-power (non-thermal) millimeter range electromagnetic radiation can act on tumor of mice in vivo without cytostatic agents. The present study has demonstrated the potential clinical application of low power coherent millimeter electromagnetic waves without damaging other tissues, without antitumoral drugs and harmful ionising radiotherapy.

It is known that with the help of differential melting curves (DMC) it can be distinguished DNA tumor sarcoma from DNA isolated from the liver of healthy mice. DMC-2 of tumor DNA are shifted relatively DMC-1 of the DNA healthy animals to lower temperatures, and in the DMC of tumor DNA there are appeared the additional peaks in the 52-60ºC, which is absent for DMC of liver DNA of healthy animals. The effect of MM waves with a frequency of 42.2 GHz is investigated in vivo on the structure of DNA secondary structure of sarcoma 37.

After 15 sessions of MM-therapy without cytostatic drugs, at animals of the irradiated 0,5hour was observed an inhibition of tumor growth by 33.5% compared with a control group and a

sharp suppression of DNA-methylation level 2.5 times as much. The DNA-2 has the high level of methylation (4,7 mol%), which after 0.5 hour influence of MM-radiation becomes (2.2 mol%) close to the corresponding value for DNA-1 (1,9 mol%). The received results are correlated with the spectrophotometric data. Under the influence of MM-radiation the values of temperature (Tm0C) and interval (T0C) of melting of DNA-2 are changed and approach to the corresponding values of DNA-1.

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Abstract

Genetic Polymorphisms Modifying Oxidative Stress and Response to Acute Antipsychotic Treatment

It has been suggested that genetic polymorphisms modifying oxidative stress may influence the response to antipsychotic treatment. In the present study we investigated the influence of polymorphisms in the Catalase (CAT), Superoxide dismutase (MnSOD) and Cytochrome P 450 17-hydroxylase (CYP17) genes on the response to acute antipsychotic treatment of schizophrenia in 74 patients acutely treated with haloperidol or risperidone. CAT C-262T, MnSOD Ala-9Val and T-C transition (A2 allele) in the 5' polymorphism in the promoter region of the CYP17 were genotyped by real time PCR assay and sequence specific PCR. Psychopathological symptoms were assessed with BPRS and CGI twice: 8-12 and 36-40 days after the first dose of antipsychotic. Adverse events were assessed with the SAS, BARS and AIMS scales. The respective genotypes frequencies were: CAT C-262T: CC 0.384; CT 0.507 and TT 0.110; MnSOD Ala-9Val: ValVal 0,338; ValAla 0,568; AlaAla 0,095 and CYP17: TT 0,243; TC 0,527 and CC 0,230. When controlled for age, gender, BMI, illness duration, number of previous hospitalizations, drug type and dosage patients with at least one CAT T allele (CT + TT genotype) had significantly higher total AIMS scores (P=0.022) and total BARS scores (P=0.010) than patients with two CC genotype. We did not observe any statistical significant association between CAT C-262T genotype and the efficacy of treatment although it did affect the baseline BPRS score (P=0.044). MnSOD Ala-9-Val and CYP17 (A2 allele) gene polymorphisms did not significantly influence neither the EPS neither the efficacy of treatment. Our results support the impact of CAT C-262T polymorphism on the occurrence of side effects in acute antipsychotic treatment in Slovenian schizophrenia patients.

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Abstract

Selected Gene Polymorphisms in Ischemic Stroke and Depressed Patients: Possibilites for Tailored Therapy

The neurobiological basis of ischemic stroke and postischemic depression is not yet clarified. We have focused on several genes which could be connected with the pathogenesis of ischemic stroke and depression. Angiotensin converting enzyme (ACE), as a part of the renin-angiotensin system, is important factor in blood pressure regulation. Incidence of D allele is associated with higher protein level and its activity. Serotonin-transporter-linked promoter (HTTLPR) is a degenerate polymorphic region in the gene that codes the serotonin

transporter. Its polymorphism is connected with neuropsychiatric disorders. Likewise, S allele is associated with the functional reduction as compared to L allele.Glutathione-S-tranferases (GST) detoxify a broad range of xenobiotics and carcinogens. The most studied polymorphisms are in families of GSTM1, GSTT1 and GSTP1. In our study we tested the gene polymorphisms in three groups of patients, with: i) ischemic stroke ii) depression, and iii) healthy controls. In the DD polymorphism of ACE gene, the depressed pacients exhibit higher frequency of DD genotypes in comparison to controls. Stroke patients exhibit only non-significantly lower frequency in comparison to controls. So far, we did not observe any significant differences in allelic frequency for HTTLPR gene neither for depressed nor ischemic groups in comparison to controls. Our results suggest that ACE DD genotype is increased in depressed pacients. Analysis of selected polymorphisms of GSTM1 and GSTT1 genes show higher frequency of GSTM1 null and GSTT1 wild genotypes.

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Abstract **Pro inflammatory genetic risk profile in periodontal disease**

Background: Periodontal disease caused by dental plaque is characterized by the clinical signs of infection, chronic inflammation and loss of periodontal tissue support. Bacteria and other pathogens colonize tooth surface and gingival sulcus, trigger chronic inflammatory responses with the release of cytokine and other inflammatory mediators which contribute to the loss of the connective tissue and the supporting bone of the teeth. Periodontitis is a multi-factorial disease and several risk-factors are involved in its pathogenesis. In fact, with infections other environmental, metabolic and genetic factors able to interfere with host immune responses may increase the propensity to develop the disease. Here, pro-inflammatory genetic background in patients with periodontal diseases was investigated to identify genetic risk factors associated with the disease.

Methods: Single nucleotide polymorphism (SNP) of Vascular Endothelial Growth Factor (VEGF), Alpha-1-Antichymotripsin (ACT), Idrossi-Methyl-Glutaril-CoA-Reduttase (HMG-CR), Interferon Gamma (INF-γ), Interleukin-1 Beta (IL-1ß), Interleukin 10 (IL-10), Interleukin 6 (IL-6) and Tumor Necrosis Factor Alpha (TNF-α) genes in patients and controls were investigated. SNPs were assessed by a PCR or by Real Time-PCR methods.

Results: The C allele of VEGF, the A allele of IL-10 and the GG genotype of TNF-α were more frequent in patients with periodontal diseases than in controls. The concomitant presence of the three genetic factors strongly increased the risk of periodontitis.

Conclusion: Our data support the notion that impaired regulation of inflammatory responses plays a role in the history of periodontal disease and VEGF, IL-10 and TNF-α genes show a synergistic role in the disease. Genetic risk factors may be used to set up a genetic risk profile and implement the screening of unaffected subjects with an increased individual susceptibility of developing periodontitis.

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Abstract **Rational design of Argyrin-based analogues as selective inhibitors of the**

proteasome

Proteasomes recognize and digest protein substrates that have been marked for degradation by the attachment of an ubiquitin moiety. Owing to their broad involvement in many cellular processes, proteasomes play a key role in many diseases, such as cancer. Therefore, proteasomes have been regarded as an attractive but complicated target for drug design. In eukaryotes, association of the 20S proteasome with the 19S regulatory 'cap' complex yields the 26S proteasome. The proteolytic core, active sites β1, β2 and β5 that exert caspase-like, trypsin-like and chymotrypsin-like activity, respectively, resides within the 20S subunit.

Inhibitors of the proteasome have to be highly specific, because proteasomes are very abundant in eukaryotic cells. The therapeutic index of proteasome inhibitors that specifically inhibit only one or two of the eukaryotic proteasome's active sites is expected to be larger than of broad proteasome inhibitors. Natural products have shown an excellent track record as medicinal agents and continuously find clinical applications despite the large number of synthetic drugs.

Herein, we report the results of our effort to design new inhibitors, inspired by nature, that selectively inhibit each of the proteasome activities, independently. We selected Argyrin A, a cyclic peptide isolated from the myxobacterium Archangium gephyra, and potent proteasome inhibitor, as our starting point upon which new compounds will be built. We performed an in-depth analysis of the binding conformation, binding site interactions and energetics of binding using DFT optimized molecular-docking simulations of Argyrin A to the three active sites utilizing a "humanized" 20S proteasome model. We describe the spatial orientation of Argyrin A in each active site, and identify the determinants of selectivity and binding activity. Through this we provide our rational for the design of new argyrin-based analogues, each ranked independently by several docking algorithms to identify potent and most importantly selective proteasome inhibitors.

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Abstract

(Iso)Ellipticines and derivatives as selective CNS cancer therapeutics

The natural product ellipticine (5,11-dimethyl-6H-pyrido[4,3-b]carbazole) exhibits potent anti-cancer activity and has been subject to much study since its isolation in 1959.(1) Its mechanism of action is multimodal, including DNA intercalation, topoisomerase II inhibition and inhibition of several kinases.(2-5)

Although synthetic routes to ellipticines and their biological activity have been well documented, a simple synthetic analogue of ellipticine, namely isoellipticine, has not been extensively investigated. Given their structural similarity and likely bioactivity, we have embarked on a programme of drug discovery centered on the isoellipticine template.

We hereby report the synthesis of a panel of novel ellipticine and isoellipticine derivatives, including 7 & 11 substituted isoellipticines and isoellipticinium salts.(6) Biological evaluation of selected compounds has led to the discovery of excellent potency for growth inhibition of numberous cancer cell lines and in particular for one subgroup, selectivity against the growth of CNS cancers.

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Abstract **Optically Activatable "Mitocans" as Molecular Probes for Colon Cancer Specific Targets**

Optical imaging is an important tool in the life sciences for the detection of gene expression and protein-ligand interactions. Although many of the techniques are restricted to in-vitro applications, due to problems with optical access or labeling, optical imaging is being increasingly used for in-vivo imaging as well. Absorption, reflectance, fluorescence, or bioluminescence can be used as the source of contrast. Endoscopic, fiber optic based, instrumentation is being developed to allow non-invasive imaging of internal organs. Usually, optical contrast agents have to be used to obtain high specificity and sensitivity. Highly specific probes are available that can label a single molecular species (e.g. GFP-fusion proteins). Metabolic processes can be investigated with probes that are activated by molecular interactions (e.g. BRET/FRET) or enzymatic reactions. Optical techniques can even map the activity of genes. In the context of the widely approved new roadmap to drug development, molecular imaging application for both identification and validation of response biomarkers defines one of the major pillars in the process.

Here in we present a new approach to introduce potent optically active pro-apoptotic derivatives of nutrient-derived lipid-soluble isoprenoids, as target-specific anti-cancer agents. Cell trafficking studies disclosed potent mitochondriotropic effect. Enzymatic hydrolysis of these "mitocans" results in alteration of optical properties which were further verified in colon cancer cell lines with differential expression of EGFR and in vivo pharmacokinetic and biodistribution studies. Introduction of the optically active "mitocans" to Bioluminscent Resonance Transfer Energy (BRET) studies in cells expressing interactive pairs of fluorescently-tagged targets downstream the EGFR pathway, reveals promising potential targets of these natural agents. Target verification is achieved with fluorescent molecular endoscopy in orthotopic colon cancer models in mice. These findings are expected to lead the way to the identification of specific therapeutic targets for minimally toxic natural agents and further decipher their mechanisms of action, thus enabling their development and approval as cancer therapeutics.

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Abstract **COST Action: European Network for Translational Immunology Research and Education (ENTIRE): From immunomonitoring to personalized immunotherapy**

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Abstract

Fluorescence based low-cost microbiosensors using simultaneously microfabrication process and enzyme immobilisation

A novel one-step microfabrication process of SU-8 films is proposed for developing inexpensive, small size and light-weight optical glucose micro-biosensors. Experimental work was performed in order to investigate whether the widely used in MEMS applications SU-8 photoresists polymers, can be utilised as immobilisation matrices for the simultaneous encapsulation of an oxygen-sensitive fluorescent indicator and glucose oxidase. The enzyme immobilisation, the encapsulation of the indicator and the patterning of the SU-8 take place simultaneously, thus offering a significant simplification of the microfabrication process. Despite the process involved contact with organic solvents, UV-light exposure and heating for pre- and post-bake, and the embedding of the enzyme in a hard and rigid epoxy resin matrix, it was observed that the enzyme demonstrated activity after encapsulation in SU-8. Testing of the immobilised enzyme´s activity inside the SU-8 matrix, was carried out with the measurement of oxygen consumption using an oxygen-sensitive indicator during the enzymatic oxidation of glucose. Negligible variation in fluorescence intensity upon the addition of glucose was observed in films without enzyme, whereas films with encapsulated enzyme and oxygen-sensitive fluorescent indicator showed a very clear increase in fluorescence intensity upon addition of glucose. A high transparency and negligible fluorescence of the SU-8 films were observed. The presented work opens up new possibilities for combining BioMEMS, advanced optoelectronic components with smart biosensor technology for personalised medicine diagnostic applications.

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Abstract

Nucleobase-containg molecules and biomedicine

Nucleobase-containing amino acids, (nucleoamino acids) and peptides (nucleopeptides) are molecules of increasing interest in biomedicine due to their useful binding properties towards natural targets such as nucleic acids and proteins [1], as well as their high resistance to enzymatic degradation [2]. More particularly, the binding ability of such molecules towards DNA, RNA and proteins is a fundamental feature useful to modulate those biochemical processes in which nucleic acids and proteins play a key role. The stability in sero is another appreciable characteristic of nucleoamino acid-based molecular probes, also in consideration of the scarce enzymatic resistance of natural oligonucleotides. Some nucleoamino acids and nucleopeptides are natural like the antimicrobial peptidyl nucleosides or the wiillardiine-containing peptides recovered from vegetal sources (Fagus sylvatica). However, many examples are also known of artificial nucleobase-containing amino acids and peptides which were obtained by chemical synthesis both in solution and in solid phase as previously reported in literature [2]. In this work, we report some examples of nucleoamino acid-based compounds which were recently studied for their possible utilization in biotechnological and medical strategies. More particularly, a description not only of their structural characteristics

but also of the synthetic routes to these hybrid molecules, as well as some properties of molecular interaction which could be beneficial in the development of innovative drugs for anticancer and antiviral therapies will be presented.

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Abstract

Drug metabolism and individualized medicine

“Personalized medicine” is a new concept in healthcare, one aspect of which defines the specificity and dosage of drugs according to effectiveness and safety for each patient. Dosage strongly depends on the rate of metabolism which is primarily regulated by the activity of cytochrome P450. In addition to the need for a genetic characterization of the patients, there is also the necessity to determine the drug clearance properties of the polymorphic P450 enzyme.

It is well-recognized that patients administered a particular drug will exhibit significant inter-individual variability in their response to treatment. Unfortunately some patients will fail to respond to the therapy entirely, while some others will suffer dose-related side effects, resulting in significant costs and fatalities. For these reasons, polymorphism in genes encoding the drug metabolizing cytochromes P450 is a very important factor that can no longer be neglected in the development of new drugs.

Progress in the human genome analysis has recently made it possible to identify a patient’s cytochromes P450 make up by genotype analysis using the AmpliChip CYP450 Test available from Roche Diagnostics.

However, genotyping needs a parallel enzyme-based platform capable of rapidly measuring a drug’s pharmacokinetics and clearance by the polymorphic P450 enzymes typical for a given genotype, and to this date, such platform is not available; this will be the subject of the current presentation.

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Abstract

Guar gum-graft-poly(ε-caprolactone) nanocarrier for anti-cancer drug delivery

Amphiphilic guar gum grafted with poly(ε-caprolactone) (GG-g-PCL) was fabricated as a drug delivery carrier using microwave irradiation technique. The structure of the GG-g-PCL copolymer was characterized by 1H NMR spectroscopy. By microwave irradiation, the GG-g-PCL with high grafting percentage (>200%) was achieved in a short reaction time. The GG-g-PCL copolymer is capable of self-assembling into nanosized spherical micelles in aqueous solution with the diameter of around 75-135 nm and 60-100 nm determined by DLS and TEM, respectively. The critical micelle concentration (CMC) of GG-g-PCL was found to be ~0.56

mg/L in a phosphate buffer solution. The drug release profile showed that the GG-g-PCL micelles provided an initial burst release followed by a sustained release of the entrapped hydrophobic model drug, ketoprofen, over a period of 10 to 68 h. The GG-g-PCL copolymer hydrolytically degraded into lower molecular weight fragments within a seven-week period under physiological conditions. These results suggest that the GG-g-PCL micelles could be used as a nanocarrier for in vitro controlled drug delivery.

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Abstract **Towards a Personalised Virtual Diabetic Patient Simulator**

The development of a diabetes simulator, an educational software tool which can help diabetic patients to better manage their disease, is described. Education of patients with diabetes mellitus is a fundamental part of diabetes care. One of the goals of diabetes education is to support the patients to understand the nature of their illness and its treatment. Diabetes patients should be aware of the impact of nutrition, physical activity and insulin injections on blood glucose excursions. They should be able to identify emerging health problems like severe hyperglycemia or hypoglycemia in early stages. This will enable them to adapt to and prevent these conditions.

Personalised ICT services provide several possibilities to improve patient education and therefore diabetic care. In particular the development of an educational diabetes simulator is considered. Only one diabetes simulator, called AIDA, is currently available. AIDA is designed only for type-1 diabetes patients (5-10% of the whole diabetic population), and does not use patient-specific data.

We are developing the Virtual Diabetic Patient Simulator (VDPS) for both type-1 and type-2 diabetes. The VDPS represents the key characteristics and behaviour of the main processes of glucose metabolism involved in diabetes for a period of one day (24 hours). Based on patient-specific information (parameters) and daily life situations the VDPS can be used to train the patient in a virtual environment with realistic scenarios.

The core of the simulator is a computational model which calculates temporal glucose and insulin plasma profiles in response to known inputs (food, insulin, etc.). As a first step we have coupled and modified existing literature models. The current model can predict plasma glucose concentrations with acceptable accuracy for education purposes. In conclusion, the model provides a solid background for further developments of the diabetes simulator.

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Abstract **Machine Learning Methods for the Prediction of Human Prostate Cancer Diagnosis and Prognosis, based on Real-Time RT-PCR data from formaline-fixed and paraffin embedded tissue**

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Background: Prostate cancer (PC) is the most common cancer diagnosed in men today. At present, screening methods lack for early stage diagnosis, and new tools are needed in order to improve the sensitivity of conventional diagnosis.

The aim of the study was to evaluate the diagnostic and prognostic power of an 8-gene signature in PC detection, using real-time RT-PCR data to train computational predictors based on supervised learning methods.

Methods & Findings: Molecular profiling was obtained from a previously characterized set of 90 formaline-fixed and paraffin embedded (FFPE) tissue samples from prostate gland: 64 were diagnosed with PC and 26 were used as negative controls.

We focused our attention on 8 genes previously shown to be correlated with prostate tumor progression: growth arrest-specific gene 1, histone H3, spermidine/spermine N(1)-acetyl transferase, ornithine decarboxylase, ornithine decarboxylase antizyme, denosylmethionine decarboxylase, clusterine, glyceraldehyde 3-phosphate dehydrogenase.

The real-time RT-PCR data were used to create different dataset from different PC tissue specimens and from negative controls. In order to obtain an effective predictor capable of discriminate between the two conditions, we evaluated the performance of various state of art supervised learning methods (Support Vector Machines, k-Nearest Neighbours, Random Forest) selecting the optimal parameters and features (subset of the 8 signature genes) in order to achieve the higher prediction.

We found that the SVM-based predictor showed a very good performance discriminating PC specimens from negative controls through a subset of 4-genes expression profile. The concordance of our 4-gene signature with the histological classification is 90.25%, with 93.4% sensitivity for prostate cancers and 80.95% specificity for negative controls. We then used the same approach to give a prognostic prediction of PC cases, classifying patient's molecular data in three different classes based on Gleason score's intervals, which represent the best predictor of final outcome routinely used in clinical practice.

The best prognostic prediction was achieved using a Support Vector Machines classifier with a 2-genes expression profile which brings to a 73.02% of concordance with the Gleason histological classification. All the computational predictors developed in this work were also integrated in a prediction server (PCPred) that allows the management of database of cases and the submission of prediction jobs via internet browser.

Discussion: The use of a subset of the original panel of 8 genes (feature selection) in order to optimize the performance of different classifiers allows the selection of an optimal predictor (Support Vector Machines here) capable to distinguish with high accuracy between tumours and benign samples. The method may be of help in supporting conventional PC diagnosis and provides an useful prognostic evaluation of the clinical outcome of patients with prostate cancer.

Keywords: prostate cancer, diagnosis, prognosis, prediction, biomarkers, bioinformatics, machine learning, prediction server

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Abstract **Non-inasive Investigation of Tissue Morphochemistry by All-Optical Methods**

"In this contribution we will discuss the combination of different optical microspectroscopic tools to non-invasively investigate the morphochemistry of human tissue. In particular, we combine the chemical sensitivity of nonlinear Raman-scattering (using coherent anti-Stokes Raman scattering, CARS) with second-harmonic generation (SHG) imaging to visualize the distribution of collagene and two-photon excited-fluorescence (TPF) imaging highlighting the distributions of fluorescent cofactors in the tissue. As the nonlinear optical tools are non-

invasive they can principally be used in personalized medicine for an in-vivo accessment of the physiological state of tissue. Furthermore, we shall discuss recent approaches towards automated image segmentation, pattern recognition and data classification, which present indispensible bioinformatic tools to bring this all-optical approach into the clinics."

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Abstract

Even stressed cells are individuals: Second messengers of free radicals in pathophysiology of stress associated diseases

"Pathophysiological processes associated with misbalance of oxidative stress and tissue homeostasis are associated also with lipid peroxidation. The end products of oxidative stress are therefore reactive aldehydes such as 4-hydroxy-2-nonenal (HNE), which act as a “second messengers of free radicals”.

Findings of growth regulating activities of HNE that overlapped with the development of the monoclonal and polyclonal antibodies specific for the HNE-protein adducts led to the introduction of qualitative determinations of the HNE presence in various (patho)physiological processes and to the change of consideration of the aldehyde’s bioactivities from cytotoxicity into cell growth regulation and signalling.1,2

However, the appearance of HNE in various organs indicates that it pathophysiology might be related to the cellular individuality of the stress reaction and adaptation that are not understood yet.

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Abstract

Finding combinatorial drugs from traditional Chinese medicines

To address the “more investments, less drugs” challenge in drug development, more and more attention is paid to multicomponent therapeutics. This drug discovery strategy will take many advantages over the prevalent single-component paradigm. However, to implement the new strategy, we still have to cope with some challenges, such as the explosive increase of drug combination quantities, the unpredictable pharmacokinetic properties of multiple components and the potential risks of drug-drug interactions. In spite of the rapid technical progresses in high-throughput screening, high-content screening and systems biology and various “omics”, we still need a long time to perfect the related techniques. Since traditional medicines, in particular traditional Chinese medicine (TCM), have accumulated rich experiences in combinatorial use of natural medicines (for instance, more than 100,000

formulae have been documented in TCM). We speculate that we can start with traditional medicines to find modern drug combinations. This tactic is preliminarily supported by the finding that a certain part of TCM components have counterparts of modern Western drugs or candidates and the synergistic effects of some TCM formulae can be understood in terms of the Western-medicine-justified activities [1]. In addition, starting with traditional medicines will take the advantages of controlling the pharmacokinetics and drug-drug interactions of multiple components, because most combinatorial modes of TCM combinations have been used clinically for hundreds years and by thousands of patients (if not millions). To further evaluate the potential of this tactic, we will focus on anti-dementia TCM formulae to examine whether some clues can be derived from these prescriptions to help find anti-dementia combinatorial drugs [2].

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Abstract

In-body positioning using enhanced radio signal strenght

Specifics of in-body positioning of a wireless capsule using received radio signal strength (RSS) on the body's surface will be presented. Limits on three axial accuracy for capsule positioning and orientation will be discussed. A new method for enhanced RSS positioning using a sensor network will be presented. Energy and space requirements will be compared with physical capsule limitations as well as those of other positioning and orientation detection methods. Simulation results using SEMCAD X Medical full human body phantoms to acquire radio signal data and software package for wireless capsule positioning developed in MATLAB will be presented. Finally, conclusion on achievable accuracy and feasibility of enhanced RSS in in-body positioning will be given.

List of Accepted Posters

1	**Aristos Aristodemou**	University of Cyprus, CY 'Linked2Safety - A next generation, secure linked data medical information space for semantically-interconnecting electronic health records and clinical trials systems advancing patients safety in clinical research'
2	**Jaime Castillo**	Technical University of Denmark, DK Self-assembled Peptide and Protein Nanostructures in Diagnosisrelevance
3	**Inga Dadeshidze**	Institute of Pharmacochemistry, GE Antioxidant natural compounds transermal delivery and hypoglicamic effect - personalized approach
4	**Simeone Dal Monego**	CBM Scrl, IT Combined high resolution and functional CT imaging in an asthma mouse model, utilizing synchrotron radiation
5	**Sarah Denford**	University of Exeter, UK Methods of individualising treatments for patients with chronic conditions
6	**Liudmila Dolmatova**	V.I. Il'ichev Pacific Oceanological Institute, RU Apoptosis-modulating Action of the New Extract from Far-Eastern Holothurians
7	**Gunars Duburs**	Latvian Institute of Organic Synthesis, LV Self-assembling synthetic lipids comprising privileged pharmaceutical structures
8	**Andrea Evers**	Radboud University Nijmegen Medical Centre, NL Personalised E-health care for patients with chronic somatic diseases
9	**Nuno Garcia**	University of Beira Interior, PT Challenges and Opportunities in Ambient Assisted Living
10	**Iulian Ionita**	University of Bucharest, RO Monte Carlo simulation for personalized laser treatment of inflammatory process
11	**Vitali Kalantaryan**	Yerevan State University, AM Millimeter Wave Induced Suppression of Sarcoma Growth in Mice
12	**Matej Kastelic**	Faculty of Medicine, Institute of Biochemistry, SI Genetic Polymorphisms Modifying Oxidative Stress and Response to Acute Antipsychotic Treatment
13	**Jan Lehotsky**	Comenius University, SK Selected Gene Polymorphisms in Ischemic Stroke and Depressed Patients: Possibilites for Tailored Therapy
14	**Federico Licastro**	University of Bologna, IT Pro inflammatory genetic risk profile in periodontal disease
15	**Eriketi Loizidou**	Univerity of Cyprus, CY Rational design of Argyrin-based analogues as selective inhibitors of the proteasome
16	**Florence McCarthy**	University College Cork, IE (Iso)Ellipticines and derivatives as selective CNS cancer therapeutics
17	**Andreani Odysseos**	EPOS-Iasis, R&D, CY Optically Activatable "Mitocans" as Molecular Probes for Colon Cancer Specific Targets
18	**Dusan Popadic**	University of Belgrade, Faculty of Medicine, RS COST Action: European Network for Translational Immunology Research

		and Education (ENTIRE): From immunomonitoring to personalized immunotherapy
19	**Sotiria Psoma**	University of Western Macedonia, EL Fluorescence based low-cost microbiosensors using simultaneously microfabrication process and enzyme immobilisation
20	**Giovanni Roviello**	Consiglio Nazionale delle Ricerche - CNR, IT Nucleobase-containg molecules and biomedicine
21	**Sheila Sadeghi**	University of Torino, IT Drug metabolism and individualized medicine
22	**Ashutosh Tiwari**	Linköpings Universitet, SE Guar gum-graft-poly(ε-caprolactone) nanocarrier for anti-cancer drug delivery
23	**Natal van Riel**	Eindhoven University of Technology, NL Towards a Personalised Virtual Diabetic Patient Simulator
24	**Anna Vendramin**	EuroClone S.p.A., IT Machine Learning Methods for the Prediction of Human Prostate Cancer Diagnosis and Prognosis, based on Real-Time RT-PCR data from formaline-fixed and paraffin embedded tissue
25	**Nadine Vogler**	Institute of Photonic Technology, DE Non-inasive Investigation of Tissue Morphochemistry by All-Optical Methods
26	**Roland Wohlgemuth**	Sigma- Aldrich, CH Metabolite Synthesis and Protein Function
27	**Neven Zarkovic**	Rudjer Boskovic Institute, HR Even stressed cells are individuals: Second messengers of free radicals in pathophysiology of stress associated diseases
28	**Hong-Yu Zhang**	Huazhong Agricultural University, CN Finding combinatorial drugs from traditional Chinese medicines
29	**Damir Zrno**	Faculty of Electrical Engineering and Computing (FER), HR In-body positioning using enhanced radio signal strenght

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