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 **UK-Japan Workshop:**

***How do we identify new targets for new medicine?***

 **28-29 January 2013**

**sponsored by the British Embassy, Tokyo**

**with support from**

**Royal Society of Chemistry**

**Participant List**

UK Speakers

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Name** |  **Department** | **Affiliation** | **e-mail** |
|  | Prof Chas Bountra | Structural Genomics Consortium | University of Oxford | chas.bountra@sgc.ox.ac.uk |
|  | Prof Rab Prinjha | Target progression departmentand external academic alliances  | GlaxoSmithKline | Rabinder.Prinjha@gsk.com |
|  | Prof Praveen Anand | Centre for Clinical Translation | Imperial College London | p.anand@imperial.ac.uk |
|  | Prof Andrew Lee Hopkins | College of Life Sciences | University of Dundee | A.Hopkins@dundee.ac.uk |
|  | Dr Dafydd Owen | Worldwide Medicinal Chemistry | Pfizer Worldwide R&D, US | Dafydd.Owen@pfizer.com |

Japanese Speakers

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Name** | **Department** | **Affiliation** | **e-mail** |
|  | Prof Toshio Tanaka | Department of Pharmacogenomics and Systems Pharmacology | Mie UniversityGraduate Schoolof Medicine | tanaka@doc.medic.mie-u.ac.jp |
|  | Prof Toshio Miyata | Graduate School of Medicine | Tohoku University  | miyata@med.tohoku.ac.jp |
|  | Dr Tetsuyuki Maruyama | Pharmaceutical Research Division | Takeda Pharmaceutical Research Division | paul.chapman@takeda.com |
|  | Dr Yoshiya Oda | Biomarkers & Personalized Medicine Core Function Unit | Eisai Co., Ltd. | Yoshiya\_Oda@eisai.com |
|  | Prof Masanari Itokawa | Schizophrenia & Affective Disorders Research | Tokyo Metropolitan Institute of Medical Science | itokawa-ms@igakuken.or.jp |
|  | Prof Tatsuo Kurokawa | Faculty of Pharmacy | Keio University | kurotats@da2.so-net.ne.jp |
|  | Dr Yuji Yamamoto | Office of Medical Innovation | Cabinet Secretariat of the Japanese Government | yyamamoto07@gmail.com |

Observers

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Name** | **Department** | **Affiliation** | **e-mail** | **availability** |
|  | Dr Osamu Asano | Eisai Product Creation Systems | Eisai  | o-asano@hhc.eisai.co.jp | 28-29 & reception |
|  | Dr Takehiko Miyagawa | Open Innovation, Neuroscience product creation unit | Eisai | t-miyagawa@hhc.eisai.co.jp | 28 & reception |
|  | Dr Koji Chiba |  | Keio University | Chiba-kj@pha.keio.ac.jp | 28-29 & reception |
|  | Dr Kazuhiro Fujita |  | The Systems Biology Institute | kaf@sbi.jp | 28 & reception |
|  | Dr Samik Ghosh |  | The Systems Biology Institute | ghosh@sbi.jp | 28-29 & reception |
|  | Prof Hiroaki Kitano |  | The Systems Biology Institute | kitano@sbi.jp | 28 & reception |
|  | Ms Akiko Kobori |  | Tokyo Metropolitan Institute of Medical Science | kobori-ak@igakuken.or.jp | 28 & reception |
|  | Prof Noriyasu Hirasawa | Graduate School of Pharmaceutical Sciences | Tohoku University | hirasawa@m.tohoku.ac.jp | 28-29 & reception |
|  | Dr Tiago Lopes | ERATO Kawaoka Infection-induced Host Reponses Project  |  | tiagojab@yahoo.com.br | 28 & reception |
|  | Dr Toru Maruyama |  | Ono Pharmaceutical Co., Ltd. | to.maruyama@ono.co.jp |  |
|  | Ms Yukiko Matsuoka |  | The Systems Biology Institute | myukiko@sbi.jp | 28-29 & reception |
|  | Dr Fumiyoshi Matsuura |  | Eisai Product Creation Systems | f-matsuura@hhc.eisai.co.jp | 28-29 & reception |
|  | Dr Terumasa Mino |  | Dainippon Sumitomo Pharma Co., Ltd. | terumasa-mino@ds-pharma.co.jp |  |
|  | Prof Toshio Miyata | United Centres for Advanced Research and Translational Medicine, Graduate School of Medicine | Tohoku University | miyata@med.tohoku.ac.jp | 28-29 & reception |
|  | Mr Kazuhiko Miyata | Third Patent Examination Department | Japan Patent Office | kazuhiko.miyata@gmail.com | 28-29 & reception |
|  | Ms Mika Mizunuma | Graduate School of Pharmaceutical Sciences | The University of Tokyo | m.mizunuma@gmail.com | 28-29 & reception |
|  | Dr Aya Nakae | Department of Anesthesiology & Intensive Care, Graduate School of Medicine | Osaka University  | anakae@anes.med.osaka-u.ac.jp | 28-29 & reception |
|  | Dr Kunihiro Nakai | Dept of Plastic & Reconstructive Surgery | Sakai City Hospital | Ckadn610@sutv.zaq.ne.jp | 29 & reception |
|  | Prof Yoshiteru Ohshima | Graduate School of Pharmaceutical Sciences | Tohoku University | oshima@mail.pharm.tohoku.ac.jp | 28 & reception |
|  | Dr Norihisa Okada | United Centres for Advanced Research and Translational Medicine, Graduate School of Medicine | Tohoku University | okada-norihisa@pmda.go.jp | 28-29 & reception |
|  | Dr Jason Shoemaker | ERATO Kawaoka Infection-induced Host Responses Project |  | jshoe@ims.u-tokyo.ac.jp | 28 & reception |
|  | Dr Kazuhiro Takahashi | Research Strategy & Planning Department | Mitsubishi Tanabe Pharma Corporation | Takahashi.Kazuhiro@mg.mt-pharma.co.jp | 28-29 & reception |
|  | Mr Yoshiaki Takahashi | International Science Cooperation Division | Ministry of Foreign Affairs | yoshiaki.takahashi@mofa.go.jp | 29 &reception |
|  | Prof Toshio Tanaka | Department of Pharmacogenomics and Systems Pharmacology, Graduate School of Medicine | Mie University | tanaka@doc.medic.mie-u.ac.jp | 28-29 & reception |
|  | Dr Kazuhiko Tanzawa |  | RIKEN | yoshiaki.takahashi@mofa.go.jp | 28 &reception |
|  | Ms Nanae Watanabe | United Centres for Advanced Research and Translational Medicine, Graduate School of Medicine | Tohoku University | nanae.watanabe@med.yohoku.ac.jp | 28 & 29am |
|  | Dr Mitsuhiro Yamaguchi |  | Daiichi Sankyo Co., Ltd. | Yamaguchi.mitsuhiro.bu@daiihisankyo.co.jp | 28-29 & reception |
|  | Prof Akio Yamakawa |  | The University of Tokyo | a2yamaka@ims.u-tokyo.ac.jp | 28-29 & reception |
|  | Prof Mitsuru Hashida | Graduate School of Pharmaceutical Sciences  | Kyoto University | hashidam@pharm.kyoto-u.ac.jp | 28 pm & 29 reception |
|  | Dr Noboru Yamamoto | Eisai Product Creation Systems | Eisai  | n-yamamoto@hhc.eisai.co.jp | 29 |
|  | Dr Yoshinobu Hashizume | Drug Discovery Chemistry Platform Unit | Center for Molecular Imaging Science, RIKEN | yhashizume@riken.jp | 28 & reception |
|  | Dr Chiaki Sato | Policy Alternatives Research Institute  | The University of Tokyo | chiakist@pp.u-tokyo.ac.jp | 28-29 & reception |
|  | Mr Shinichi Horie | CRO Business Dept | Trans Genic Inc. | horie@transgenic.co.jp | 28-29 & reception |
|  | Ms Jane Weng | Dept of Cellular Signaling and Molecular Medicine, IMSUT | The University of Tokyo | janescweng@gmail.com | 28-29 & reception |
|  | Dr Osamu Nakayama | Dept of Industry-Academic Collaboration | Japan Science and Technology Agency (JST) | O2nakayama@jst.go.jp | 28-29 & reception |
|  | Dr Hiroshi Otake | Center for Research and Development Strategy | JST | hiroshi.otake@jst.go.jp | 28 & reception |
|  | Dr Daiji Naka  | Dept of International Affairs | JST | d2naka@jst.go.jp | 28 & reception |
|  | Prof Yoshiharu Iwabuchi | Graduate School of Pharmaceutical Sciences | Tohoku University | iwabuchi@mail.pharm.tohoku.ac.jp | 29 |
|  | Dr Atsuhiko Ichimura | United Centres for Advanced Research and Translational Medicine | Tohoku University | aichimura@med.tohoku.ac.jp | 28-29 & reception |

**Workshop Programme**

 **How do we identify new targets for new medicines?**

 **28-29 January 2013**

**WORKSHOP OBJECTIVES:**

Improve collaboration between researchers working on target validation (translational

 medicine) in the UK and Japan

Highlight the importance of target validation in healthcare and to society at large

Present leading developments in target validation from UK and Japan

Identify the challenges facing target validation and how these challenges should be met

Identify areas of collaboration and outline actions

Give an overview of science policy relating to target validation

**Monday 28 January**

|  |  |
| --- | --- |
| Time | Activity  |
| 0845 – 0910 | **Registration + Coffee** (presentation check for Session 1 & 2 speakers) |
| 0910 - 0915 | **Opening remarks (British Embassy)** |
| 0915 - 10450915-09400940-10051005-10301030-1045 | **Session 1: Scene Setting**  \*Each slot 25 minute presentation **Prof Chas Bountra** (SBC Oxford) *To provide an introduction to the workshop, detailing the workshop overall objectives (What is target validation) and outlining it is important/challenge within drug discovery programmes.* **Prof Toshio Tanaka** (Mie University) **Dr Tetsuyuki Maruyama** (Takeda)**Q&A and discussion**  |
| 1045 - 1100 | Coffee Break |
|     1100-11251125-11501150-12151215-12401240-1255 | **Session 2:** **Current Overview of Research-Japan***Objective(s): To provide an overview of current drug discovery process in Japan from academic, industrial, clinical perspectives.*\*Each slot 25 minute presentationChair: Prof Toshio Tanaka (Mie University)**Prof Toshio Miyata** (Tohoku University)**Prof Masanori Itokawa** (Tokyo Metropolitan Institute of Medical Science)**Prof Noriyasu Hirasawa** (Tohoku University)**Dr Yoshiya Oda** (Eisai)**Q&A and discussion** |
| 1255 - 1400 | Lunch |
|  1400-14251425-14501450-15151515-15401540-1555 | **Session 3:** **Current Overview of Research –United Kingdom***Objective(s): To provide an overview of current drug discovery process in the UK from academic, industrial and clinical perspectives.* \*Each slot 25 minute presentationChair: Prof Chas Bountra (Oxford) **Prof Andrew Hopkins** (University of Dundee) **Dr Dayfdd Owen** (Pfizer)**Dr Rab Prinjha** (GSK)**Prof Praveen Anand** (Imperial College London)**Q&A and discussion** |
| 1555 - 1610  | Coffee Break |
|  1610-1630 1630-1650 1650-1715 1715-1730 1730- | **Session 4: Policy Considerations**Chair: Prof Bountra and Prof Miyata**Prof Tatsuo Kurokawa** (Keio University)**Dr Yuji Yamamoto** (Cabinet Office)**Prof Chas Bountra** (Oxford)**Q&A and discussion**Day 1 close |
| 1730 – 1900 | **Reception** |

**Tuesday 29 January**

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| --- | --- |
| Time | Activity  |
|  0915-0930 | Registration & coffee |
|  0930-1050 | **Session 5:** **What are the challenges and how can these be addressed?***Objective(s):* *To identify the gaps and challenges within Target Validation in relation to Drug Discovery;* *To identify topics of mutual interests for collaboration or areas requiring the development of new scientific strategies**To establish dialogue and means for achieving collaboration and joint projects*Chair: Prof Bountra and Prof TanakaTable Discussions-Gaps/Challenges with Target Validation-Solutions and Actions |
| 1050 – 1100 | Coffee Break |
| 1100 – 1145 | Summary Findings + Group Photo |
| 1145 – 13201330- | LunchWorkshop participants to move  |

**Open seminar:**

 **‘Challenges facing drug discovery in Japan and the UK**

 **-how can these challenges be met?’**

Venue: Kagaku Kaikan Hall 7th floor

**Objective(s):**

* *To provide an overview to a range of stakeholders on the current drug discovery processes in Japan and the UK.*
* *To create a forum for the open discussion of current challenges facing translational medicine and thoughts on how these should be addressed.*

**1400-1430 Registration**

**1430-1435 Opening remarks (Royal Society of Chemistry and British Embassy)**

**1435-1455 Introduction to the session - Dr Dayfdd Owen (Pfizer)**

* *Provide a very brief introduction on Target Validation*
* *Summarise key points from previous 1.5 days workshop at the British Embassy*
* *Similarities/Differences between UK and Japan*

**1455-1500 Q&A**

**1500-1520 Prof Chas Bountra (University of Oxford)**

 *Drug discovery landscape in the UK*

**1520-1540 Dr Yoshinobu Hirayama (MHLW)**

 *TBA*

**1540-1545 Q&A**

**1545-1600 Coffee break**

**1600-1625 Professor Toshio Tanaka (Mie University)**

 *Target Validation and Zebrafish-based Systems Pharmacology*

**1625-1650 Prof Andrew Hopkins (University of Dundee)**

 *TBA*

**1650-1715 Professor Toshio Miyata (Tohoku University)**

 *Drug Discovery and Development from Academia*

**1715-1740 Professor Praveen Anand (Imperial College of London)**

 *Target Validation for Novel Analgesics: Paradigm for Clinical Translation*

**1740-1745 Closing remarks**

**1745-1900 Networking reception**

**CV & Abstracts**

**Professor Chas Bountra**

Chas Bountra has had a unique industrial and academic career. He is currently Head of the Structural Genomics Consortium (SGC), Professor of Translational Medicine, and an Associate Head of Medical Sciences at the University of Oxford. He serves on numerous public/ charitable funding committees, journal review panels, scientific advisory boards for academic drug discovery programmes, biotechs, pharmas and VCs. He has in the past five years helped attract nearly £65M of research funding to the University, has led the organisation of several international scientific conferences in Oxford and is facilitating the university’s reputation as a centre for drug discovery.

The SGC comprises 12 PIs, and more than 90 research fellows, postdocs, students and support staff. The group’s technical focus is protein biochemistry, structural biology, crystallography, bio-informatics, assay development, screening and medicinal chemistry. The group is now driving the identification of new targets for the discovery of new medicines, publishes all findings immediately (>1 per week), works closely with more than 100 academic labs and eight large pharmaceutical companies, and shares all reagents and expertise freely. The SGC has become a leader in human protein structural biology and epigenetics chemical biology, and is arguably one of the largest and most successful public private partnerships in the world. Chas is an advocate for pre-competitive science up to and including Phase I. In 2012 he was voted one of the “top innovators in the industry”.

Prior to coming back to Oxford five years ago, Chas was Head of Biology at GSK (nearly 200 molecular biologists, pharmacologists, histologists, in vivo and translational scientists). During a six year period, his group generated >30 clinical candidates, facilitated >20 POCM studies, progressed 5 assets into Phase III studies and established two new Translation research units in Singapore and Ireland. Chas built the biological rationale leading to the development and launch of Alosetron, and was the first to show that neurokinin NK1 receptor antagonists are anti-emetic (drugs now on market). He has therapeutic expertise in neuro-psychiatry, gastro-intestinal and inflammatory diseases, and “know- how” of all stages of the drug discovery and development process. His research interests are mechanisms underlying synaptic plasticity, neuronal hyper-reactivity, inflammation, degeneration and regeneration. He has given over 300 invited lectures (61 in past two years).

**Abstract**

**Scientists in Japan and UK must work together to accelerate the discovery of new medicines for many chronic diseases**

The discovery of “pioneer medicines” (i.e. those acting via novel molecular targets) has proven to be an immensely complex, long term, expensive and high risk endeavour. Despite formidable investments by the pharmaceutical industry and public/ charitable funders, over the past few decades in both infrastructure and technology, the success rates have remained low, and flat at best. There are several reasons for this: inadequate understanding of human disease and of the mode of action of existing drugs, poor clinical biomarkers and preclinical models, and a large choice of potential drug targets. Furthermore, many academic groups and private organisations continue to work “in parallel and in secret” on a relatively narrow sub-set of targets, most of which are destined for failure in subsequent clinical studies. This duplication of effort and hence wastage is perpetuated by the many clinical studies which are not published (or published after a delay, or in insufficient detail). Several groups therefore waste increasingly limited resources on such “failed” targets. This poses an ethical dilemma, because current practice is resulting in patients being exposed to molecules for such targets.

During my presentation, I will discuss strategies to de-risk or to identify better targets, and ways in which we can pool resources to share risk, reduce duplication, minimise patient harm and help industry discover new medicines for society.

**Professor Toshio Tanaka M.D., Ph.D**

Target Validation and Zebrafish-based Systems Pharmacology

Department of Pharmacogenomics and Systems Pharmacology

Mie University Graduate School of Medicine

**Research Career**

1975 Graduated from Mie University School of Medicine, MD

1980 Graduated from Mie University Graduate School of Medicine, PhD of Pharmacology

1980 Research Associate at the Department of Pharmacology, Mie University School of Medicine

1982 Assistant Professor at the Department of Pharmacology, Mie University School of Medicine

1982 Post-Doctoral Research Associate at Baylor College of Medicine, USA

1983 Assistant Professor at the Department of Pharmacology, Mie University School of Medicine

1988 Professor at the Department of Pharmacology, Mie University School of Medicine

2003 Joint Professor at the Department of Bioinfomatics, Mie University

2013 Professor at the Department of Pharmacogenomics and Systems Pharmacology,

 Mie University Graduate School of Medicine

Chairman of the Council for Genomic Drug Discovery Forum Japan

President of Japanese Sociaty for Circulation Research

**Abstract**

Although the rate of progress in preclinical biomedical science is high, it remains difficult to translate these findings into potential drug discovery. The major cause of attrition in the pharmaceutical industry is the lack of efficacy in phase II and III clinical trials, which may be due to insufficient target validation. Systems pharmacology is a recently introduced term that refers to the area dealing with the representation of therapeutics mechanisms of action and to improve the efficiency of innovative drug discovery and development. Previously, we reported that heme oxygenase-1 and heat shock protein 72 as potential drug targets by using rat model of cerebral vasospasm. However, there is serious problems of throughput in mammalian target validation system. In recent years in vivo chemical and genetic screening in zebrafish has emerged as a rapid and efficient method to identify drug target that modulate specific human disease processes. By performing primary screening of drug in vivo, the bioactivity, toxicity, and off-target side effects are determined from the onset of drug development. We would like to present our rencent data which suggest that zebrafish-based systems pharmacology will be powerful next generation strategy for therapeutic target validation.

**Professor Tetsuyuki Maruyama, Ph.D**

The scientist formerly known as Paul Chapman was born and raised in the US, obtaining his PhD in neuroscience from Stanford University. He began his academic career as Assistant and then Associate Professor at the University of Minnesota before moving in 1996 to Cardiff University, where he became Professor of Neurobiology in the Cardiff School of Biosciences. His professional interest in the neural mechanisms of learning and memory led to research on Alzheimer ’s disease and other diseases associated with cognitive dysfunction, which eventually induced him to move from academics into industry in order to pursue treatments for these high unmet medical needs. After working at Merck Sharp and Dohme in England he moved to Singapore to become Director of GlaxoSmithKline’s Center for Cognitive and Neurodegenerative Disorders. In 2010 he moved to Japan and Takeda Pharmaceutical Company, where he now heads Takeda’s global Research efforts. Dr Chapman was so taken by the culture, heritage and quality of life in Japan that he has now become a Japanese citizenship and taken the name of Tetsuyuki Maruyama.

**Abstract**

The process of identifying drug targets is at the same time very simple and almost impossibly complicated. Advances in biotechnology have enabled high-throughput approaches based on genetics and genomics as well as the use of phenotypic screens employing sophisticated imaging and robotics. Similarly, rapid technical evolution of medicinal chemistry approaches has contributed to screening, real or virtual, and to an expansion of what is considered "druggable," as has the increasingly successful use of large molecules. And yet, the number of truly novel targets that promise breakthroughs in the treatment of unmet medical needs has not increased significantly. The way to identify targets that will change the standard of medical care will most likely come from renewing our focus on the biology of the diseases we seek to treat. By making greater use of cellular, molecular and systems biology, and by cross-fertilizing the understanding gained from studies of seemingly disparate diseases, we may be in a better position to create medicines of value.

## Professor Toshio Miyata, M.D., Ph.D.

**Affiliation** Professor, Tohoku University

 **・**Special Advisor to the President

 **・**Vice Executive Director, Office of Research Promotion

 **・**Director, United Centers for Advanced Research and Translational

　　　　　　　　 Medicine (ART) (http://www.art.med.tohoku.ac.jp/e/index.html)

**Concurrent post**

 Member of Royal Academy of Medicine in Belgium, Permanent (2004~)

 Member of the Executive Committee and Council, The International Society of Nephrology (~2013)

 Vice President, The International Society of the Maillard Reaction(~2011)

**Total publications in English**

Total of 245 peer-reviewed contributions in English (h-Index 54, Total citation factors 10,264 point. Invited speaker at international conferences: 62 times

**Abstract**

In the field of new drug discovery, basic research has yielded many fruits, and we have an abundance of information on drug targets, together with the infrastructure needed for drug discovery. Researchers in universities are now able to use high-throughput screening using large-scale compound libraries. They also have access to various *in silico* technologies which use computers for compound design. This means that with the right effort, using the latest science and technology and working smartly in cooperation with contracting research organizations (CRO), it is possible even for universities to start from *in silico* searching for hit compounds, move through GMP synthesis and formulation as well as non-clinical GLP studies, and reach phase 2a clinical trials in humans. Universities now have a solid infrastructure for drug discovery and development, but the question for the future is to what extent we can build cost-effective mechanisms for obtaining new, innovative medicines in the context of limited budgets, labor, and time.

**Professor Masanori Itokawa, M.D., Ph.D.**

**Education**:

 1989 M.D. Saitama Medical School

 1996 Ph.D. Tokyo Medical and Dental University/ School of Medicine

**Professional Training, Employment and Fellowships:**

1989-1990 Resident in Department of Neuropsychiatry, Tokyo Medical

 and Dental University/ School of Medicine, Tokyo

 1991-1993 Research Fellow in Department of Medical Genetics,

 Institute of Basic Medical Sciences, University of Tsukuba,

 1993-1994 Research Associate and Psychiatrist in Department of

 Neuropsychiatry, Tokyo Medical and Dental University/

 School of Medicine, Tokyo

 1994-1996 Research Association in Department of Biochemistry,

 Institute for Brain Research, Faculty of Medicine,

 University of Tokyo, Tokyo

 1997-1999 Visiting Fellow in Molecular Neurobiology Branch,

 National Institute on Drug Abuse, National Institute of

 Health, Baltimore, MD, USA

1999-2001 Researcher in Lab. for Molecular Psychiatry, BSI, RIKEN,

 2001-present Leader, Project for Schizophrenia & Affective Disorders Research,

Tokyo Metropolitan Institute of Medical Science

**Abstract**

**Discovery of a novel drug for schizophrenia：Challenge from academia**

Drug discovery for mental disorders, such as schizophrenia, is hampered partly by the lack of experimental animals close to human mental disorders and by the absence of appropriate surrogate biomarkers able to substitute for mental abnormalities. Despite the difficulty of target validation, there are unmet medical needs in the field of mental disorders. I am happy to share with you some of our data of a novel drug (pyridoxamine) for schzophrenia.

 We found an interesting pedigree containing multiple individuals with schizophrenia as three brothers and their two uncles are patients. We detected a frameshift mutation of glyoxalase (GLO1) gene in a case of the pedigree. GLO1 detoxifies toxic carbonyls, which modify proteins and eventually form advanced glycation end-products (AGEs), such as pentosidine, by the maillard reaction. The mutation reduced enzymatic activity of GLO1 by 50%, resulting in increased plasma pentosidine by 3.7 fold and decreased serum vitamin B6 less than 20% as compared to that of controls. We measured pentosidine and vitamin B6 in 45 schizophrenia and 61 controls. Plasma pentosidine were significantly high (P<0.0001) and vitamin B6 levels were significantly low (P<0.0001) in patients with schizophrenia compared to that of control subjects. A subpopulation of schizophrenic patients thus suffers from enhanced carbonyl stress. An investigator-driven clinical trial (exploratory phase 2a) with pyridoxamine (an isoform of vitamin B6), a scavenger of toxic carbonyls, has been conducted in 10 schizophrenics with carbonyl stress and low vitamin B6 to test its effectiveness.

**Dr. Yoshiya Oda, Ph.D**

**President of Biomarkers & Personalized Medicine Core Function Unit, Eisai Inc.**

Dr Yoshiya Oda received his BS degree in Pharmaceutical Science from Kyoto University (Japan), and he earned his PhD from Kyoto University. He is working in Eisai (Japanese pharmaceutical company) for 24 years. At the same time, Dr. Oda also served as an associate professor at Medical Institute of Bioregulation in Kyushu University, Graduate School of Medicine at the University of Tokyo and as a professor at Graduate School of Medicine at Chiba University. Dr. Oda has published 72 original papers, 8 international review papers and 3 international book chapters. Among them, Dr. Oda has made several major contributions to the field of proteomics including metabolic stable isotope labeling method for quantitative proteomics. Dr. ODA has received several awards: Research Award from the Society of Chromatographic Sciences, Japan (1999), Division Award from Pharmaceutical Research Vision in the Pharmaceutical Society of Japan (2005), Research Award from the Mass Spectrometry Society of Japan (2005), and Nature-Invitrogen Award (2006). Dr. Oda is currently leading Biomarkers & Personalized Medicine Core Function Unit in Eisai. Dr. Oda has also established preclinical imaging facility in Eisai. The primary purpose of his biomarker group is to provide “Personalized Medicine” to patients and their families. His group contributes to enhance the accuracy of product creation delivering the right products to the right patients at late stage of clinical development based on biomarkers. He believes that biomarkers enable the rapid decision-making with scientific rationales at discovery and early clinical stage and biomarkers enhance the speed of product creation during the entire drug development process.

His group oversees biomarker activity including discovery, assay development, clinical testing, informatics, and tissue banking for all therapeutic areas. Their core technologies are genomics (array, quantitative PCR, nano-String, Ion torrent, siRNA screening, miRNA etc), proteomics/metabolomics (ELISA, multiplex assay, mass spectrometry, HPLC etc), preclinical imaging (MRI, PET, SPECT, CT and optical imaging), tissue/biofluid banking (LIMS, IHC, ISH, Flow cytometer etc) and bioinformatics.

**Abstract ;Biomarker-driven Product Creation**

Pharmaceutical industry is now facing very difficult situation to create new products. The amount of investment is increasing, but outcomes (products) are decreasing. Therefore pharmaceutical industry has to enhance the efficiency and the productivity under limited resources. Biomarkers play important roles in drug development to confirm target engagement of drug candidates, to determine right dose, to select right patients and to supply right medication. Pharmacodynamics (PD) is the study of the biochemical and physiological effects of drugs on the body by interacting drugs with the target molecules. PD is deeply related with mode-of-action of drug candidates, therefore PD biomarkers can achieve proof-of-mechanism (POM). Recent progress of disease etiology has provided sub-category of the disease. It is now highly important to identify right patient population among several disease sub-categories to increase response rate of the drug candidates and reduce number of subjects in phase II and /or phase III studies. Patient stratification is expected to increase the success rate and accelerate product creation, and leads patients toward personalized medicine era. To determine “right patients”, we need to enhance the technology platform and covert biomarkers to diagnostics. Response/efficacy markers, which can be detected in early clinical study to increase confidence of projects, and exclude poor-response patients from clinical trials at earlier time points, which is useful to avoid unnecessary adverse effects on poor-responders. Efficacy biomarkers can also encourage patients to continue taking right medicine. Therefore, using the response markers brings a benefit to patients as “right medication”. Biomarkers are also keys to diagnose disease and monitor disease situation. Several biomarker examples will be discussed.

**Professor Andrew Lee Hopkins D.Phil. FRSC FSB**

Professor Hopkins is Chair of Medicinal Informatics and SULSA Research Professor of Translational Biology, in the College of Life Sciences, University of Dundee, where he is also the Director of SULSA – the Scottish Universities Life Sciences Alliance. The Hopkins Laboratory is focused on developing new informatics and experimental methods for drug discovery, and applying these to the discovery and optimisation of novel leads. His research focuses on developing novel computational methods for automating drug design and chemogenomics. Experimentally, his lab is interested in advancing biosensor based screening, with particular interesting in developing fragment-based drug discovery for GPCRs.

In 1993 Prof. Hopkins won a British Steel scholarship to attend University of Manchester graduating with a First Class Honours in Chemistry. Following a spell in the steel industry, Professor Hopkins undertook a doctorate in molecular biophysics under at the University of Oxford. Directly from Oxford he joined Pfizer, in 1998, where he established various new functions for the company including the Target Analysis Group, Indications Discovery and Knowledge Discovery. Prof Hopkins is a Fellow of the both the Royal Society of Chemistry and the Society of Biology. He has won several awards including the Royal Society of Chemistry’s Capps Green Zomaya medal (2008); Corwin Hansch Award (2007); Pfizer Team Achievement Award (2004); Pfizer Achievement Award (2002); Pfizer Leadership Award (2002). He has over 50 scientific publications and patents, including twelve papers with over 100 citations. Prof Hopkins is the co-founder of Kinetic Discovery Ltd, a company offering biosensor-screening services to the pharmaceutical industry. In 2012 he founded *ex scientia* Ltd to apply automated design methods to the challenge of improving drug discovery productivity.

**Abstract: The endless cycle of idea and action: adapting the concept of a drug target**

A paradox lies at the heart of current approaches to the discovery and development of new medicines. As our knowledge of the mechanism of disease improves, concurrent with a continuous growth in private and public investment in biomedical research we are simultaneously witnessing a decline in the productivity of drug discovery and development. Despite the thousand of potential new drug targets that have been discovered over the past decade, as a result of the sequencing of the human genome, on average only around five breakthrough (also called “first-in-class”) drugs are approved for use each year. The increasing costs of pharmaceutical research and development are largely driven by an increasing number of clinical failures. As lack of efficacy in patients is generally only concluded in the later stages of drug development at Phase II or Phase III: accounting for a significant share of the rising research costs. Translating new knowledge into new therapies is the challenge at the heart of this paradox. How do we improve the success of science in converting discoveries in the laboratory into benefits for the patient? The challenge to biomedical research is to understand not only the science but also our underlying assumptions of how we turn invention into innovation. One common assumption in medical research over the past two decades has been the philosophy of genetic reductionism: the assumption that the “causes” of diseases can often be traced to single identifiable gene mutation. However the vast majority of the disease burden of mankind is not the result of single gene disorder but diseases of complex etiology from the combination of interdependent multiple genes acting in a network, perturbed by the environment. However the assumption that one gene can cause one disease that can be targeted by a single, selective drug - the ‘one gene, one drug paradigm’ - has permeated much of our thinking of how to discover drugs. The replacement of the paradigm of the gene with the paradigm of a network suggests for any disease states the discovery effective treatments may require design therapies that act on multiple nodes in the gene network rather than on single genes. A second assumption that underlies our approaches to drug discovery is that our increase knowledge of disease will inexorably enable us design new medicines. In contrast to the hypothesis-driven philosophy of modern drug discovery, many highly successful treatments have been discovered by serendipity. An interesting area of investigation is whether there are the lessons from examples of serendipity that we can exploit rationally as new methods of scientific discovery? If there is a common lesson from serendipity it is the how do we create of a new connection between previously unconnected areas of knowledge, in short how do we generate new hypothesis form the evidence. The eighteen century German romantic poet, Novalis, elegantly expressed the problem: “Hypotheses are nets: only he who casts will catch”. Taking inspirations from Novalis we can now design computational systems to help us make the creative connection between ideas in order to generate new hypotheses.

**Dr. Dafydd Owen FRSC**

**Worldwide Medicinal Chemistry, Pfizer Worldwide R&D**

Dafydd Owen has thirteen years experience as a medicinal chemist in the design and synthesis of drug-like molecules for Pfizer at its Sandwich UK and Cambridge MA research sites. He is currently an Associate Research Fellow within Pfizer Worldwide Medicinal Chemistry where he leads a leads an outward looking, academically collaborative group for Pfizer, researching chemical probes for epigenetic targets. He obtained his first degree at Imperial College in 1994 before moving to the University of Cambridge to gain a PhD under the supervision of Professor Steve Ley FRS in 1997. Having won a research fellowship for postdoctoral work, he spent 1998 with Professor Leo Paquette at Ohio State University. During his research career has delivered over forty invited lectures and is also an author on over thirty research papers and patents. He has made contributions to three compounds currently in Pfizer’s Phase I/II portfolio. He is the only Pfizer medicinal chemist to have won the reaction (2001), synthesis (2003) and molecular design of the year (2010) awards at Pfizer’s UK Sandwich site since they began in 2001. In 2009 he was the recipient of a Pfizer Worldwide R&D People Leader Award for his scientific direction of over 80 scientists in organic synthesis. In the same year he was selected as an ACS Organic Division Young Industrial Investigator, receiving his award at the 2009 Fall ACS National Meeting in Washington DC.

**Abstract**

**How Can Pfizer Help Target Validation in the Field of Epigenetics?**

Research into the role of epigenetics in disease could be significantly accelerated if cell active chemical probes for such targets were available to the research community, through a collaborative, open innovation model. Pfizer is a member of a public-private partnership led by the Structural Genomics Consortium (SGC) to help identify a suite of high-quality chemical probes for epigenetic targets. This partnership is unique in that it brings the medicinal chemistry expertise within industry together with biological expertise in academia to drive basic research in an emerging area of important biology of potential relevance to many diseases.

Chemical modifications of histones that influence epigenetic regulation include changes such as methylation of lysine/arginine residues and acetylation of lysine residues. A number of epigenetic enzymes have now been identified that either introduce these epigenetic marks (‘writers’) or remove them (‘erasers’). In addition, regulatory proteins have been discovered that directly recognize histone modification status (‘readers’) and drive the localization of complexes which control gene expression. Many of these target classes have little or no chemical matter and Pfizer has committed to discovering and disclosing chemical probes, free from restriction on use to the scientific community for further research and publication. This presentation will describe recent progress in this collaboration and highlight the discovery of novel chemical probes for epigenetic proteins that may have an important future role in disease. It will also discuss the value of novel, open innovation models in target validation to Pfizer and their role in drug discovery.

**Identification of a chemical probe for BET bromodomain inhibition through optimization of a fragment-derived hit** Paul V. Fish, Panagis Filippakopoulos, Gerwyn Bish, Paul E. Brennan,Mark E. Bunnage, Andrew S. Cook, Oleg Federov, Brian S. Gerstenberger, Hannah Jones, Stefan Knapp, Brian Marsden, Karl Nocka, Dafydd R. Owen, Martin Philpott, Sarah Picaud, Michael J. Primiano, Michael J. Ralph, Nunzio Sciammetta, John D. Trzupek *Journal of Medicinal Chemistry* (2012), 55, 9831

**Professor Rab Prinjha**

**Education, Key Responsibilities, Milestones, Awards and Promotions:**

**2012** Appointed VP Head of Epinova Epigenetics DPU

**2010** Leading Target Progression department and external academic alliances

**2009** Joined Epinova leadership team

**2008** Appointed to post in II-CEDD DDPS

**2007** Appointed Target Validation Department Leader.

**2007** LedAnti-Nogo programme to successful Candidate Selection.

**1997-Current** Recruited to SmithKline Beecham in Neuroscience Department to develop CNS regeneration/ plasticity area. Contributed to Nogo, Neuropilin-semaphorin, MAG, VR1, MICAL, LRRK2, Brd4 and BET programmes amongst others.

**1995-1997** Post-doctoral Fellowship (Muscular Dystrophy Association UK funded). Supervisors: Professor Frank Walsh and Dr Pat Doherty.
Role of Agrin and Dystroglycan in Synapse Formation at the Neuromuscular Junction.

**1988-1994** University College London, Molecular Cell Biology. PhD and EU funded Post-Doctoral Fellow working on cytoskeleton, target cloning and functional characterisation.

**1985-1988** King’s College London, Biotechnology BSc (Hon) (2(i)).

**A and S Levels** Biology, A1; Chemistry, B2; Physics, B; General Studies, A.

# Publications

Bandukwala,H.S., Gagnon,J., Togher,S., Greenbaum,J.A., Lamperti,E.D., Parr,N.J., Molesworth,A.M., Smithers,N., Lee,K., Witherington,J., Tough,D.F., **Prinjha,R.K.,** Peters,B., and Rao,A. (2012). Selective inhibition of CD4+ T-cell cytokine production and autoimmunity by BET protein and c-Myc inhibitors. Proc. Natl. Acad. Sci. U. S. A *109*, 14532-14537.

**Prinjha,R.K.**, Witherington,J., and Lee,K. (2012). Place your BETs: the therapeutic potential of bromodomains. **Trends Pharmacol. Sci.** *33*, 146-153.

Marazzi,I., Ho,J.S., Kim,J., Manicassamy,B., Dewell,S., Albrecht,R.A., Seibert,C.W., Schaefer,U., Jeffrey,K.L., **Prinjha,R.K.,** Lee,K., Garcia-Sastre,A., Roeder,R.G., and Tarakhovsky,A. (2012). Suppression of the antiviral response by an influenza histone mimic. **Nature** *483*, 428-433.

Fang,T.C., Schaefer,U., Mecklenbrauker,I., Stienen,A., Dewell,S., Chen,M.S., Rioja,I., Parravicini,V., **Prinjha,R.K.,** Chandwani,R., Macdonald,M.R., Lee,K., Rice,C.M., and Tarakhovsky,A. (2012). Histone H3 lysine 9 di-methylation as an epigenetic signature of the interferon response. **J. Exp. Med**. 209(4):661-669.

**Abstract**

**Can and should we drug the undruggable? Building a case for new targets**

Rab Prinjha who currently leads the Epinova Discovery Performance Unit at GSK and has previously headed up Target Progression and before that Target Discovery and Validation departments in GSK will outline the key issues concerning the pharmaceutical industry in terms of target selection. He will discuss the key technologies and data-sources that can be used to identify and triage targets for drug discovery. Using two distinct examples he will illustrate how data-packages can be generated to support discovery investment decisions. The first will be the CNS regeneration inhibitor Nogo-A currently in trials for ALS and the second will be the BET Bromodomain containing proteins where our inhibitors are now progressing in trials for NMC and solid tumors. How were the targets discovered, what data was generated to validate them and provide confidence to move forward.

**Professor Praveen Anand**

Dr Praveen Anand is Professor of Clinical Neurology and Head, Centre for Clinical Translation, at Imperial College London. His medical education was at the Universities of Oxford and Cambridge, and post-graduate training was at the Royal Postgraduate Medical School, Hammersmith Hospital, and the National Hospital for Neurology and Neurosurgery, Queen Square, London. His research focuses on pathophysiological and molecular mechanisms in the human sensory neuropathies and chronic pain syndromes. Collaborations with pharmaceutical companies and clinical colleagues are directed to projects which bridge the gap between pre-clinical developments and their clinical applications, including 3 recent successful clinical trials of novel agents for neuropathic pain. He has published over 200 peer-reviewed and invited publications in journals including Nature, Nature Medicine, Nature Genetics, Science and The Lancet.

**Abstract**

Target validation has been a major cause of attrition in Phase 2 efficacy trials, particularly of novel medicines for pain. There have been great advances in understanding the neurobiology and molecular mechanisms underlying pain, yet pain conditions represent an increasing unmet clinical need. Current treatment for chronic neuropathic (nerve) pain is least effective, we need to treat around 4 patients before even one patient has 50% pain relief, and these drugs have significant side-effects. Clinical trials of new drugs for neuropathic pain have seen a number of high profile failures in recent years, as animal *in vivo* model results did not predict responses in patients. The reason was not a failure to identify potential pain targets in preclinical studies, but to translate these successfully to chronic pain patients.

We have adopted a translational approach based on clinical validation of novel drug targets in common pain states, using: 1) *in vitro* human DRG neuron (nociceptor) pain models for pharmacological studies (“clinical trial in a dish”); 2) clinical objective biomarkers and surrogates, including skin biopsy, pain evoked cerebral potentials and functional MRI; and, 3) new human volunteer/patient models linked to the drug target mechanism, for validation and use in Phase I / IIa trials (“matchmaking”). The aim was to deliver pre-clinical to POC / Phase II success (and PK/PD in Phase I / IIa) by conducting rational mechanistic trials in homogenous patient cohorts. The selection and assessment of patients with target related biomarkers would better predict clinical outcome.

Our approach has supported target validation and guided the success of 3 novel pain drugs in Phase II trials for neuropathic pain, which will be illustrated by the Angiotensin II Type 2 receptor antagonist EMA401, and others in development.

These studies have been conducted in collaboration with pharma, including two Japanese companies. A current pain evoked potential biomarker study involves collaboration with a Japanese academic. We have strong links with a UK Contract Research Organisation which specialises in Caucasian-Japanese bridging studies, and have made joint presentations to several leading Japanese pharma regarding development of their novel pain drugs, and of pain and nerve regeneration biomarkers.

We aim to build on these links to further our research collaborations between UK and Japan. The Workshop and visits to companies will provide an opportunity to facilitate new research collaborations. These may lead to greater success in clinical translation of new drugs, especially for chronic pain.

**Professor Tatsuo Kurokawa Ph.D.**

In 1973, he graduated from the Faculty of Pharmaceutical Sciences, Chiba University and joined Ministry of Health and Welfare Japan (MHW). In 1980-82 he worked for WHO HQs and Western Pacific Regional Office and then moved to Science and Technology Agency Japan. In 1984 he came back to MHW, International Division of the Minister's Secretariat. From 1989 He was deputy director of New Drug Division and served as Japan's representative to the ICH Steering Committee.

After experience of safety affairs, he was assigned as Councilor for Pharmaceuticals and Food Safety, Minister's Secretariat, MHLW in 2004. In 2008, After retiring from MHLW, he was Professor of Graduate School of Pharmaceutical Sciences, Chiba University, and now he is Professor of Division of Regulatory Sciences, Faculty of Pharmacy, Keio University since April 2011. He is a pharmacist.

**Abstract: UK-Japan Collaboration for Drug Discovery and Clinical Trial**

UK is well known and has been respected as a country first in the world introduced and conducted a comparative randomized clinical trial in 1948 on the effectiveness of Streptomycin on pulmonary tuberculosis. We can easily recognize many of scientific and technological findings were first applied and made up into practical measures in UK. Japan has enjoyed and benefitted by such UK’s contribution so far. Probably Japan is good at make such findings into very best productive and advanced measures with very reliable manner and quality. That may form a typical understanding on the comparison of both countries, although now the situation of two countries became much closer. Probably Japan can learn fundamental approaches to put basic findings into practical technology and/or applicable measures from UK’s experience and culture. UK may be benefitted by Japan’s efforts and thinking way of improvement and gaining maximum quality as well as reliability. I would like to suggest that such mutual stimulation and learning could be multiplied by one or two step more collaboration and dialogue among us. I also wish to underscore that we can learn about clinical attitude and how to establish productive and functional collaboration system among Government, academia and industry from UK’s experience and wisdom.

We know we have a long history of close friendship. I am rather optimistic on our future collaboration and communication.

**Dr Yuji Yamamoto, MD, MBA**

Dr Yuji Yamamoto is a director at the Office of Medical Innovation, the Cabinet Secretariat. He joined the office in 2012 and is responsible for planning health care innovation policy for the cabinet. Stratified medicine, health technology assessment, and preemptive care are his focus in policy research.

He also serves concurrent positions in health care field including a visiting associate professor of the Centre for Clinical Research (CCR) at Keio University School of Medicine, the chief executive officer at MinaCare, co. ltd which manages over one million people health through their health-related data, and as a researcher at Sony Computer Science Laboratories, Inc.

Yuji received his M.D. degree from University of Tokyo and his medical license in1999, worked as a cardiologist in Japan, specialized in electro-physiology. He qualified as a board certified member of the Japanese Society of Internal Medicine, and holds an M.B.A. from Harvard Business School in 2007.

**Abstract**

5-year strategy for health care innovation was issued in June, 2012. This strategy emphasized on enabling industrialization of research and development activities in health care. Four targeted R&D areas are drug, medical device, regenerative medicine, and personalized medicine, and public and private collaboration is strengthened for supporting these areas. The strategy has been in implement stage and its status would be shared in the meeting.