

## In vivo molecular imaging for translational research

Keon Wook Kang, M.D., Ph.D.

*Department of Nuclear Medicine & Cancer Research Institute, Seoul National University College of Medicine, Seoul, Republic of Korea*

*Email: kangkw@snu.ac.kr*

### Abstract

In vivo imaging has been playing an important role in diagnosing diseases and monitoring treatment. Recently, it is widening its field through revealing molecular events in cells and tissues. In vivo molecular imaging is useful not only for clinical studies but also for developing new drugs and new treatment modalities. Pre-clinical molecular imaging using animals such as mice shows biodistribution, pharmacokinetics, mechanism of action, and efficacy. In vivo imaging not only reduces the number of animals for the experiment, but also increases the confidence of results by removing the factor of variability among individual animals. There are several strategies in the molecular imaging targeting biomarkers. Radiolabeled antibodies, peptides, and aptamers can be used on PET imaging. For the imaging sources, fluorescent materials, radioisotopes, and MRI enhancers can be used. Multimodal technique combining PET/MRI/optical imaging will overcome the limitations of each modality. We validated several targeted nano-drug delivery systems in mouse models using in vivo multimodal imaging after radiolabeling nano-particles. If we combine nanotechnology and in vivo whole body imaging, personalized targeted therapy can be realized through validating the targeting efficiency of each nano-drug in every treatment.

### Short biography



*Dr. Keon W. Kang, a nuclear medicine physician, is Professor, Department of Nuclear Medicine, Seoul National University College of Medicine (2007-). He received M.D. degree from Seoul National University College of Medicine (1991). He was trained as an intern and a resident for Internal Medicine at Seoul National University Hospital (1991-1996). He received Ph.D. in Medical Science at Seoul National University College of Medicine (2001). He has worked as Chief, Department of Nuclear Medicine, National Cancer Center, Korea (2000-2007). He studied molecular imaging and researched "Preclinical efficacy of the c-Met Inhibitor from Pfizer Inc. by small-animal PET" with Pf. Sam Gambhir as a visiting scientist of Molecular Imaging Program at Stanford (2003-2004). Since 2011, he has served as an Editor of Nanomedicine. His research areas are in vivo molecular imaging of cancer using PET & nanoparticles.*

# illuminating biomedical discovery with advanced photonic imaging

Vasilis Ntziachristos

*Institute for Biological and Medical Imaging Helmholtz Zentrum München & Technical University of Munich, Germany*

*Email: v.ntziachristos@helmholtz-muenchen.de*

## Abstract

Optical imaging is unequivocally the most versatile and widely used visualization modality in the life sciences. Yet it is significantly limited by photon scattering, which complicates imaging beyond a few hundred microns. For the past few years however there has been an emergence of powerful new optical imaging methods that can offer high resolution imaging beyond the penetration limits of microscopic methods. Of particular importance is the development of multi-spectral opto-acoustic tomography (MSOT) methods that bring unprecedented imaging performance in visualizing anatomical, physiological and molecular imaging biomarkers through several millimetres to centimetres of tissue. Some of the attractive features of the method are the 10-100 microns resolution achieved, the real-time imaging performance and the ability to visualize several classes of nanoparticles such as gold, carbon and iron-oxide nanoparticles or dye-tagged liposomes and micelles. In parallel we have now achieved the first-in-human clinical translation of targeted fluorescent probes, which opens the way for advanced surgical and endoscopy procedures and personalized theranostics and screening.

Coupled to the increasing availability of photo-absorbing molecules and nano-particles with physiological and molecular specificity, including common fluorescent proteins and probes, MSOT enables unprecedented insights to cellular and sub-cellular processes through entire small animals, embryos, fish and insects and has revolutionized the role of imaging on the laboratory bench, well beyond the capability of conventional microscopy. This talk describes current progress with instruments, methods and applications for in-vivo optical and opto-acoustic tomography of whole intact animals and model biological organisms. We show how new opto-acoustic and fluorescence imaging concepts are necessary for accurate and quantitative molecular investigations in tissues and why they might become a valuable tool for accelerated investigations on therapeutic efficacy and outcome. We further demonstrate that cellular function and bio-chemical changes can be detected in-vivo, through intact tissues at high sensitivity and molecular specificity. Pre-clinical and clinical results are presented and the advantages and limitations of these methods and future directions are discussed.

## Short biography



*Vasilis Ntziachristos Ph.D. is a Professor and Chair for Biological Imaging at the Technische Universität München and the director of the Institute for Biological and Medical Imaging at Helmholtz Zentrum München. Prior to this appointment he has been faculty at Harvard University and the Massachusetts General Hospital. He has received his M.Sc. and Ph.D. from the Bioengineering Department of the University of Pennsylvania and the Diploma on Electrical Engineering from the Aristotle University of Thessaloniki, Greece. His main research interests involve the development of optical methodologies for probing physiological and molecular events in tissues using non-invasive methods.*

# The use of microSPECT/CT imaging as a screening tool in drug and radiopharmaceutical development

Jane Sosabowski

*Centre for Molecular Oncology, Barts Cancer Institute, UK*

*Email: j.k.sosabowski@qmul.ac.uk*

## Abstract

In-vitro assays often poorly predict the in-vivo behaviour of novel drugs but much time and resource is normally expended on such assays before studies in living animals are envisaged. Recent developments in small animal imaging technology provide an opportunity to inform such investigations through in vivo screening of drug candidates prior to selection of the most promising candidates for more intensive in vivo studies. The aim of this study was to compare and rank twelve peptides binding the CCK2-R in vivo using small-animal SPECT/CT imaging in just two animals per candidate. This ranking was then compared with that obtained from high animal number/low dose ex vivo biodistribution studies carried out in parallel in the selection of a single candidate for further clinical evaluation.

## Short biography



*Dr Jane Sosabowski studied Chemistry to Masters level at the University of Natal, Durban, South Africa and then moved to the UK to complete her PhD at the Joint Department of Physics, Institute of Cancer Research, Sutton, Surrey, looking at imaging multidrug resistance in vivo using PET. Thereafter she joined what was then the Nuclear Medicine Research Laboratory at Bart's and the London School of Medicine and Dentistry headed by Prof Steve Mather. With the development of small animal PET/CT, SPECT/CT capabilities the laboratory became the Cancer Imaging Laboratory within Barts Cancer Institute at Charterhouse Square, London and she is now head of this facility. In addition to radiochemistry and radioisotope/CT imaging facilities, the BCI has bioluminescence/fluorescence and pre-clinical ultrasound imaging capabilities.*

# Nanostructured conjugated polymers for diagnostic applications

Dong June Ahn

*Department of Chemical & Biological Engineering, Korea University, Seoul 136-701,  
Republic of Korea.*

*E-mail: ahn@korea.ac.kr*

## Abstract

Conjugated polymer nanoarchitectures based on polydiacetylene materials are interesting biomimetic materials in view of application to chemical and biological sensors. These conjugated materials are unique in changing color from blue to red and/or in altering fluorescence emission, caused by perturbation of materials' electronic state and energy transfer upon specific binding events. Based on these optical characteristics, we can utilize the conjugated polymers as label-free detection agents for chemical and biological targets. In this presentation, we demonstrate strategy of interfacial design of soft nanoarchitectures achieving the label-free and/or rapid detection capability. Their sensitivity and specificity were analyzed in the range of nM to sub-fM depending on the kind of target species. The printed array patterns, characters, and images were found to detect the target substances successfully out of mixture samples. In addition, a strikingly rapid detection of biological targets within ca. 10 min. was also enabled by designing 3-dimensional architectures involving columnar and/or porous interfaces showing higher surface area that enhanced the accessibility and the mass transfer rate of the target molecules.

## Short biography



*Dong June Ahn received his B. S. and M. S. degrees in Chemical Engineering from Seoul National University, respectively, in 1986 and 1988, and his Ph. D. degree in the field of Interfacial Engineering in Chemical Engineering major from Purdue University in 1993. He worked as a postdoctoral fellow at Purdue University during 1993-1994, and a research scientist of the Center for Advanced Materials at Lawrence Berkeley National Laboratory during 1994-1995. In 1995, he joined the faculty of the Department of Chemical and Biological Engineering at Korea University, where he is now a professor and serves as the departmental head. He is also the director of the Center for NanoBio Engineering of Korea University. He was a visiting professor at the Bioorganic Chemistry Group of Chiron Research Center during 2001-2002, and at the Department of Applied Chemistry and the Nanotechnology Research Center of Waseda University during 2009-2010.*

*His research interests include nano-to-macro scale molecular and supramolecular assemblies, surface engineering, and nanobiotechnology. Toward fundamental knowledge, he investigates molecular-level interaction of chemical and biological materials. In applied regime, he develops rapid on-site detection devices for chemicals of environmental and safety issues, and ultra-sensitive label-free diagnostic sensor chips for DNAs, proteins, and cells. His major scientific contributions have been published in high-profile journals including Science, JACS, Adv. Mater., Acc. Chem. Res., and others.*

# Designing delivery systems via molecular bionics

Giuseppe Battaglia

*The Krebs Institute, The Centre for Membrane Interactions and Dynamics & Department of Biomedical Science, University of Sheffield, UK.*

*Email: g.battaglia@sheffield.ac.uk*

## Abstract

Bionics (from greek Βιονικός Bio -unit of life and νικός -derived from) is the study of making artificial systems implementing functions and features found in biological structures. With advent of nanotechnology we can now translate this approach at molecular level and construct novel structures that mimic (and possibly improve) biological functions. We apply this approach to research problems that require a considerable understanding of biology to tackle clinical challenges. We start identifying the tools necessary to address the specific clinical problem, we subsequently study in details the interactions between the nanostructured materials and the living system often adapting and/or developing new techniques. Finally we test our devices using detailed pharmacological and medical characterisations. This approach is highly interdisciplinary and combine fundamental science with engineering coalescing expertise from across disciplines such as synthetic chemistry, polymer science, soft matter physics, biophysics, cell biology, immunology, oncology, and neuroscience. I will discuss briefly our molecular tools based on waterborne self assembly, the chemistry and the physics behind the resulting structures, how these can be combined to engineer simple or complex structures and how parameter such size, shape, topology and surface topography affect their interaction with biological systems. Finally I will show few examples how such an approach can lead to new clinical applications.

## Short biography



*Giuseppe Battaglia obtained his Laurea in Chemical Engineering from the Università degli Studi di Palermo in Italy in July 2001 specialising in Macromolecular Biomaterials. Straight after his graduation, he joined the ICI Strategic Technology Group (now part of AkzoNobel) at Wilton, UK, as research process engineer member of the Product Pathway Engineering Team. In October 2002, he joined the Prof. Anthony Ryan's research group for an ICI sponsored PhD in Physical Chemistry in the Department of Chemistry at the University of Sheffield (UoS). In February 2006 immediately after submitting his PhD thesis (viva date: 21.03.2006), he was appointed to a fixed term lectureship within the Biomaterials and Tissue*

*Engineering group in the Dept. of Materials Science and Engineering in the University of Sheffield. 3 years later he relocated to a permanent position within the Department of Biomedical Science in the same university where he was promoted to a Senior Lecturer in 2009 and Professor in 2011. From March 2013, he will be relocating to the University College London to a Personal Chair of Molecular Bionics between the Department of Chemistry and the Division of Infection and Immunity.*

*Giuseppe Battaglia's research is focused on the investigation of the specific design rules behind inter/intramolecular interactions and self-assembly of soft matter systems often taking inspiration from biological systems such as cells and viruses. These are subsequently translated into the engineering of nanostructured biomaterials. Such an effort is allowing the fast translation of cutting-edge science through rigorous engineering evaluation and characterisation.*

# A new theranostic nano hydrogel to treat the ischemic lesions

Hwan-Jeong Jeong

*Department of Nuclear Medicine, Chonbuk National University Medical School and Hospital, Jeonju,  
Jeonbuk, Republic of Korea*

*E-mail: jayjeong@chonbuk.ac.kr*

## Abstract

**Purpose:** Vascular endothelial growth factor (VEGF) is a primary stimulant of angiogenesis, and is a survival factor that induces proliferation and migration of endothelial cells. Angiogenesis is stimulated not only during cancer but is also induced for the healing of ischemic lesions. Expression of VEGF receptors (VEGFRs) increases in ischemic lesion to recover the pathologic condition by enhancement of angiogenesis. However, there are few reports that VEGF injection to the ischemic lesion induced the angiogenesis effectively. We developed a nano-hydrogel (nanogel) containing VEGF and we were able to track its position due to labeling with Tc-99m. Using this theranostic system, we investigated improvement of ischemic lesions. **Methods:** To prepare ischemic models the femoral artery of rats and its branches were ligated through skin incision with 5-0 silk. The nanogel used for VEGF delivery was conjugated with DTPA and was labeled with <sup>99m</sup>Tc. The nanogels containing VEGF were prepared by addition into crosslinking solution. One day after arterial dissection, the rats were injected with <sup>99m</sup>Tc-sodium pertechnetate for noninvasive physiological evaluation of blood flow of hind limbs. PBS, VEGF, and <sup>99m</sup>Tc-VEGF-nanogels were injected into femoral artery of hind limb, respectively. At 1 week after VEGF treatments, neovascularization in the hind limb were monitored by gamma perfusion imaging with <sup>99m</sup>Tc-sodium pertechnetate. **Results:** <sup>99m</sup>Tc-VEGF-nanogels were accumulated in the ischemic lesions after femoral artery of hind limb and were retained for monitoring time. We could calculate the retention ratio and accumulated amount of injected VEGF-nanogels by gamma imaging. Compared with the groups of PBS, VEGF, and VEGF-nanogels, PBS and VEGF-treated rats showed no improvement in blood perfusion, whereas VEGF-nanogles-treated rats showed higher perfusion in the ischemic lesions to level of blood flow in a healthy hind limb. **Conclusion:** <sup>99m</sup>Tc-VEGF-nanogels have a theranostic angiogenic effect on peripheral ischemia. Therefore, our traceable angiogenic nanogel may be a promising theranostic agent for the treatment of ischemic diseases and other vessel disorders

## Short biography



*Hwan-Jeong Jeong received his degree of master and doctor of philosophy from Medical School of Chonnam National University (Gwangju, Korea) in 2000 and 2003. He worked at Seoul National University Hospital as a postdoctoral, clinical and research fellow under guidance of professor June-Key Chung, who was a chairman of department of nuclear medicine. In 2002, he moved to Wonkwang National University and Hospital as an instructor. Thereafter, he also moved to Chonbuk National University and Hospital as an assistant professor in 2005 and has been working there until now as an associate professor. His research interest focus on molecular imaging using nuclear medicine and nanotechnology and translational research.*



# Biomedical applications of magnetic nanoparticles

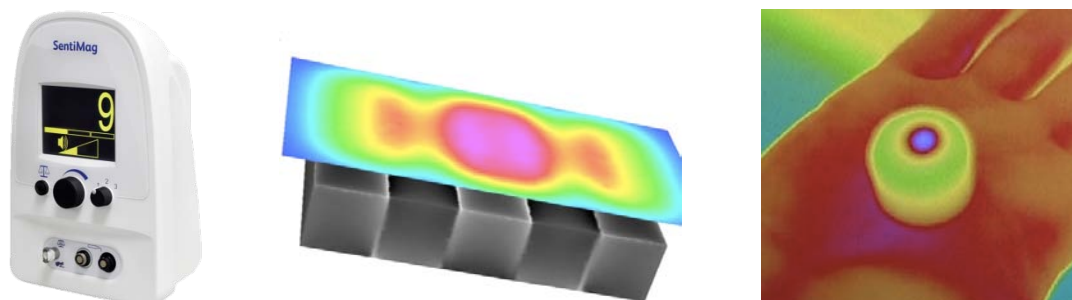
Quentin Pankhurst

*Institute of Biomedical Engineering, University College London, London, UK*

*Email: q.pankhurst@ucl.ac.uk*

## Abstract

'Healthcare Biomagnetics' – the sensing, moving and heating of magnetic nanoparticles in vitro or in the human body – is a rapidly changing field that is attracting interest worldwide.[1] It offers the potential to develop safe and convenient alternatives for a diverse range of therapeutic and diagnostic healthcare applications, using injectable materials of proven safety and reliability. In doing so, it makes use of the three fundamental 'action-at-a-distance' properties of magnetic materials – their ability to act as remote sensors,[2] mechanical actuators,[3] and heat sources.[4]



Representative images related to (from left to right): magnetic sensing, actuation and hyperthermia.

The versatility of the field is leading to the emergence of multi-modal applications, combining two or more of the sensing-moving-heating properties in the same product. Similarly, certain applications are now entering or are close to beginning Phase I/II clinical trials, or in the case of in vitro products, are already in the marketplace. Pertinent examples of work in the fields of targeted delivery of drugs and other therapeutic agents, and others, will be presented and discussed.

[1] Q.A. Pankhurst et al.: J. Phys. D, 36, R167, (2003); Q.A. Pankhurst et al.: J. Phys. D, 42, 224001 (2009). [2] U.A. Gunasekera et al.: Targeted Oncology, 4, 169 (2009); M.R. Loebinger et al.: Cancer Research, 69, 8862 (2009); K.L. Vigor et al.: Biomaterials, 31, 1307 (2010). [3] E. Stride et al.: Ultrasound Med. Biol., 35, 861 (2009); J. Riegler et al.: Biomaterials, 31, 5366 (2010); J. Riegler et al.: J. Phys. D, 44, 055001 (2011). [4] M. Kallumadil et al.: J. Magn. Magn. Mater., 321, 3650 (2009); L.A. Thomas et al.: J. Mat. Chem., 19, 6529 (2009); K. Parcell et al.: Thorax, 65, A41 (2010).

## Short biography



*Quentin Pankhurst is the Director of the Institute of Biomedical Engineering at University College London. The objective of the IBME is to bring together UCL's excellence in academic and clinical R&D – around a thousand staff, fellows, nurses and students in 35 different centres, departments and institutes – to create the world's best research centre for biomedical engineering. The IBME's goal is to be the world's fastest and most cost-effective deliverer of patient benefit by harnessing the power of university-based innovation and experimental medicine in the UK.*

*He is also the Director of the Davy-Faraday Research Laboratory and Wolfson Professor of Natural Philosophy – a post once held by Lord Ernest Rutherford – at the Royal Institution of Great Britain, in London. Here he runs research programmes in bio- and nanomagnetism aimed at making practical advances in the use of magnetic nanoparticles in healthcare. These include medical imaging devices, targeted regenerative medicine, molecular imaging microscopy for living cells, and the development of multi-functional nanoparticles for therapy and diagnostics. He is a founder and CTO of Endomagnetics Ltd, a spin-out company which is commercialising the SentiMag™, an intra-operative device for breast cancer surgery.*

## Biomedical applications of graphene derivatives

Dal-Hee Min

*Department of Chemistry, Seoul National University, Seoul 151-747, Republic of Korea*

*E-mail: dalheemin@snu.ac.kr*

### Abstract

Recently, various nanomaterials are being harnessed as critical components of bioanalytical systems such as gold nanoparticles for sensing DNA-related biochemical changes. To design “good” bioanalytical systems using new nanomaterials, one should be able to understand and fully utilize chemical/physical properties to detect molecular changes during certain biochemical transformations in a biological system. Moreover, the new system should overcome limitations of conventional assay methods—detection limits, cost issues, labors, efficiencies, quantitiveness, reproducibility, etc. In this talk, I will introduce recent efforts to utilize “graphene oxide” for the development of bioanalytical systems and biotechnological tools. In addition, I will discuss on the efforts towards successful interfacing of graphene for biosystems.

### Short biography



*Dal-Hee Min received her master's degree from Seoul National University (Seoul, Korea) in 1999, and her Ph D. from University of Chicago (Chicago, USA, Prof. M. Mrksich) in 2005. She joined a group of Prof. Sangeeta Bhatia as a postdoctoral researcher in Division of Health Science and Technology, MIT (Massachusetts Institute of Technology, USA) for two years. In Oct. 2007, she moved to KAIST (Korea Advanced Institute of Science and Technology) as an Assistant Professor of the Department of Chemistry and recently, moved to Seoul National University as an Associate Professor. Her recent research especially focus on development of bioanalytical platforms based on various nanomaterials for diagnostics, biosensing, drug discovery and drug delivery system development*

*with collective understanding on nano-surface chemistry, cellular behavior and the interactions of biomolecules with nanomaterials.*



# Structure-toxicity relationships for metal oxide nanoparticle–induced lung inflammation

Wan-Seob Cho

*Department of Medicinal Biotechnology, College of Natural Resources and Life Science, Dong-A University, Republic of Korea.*

*E-mail: [wcho@dau.ac.kr](mailto:wcho@dau.ac.kr)*

## Abstract

The toxicology of nanoparticles (NPs) is an area of intense investigation that would be greatly aided by structure/toxicity relationships that would enable prediction of toxicity based on physicochemical structure. To evaluate the structure/toxicity relationship of metal oxide NPs and acute lung inflammogenicity, we assembled a panel of 15 NPs and attempted to relate various physicochemical parameters, including zeta potential ( $\zeta$ P) and solubility, to lung inflammogenicity in vivo. The acute pulmonary inflammogenicity of 15 metal oxide NPs was accurately predicted by one of two structural parameters –  $\zeta$ P under acid conditions for low-solubility NPs and solubility to toxic species for high-solubility NPs.  $\zeta$ P is the electrical potential created between the surface of a particle, with its associated ions, and the medium it exists in and provides information concerning the particle surface charge. We suggest that inside the phagolysosome under acid conditions, a high positive  $\zeta$ P may allow NP to damage the integrity of the phagolysosomal membrane leading to inflammation. In the case of high-solubility NP, inflammogenicity depends on the ions that are produced during dissolution of NP inside the acidic phagolysosomes; if the ions are toxic then phagolysosomes will be destabilised and causes inflammation. Our prediction models may have utility in preliminary assessment of the potential lung inflammation hazard of the large number of NP that requires testing. These results should provide a momentum for more research towards surface charge and solubility as structure/toxicity relationships for NPs.

## Short biography



*Wan-Seob Cho was born in 1977 in Korea and attended the Seoul National University obtaining a B.Sc. in Veterinary Medicine (2000), M.Sc. (2002), and Ph.D. (2004) in Veterinary Pathology. He was a Scientific Officer in the Korea Food and Drug Administration (2002 - 2008) and a postdoctoral fellow at the University of Edinburgh (2008 - 2011). At the moment, he is an Assistant Professor of Toxicology in Dong-A University, Korea. He has published over 50 peer-reviewed papers and book chapters on toxicology and his current interests are structure-toxicity relationships of metal/metal-oxide nanoparticles.*