

Recombinant pharmaceutical manufacturing from plants - the future of molecular farming

The BioPark Hertfordshire, Welwyn Garden City, AL7 3AX: Friday, October 15, 2010

After our very successful 'Molecular Farming - plant biologicals' event in 2008 we are pleased to announce this follow up event which will be chaired again by Professor Julian K-C. Ma, Hotung Chair of Molecular Immunology, St. George's, University of London, UK

This meeting has CPD approval

- 9:00 – 9:45 **Registration**
- 9:45 – 10:00 **Introduction by the Chair:** *Professor Julian Ma*, Hotung Chair of Molecular Immunology, St. George's, University of London, UK
- 10:00 – 10:30 **Talk title to be confirmed**
Dr. George Lomonosoff, John Innes Centre, UK
- 10:30 – 11:00 **Increasing yields of medicinals by plant molecular breeding**
Professor Ian A Graham, CNAP Director & Weston Chair of Biochemical Genetics, The University of York, UK
Modern molecular breeding methods will be introduced and used to demonstrate the new timelines that are now possible for the rapid improvement of medicinal plants as robust production systems
- 11:00- 11:05 **Speakers photo**
11:05 – 11:30 **Mid-morning break**
- 11:30 – 12:00 **Tackling chronic disease through improvements to foods**
Professor Cathie Martin, Norwich Research Park, UK
A major challenge for society is to reduce the frequency of the chronic diseases; cardiovascular disease, cancer and age-related degenerative diseases. Epidemiological studies have demonstrated the efficacy of diets high in fruit and vegetables in reducing the incidence of chronic disease because they contribute important phytonutrients which serve to promote antioxidant defence mechanisms. Plant biotechnology can make a very significant contribution to dietary improvement through model foods that test the importance of specific bioactives in promoting particular aspects of health, markers that allow molecular breeding for enhanced levels of bioactives and genetic engineering that provides novel, health-promoting (functional) foods.
- 12:00– 12:30 **Selected Abstracts**
- 12:30 – 13:30 **Lunch and Poster Viewing**
- 13:30 – 14:00 **Using thin-layer chromatography (TLC) to detect biologically-active compounds in plant extracts**
Professor Peter Houghton, Emeritus Professor Pharmaceutical sciences Division, Kings College London
In the last 20 years bioassay-guided isolation of active compounds from plant extracts has been widely used in the discovery of new lead compounds. One disadvantage of the conventional method of testing each fraction is the large number of fractions that have to be tested. The use of TLC together with various spray reagents for activity of biological interest enables the early rejection of fractions showing no activity and also helps to quickly identify the type of phytochemical and its rapid isolation.
- 14:00 – 14:30 **Containment strategies in biopharming**
Professor Denis J Murphy, University of Glamorgan, UK
This paper examines the challenges of segregating biopharmed crops from mainstream crops, particularly those destined for food or feed use. One commercially viable strategy to limit or avoid biopharming intrusion into the human food chain is the rigorous segregation of food and non-food varieties of the same crop species via a range of either physical or biological methods. Even more secure segregation is possible by use of non-food crops, non-crop plants, or *in vitro* plant cultures as production platforms for biopharming. Such platforms already under development range from outdoor-grown *Nicotiana* spp. to glasshouse-grown *Arabidopsis*, lotus and moss. Even more effective methods for secure biocontainment include plastid expression of transgenes, inducible and transient expression systems, and physical containment of plants or cell cultures. In the current atmosphere of heightened concerns over food safety and biosecurity, the future of biopharming may be largely determined by the extent to which the sector is able to

maintain public confidence via a more considered approach to containment and security of its plant production systems.

- 14:30 – 15:00 **Engineering JA-regulated secondary metabolism in plants**
Dr Alessandra Devoto, Royal Holloway - University of London, UK
Plants produce small molecules useful as pharmaceuticals, insecticides, flavours, and fragrances which derive from secondary metabolism. The plant hormone jasmonic acid (JA) induces the biosynthesis of defence proteins and protective secondary metabolites. We propose here to manipulate jasmonate-responsive genes controlling a pathway of potential importance for the production of therapeutic drugs in plants with the dual aim of developing a greater understanding of plant secondary metabolism and developing precursors for new medicines. Success in manipulation of the targeted metabolic pathway will be analyzed by LC-MS, GC-MS and through a novel functional screening system.
- 15:00 – 15:30 **Afternoon Tea/Coffee and Last Poster Viewing**
- 15:30 - 16:00 **Talk title to be confirmed**
- 16:00 – 16:30 **Metabolic engineering of high-value and nutritional isoprenoids in plants**
Dr Paul Frazer, Royal Holloway University London, UK
Over the past decade genetic/metabolic engineering of isoprenoid biosynthesis and accumulation has resulted in the generation of transgenic varieties containing enhanced or altered isoprenoids. In achieving this important goal many fundamental lessons have been learnt. Most notably is the observation that the endogenous pathways in higher plants appear to resist engineered changes. Typically, this resistance manifests itself through intrinsic regulatory mechanisms that are “silent” until manipulation of the pathway is initiated. In the present presentation the progress made in the genetic engineering of isoprenoids in tomato fruit and other Solanaceae will be reviewed.
- 16:30 – 17:00 **Chairman’s summing up.**

This meeting was organised by Euroscicon (www.euroscicon.com), a team of dedicated professionals working for the continuous improvement of technical knowledge transfer to all scientists. Euroscicon believe that they can make a positive difference to the quality of science by providing cutting edge information on new technological advancements to the scientific community. This is provided via our exceptional services to individual scientists, research institutions and industry. The event was hosted by 'BioPark (www.biopark.co.uk), a research and development centre in Welwyn Garden City providing specialist facilities and support for bioscience and health technology businesses to grow, and to develop new products and technologies

About the Chair

Professor Julian Ma holds the Hotung Chair for Molecular Immunology at St. George's Hospital Medical School, University of London. He graduated in dentistry at Guy's Hospital in 1983, and went on there to gain his PhD in Immunology, studying topical anti-microbial immunotherapy using monoclonal antibodies. He was a post-doctoral fellow at The Scripps Research Institute, La Jolla, in Andrew Hiatt's laboratory where he worked on the expression of recombinant antibodies in transgenic plants. On his return to Guy's Hospital in 1992, he continued this work which led to the first description of a monoclonal secretory antibody expressed in plants and its clinical applications in human immunotherapy against dental caries. In 1998, he was made Consultant in Immunology and Oral Immunotherapy at Guy's Hospital Dental School, the first consultant appointment in Oral Immunology in the UK. He heads a research group which also studies basic mechanisms of protein assembly, processing and expression in plant cells, design and engineering of novel recombinant proteins in plants for systemic and mucosal human vaccination. The group are leading proponents in Europe for the development of plant biotechnology for medicines for human health.

About the Speakers

Denis J Murphy; PhD at Univ of York, UK; Fulbright postdoc fellowship at Univ California Davis; Royal Society postdoc fellowship at Australian National Univ, Canberra; Lecturer in Molecular Biology at Univ Durham; Head of Oilseeds Research Dept at John Innes Centre UK. Currently Head of Biotechnology Unit at University of Glamorgan, UK. Also Biotechnology Advisor to United Nations Food and Agriculture Organization and Chair, Biology Advisory Committee, Malaysian Palm Oil Board.

Dr Alessandra Devoto (AD) has expertise in plant stress biology, specifically hormones and their signalling pathways. AD investigates the role of jasmonates (JAs) as distress signals blocking cell cycle during defence responses. Genomics and biochemistry are used to

manipulate natural compounds to obtain therapeutic drugs. A model system is being developed to study the effect of JAs on normal and tumour cells. Transcriptomics and bioinformatics are used to model and infer signalling networks. Other work is aimed to developing of novel plant varieties more prone to saccharification. AD's work is documented by 25 publications in international peer-reviewed journals.

Professor Houghton retired as Professor in Pharmacognosy at KCL in 2008, after over 30 years working there. He has published over 250 research papers on the chemistry and biological activity of plants and their constituents. His research areas include substances from plants potentially useful in wound healing, cancer and neurodegenerative disease.

Cathie Martin is a group leader at the John Innes Centre, the leading plant research institute in Europe. She is Professor at the University of East Anglia and Niels Bohr Professor in the Faculty of Life Science, University of Copenhagen, Denmark. Recently she has been co-ordinating research into how diet can help to maintain health and reduce the risk of chronic disease, and how crops can be fortified to improve diets. Her interests span from fundamental to applied plant science. She is Editor-in-Chief of *The Plant Cell*, and the first woman and the first non-American to hold this post.

Ian A Graham, graduated from the Queen's University of Belfast with a first class honours degree in Botany and Genetics in 1986. He obtained his PhD in Plant Molecular Biology from the University of Edinburgh in 1989, after which he went on to do postdoctoral research at the University of Oxford and The Carnegie Institution Plant Biology Laboratory at Stanford University. He took up his first faculty position at The University of Glasgow in 1993 and moved to the University of York in 1999 where he holds the Weston Chair of Biochemical Genetics and is current Director of CNAP (<http://www.york.ac.uk/org/cnap/>)

Paul Fraser has over 20 year's experience working both in academia and industry within the UK and abroad. During this period Dr Fraser has worked on the analysis, biosynthesis, regulation and metabolic engineering of carotenoids and isoprenoids, both in plant and microbial systems.

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Poster Presentations

Molecular Farming in *Dunaliella salina*

Barzegari, A.,¹ Hejazi, M. A.,¹ Rustayi, M.²

¹North and North-West Agricultural Biotechnology Research Institute of Iran, ²Bu Ali Sina University, Agricultural Faculty, Hamadan

At present, several heterologous protein expression systems are available for the production of recombinant proteins for using in human and animal healthcare. Each of these expression hosts offers distinct advantages consisting soluted protein enhancement, ease of manipulation, and cost of production. Bacteria are the expression host systems that are often used to attempt to produce recombinant proteins. However, the bacterial protein expression system is incapable of reproducing the complexity of eukaryotic proteins which often require extensive folding and post-translational modification. Plant cells carry out many of the post-translational modifications required for optimal biological activity of mammalian proteins. However, there are several problems to use them to produce therapeutic proteins including long period from the initial transformation event to the delivery of usable quantities of antibody that may take even in year scale. The second problem in plants is the potential for genflow (via pollen) surrounding crops. The last problem is herbicide resistance genes. The production of pharmaceutical substances in animal cell cultures is often associated with the risk of product contamination with pathogens dangerous to human health. Therefore, *D. salina* has many advantages compared with traditional systems for the molecular farming of pharmaceutical proteins.

- 1.lacking of cell wall, therefore being easy to manipulate.
2. the single, large, cup-shaped chloroplast present in the cell. The chloroplast transformation is harmless to the environments and does not induce gene silencing.
3. The low cost of their culture. *D. Salina* is an autotrophic organism in media containing inorganic salts.
4. Lack of proteins and pathogenes similar to human's in *D. salina*.
5. post-translational processing for proteins.
6. The availability of a wide variety of promoters regulated by factors such as light or specific nutrient levels in the medium.

7. The ability to produce secreted proteins
8. High growth rate in shorter time, which allows it easy to screen transformed cells.

References

- 1- Armin, H. 2007. Algal Transgenics and Biotechnology, *Transgenic Plant Journal* 1(1), 81-98
- 2- Geng, D.G., Y.Q. Wang, W.B. Li, and Y.R. Sun. 2002. Transient expression of GUS gene in *Dunaliella salina*. *High Tech. Lett.* 12, 35-39.
- 3- Scott E F. and Mayfield, S. P. 2004. Prospects for molecular farming in the green alga *Chlamydomonas reinhardtii*, *Plant Biology*, 7:159–165
- 4- Mewett, O., Hilary, J. and Ruth, H. 2007. Plant molecular farming in Australia, www.ag.gov.au/cca

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