

Molecular Farming - plant biologicals

The BioPark Hertfordshire, Welwyn Garden City , AL7 3AX

29th Jan 2008

- 9:00 – 9:45 **Registration**
- 9:45 – 9:50 **Introduction by the Chair:** Professor Julian Ma, St Georges Hospital-University London
- 9:50 – 10:20 **The developing regulatory oversight of plant made pharmaceuticals**
Professor Philip J Dale OBE, John Innes Centre, UK
 The production of pharmaceuticals in plants has several important potential benefits, but also presents challenges, including the choice of crop and production protocol, and managing production to ensure batch to batch consistency. The current regulatory mindset for pharmaceutical production has evolved through extensive experience with contained and highly controlled production systems. In order to evaluate and hopefully exploit the benefits of large scale pharmaceutical production in plants, it is important to question the relevance of some of the current regulatory guiding principles to other production systems, and where necessary, to modify them or develop new ones
- 10:20 – 10:50 **Pharma-Planta – an academic consortium advancing Molecular Farming in Europe and South Africa**
Professor Julian Ma, St Georges Hospital-University London
 The Pharma-Planta Project is an academic led consortium of 39 principal investigators from institutions including SMEs in Europe and Africa. Pharma-Planta has been funded by the European Commission as part of the Sixth Framework Programme in the area of “Plant platforms for immunotherapeutic biomolecule production.” This talk will describe the work that is being done by this consortium, and the progress that is being made towards the main objective of performing a Phase I clinical trial using a cGMP compliant plant derived monoclonal antibody.
- 10:50- 11:00 **Speakers photo**
- 11:00 – 11:30 **Mid-morning break**
- 11:30 – 12:00 **Recombinant pharmaceutical proteins from cereal grains**
Dr Eva Stoger, Aachen University RWTH, Germany
 Among the many plant-based production systems that have been developed for pharmaceutical proteins, seeds have the useful advantage of accumulating proteins in a relatively small volume, and recombinant proteins are very stable in dry seeds allowing long-term storage and facilitating distribution prior to processing.
 To take full advantage of these properties for the production of glycoproteins, including therapeutic antibodies, it is important to study the tissue-specific factors involved in intracellular protein accumulation and post-translational modification. N-glycan structures, for example, are generally influenced by the plant species, tissue, cell type and age, with potential implications for the performance of pharmaceutical proteins.
- 12:00 - 12:30 **Maximising production and improving uniformity of transgenic plants for the manufacture of an IgG monoclonal antibody**
Dr. Richard Colgan, East Malling Research, UK
 Tobacco is emerging as a transgenic production crop of choice for plant made recombinant pharmaceuticals (PMP). A range of recombinant proteins including monoclonal antibodies have been successfully produced in tobacco. The primary goal in horticultural management of plants for PMP production is to maximise recombinant protein synthesis while maintaining inter and intra plant uniformity of production.
 Here, the horticultural considerations for cultivation of two transgenic lines in greenhouse containment have been studied. The effect of environmental variables such as light intensity, day length, temperature, plant density and nitrogen availability have been investigated in terms of impact not only on plant growth and biomass production but also with regards to the concentration and total yield per plant of two recombinant pharmaceutical proteins.
- 12:30 – 12:50 **Tour of the BioPark**

- 12:50 – 14:00 Lunch and Poster Viewing
- 14:00 – 14:30 **New generation technologies for expressing recombinant proteins in green plants**
Professor Yuri Gleba, Icon Genetics GmbH, Germany
 The traditional plant-based production platforms fall into several categories: nuclear transformation, plastid transformation, and transient expression based on delivery by *Agrobacterium* or viral vectors. All 'first generation' expression methods suffer from various limitations, such as the long time frame necessary for stable transformation, low yield, biosafety concerns around open field cultivation of transgenic crops, etc. The new generation processes such as recently developed magniflection offer dramatically better solutions that combine speed of transient systems, expression level/yield that approaches biological limits, and posttranslational capabilities and low production cost of a plant
- 14:30 – 15:00 **How does the plant endoplasmic reticulum cope with the synthesis of heterologous proteins?**
Dr Lorenzo Frigerio, University of Warrick, UK
 The endoplasmic reticulum (ER) is the key subcellular compartment for the folding, assembly and quality control of any recombinant protein that is targeted to the plant secretory pathway. Using immunoglobulins as a model, we have assessed the capacity of the ER to handle multimeric recombinant proteins. We have compared the response to antibody overexpression with chemically - induced ER stress. We have also initiated the study of a novel protein family that is involved in regulating the shape of the ER. We will discuss the potential of these proteins to modulate ER expansion following expression of heterologous polypeptides
- 15:00 – 15:30 **Afternoon Tea/Coffee and Last Poster Viewing**
- 15:30 – 15:50 Rhizosecretion for harvest of molecular farming products - A contained and controlled manufacturing system
Dr. Pascal Drake, St. George's Hospital Medical School, London
 Rhizosecretion is an attractive method for the production of recombinant pharmaceuticals in genetically modified plants, as extraction and purification from hydroponic medium is simpler and less expensive than from more complex plant tissues. In addition, plants are grown under contained conditions and rhizosecretion allows continuous production of pharmaceutical over the lifetime of the plant.
 In this paper we will be summarising developments in the field to date, including our demonstration of assembled full-length antibody and cyanovirin rhizosecretion in transgenic tobacco hydroponic cultures. Finally, we shall focus on possible methods to improve the efficiency of rhizosecretion. Such strategies include the optimisation of conditions for root growth, the simplification of hydroponic medium to ensure facile, inexpensive, purification of pharmaceutical, the use of root-specific promoters, and the minimisation of protein degradation by plant-expressed proteases.
- 15:50 – 16:20 **Expression of self-assembling macromolecular complexes using a plant virus vector**
Dr George Lomonosoff - John Innes Centre, Norwich
 Vectors based on wild-type RNA plant viruses have already proved useful for the production of foreign proteins in plants and we have used such vectors based on the legume virus, *Cowpea mosaic virus*, to produce both antigens and antibodies. However, vectors based on fully competent viruses have disadvantages both in terms of the size of insert that can be tolerated and problems of biocontainment. To address these problems we have developed systems based on defective versions of CPMV and have used these to express multi-subunit proteins of pharmaceutical interest.
- 16:20 – 16:50 **Freedom to Operate and Molecular Pharming**
Dr Harry Thangaraj, Director of Research, Centre for the Management of IP in Health R&D, UK
 Expression methodologies in plants are a potentially cost-effective way for large scale production of biopharmaceuticals for diseases that disproportionately affect poorer populations. The Pharma-Planta Consortium is actively developing products and processes, with a focus on combating diseases such as TB, Malaria and HIV infection, keeping access and affordability considerations in mind. Access considerations are not limited to scale up of production. Creative access strategies extend far beyond scientific methodologies and involve broader considerations such as Intellectual Property and Risk Management, examples of which will be presented here
- 16:50 – 17:00 **Chairman's summing up & close.**

*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 Hertfordshire'** (www.biopark.co.uk), a new 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*