

MolPAGE: Molecular Phenotyping to Accelerate Genomic Epidemiology.

Thematic Area: Life Sciences Genomics and Biotechnology for Health

Instrument: Integrated Project

Co-ordinated by: University of Oxford

Total budget: 12m€

Duration of project: Four years from 2004

Number of partners: 18

Subjects of case study: University of Oxford and Oxford Gene Technology.

Project website: <http://www.ocdem.com/composite-108.htm>

The Challenge

A number of biobank efforts are ongoing in the UK and worldwide. These programmes will soon produce an unprecedented number of samples for molecular phenotyping. Although the development of genotyping technologies for the analysis of DNA markers is already mature enough to allow for their use on an epidemiological scale it is not yet clear how to tackle the application of post-genomic technologies such as metabonomics and proteomics where standardisation procedures and high throughput approaches are less well established. The concept of the MolPAGE project is to design a programme to bridge this gap. In the first instance post-genomic technologies from the project will be applied to biomarker discovery and typing in metabolic disease.

Diabetes and its associated vascular complications is a major cause of ill health and premature death and is reaching epidemic proportions in Europe and worldwide. Scientific advances in molecular phenotyping now offer the potential for discovering and validating biomarkers so as to identify individuals who are likely in the future to suffer from diabetes and vascular disease, long before they show symptoms or the biochemical abnormalities usually used as the basis for diagnosis. If those at risk can be diagnosed earlier, then there is the prospect for more effective prevention and better treatment.

The Project

Developments in genomics, proteomics and metabonomics now enable much more detailed study of genes, proteins and other molecules involved in disease progression. The major opportunity for the project MolPAGE is to further develop technologies for high-throughput use to define the relationship between different biomarkers (and their patterns) and disease, on an epidemiological scale. This project brings together a range of techniques to characterise diabetes, metabolic and vascular disease. The programme has three parts:

- (i) Evaluation of sample collection and storage methodology to reduce sample variation and improve stability.
- (ii) Development of new tools for molecular phenotyping at the population level – including metabonomics, transcriptomics, proteomics, DNA methylation patterns and genetics.
- (iii) Development of new bioinformatics tools for data collection and integrated data analysis.

The Consortium

MolPAGE is now in its second year of the four year programme (12m€). The consortium is led by Professor's John Bell and Mark McCarthy from the University of Oxford and comprises 18 leading academic groups, pharmaceutical and biotech companies (companies account for 40% of the partners). Involvement of clinical academic specialists provides insight into disease pathophysiology and access to clinical samples and the consortium as a whole represents a highly valuable mix of clinical and basic research experience and proprietary technology expertise.

The View from Oxford Gene Technology

One of the SME partners, Oxford Gene Technology (OGT) is a company specialising in the development of molecular tools, built on the original success of DNA microarray technology and represented in the consortium by John Anson.

OGT recognises that 50% funding of their research costs is useful, but probably of much greater value to OGT in participating in MolPAGE is the opportunity to network with leading scientists across Europe. OGT as a company aims to remain at the forefront of emerging technology and needs to have early intelligence of new research developments and of the scientific challenges faced by the leading laboratories. OGT is also a member of the MolTOOLS consortium in Framework Programme 6, which is complementary to MolPAGE in important respects in technology development. There is also good potential for further development of the general area of high throughput molecular phenotyping in Framework Programme 7.

Flexibility of roles

The contribution made by OGT to MolPAGE Work Packages has already evolved from an initial focus in year one in proteomics to their current role in the development of a micro RNA array. Some of the initial technical aims of the consortium have been revised accordingly to the current needs of the consortium. The underpinning technology is advancing rapidly – in particular there are now commercially available microarray products for re-sequencing known regions of the genome.

During the course of the MolPAGE project the role of micro RNAs as biomarkers in human disease, including diabetes has emerged. Analysis of these molecules was not part of the original deliverables for the consortium, but the project Steering Committee felt that this was a gap in the programme. Because of their expertise in microarray design and construction, OGT were approached by the Steering Committee to produce a micro array product to tackle the analysis of micro RNA for the consortium. The availability of a range of alternative technologies customised by OGT enables the company to be flexible and to contribute to different work packages as necessary.

Handling Intellectual Property

A significant concern for OGT when considering whether to join MolPAGE was the handling of Intellectual Property. OGT is a company that exists by licensing its technology and it holds fundamental patents on microarrays. Hence, it was possible that involvement in the consortium would leave OGT exposed to the use of its technology by others without payment of licensing fees. The solution was to stipulate clearly in the consortium agreement what IP was to be included or excluded from the project. OGT also notes that it is important to be clear about the demarcation of roles among the partners at the start to avoid future confusion or conflict.

Management and Communication

OGT emphasises the general importance of:

- Good internal communication and leadership, to clarify the scientific responsibilities and to encourage individual partners to come together as a team.

- The decision to allocate dedicated resource for project management during the first year of MolPAGE operation, which has provided very significant support to the scientific leadership.
- Commitment to internal communication, which is vital to raise awareness within the company, in particular to explain the necessity for recording and costing research done for MolPAGE so as to prepare for external audit. There is a continuing concern that EU audit rules for FP6 are too challenging for SMEs, in not allowing adequate time to conduct the independent audit.

In summarising the experience of OGT in MolPAGE:

- The research being conducted in MolPAGE is highly relevant to OGT's core business and the benefits of networking have been greatly appreciated.

In terms of "tips for success" that might aid other SME researchers thinking about future participation in Framework Programmes:

- It is judged important to take a flexible approach so as to be able to adapt to the changing science and technology.
- It is also important to generate internal awareness of participation throughout the company early on in order to allocate sufficient management time and prepare for reporting and auditing requirements.

The View from Project Management

As Programme Director, Maxine Allen (University of Oxford) provides additional perspective on consortium coordination. The consortium has collectively made a major commitment to training, by organising annual training courses and technology workshops open to the wider scientific community to showcase developments in the project. In addition the project encourages mobility between partners through the provision of financial 'mobility awards' to support the secondment of researchers between consortium laboratories for cross training and career development. MolPAGE dissemination activities are also open to the wider community and these are seen as an important mechanism for contributing to standard-setting and to the interaction with other EU projects.

The University of Oxford, as Project Coordinator, has important responsibilities

- in providing the main contact point with DG Research,
- in providing the central administration and support for partners,
- in acting as the public champion of the project,
- in managing change and coordinating dissemination activities and IP reviews.

Underpinning these specific duties is the need to ensure project momentum is maintained by the regular monitoring of scientific progress and by promoting interaction between the partners.

There is also recognition by of the importance of a well-written consortium agreement and explicit explanation of the project plan and IP management. There is continuing need for high-level interaction between partners and good internal and external communication procedures. Ongoing close contact with the project officer in DG Research is crucial to ensure that there is flexibility if necessary to change protocols and scientific deliverables.

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