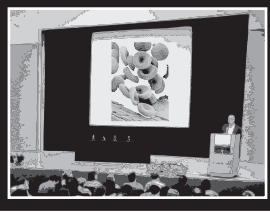
Conference Scene

Progress and challenges for pharmacogenetics in Europe



5th Anniversary Meeting of the European Research Network Pharmacogenetics/Pharmacogenomics
8–9 December 2011, Utrecht, The Netherlands

The European Research Network Pharmacogenetics/Pharmacogenomics (PGx) is a specialist group of scientists and clinicians who share a common interest in research in PGx and its implementation to improve clinical care. This 5th anniversary meeting focused on progress and future challenges for PGx in Europe. A series of expert presentations were made, and are summarized below. The meeting concluded with an open debate on the current challenges facing the field in a time of limited funding.

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Opening & progress

This 5th anniversary meeting of the European Research Network Pharmacogenetic/Genomics (PGx) was organized in Utrecht, The Netherlands, and attended by more than 30 researchers from many different European countries. Anke-Hilse Maitland-van der Zee (University of Utrecht, Netherlands), host and organizer, opened the meeting with an overview of the Network's history and achievements to date. It was encouraging to see the progress made within this specialized field. During the first day of the meeting the progress in research, education and implementation of PGx in Europe were discussed. The second day of the meeting considered the challenge of finding funding for new research within a fiscally constrained European environment.

Update on European/international research

An appreciation that collaboration and cooperation are key components for the success of PGx has delivered a range of ongoing projects including; European Pharmacogenetics of AntiCoagulant Therapy (EU-PACT), The International Drug-Induced Liver Injury Consortium (iDILIC) and International Consortium on Drug Hypersensitivity (ITCH). Updates on the aforementioned large European/International studies demonstrated progress towards a better understanding in these important areas [1–3]: Ann Daly (Newcastle University, UK) described the growth of iDILIC from the UK DILIGEN network, established in 2004 with UK Department of Health funding, to the now truly international group of scientists who are pooling their resources (now included with European groups are Chinese, Australian, Canadian, South American and New Zealand participants) with funding from the International Serious Adverse Consortium (iSAEC). As of November last year, iDILIC have in excess of 600 samples and datasets, a remarkable achievement given the scarcity of the phenotype (rare, serious, drug-induced idiosyncratic liver toxicity occurs in only one in every 10,000/100,000 patients). Plans for the application of the latest genome interrogation approaches, for the detection of rarer sequence variation, to the iDILIC resource are underway, with results expected later in 2012.

As for iDILIC, the ITCH group have benefited from support by the iSAEC. Ana Alfirevic (University of Liverpool, UK) described a similar, international approach important not only to improve sample numbers but also to ensure a range of medicines and patient ancestry are investigated. Encouraging demonstration of the potential for avoidance of serious adverse events has recently been published for a Taiwanese population [4] providing hope that further work will yield similar successes in the clinic. The iSAEC includes representation from many of the world's pharmaceutical companies and regulatory bodies, emphasizing the priority that drug safety has for all pharmaceutical stakeholders; patients, providers, regulators and industry partners alike.

Clinical implementation

Thomas Bergmeijer (St Antonius Centre for Platelet Function Research Nieuwegein, The Netherlands) spoke on the clinical implementation of PGx, with specific

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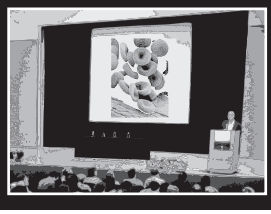


reference to *CYP2C19* testing in cardiology. Interestingly, Dr Bergeijer's study demonstrated carriers of *CYP2C19* loss-of-function alleles (**2*, **3*) do have increased platelet reactivity and atherothrombotic event rates when using clopidogrel to minimize atheromthrobotic events following stent implantation, although further work is required to develop the optimal management strategy.

Integrating other 'omics

The staggering range of technical possibilities now available to the PGx research community presents opportunities as well as new challenges. In addition to the current funding situation, the nature and volume of data it is possible to assimilate have created a new set of problems, and is considered to be the next 'bottleneck' for genomic sciences [5]. In this vein, Ingolf Cascorbi (Christian Albrechts University Kiel, Germany) provided an excellent overview of 'omics technologies, starting with a discussion of the (sometimes confusing) terminology in this area. It is good to see that the WHO has at least provided a clear and simple differentiating description of genetics versus genomics and it must be hoped that similar clarity develops for the other, technology-driven, fields attracting the 'omics suffix [101]. Genomics (quantitative study of genes, regulatory/noncoding sequences); transcriptomics (RNA/gene expression); proteomics (protein expression); metabolomics (metabolites/metabolic networks) and PGx (quantitative study of how genetics affects hosts' responses to drugs) have progressed significantly in the last decade. Dr Cascorbi's presentation concluded, via the search for biomarkers, with the current drive for personalized medicines, providing an excellent link to Ron van Schaik's (Erasmus Medical Center, Rotterdam, The Netherlands) clinically focused overview of his experience in moving current knowledge to where it really matters, improving the treatment and outcomes for patients.

Optimizing robust systems

The clinical PGx services established at the Erasmus MC (University Medical Centre Rotterdam, The Netherlands) ensure that real-world learning on the implementation of genetic testing for dose adjustment or drug selection is developed. By optimizing test platforms, data interpretation and recommendations to physicians, it has been possible to assimilate new data on the cost–effectiveness of PGx testing, challenging conclusions drawn from different healthcare environments, for example, the USA [6].

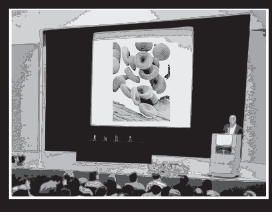
Courses: meeting training gaps

The final session of the first day focused on current efforts to bridge the PGx education gap in Europe. Both the Universities of Liverpool and Newcastle are developing courses and training opportunities designed to meet the needs of students at all career levels. For example, via the EU FP7 Marie Curie Initial Training Network: Fighting Drug Failure, co-ordinated by Hiltrud Brauch (Dr Margarete Fischer-Bosch-Institute of Clinical Pharmacology, Stuttgart, Germany), training and research experience programs in PGx are provided for early-stage researchers (less than 4 years research experience and without a PhD, 13 placements) and more experienced PhD level/>4 years experience researchers (two placements). The students are supported for a period ranging from 3–36 months, subject to project and funding guidelines. At Newcastle, Ann Daly offers a specialist undergraduate module to BSc students in Pharmacology (Advanced PGx), thus providing an option to gain up-to-date knowledge of the field. Finally, in the EU2P training program (the European IMI Education and Training e-learning Master and PhD programme, funded by the European Commission and the pharmaceutical industry) PGx knowledge is delivered within the context of pharmacovigilance and pharmacoepidemiology. With input from a wide European partnership of countries and specialist groups this course too promises to deliver a good grounding in the field.

The future of PGx research in Europe was discussed on day two. Key topics and important conclusions from this debate are summarized below.

Funding

The European Research Network considers it important to identify European funding for PGx. In addition to FP7, researchers may consider academic–industrial collaborations, not least within the Innovative Medicine Initiative (IMI) framework.



Christian Noe (Scientific Committee Chair, IMI) mentioned that personalized medicine is high on the IMI strategic agenda and that IMI calls are directed to address pharmaceutical company challenges. It was decided, therefore, that in 2012 the Network will organize a workshop in preparation of a call on genomic biomarkers, including new ways of collaboration/coordination, with participation from academia and industry.

PGx in the next decade

Discussion led to the identification of several important areas: first, phenotypes of both efficacy and adverse drug reactions. Phenotypes, across Europe, should be standardized, facilitating collaboration/meta-analysis. Furthermore, a European database of genomic datasets (including phenotypes) would be helpful, with the Network playing a role in developing this tool. Next, extreme phenotype approaches are still considered important in gene–drug interaction work. Lastly, the most successful areas in PGx research are oncology and adverse drug reactions. IDILIC and ITCH (within iSAEC) make it possible to perform research on rare severe adverse drug reactions, and European researchers should continue to lead and contribute to these and similar initiatives.

Implementation

Although several gene–drug interactions have potential for clinical implementation (e.g., those added to drug labels by US FDA), the clinical uptake of PGx is still low. The Network might play a role in providing recommendations for which gene–drug interactions are ready for clinical implementation. Furthermore, the nomenclature of genetic variation is confusing, and better standardization would help nonexperts. Finally, parallel standardization of genotyping tests is of utmost importance for clinical implementation of PGx.

Education & training

Competences needed to be a 'pharmacogeneticist' should be defined. Indeed, although centers of excellence exist, the breadth of Europe-wide knowledge and training opportunities is unclear. If, on review, gaps are identified, the Network could engage in organizing a European PGx Course.

Research network: the future

Easy interparticipant communication was considered a key to success; therefore, a European Research Network LinkedIn [102] Group will be established. Increasing the number of participants in European projects is important, and the Network could help in this regard. However, funding for Network activities is required. Ensuring ambitious projects, such as delivery of the proposed European PGx database, is not a trivial task and the Network will need further support to ensure success.

Financial & competing interests disclosure

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