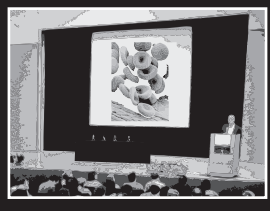
Conference Scene

Golden Helix Pharmacogenomics Days: educational activities on pharmacogenomics and personalized medicine



4th and 5th Golden Helix Pharmacogenomics Days
7 October 2011, Cagliari, Italy and 3 December 2011, Msida, Malta

The Golden Helix Pharmacogenomics Days are high-profile international educational scientific meetings discussing pharmacogenomics and personalized medicine. Here, we provide an overview of the scientific lectures and the topics discussed during the 4th Golden Helix Pharmacogenomics Day, held in Cagliari, Italy, on 7 October 2011, and the 5th Golden Helix Pharmacogenomics Day, that was held in Msida, Malta, on 3 December 2011. The scientific programs of both events included scientific and company lectures on pharmacogenomics, bioinformatics and personalized medicine by local and international speakers from Europe and the USA.

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The Golden Helix Pharmacogenomics Days

The Golden Helix Pharmacogenomics Days are international educational scientific meetings that are organized by the Golden Helix Institute of Biomedical Research jointly with local academic institutions in major cities with large academic hospitals [1,101]. The aim of these meetings is: to provide timely updates on the field of pharmacogenomics and personalized medicine to the local biomedical scientists, healthcare providers and biomedical students; to educate and inform them on the application of pharmacogenomics in modern medical practice; and to bring together faculty members from universities and research institutes from the local scientific arena working in the field of pharmacogenomics in order to initiate collaborative projects in this field to the benefit of society. Previous Golden Helix Pharmacogenomics Days have been organized in Athens (Greece; 7 May 2009), Thessaloniki (Greece; 15 April 2010) and Alexandroupolis (Greece; 8 April 2011).

The 4th Golden Helix Pharmacogenomics Day was organized in Cagliari (Italy) by the Golden Helix Institute of Biomedical Research and the Bernard B Brodie Department of Neurosciences of the University of Cagliari (Cagliari, Italy) and supported by the Foundation of the Bank of Sardinia and Beijing Genome Institute. The 5th Golden Helix Pharmacogenomics Day was organized in Msida (Malta) by the Golden Helix Institute of Biomedical Research and the Faculty of Medicine of the University of Malta and supported by the Foundation of Medical Sciences, Affymetrix, Illumina, QIAGEN, and the Mediterranean Bank. Both meetings were under the auspices of the European Society of Pharmacogenomics and Theranostics [102] and were attended by over 160 registered participants each. Here, we provide a report and present the highlights of these meetings.

4th Golden Helix Pharmacogenomics Day

Pharmacogenomics has an integral part in modern medical practice. George P Patrinos (University of Patras, Greece) outlined the key aspects of pharmacogenomics, their implications in personalized medicine, and the most important applications in cancer, cardiovascular and psychiatric disorders, both in terms of drug efficacy and toxicity. Patrinos, also alluded to the importance of the incorporation of pharmacogenomics in developing countries in Europe, not only to rationalize drug use but also to reduce the overall healthcare costs [2]. Next, Giovanni Severino (University of Cagliari) also stressed the importance of pharmacogenomics to predict adverse drug reactions so that the patient's quality of life is improved. Successful implementation of pharmacogenomics strongly relies on regulatory agencies. Roberto De Lisa (EMA, London, UK) presented the regulatory activities related to pharmacogenomics and personalized medicine at the level of the EMA. The Pharmacogenomics Working Party (PgWP) provides recommendations to the Committee for Medicinal Products for Human Use (CHMP) on all matters relating directly or indirectly to pharmacogenomics. Some examples of product

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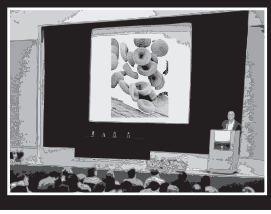


information recently updated to include information on pharmacogenomics on the basis of pharmacovigilance data are carbamazepine in relation to *HLA-A*1502*.

Federico Innocenti (University of North Carolina, NC, USA) discussed about the discovery of pharmacodynamic and pharmacokinetic biomarkers for drug response in cancer patients. Innocenti presented some recent work on the discovery of genetic variants in genes of the VEGF (angiogenesis) pathway (pharmacodynamics), and genetic variants involved in the regulation of gene expression in the human liver, the main organ of drug disposition (pharmacokinetics). In these studies, integrated approaches using clinical and molecular data were performed [3].

In the current post-human genome project era, next-generation sequencing (NGS) technologies promise to accelerate human genetic studies tremendously. Grover Yu (Beijing Genome Institute, China) presented the various NGS applications offered by BGI to identify important rare variants, understand disease inheritance and realize the goal of therapies based on personal genomics. NGS technologies make these goals possible and promise a way to exploit the complexity of the human genome.

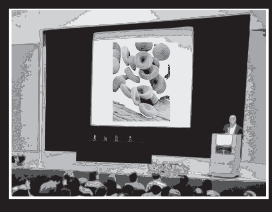
Hemoglobinopathies are the commonest single gene disorders in the Mediterranean basin. Renzo Galanello (University of Cagliari) presented recent data outlining the impact of pharmacogenomics in iron-overload treatment, while also stressing the importance of *KLF1* mutations in increasing fetal hemoglobin production in adults, which holds promise for novel therapeutic modalities for hemoglobinopathies [4]. Giovanni Caocci (Bone Marrow Transplant Center, R Binaghi Hospital, Cagliari, Italy) described the application of tyrosine kinase inhibitors to treat chronic myeloid leukemia (CML), in particular the use of imatinib and the second generation of tyrosine kinase inhibitors that are also available today (dasatinib and nilotinib). Overall survival of CML patients has increased up to 85–90% after 5 years of therapy, transforming CML from a fatal leukemia in a chronic illness with a good quality of life.

Finally, Alessio Squassina (University of Cagliari) presented a wide overview of the pharmacogenomics of lithium response in bipolar disorder. Squassina presented evidence based on a genome-wide association study study on bipolar patients of Sardinian ancestry characterized for lithium response, suggesting that *ACCN1* may play a key role in lithium treatment response [5].

As with every genomics approach, bioinformatics and data management are of utmost importance. Patricia Rodriguez-Tomè (CRS4, Pula, Cagliari, Italy) outlined the importance of bioinformatic tools in the analysis of large amounts of genomic data, and presented examples of their use, focusing on genomic databases. Similarly, Stefano Calza (University of Brescia, Italy) illustrated how data mining and machine-learning algorithms can be applicable in the context of modern life sciences, in particular developing predictive models, designing better clinical trials and understanding how (candidate) genomic markers can be incorporated into study design for the development of new drugs. Finally, Valeria Deiana (University of Cagliari) presented a clinical database that has been developed to document detailed clinical and phenotypic information of bipolar disease patients, such as the longitudinal course of illness, presence of psychotic symptoms and suicidal behavior, and psychiatric comorbidity.

5th Golden Helix Pharmacogenomics Day

The importance of pharmacogenomics and personalized medicine was emphasized by European Commissioner for Health and Consumer Policy, John Dalli, who officially opened the event [103]. Christian Scerri (University of Malta) presented the opportunities that a small island like Malta can offer to pharmacogenomics, strongly related to the participation of Malta to the Pharmacogenomics for Every Nation Initiative (PGENI) [104], which also endorsed this event. Pharmacogenomics should be successfully incorporated in the clinic to maximize their usefulness to the patients. Ron van Schaik (Erasmus University Medical Center, Rotterdam, The Netherlands) presented the experiences of one of the biggest hospitals in The Netherlands in the integration of pharmacogenomics into mainstream



clinical practice and how pharmacogenomic information can be communicated between various healthcare professionals across the country.

Marisa Papaluca-Amati (EMA) delivered her presentation by live videoconferencing and described the contribution and activities of a major regulatory agency to the development and applications of pharmacogenomics [105]. Pharmacogenomics has fast entered the clinical arena, and the EMA emphasis now focuses on clinical translation of pharmacogenomic data for personalized medicines, encouraging the incorporation of pharmacogenomic methods into clinical trials, and entering into dialogue with industry in order to explore the therapeutic benefits and risks within genetically defined patient subgroups. In addition, Jean-Luc Sanne (Directorate General for Health, European Commission, Belgium) outlined the central role of personalized medicine into framework program 7 (FP7) for health.

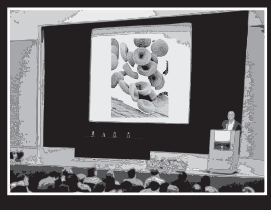
There are currently very few clinical applications for pharmacogenomics on the market. Laura Uribe (Affymetrix Ltd, Singapore) discussed microarray technology as a tool for genotyping pharmacogenomic markers and generating information which is translatable to bedside applications. Uribe focused on the DMET+ array, which genotypes 1936 known pharmacogenomic markers in 225 genes related to drug metabolism and transport, including 99% of the absorption, distribution, metabolism and excretion core markers as defined by the PharmaAdme Group [106]. The DMET+ array is the basis for the ongoing PGENI project [104], which aims to produce a worldwide map for ethnic-specific pharmacogenomic marker allele frequencies.

The keynote lecture was delivered by Patrinos, who presented the impact of pharmacogenomics not only to modern medical practice but also to society. He also presented preliminary data from the analysis of healthy Maltese volunteers for the PGENI project, which indicate some very interesting deviations from certain pharmacogenomic marker allele frequencies compared with the Caucasian group, further supporting the importance of PGENI to rationalize drug use in developing countries [2].

Andrew Webb (QIAGEN GmbH, Germany) gave an overview of the current trends in personalized healthcare and the roles of the pharmaceutical and diagnostic industries in the development of companion diagnostics to predict which patients are most likely to benefit from a particular therapy in advance. Webb highlighted that the use of companion diagnostics will provide a solution to stratify patients into therapeutic groups and eliminate the 'trial and error' approach. He also discussed the current companion diagnostic tests and the technologies used for implementation. In addition, Gustav Karlberg (Illumina Ltd, UK) gave an overview of the current tools and methods for Pharmacogenomics.

Godfrey Grech (University of Malta) presented an overview of the molecular aspects of pharmacogenomics. He emphasized that the use of biomarkers to derive knowledge required for the classification of patients into therapeutic groups has been extensively used in various malignancies [6,7]. Following on from Grech, Anthony Fenech (University of Malta) discussed molecular aspects of pharmacogenomics throughout the process, from drug development applications to bedside personalized medicine. Fenech finished by discussing the roles of microarrays and whole-genome sequencing in pharmacogenomic analysis, and commented that further answers to interpatient drug-response variability questions may not only be found in the genome.

Alessio Squassina (University of Cagliari) discussed pharmacogenetic testing of bipolar disorder and presented a comprehensive overview of all candidate genes known thus far to influence or predispose to bipolar disorder. Squassina presented data indicating that an important variant in *ACCN1* was associated with response to lithium treatment in Sardinian patients with bipolar disease [5]. He also stressed the 'Consortium on Lithium Genetics' (ConLiGen) initiative is also involved in the validation and identification of the key genes responsible for lithium therapy and personalized medicine [107]. Finally, Joseph Borg (University of Malta) presented the impact of pharmacogenomic testing on hemoglobin related disorders. Borg presented data suggesting that genomic biomarkers can be



correlated to response to fetal hemoglobin augmenting therapies, while a novel gene can be related to increased fetal hemoglobin in adults and as such can be targeted for novel therapeutic modalities for thalassemia [8].

Conclusion

The 4th and 5th Golden Helix Pharmacogenomics Days highlighted various areas of interest in pharmacogenomics, where many internationally renowned scientists gave excellent overviews of the existing applications and demonstrated the rapid pace and the direction in which the field is moving. The Golden Helix Institute of Biomedical Research aims to establish the Golden Helix Pharmacogenomics Days as one of the main educational and outreach activities for PGENI [104] in developing countries in Europe. Educational and training activities for healthcare professionals on pharmacogenomics will significantly contribute to the adoption of pharmacogenomics particularly in developing countries and, reciprocally, to the spread of pharmacogenomics applications to the benefit of the general public in these countries [1,2]. Finally, these events have also laid the foundations for the 6th and 7th Golden Helix Pharmacogenomics Days scheduled for 5 June 2012 and 20 October 2012 in Belgrade, Serbia, and Patras, Greece, respectively.

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