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Genetic analysis in translational medicine

George P. Patrinos[1], **Federico Innocenti**[2], **Nancy Cox**[3], and **Paolo Fortina**[4,5]

George P. Patrinos: gpatrinos@upatras.gr; Federico Innocenti: finnocen@medicine.bsd.uchicago.edu; Nancy Cox: ncox@medicine.bsd.uchicago.edu; Paolo Fortina: paolo.fortina@jefferson.edu

[1]University of Patras, School of Health Sciences, Department of Pharmacy, Patras, Greece

[2]University of Chicago, Department of Medicine, Section of Hematology/Oncology Chicago, IL, United States of America

[3]University of Chicago, Department of Medicine, Section of Genetics, Chicago, IL, United States of America

[4]Thomas Jefferson University, Jefferson Medical College, Laboratory for Cancer Genomics, Kimmel Cancer Center, Philadelphia, PA, United States of America

[5]Dipartimento di Medicina Sperimentale, Universita' La Sapienza, Rome, Italy

Abstract

The 2010 GOLDEN HELIX Symposium ‘Genetic Analysis in Translational Medicine' was held in Athens, Greece, Athens, Greece, 1-4 December 2010. The scientific program covered all aspects of this discipline, including genome-wide association studies, genomics of cancer and human disorders, molecular cytogenetics, advances in genomic technology, next-generation sequencing applications, pharmacogenomics and bioinformatics. In addition, various topics on genetics and society and genetic analysis in clinical practice were discussed. Here, we provide an overview of the plenary lectures and the topics discussed in the symposium.

The GOLDEN HELIX Symposia

The GOLDEN HELIX Symposia (http://www.goldenhelixsymposia.org) are 2-3 day high profile interdisciplinary scientific meetings aim to advance biomedical and life sciences by bringing together scientists in the fields of human genomics and personalized medicine. This symposium series is named after the house of Francis Crick (‘The Golden Helix’; 19/20 Portugal Place, Cambridge, UK) to emphasize their focus on human genomics and personalized medicine. The symposia aim to maximize information exchange and promote collaborative relationships between regional research institutes and research centers of excellence in North America and Europe. Such information exchange and collaboration ties are strengthened by interactions between participants and lecturers, the latter being internationally renowned scientists and recognized leaders in their fields.

Previous Golden Helix Symposia were held in Athens, Greece, and dealt with developments in the areas of Copy Number Variation and Genomic Alterations in Health and Disease [2008; Patrinos and Petersen, 2009] and Pharmacogenomics and Personalized Medicine [2009; Patrinos and Innocenti, 2010]. Selected mini-reviews from the topics discussed in the symposia have been published in *Human Genomics and Proteomics* (http://www.sage-hindawi.com/journals/hgp).

The 2010 Golden Helix Symposium was devoted to Genetic Analysis in Translational Medicine and was under the auspices of His Excellency the President of the Hellenic Republic, Dr. Karolos Papoulias. The meeting was attended by over 220 registered participants from 26 countries, supported by 10 national and international corporate entities,

the European Commission FP7 program, the University of Patras and the Human Genome Variation Society, endorsed by the University of Chicago Department of Medicine, the Kimmel Cancer Center at Thomas Jefferson University Jefferson Medical College, the Pharmacogenomics for Every Nations Initiative (PGENI; http://www.pgeni.org), the Hellenic Cancer Society and the Hellenic National Organization for Medicines. Human Mutation and "VIMA Science" kindly served as communication sponsors of this event.

Here, we provide a report and present the highlights of this meeting.

Omics

The 1st session of the 2010 Golden Helix Symposium was devoted to the genomic etiology of human inherited disorders. Molecular heterogeneity of cancer is associated with differential prognosis and response to therapy. However, in spite of extensive molecular classification, specific pathways that can be targeted to understand the basis of disease and improve treatment remain poorly understood within specific subtypes of disease. Professor Erik Knudsen (Philadelphia, PA, USA) presented on the role of the retinoblastoma tumor suppressor (RB) pathway as a functional determinant of cancer subtypes and the relationship to therapeutic response [Knudsen and Knudsen, 2008]. In particular, mining gene expression data demonstrated that an RB loss gene expression signature differentiates the behavior of both ER-positive and ER-negative breast cancer cases [Ertel et al., 2010]. In ER-positive breast cancer, disruption of RB-pathway function was associated with poor prognosis and failure of endocrine therapy. Functional studies demonstrate that such therapeutic failure largely occurs in the presence of an intact *Rb* gene, as a result of deregulated mitogenic signaling. In models of hormone-refractory disease pharmacological activation of RB is a potent second-line therapy. In contrast, in ER-negative tumors complete loss of RB protein as occurs through genetic or epigenetic mechanisms in 40-50% of cases. Strikingly, in ER-negative disease RB loss is associated with improved response to chemotherapy and longer relapse-free survival. Complementary studies have shown that this paradigm from breast cancer holds significance in diverse tumor type including prostate cancer [Sharma et al., 2010]. In total, these studies define a clear role for RB-pathway as a determinant of tumor heterogeneity that can be leveraged as a molecular diagnostic to more effectively treat cancer. Professor Nancy Cox (Chicago, IL, USA) presented an overview of genome-wide association studies of complex disorders and stressed that we need to identify enough genes to get an idea of biological pathways, using examples from trait-associated SNPs for type I and II diabetes, bipolar disorder, cancer, hypertension and rheumatoid arthritis. Professor Cox also discussed the role of distant regulators and genomic architecture as a common mechanism of action for SNPs associated with multifactorial disorders.

The first keynote lecture was given by Professor Jean Jacques Cassiman (Leuven, Belgium) and was about the policies and guidelines for genetic testing, focusing on the current situation in Europe. He stressed that there is a highly variable quality in genetic services and a multitude of rules and guidelines governing genetic testing, requiring cross-continent harmonization. EuroGenTest (http://www.eurogentest.org) is a network of excellence aiming to establish norms and guidelines for quality, criteria, training in genetics, to provide centralized information for everybody involved in genetic testing and to validate new technologies. Also, a European database was constructed within Orphanet, documenting the quality of laboratories in Europe providing genetic analyses. Professor Cassiman finally stressed that there is a need to increase the quality of the services by both National and European regulation and this opportunity should not be missed.

The elucidation of the molecular basis governing human fetal globin gene silencing was under extensive study for over 40 years with the aim of providing a therapeutic intervention

to patients suffering from β-thalassemia. George P. Patrinos (Patras, Greece) presented results from a collaborative study with the University of Malta and Erasmus Medical Center in Rotterdam, the Netherlands, revealing that KLF1, a fundamental erythroid transcription factor, has a key role in fetal globin gene silencing. A genome-wide scan of a consanguineous Maltese family revealed a single nucleotide variation truncating the DNA binding domain of KLF1 [Borg et al., 2010]. KLF1 knockdown in human erythroid progenitors derived from healthy donors demonstrated significantly increased γ-globin gene expression upon KLF1 knockdown, while overexpression of the full-length, but not the truncated KLF1 protein in human erythroid progenitors derived from the Maltese family members expressing high HbF levels resulted in considerable downregulation of γ-globin gene transcription. Chromatin immunoprecipitation studies indicated that KLF1 silencing effect is mediated by *BCL11A* gene promoter binding. These data suggest that KLF1 has a dual regulatory role on fetal-to-adult globin switching in humans, by acting on the *HBB* locus as a preferential activator of the *HBB* gene and by repressing the fetal globin gene expression, mediated by BCL11A. George Patrinos also presented recent evidence for another transcription factor putatively implicated in fetal globin gene silencing which can potentially provide the basis for the development of novel therapeutic modalities for β-thalassemia.

Epilepsy consists of a multifactorial neurological disorder with a multitude of genes identified as the underlying genetic basis of disease pathogenesis. Dr. Gianpiero Cavalleri (Dublin, Ireland) provided the results from a genome-wide analysis applying genetics to epilepsy therapeutics and predisposition that provided no clear evidence for a common genetic variation associated with the disease. However, rare genetic variation and copy number variation (CNVs) seems to contribute to the commonest forms of epilepsy, while recent experimental evidence suggests that common variation is most likely relevant to treatment-related traits.

Nowadays, direct access (DAT) or direct to consumer testing (DTC) encompasses a wide range of tests. Simple self-performed home tests (e.g., pregnancy tests) are readily available from pharmacies or online, but more recently there has been a significant growth in more complex tests that are directly available to the general public from laboratories without the intermediacy of a physician. Professor Larry J. Kricka (Philadelphia, PA, USA) gave an overview of these SNP-based genetic tests, that are available from several companies (23andMe, DeCodeMe, Navigenics, etc) and their cost has steadily fallen making them more affordable, and it is reasonably anticipated that progress with the $1000 genome will serve to further reduce test prices. This type of genetic profile test has been controversial in terms of the value of the information and has raised a number of ethical issues and also concerns, not only over the privacy and security of the information, but also, over the accuracy of the results. A concordance study of data from three DAT services and a genomics service showed a high degree of agreement but also instances of considerable disagreement. Professor Kricka stressed that the intermediacy of a physician in this process, may ensure correct interpretation of the results and necessary intervention.

The session ended with Dr. Kevin Long (Chapel Hill, NC, USA) who emphasized the need to implement pharmacogenomics in developing countries. Dr. Long presented the aims and goals of the Pharmacogenomics for Every Nation Initiative (PGENI; http://www.pgeni.org), a worldwide effort to: (a) promote the integration of genetic information into public health decision making process, (b) enhance the understanding of pharmacogenomics in the developing world, (c) provide guidelines for medication prioritization for individual countries, using pharmacogenetic information, and (d) help build local infrastructure for future pharmacogenetic research studies. PGENI is active throughout the world with 8 regional centers of excellence in the Americas (Mexico, Brazil), Europe (Greece; http://

www.goldenhelix.org), Africa (Ghana, South Africa) and Asia (Jordan, India, China). The tangible benefits from the PGENI initiative will be both in terms of surveillance, by identifying population subgroups at higher risk of toxicity or treatment failure and prioritization, and by assisting the treatment selection from among WHO recommended therapies.

This session was followed by two company lectures from Illumina (http://www.illumica.com) and Life Technologies (http://www.lifetech.com) that presented their next-generation sequencing platforms and applications.

Molecular Cytogenetics

The field of molecular cytogenetics assumes an increased importance in the field of modern genetic analysis. Dr. Nigel Carter (Hinxton, UK) gave an overview of the various applications of array-based comparative genomic hybridization (array-CGH) in deciphering the molecular basis of developmental disorders, e.g. the 9q22.3 and 17q21.3 microdeletion syndromes. He also described DECIPHER, an online resource to upload bulk amount of genomic data and to perform queries for phenotype entries and interpret CNVs. Dr Carter also noted the use of next-generation sequencing for array-CGH analysis and concluded that (a) array-CGH analysis will soon replace karyotyping, (b) high resolution array data will identify small pathogenic copy number changes, such as in exons, regulatory sequences, (c) CNV genotyping arrays will identify the role of normal variants in disease and penetrance, and (d) SNP genotyping will identify the role of segmental uniparental disomy in disease.

Molecular cytogenetics play an important role in oncology, since chromosomal aberrations are one of the hallmarks in cancer, and Dr. Bauke Ylstra (Amsterdam, the Netherlands) gave an overview of the various applications of molecular cytogenetics in oncology. He presented various examples of diagnostic applications of array-CGH to diagnose various types of cancer from many patients and from multiple lesions. Also, he presented data from a meta-analysis of 373 primary tumors indicating that these tumors cluster according to their embryonic origin, while hierarchical clustering of gastrointestinal tumors suggest that small intestinal adenocarcinomas should be treated according to the regimen used in colorectal cancer patients. The latter indicate that the use of array-CGH can also give valuable insights not only for diagnosis but also for the optimal selection of therapy.

Chromosomal aberrations are a frequent cause of genomic disorders and Professor Beverly Emanuel (Philadelphia, PA, USA) presented an informative overview of CNVs as the cause and susceptibility factor for recurrent genomic disorders. She presented cases with the 22q11.2 deletion syndrome, characterized by congenital malformations and mental retardation, and underlined sequence misalignment and recombination as the most likely mechanism to lead to this deletion. Professor Emanuel also presented evidence indicating that another mutagenic event, e.g. a *de novo* CNV (a 2nd hit) possibly occurs in the 22q11.2 deletion syndrome cases, that alters the observed phenotype and perhaps the 22q11.2 deletion represents a 1st hit that requires one or more additional “lesions” to manifest either psychopathology or a heart defect. The 2nd session ended with the lecture of Dr. Cedric Le Caignec (Nantes, France) who gave an extensive overview and numerous examples of diagnostic applications of array-CGH in detecting causative *de novo* or inherited chromosomal imbalances, and discussed the possibility an inherited imbalance with no mutations in the gene to lead to a phenotypic effect due to a deletion in a distant regulatory element [Lecointre et al. 2009]. Finally, he described families with Mesomelia-synostoses syndrome, caused by deletions of the *SULF1* and *SLCO5A1* genes, to outline that array-CGH analysis can often be the gateway to translational research projects [Isidor et al. 2010].

Next-generation sequencing applications

The 1st session of the second day, introduced by Professor Paolo Fortina (Philadelphia, PA, USA), was fully dedicated to next-generation sequencing, the latest cornerstone of the genome revolution that has emerged in the last 5 years. Professor Wilhelm Ansorge (Lausanne, Switzerland) surveyed the scope of next-generation sequencing platforms, the principles on which they are based and some applications. He also alluded to the contribution of nanotechnology in the evolution of the various platforms to increase the length and accuracy of the reads, while reducing the overall costs and analysis time, and concluded that DNA sequencing will not only be affordable but will also be incorporated in clinical applications reasonably soon. Next-generation sequencing also has various applications in the study of transcriptional regulation. Professor Frank Grosveld (Rotterdam, the Netherlands) presented several examples exploiting sequencing of RNA and of chromatin immunoprecipitated fragments to study long range interactions and transcription factor dynamics in erythroid cells [Soler et al., 2010]. He also presented a novel application of next-generation sequencing coupled to chromosome conformation capture (3C) technology to study long range interactions and chromatin structure. Finally, he presented recent findings suggesting that FOP is a regulator of γ-globin gene expression, while 5 other candidate genes hold promise for the design of novel therapeutic modalities for β-type hemoglobinopathies.

The second keynote lecture was given by Professor Lucio Luzzatto (Florence, Italy) and dealt with the rate of somatic mutations and the development of cancer. This relates to the number and kind of mutations, the mutational mechanism, the gene that is mutated and finally the genotype-phenotype correlations. Genetic instability, namely chromosomal, microsatellite or point mutation instability are also distinct causes of tumorigenesis. The *HPRT*, *TK* and *PIG-A* sentinel genes have been exploited to measure the rate of somatic mutation in tumor cells, while today the battery of genomic tools available has allowed whole-genome sequencing of tumors.

The 1,000US$ genome has been the ultimate goal of large-scale genome sequencing projects. Dr. Radoje Drmanac (Mountain View, CA, USA) discussed the use of patterned nanoarrays and DNA nanoballs as an alternative technology for DNA sequencing. This technology is highly accurate with a low error rate and affordable costs, because of the low concentration of inexpensive labeled probes [Drmanac et al., 2010; Lee et al., 2010]. Dr. Drmanac presented an example of use of this technology with the identification of loss-of-function mutations in both alleles of the ATP binding cassette transporter G5 as a putative cause of hypercholesterolemia in an 11-month old patient, which led to dietary change and cholesterol management protocols to treat the condition [Rios et al., 2010]. Ultimately, deep DNA sequencing has its place in a clinical setting and Professor Graham Taylor (Leeds, UK), President of the Human Genome Variation Society (http://www.hgvs.org), presented a workflow for the complete resequencing of *BRCA1* and *BRCA2* genes, coupled to long-range PCR. Professor Taylor also stated that in the future, there will be targeted resequencing of specific genes for hereditary cancers, cardiovascular disorders, namely 20-200 genes consisting of 250-3,000 megabases. The main application would be: (a) mutation detection, (b) gene dosage and chromosome counting, and (c) identification of somatic variation in tumors.

Data analysis, storage and reporting is also another daunting task that should be adequately addressed with the introduction of specific databases and data servers and, of course, dedicated tools should be available to make sense of the enormous amount of genomic information. Professor Christian Stoeckert (Philadelphia, PA, USA) gave an overview of the pitfalls and advances possible based on integrating functional genomics data, and the related

need for standards for biological research data quality, annotation and exchange [Shankar et al., 2010; Brinkman et al., 2010]. Also, he referred to the use of ontology in order to set the concepts within the genomics domain and establish a common vocabulary that would be understandable by humans and interpretable by a computer. Certain organizations and consortia such as the Functional Genomics Data (FGED) Society (involves leaders in databases and researchers in functional genomics), exploit input from journals and industry and facilitate the creation and use of software tools that build on these standards and allow researchers to easily annotate and share their data. In this respect, genetic variation data is also of utmost importance for the recording of human variome data and to this end a number of bioinformatics solutions have been developed to facilitate end-users. Such resources are known as gene variant or locus-specific databases. Professor Johan den Dunnen (Leiden, the Netherlands) presented the work done by his group and others to harmonize efforts to report and store gene variation data, using off-the-shelf solutions, such as the Leiden Open-access Variation Database (LOVD; http://www.lovd.nl). These efforts are supported by the European project GEN2PHEN (http://www.gen2phen.org).

This session was followed by workshop organized by Agilent Technologies (http://www.agilent.com), where solutions for next-generation sequencing and array-CGH were presented. The workshop was followed by two company lectures. Agilent Technologies presented solutions for target enrichment for next-generation sequencing applications and SNP microarrays and Affymetrix (http://www.affymetrix.com) presented tools for predicting drug response and to determine unique molecular signatures in tissues.

Current genetic technology in diagnostics and therapy

DNA denaturation (melting) has been used for many years to study DNA structure and composition. Recent technological improvements resulted in new instrumentation to perform so called high-resolution melting curve analysis (HRMA). Professor Johan den Dunnen (Leiden, the Netherlands) presented the principle of this technology that provides an alternative to agarose gel-electrophoresis, and gave examples of its use, such as mutation screening and SNP-typing, methylation analysis, quantification (CNV and mosaicism) and clone characterization. Sensitivity and specificity were significantly improved using newly developed saturating DNA dyes, improved temperature precision and increased measurements per time and temperature unit. Based on its combined characteristics such as ease of use, simplicity, flexibility, low cost, non-destructive nature, superb sensitivity and specificity, HRMA is quickly becoming the tool of choice to screen patients for pathogenic variants. HRMA is a multi-purpose technology that is becoming a standard tool for any laboratory studying nucleic acids. Another important method that is gaining momentum in clinical laboratories is pyrosequencing that can be employed to identify point mutations and hypermethylation in tumor specimens for diagnostic, prognostic, and therapeutic decision making. Dr. Athanasios Tsiatis (Philadelphia, PA, USA) presented results from KRAS mutational testing as a paradigm to demonstrate the utility of pyrosequencing technology, as means to predict resistance to anti-epidermal growth factor receptor therapy [Tsiatis et al., 2010]. Dr. Tsiatis also showed that tumor heterogeneity can lead to differences in mutant percentages within a resection specimen and hence caution should be exercised in attempting to correlate the percentage mutant detected with the actual percentage of tumor seen histologically. Tumor heterogeneity can also result in a relatively low percentage of mutated alleles, thus the limit of detection of the platform is important. The possibility of intratumoral heterogeneity should also be considered when attempting to use this platform for quantitative purposes in the setting of cancer diagnostics.

Proteomics, like genomics, have an equally important role in the “omics” era. Professor Thomas Joos (Tubingen, Germany) gave an overview of the use of proteomics, particularly

multiplexed sandwich immunoassays and mass spectrometry in establishing disease-specific and/or differential diagnosis biomarkers, such as in the case of schizophrenia and bipolar disorder. He also pointed out that a limiting factor in biomarker discovery in proteomics is often the lack of highly specific antibodies, which was paralleled to finding a needle in a haystack. The session ended with Professor Aglaia Athanassiadou (Patras, Greece) who demonstrated the use of episomal vectors as a vehicle for gene therapy. She presented her group's findings to develop an episomal vector for efficient delivery of a synthetic peptide in human erythroid progenitor cells that led to increased fetal hemoglobin levels in K562 cells, in cells bearing a β-globin locus YAC transgene, and in human erythroid progenitor cells. These data provide a good basis for the development of episomal vectors for β-thalassemia therapeutics.

Translating genetic analysis into clinical practice

The last session of the symposium, introduced by Professor Federico Innocenti (Chicago, IL, USA), was dedicated to translation of genomic technology into clinical practice. Pharmacogenomics deals with the influence of genetic variation on drug response in patients by correlating gene expression or single nucleotide polymorphisms (SNPs) with a drug's efficacy or toxicity. Professor Ron van Schaik (Rotterdam, the Netherlands) gave an overview of the current knowledge from the implementation of pharmacogenomics in clinical diagnostics and presented examples from the use of *TPMT* testing for 6-mercaptopurine (6-MP) treatment and *UGT1A1* testing for irinotecan therapy. Also, *CYP2D6* is another important gene that should be analyzed prior to prescribing imipramine as antidepressant and tamoxifen for breast cancer patients. In the Netherlands, a 2-platform approach has been used in the last 5 years for DNA isolation and analysis for pharmacogenetic tests and the results are reported within a week. Clopidogrel, the 2nd most widely prescribed drug in the world, is another success story in pharmacogenomics. Dr. Sandra Kirkwood (Indianapolis, IN, USA) showed that *CYP2C19* genotype can predict hazardous cardiovascular events in carriers of the *CYP2C19**2 allele, leading to a change of the drug label in Europe in September 2009 and in the United States in March 2010. Although *CYP2B6*, *CYP3A4*, *ABCB1* and *CYP2C9* are other potentially predictive genetic factors that can be exploited for clopidogrel therapy, it is consistent across the studies that *CYP2C19* is the best predictor explaining as much as the other known measured factors combined.

The recently described DNA replication-based mechanism of fork stalling and template switching/microhomology-mediated break-induced replication (FoSTeS/MMBIR) was previously shown to catalyze complex exonic, genic and genomic rearrangements. George Koumbaris (Nicosia, Cyprus) showed that FoSTeS/MMBIR can generate large-scale gross chromosomal rearrangements leading to the deletion and duplication of entire chromosome arms, thus suggesting an important role for DNA replication–based mechanisms both in the development genomic disorders and cancer. Furthermore, it has been demonstrated that most cytogenetically dicentric i(Xq) chromosomes are generated by non-allelic homologous recombination (NAHR) between palindromic low copy repeats (LCRs) and highly homologous palindromic LINE elements, while nonrecurrent-breakpoint i(Xq) have microhomology-associated breakpoint junctions and are probably catalyzed by FoSTeS/MMBIR.

These lectures were followed by a company lecture from Oxford Gene Technology (http://www.ogt.co.uk) on the available solutions for array-CGH.

Immunogenetics refers to the genetics of the immune response, namely the structure, function, sequence variation and clinical relevance of the immune response genes. Professor

Joannis Mytilineos (Ulm, Germany) stressed that certain genetic factors influence the development of immune response, such as MHC molecules (HLA), cytokine/chemokine polymorphisms and NK-KIR receptor genes. There are several methods for HLA typing, such as serological, cellular, biochemical and molecular, the latter served by a variety of low- and medium-throughput approaches. Professor Mytilineos presented the application of Luminex and fully automated DNA sequencing approaches for HLA typing. He showed that mutations in IL10 and TGF-β1 cytokine genes promoter, by altering specific transcription factor recognition sites, consequently affect transcriptional activation and cytokine production. Hereditary hearing loss has a complex genetic etiology and can be used as a paradigm for the use of prognostic markers for complex disorders. Professor Michael Petersen (Athens, Greece) explained that there are 121 genetic loci, namely 49 autosomal dominant, 66 autosomal recessive, 5 X-linked and 1 Y-linked, associated with non-syndromic hereditary hearing loss [Petersen and Willems, 2006] and presented the experience from the genetic screening for non-syndromic deafness in Greece. He concluded that although until recently genetics of deafness was thought to be a highly complex problem due to the extreme genetic heterogeneity, this complexity has now been greatly reduced since the description of a very common form of genetic hearing loss (*GJB2*), hence allowing population carrier screening, introduction of DNA testing as part of newborn hearing screening, family carrier detection and prenatal diagnosis. In particular, classical prenatal diagnosis, together with pre-implantation genetic diagnosis and non-invasive prenatal diagnosis are some of the most significant applications of translational medicine involving genetic analysis and represent valuable reproductive options for couples at risk of having a child affected with a severe inherited disorder. The hemoglobinopathies represent one of the best examples of the importance of prenatal diagnosis for combating severe inherited disease [Harteveld et al., 2009] and Dr. Jan Traeger-Synodinos (Athens, Greece) presented an excellent summary of these approaches, the new DNA sources and application of novel technologies for DNA testing, as well as the limitations and the inherent pitfalls of these methods [Harton et al., 2011].

Finally, two posters were selected for oral presentation and Dr. Mike Makrigiorgos (Cambridge, MA, USA) and Dr. Marianna Bei (Charlestown, MA, USA) gave an outline of their studies on the use of cold PCR to enrich variant DNA sequences in cancer and on the molecular genetics of epithelial appendages, respectively.

Conclusions

Overall, the 2010 GOLDEN HELIX Symposium highlighted various areas of interest in genetic analysis and genomics and their integration into clinical practice. Many internationally renowned scientists gave excellent overviews of the existing applications of genomic technologies and demonstrated the way and the rapid pace that the field is moving. Also all the key biotechnology companies with genomics products have sponsored this symposium and gave outstanding presentations of their platforms.

Once again, the 2010 GOLDEN HELIX Symposium has achieved its goal to gather some of the world's leading scientists from all these different disciplines who communicated their recent results to a multinational group of participants, from post-graduate students to senior academics and researchers, allowing for cross-fertilization of ideas. This has allowed several new collaborations to flourish and also laid the foundations for the next multidisciplinary GOLDEN HELIX Symposium, scheduled for 2012 in Europe.

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