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Chapter 15

The Genomic Medicine Alliance: A global effort to facilitate the introduction of genomics into healthcare in developing nations

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Abstract

The primary goal of genomic medicine is to make use of and examine thean individual's genomic information to support the clinical decision-making process. At present, several international organizations and research consortia exist, which aim to support the translation of genomic research into clinical practice so that genomic medicine can ultimately be used to benefit the global community. The Genomic Medicine Alliance [http://www.genomicmedicinealliance.org] is a global academic research network that seeks to establish and strengthen collaborative ties between different genomic medicine stakeholders. Its focus lies firmly with the translation of scientific research findings into clinical practice. To this end, it brings together experts from various disciplines including genome informatics, pharmacogenomics, public health genomics, as well as experts on ethical, legal and social issues in the sphere of genomics/health economics. These multidisciplinary activities are supervised by a 15-member International Scientific Advisory Committee. Its official journal, Public Health Genomics, offers members a highly respected publication forum for reviews, original research findings and policy in this field. In the short-to-medium term, the Genomic Medicine Alliance aims to promote research collaborations between developed and developing countries and to organize educational activities in the field of genomic medicine. In the longer term, it aspires to become a focal point for global collaboration in the field of genomic medicine while helping to pave the way for a smoother transition from genomics research to genomic medicine.

Key words: Genomic Medicine, pharmacogenomics, Ethics in Genomics (genethics), whole genome sequencing, genome informatics, public health genomics, economic evaluation in genomic medicine, genome literacy, genetics education

Introduction

Genomic medicine aims to utilize the individual's genomic information to support the clinical decision-making process [Manolio et al., 2015]. In recent years, significant advances have been made to-in understanding the molecular basis of a wide range of human inherited diseases and cancers with the potential to improve disease prognosis and treatment [Kilpinen and Barrett, 2013]. At the same time, genomic technology has progressed rapidly, with a variety of new high-throughput genome-wide screening and massively parallel sequencing approaches becoming available [Gullapalli et al., 2012]. As a result, genomic information is becoming more readily available with the potential to play a role in diagnosis, disease risk-stratification, medication selection and dosing, carrier screening and other emerging uses. This constitutes the basis of Genomic Medicine, a relatively new discipline that aims to enhance opportunities for disease prevention; and the customization of patient care, including the personalization of conventional and new therapeutic interventions [Lazaridis et al., 2014].

Genomic Medicine is closely linked to the concept of or Personalized Medicine, which refers to the aim to tailor diagnosis and treatment more closely to the individual characteristics of patients [European Science Foundation, 2012]. Although personalized medicine as a concept has gained particular currency within the last two decades, its central concept was proposed around 400 B.C.; Hippocrates of Kos (460–370 B.C.) stated that "... it is more important to know what kind of person suffers from a disease than to know the disease a person suffers". The first application of "Genomic Medicine" can be said to have been codified in the Talmud (Yevamot 64b), where it is stated [Rabbi Judah the Prince's ruling (2nd century B.C.)] that if a woman's first two children had died from blood loss after circumcision, the third son should be exempted from circumcision. Rabbi Simeon ben Gamliel disagreed and ruled that the third son might be circumcised, but if this infant also died then the fourth child should not be circumcised. These ancient examples could be seen to encapsulate the essence of personalized medicine

where people's personal circumstances and characteristics mean that not everybody is treated the same. Today, genomics yields important information for personalization. For this reason, several international organizations and research consortia have been formed with the stated goal of supporting the translation of genomic research into clinical practice so that genomic medicine can ultimately be used to benefit the global community.

The Genomic Medicine Alliance [GMA; www.genomicmedicinealliance.org; Cooper et al, 2014] is a newly established global academic research network, which aims to build and strengthen collaborative ties between academics, researchers, regulators and those members of the general public interested in genomic medicine, focusing in particular on developing countries and low-resource environments.

Aims and goals of the Genomic Medicine Alliance

The GMA aims to: (a) Encourage and catalyze multidisciplinary collaborative research between partner institutions and scientists, with an emphasis on developing countries; (b) Liaise between research organizations, clinical entities and regulatory agencies on topics related to genomic medicine; (c) Facilitate the introduction of pharmacogenomics and advanced 'omics technologies into mainstream clinical practice; (d) Propose international guidelines and draw up recommendations for activities pertaining to genomic medicine, in close collaboration with other scientific academic entities, agencies and regulatory bodies; and (e) Develop independently and coordinate, in close collaboration with partner institutions, educational activities in the area-sphere of genomic medicine.

The GMA aims to foster collaboration in genomics research between developed and developing/low resourced countries, seeking to ensure that such collaboration is beneficial to all parties concerned. Developing countries will should benefit from training opportunities, knowledge exchange, and expanding transnational networks whereas developed countries

could expect to benefit through comparative work on ethnically diverse populations that have not yet been well studied eurrently characterized, and by having access to families with rare diseases or unique clinical features, especially where the developing countries are characterized by a higher incidence of consanguinity and/or well-defined founder populations (see also below). This includes patients coming from ethnic communities within developed countries that are characterized by a high rate of consanguineous marriages. Considering that approximately 85% of the world's population live in developing countries, this represents a major challenge to access and engage a hitherto neglected group of individuals with rare diseases [Cooper et al., 2014]. Rare diseases are not only important in terms of improving our understanding of the pathology to benefit the affected patients and their families, but they have the potential to provide key insights that can lead to a better understanding of gene function in both health and disease [Collins, 2011].

A key aim of GMA is paving the way from genomics research to Genomic Medicine, by encouraging and undertaking multicenter research projects in key sub-disciplines. To this end, GMA activities aim to contribute to the transition from genomics and pharmacogenomics research to Genomic Medicine, viz. Public Health Genomics, Ethics in Genomics (or 'genethics'), Genome Informatics, the genetics education of healthcare professionals, the genetics awareness of the general public and health economic evaluation in relation to genomic medicine. This has been previously represented pictorially as an ancient Greek temple, where genomics and pharmacogenomics research represents the bedrock of genomic medicine, and where the various subdisciplines are held above the supporting pillars that must be carefully erected for the superstructure of Genomic Medicine to hold (Fig. 15.1). At present, although the foundations of genomic medicine are becoming stronger and being ascribed ever-increasing hopes and expectations, the pillars themselves are still largely under construction.

<Insert Figure 15.1 near here>

GMA research activities are supervised by an International Scientific Advisory Committee comprising 16 internationally renowned scientists in the field from all over the world (**Table 15.1**). Administrative assistance is provided by the Golden Helix Foundation (www.goldenhelix.org) staff. Registration with the GMA is free-of-charge in order to encourage the participation of researchers from developing/low income countries and emerging economies. Upon registration, members specify their research interests so that they can be directed to research projects and training opportunities that suit their specific needs.

<Insert Table 15.1 near here>

The GMA has recently established the concept of 'GMA Ambassadors' within the network, aiming to actively engage dynamic, mostly early-career but also senior scientists with a keen interest in Genomic Medicine, who are interested in expanding the GMA network in their own territory. In particular, the role of GMA Ambassadors is—will be to (a) increase awareness of GMA activities and events among their peers and colleagues, (b) attract new members to the GMA through social media and other means, (c) contribute and/or comment on articles posted on the GMA portal, pertaining to their area of expertise and territories, and (d) represent the GMA, if required, at scientific events and conferences that the GMA Ambassadors attend.

GMA research activities span eight different Working Groups: Genome Informatics, Pharmacogenomics, Cancer Genomics, Public Health Genomics, Genethics and Economic Evaluation in Genomic Medicine. Each of the Working Groups' activities are coordinated by the corresponding Working Group and Activity leaders in conjunction with Senior National Representatives from each of the >70 countries from which the >1200 current GMA members (January 2017) originate. Some of the key GMA research projects are outlined below.

Current research projects among GMA members

Pharmacogenomics Working Group

Pharmacogenomics aims to rationalize drug treatment by optimizing the balance between treatment efficacy and toxicity based on a comprehensive understanding of the impact of genomic variants on drug metabolism combined with other patient-based and environmental factors. The GMA Pharmacogenomics Working Group, in close collaboration with the Golden Helix Foundation. is currently taking part in the Euro-PGx project [http://www.goldenhelix.org/index.php/research/pharmacogenomics-in-europe], in which 26 European populations are participating. More specifically, the Euro-PGx project aims to (a) determine the population-specific allele frequencies of pharmacogenomics variants to optimise medication choice and dose and minimize adverse reactions by genotyping pharmacogenomically-relevant genetic variants in 231 absorption, distribution, metabolism and excretion-toxicity (ADMET)-related pharmacogenes, which would assist in prioritizing medication selection in participating developing countries and, (b) develop off-the-shelf solutions for pharmacogenomic testing in participating developing countries. There are significant inter-population pharmacogenomic allele frequency differences, particularly in seven clinically actionable pharmacogenes in seven European populations that affect drug efficacy and/or toxicity of 51 medication treatment modalities. This includes differences observed in the prevalence of high-risk genotypes in these populations in the CYP2D6, CYP2C9, CYP2C19, CYP3A5, VKORC1, SLCO1B1 and TPMT pharmacogenes, resulting in notable differences in drug response, such as the genotype-based warfarin dosing within between these populations [Mizzi et al., 2016]. These findings can be used not only to develop guidelines for medication prioritization, but most importantly to facilitate the integration of pharmacogenomics and to support pre-emptive pharmacogenomic testing. Replication of these

findings in larger population samples would <u>permit the</u> establish<u>ment of</u> a rational framework for pharmacogenomic testing in developing countries <u>that to</u> supports the incorporation of country-specific population characteristics in a standardized fashion.

At the same time, the GMA Pharmacogenomics Working Group has sought to provide proof-of-principle of the use of whole-genome sequencing for pharmacogenomic testing, by resequencing with high coverage almost 500 whole genomes, mostly from Caucasian populations. This project not only revealed a vast number of novel potentially functional variants in a total of 231 pharmacogenes, as indicated by *in silico* analysis, but has also demonstrated the value of whole-genome sequencing for pharmacogenomic testing by capturing over 18,000 variants in these pharmacogenes, in contrast to just over 250 variants that would have been identified in these genes using the most comprehensive pharmacogenomics assay currently available [Mizzi et al., 2014].

Genome Informatics Working Group

Documentation of the incidence of genetic disorders in different populations, particularly in those developing countries with a high incidence of genetic diseases and/or consanguinity can be particularly helpful in the context of adopting national prevention and screening programs [Patrinos, 2006]. GMA members have actively participated in the development of new or the update of existing National/Ethnic Genetic databases for several populations in GMA member territories, such as Greece, Serbia, Kuwait, Egypt and Tunisia, using the newly upgraded ETHNOS software [Viennas et al., 2017].

The result is that the ETHNOS software supports, in its present format, the development of National Genetic databases [Papadopoulos et al., 2014], based on the data warehouse principle and pre-existing guidelines [Patrinos et al., 2011]. These databases will be assigned to senior human geneticists in the corresponding populations in order to coordinate their curation and stimulate data enrichment and expansion.

Cancer Genomics Working Group

Identification of genomic variants and structural alterations that guide therapy selection for patients with cancer has nowadays become routine in many clinical centres. The majority of genomic assays used for solid tumour profiling <u>use-employ</u> next-generation resequencing to interrogate mostly somatic but also germline variants because they can be <u>relatively more</u> easilyer identified and interpreted.

Owing to the rapid evolution of next generation sequencing, the past decade has seen the characterization of mucleic acidboth somatic and/or germline alterations in a wide range of cancers generating a large body of information pertaining to how cancer develops, evolves, and reacts to various treatment modalities [Macintyre et al., 2016]. Also, a considerable number of genomic variants have been previously been reported to be causative of, or associated with, tumor progression or an increased risk for various types of cancer [Hanahan and Weinberg, 2011]. The GMA Cancer Genomics Working Group aims to define some of the key tools for genomic testing that primary care practitioners and specialists should know about when considering how to treat cancer patients.

At the same time, members of the GMA Cancer Genomics Working Group have undertaken a study to identify cancer predisposition (germline) variants in apparently healthy individuals with no cancer history in the family using a next-generation sequencing strategy. Such an approach aimed to identify genomic, particularly novel, variants that might predispose to various types of cancer so that such information could help in the assessment of personalized cancer-susceptibility risk from genome sequence data [Karageorgos et al., 2015]. This includes both genomic variants in genes (like e.g. *BRCA1/2* genes) that are have previously been associated with heritable risk conditions, and also risk alleles that are known to increase cancer

predisposition risk, but not in a Mendelian sense. Indeed, a small fraction (3%) of a large number of variants (571 variants in total) previously associated with cancer predisposition has been shown to be potentially pathogenic in the members of two families. This approach could be adopted for other types of complex genetic disorder in order to identify variants of potential pathological significance.

Public Health Genomics Working Group

Public Health Genomics represents the responsible and effective translation of genomebased knowledge and technologies into public policy and health services for the benefit of population health [Burke et al., 2006]. The GMA Public Health Genomics Working Group is undertaking national and transnational studies to improve our understanding of the level of public awareness of genetics, including their attitudes to genomic testing and the level of genetics education of healthcare professionals (i.e. physicians, pharmacists, etc). So far, such surveys have yielded some very interesting findings [Mai et al., 2014] highlighting the relative lack of genetics education of healthcare professionals and genetic awareness and literacy of the general public as perhaps some of the biggest obstacles to the widespread implementation of Genomic Medicine [Kampourakis et al., 2014]. A detailed stakeholder analysis which aimed to comprehend the attitudes and map the genomic medicine policy environment was undertaken, serving as a database for assessments of the policy's content, the major players, their power and policy positions. their interests and networks and coalitions that interconnect them [Mitropoulou et al., 2014]. These findings should contribute to the selection implementation of policy measures that will expedite the adoption of genomics into conventional medical interventions; such studies are currently being replicated in other countries, under the umbrella of the GMA.

These studies have also shown the general utility of genomic testing for individuals including the public's remarkable level of interest in participating in genomic research [Reydon et al., 2012; Demmer and Waggoner, 2014]. Such surveys have already been replicated in other European countries [Pisanu et al., 2014; submitted] and are currently being conducted in Southeast Asia and the Middle East, partly supported by the Golden Helix Foundation, thereby confirming initial findings and highlighting the need to harmonize genomics education and to raise genomics awareness among the general public. To this end, GMA members co-organize educational events revolving around pharmacogenomics and genomic medicine in various European countries; these are endorsed by the GMA and partly funded by the Golden Helix Foundation and other entities [Squassina et al., 2012].

Genethics Working Group

Several ethical issues confront those who are committed to the practice of Genomic Medicine, including the regulation of genetic testing, the governance of genetic research, and genomic data sharing in an ethical and publicly accountable way [Kampourakis et al., 2014]. The GMA Genethics Working group also explores the landscape of direct-to-consumer (DTC), beyond the clinic [Prainsack and Vayena, 2013] and over-the-counter (OTC) genetic tests in various European countries, including Greece, Slovenia, Italy and Serbia. From these undertakings, it is particularly important to harmonize policies that safeguard the general public and ensure that they become better informed with respect to the various attendant risks from this type of testing. Currently, regulation of these issues is lacking in many European countries, as well as at a central level in the form of a directive of the European Medicines Agency for both OTC and DTC genetic testing [Kricka et al., 2011]. The GMA has recently produced an opinion article to highlight the various types of OTC genetic tests currently available [Patrinos et al., 2013]. GMA members are also working in close cooperation with the National Genetic

Societies and National Ethics Committees to establish guidelines to cover ethical, legal and social issues pertaining to genetic testing.

Furthermore, in an effort to resolve the ambiguity regarding the utility of nutrigenomics testing given our current level of knowledge, the GMA Public Health Genomics Working Group has encouraged the meta-analysis of a number of studies related to 38 genes included in nutrigenomics tests provided by various private genetic testing laboratories, aiming to identify possible associations between the genes of interest and dietary intake and/or nutrient-related pathologies. No specific and statistically significant association was observed for any of the 38 genes, while in those cases where a weak association was demonstrated, evidence was based on a limited number of studies [Pavlidis et al., 2015]. This study has demonstrated that although nutrigenomics research is a promising area for genomic investigation, solid scientific evidence is currently lacking, and as such commercially available nutrigenomics tests cannot be recommended. This is consistent with the 2014 position statement from the Academy of Nutrition and Dietetics, indicating that "It is the position of the Academy of Nutrition and Dietetics that nutritional genomics provides insight into how diet and genotype interactions affect phenotype" [Camp and Trujillo, 2014]. On the contrary, it has been suggested that assessment and synthesis of nutrigenomics data should be carried out on an ongoing basis at periodic intervals and/or when there is a specific demand for a synthesis of the available evidence, and importantly, in ways that are transparent where potential conflict of interests are fully disclosed by the parties involved [Pavlidis et al., 2016].

Economic Evaluation in Genomic Medicine Working Group

A key factor in expediting the adoption of Genomic Medicine in clinical practice would be the demonstration of its cost-effectiveness (as the "fourth hurdle" in healthcare, after safety, efficacy and quality). The real cost-effectiveness of involving genomics in medicine is as yet unknown apart from some rather limited studies in pharmacogenomics and hereditary cancer

syndromes. Although it is vital to perform cost-effectiveness analyses for the implementation of genomic medicine in developing countries, there are only a handful of such studies reported in the literature [Snyder et al., 2014]. Realizing cost-effectiveness would be a crucial step towards convincing policy makers of the utility of genomics in healthcare as a means to reduce the overall treatment costs, as well as to reduce the overall burden and minimize consequences of disease at the national level [Payne and Shabaruddin, 2010]. Currently, the GMA Economic Evaluation in Genomic Medicine Working Group has been successfully engaged in assessing the cost-effectiveness of genome-guided treatment modalities in developing countries. In particular, GMA members have participated in a prospective study to assess the costeffectiveness of genome-guided warfarin treatment in Croatia, where it has been shown that genome-guided warfarin treatment may represent a cost-effective therapy option for the management of elderly patients with atrial fibrillation who developed ischemic stroke in Croatia, with an estimated incremental cost-effectiveness ratio of the pharmacogenomicsguided versus the control groups of €31,225/QALY -[Mitropoulou et al., 2015]. Also, a retrospective economic analysis for of genome-guided clopidogrel treatment in Serbia indicated that pharmacogenomics-guided clopidogrel treatment may represent a cost-saving approach for the management of myocardial infarction patients undergoing primary percutaneous coronary intervention in Serbia, saving €13 per person on average [GEORGE: per day, per annum? per treatment], deducted from a break-even point analysis [Mitropoulou et al., 2016].

Members of the GMA Economic Evaluation in Genomic Medicine Working Group have developed and evaluated standardized methodologies for the economic evaluation of genomic medicine [Fragoulakis et al., 2016; 2017], which, in addition to the already existing battery of economic evaluation models in genomic medicine [Annemans et al., 2013], will be of the utmost importance as innovative tools for performing cost-effectiveness analyses in such a rapidly evolving discipline. To this end, the GMA has also endorsed the production of a

related textbook, co-authored by two GMA Scientific Advisory Committee members, published by Elsevier/Academic Press in early 2015 [Fragoulakis et al., 2015].

Lastly, the issue of pricing and reimbursement was the topic for the GMA Economic Evaluation in Genomic Medicine Working Group, given the lack of harmonization between pricing and reimbursement policies between European countries, contrary to the situation pertaining in the United States [Logue, 2003].

As a first step, the general strategy towards pricing and reimbursement for genomic medicine in Europe has been outlined, providing an overview of the rationale and basic principles guiding the governance of genomic testing services, clarifying their objectives, and allocating and defining responsibilities among stakeholders, focusing on different EU countries' healthcare systems. Particular attention was paid to issues pertaining to pricing and reimbursement policies, the availability of essential genomic tests, differing between various countries owing to differences in disease prevalence and public health relevance, the prescribing and use of genomic testing services according to existing or new guidelines, budgetary and fiscal control, the balance between price and access to innovative testing, monitoring and evaluation for cost-effectiveness and safety, and the development of research capacity [Vozikis et al., 2016].

Subsequently, it is hoped that a more technical analysis would lead to a robust policy in relation to pricing and reimbursement in genomic medicine, thereby contributing to an effective and sustainable health-care system that will prove beneficial to the economy at large.

Establishment of the DRIFT Consortium

Consistent with one of the stated goals of the GMA, which is the fruitful engagement between research groups from developing and developed countries to study families with rare diseases or unique clinical features (especially countries with a higher incidence of consanguinity and/or well-defined founder populations), the GMA participated in the

establishment of the DRIFT (Discovery Research Investigating Founder Population Traits)

Consortium.

In early 2016, a call for research collaboration was made by the Regeneron Genetics Center (RGC) and the GMA, aimed specifically at developing countries. DRIFT -aims to understand the genetic architecture of founder populations throughout the world with direct impact on human health and disease. The DRIFT Consortium aims to catalogue population-specific allelic architecture, to understanding the biological and functional consequences of specific genomic variants identified, and to share and establish best-practice approaches to relieve disease burden in these populations. DRIFT is planning two tiers of collaboration models:

- a. Tier 1 aims to canvas the allelic architecture of the population by exome sequencing and DNA microarrays from relatively unrelated individuals. Several hundred de-identified samples will be analyzed at the RGC that will provide high-depth exome sequence and genome-wide association data, derived from DNA microarrays, to be returned to the collaborator <u>free of charge</u>. There would be no need to exchange phenotype information and if the joint sequence data were used for any genotype-phenotype analyses, the results would be shared with RGC. Most importantly, the collaborator is free to publish results derived from this effort.
- phenotypes of mutual interest. In this tier, an academic collaboration model is established, where the collaborator and the RGC jointly develop the research plan. In this tier, a much larger number of DNA samples (100s to 10,000s) is provided by the collaborator and again, like Tier 1, RGC provides all exome sequence data to the collaborator free of charge. Deidentified phenotype data will be shared, data analyses of the combined sequence and phenotype data set are performed collaboratively and each party is free to use the data set

for its own internal research. Again, collaborators are encouraged to publish results and each party is free to use published results for any and all purposes.

A short form material transfer agreement is used to govern the collaboration in both Tiers. For both models, data and results will be broadly shared with the research community and if exciting new results are generated from a Tier 1 or Tier 2 collaboration, there will be the potential for the design and funding of follow-up "genotype-first call-back" studies for additional collaborative research to delve more deeply into biological mechanisms and pathways. Such an approach is expected to attract institutions and research groups from developing countries in Europe, Latin America and the Middle East, which have founder populations bearing some very important features readily available for analysis.

Conclusions and future perspectives

The GMA is a new initiative in the field of Genomic Medicine, with the primary goal to develop a network focusing on the translation of genomic knowledge into clinical use, with a special focus on the participation of developing countries and of low-resource settings.

The GMA has several unique features as a research network, in which it differs from existing consortia and initiatives in this field [Manolio et al., 2015]. First, membership is free of charge, which is particularly usefulimportant to attract members from low-resource environments. Second, it has a flat governance structure, consisting of comprising the Scientific Advisory and the Steering Committees. Third, this network has a stated goal and commitment to bring together genomics research institutions from developing countries with those from developed countries [Cooper et al., 2014].

Ever since its establishment, the expansion of the GMA membership base has progressed at a very rapid pace, currently consisting of over 1,300 members from >70 countries

worldwide, from academia as well as from corporate and regulatory sectors, including developing countries in the Middle East, Asia and Latin America.

In 2014, an important milestone for GMA was the agreement with Karger to establish the international peer-reviewed journal, *Public Health Genomics* (http://www.karger.com/Journal/Home/224224), as the Official GMA journal [Patrinos and Brand, 2014]. *Public Health Genomics* is the leading bimonthly international journal, published by Karger (Editor-*In*-Chief: Prof. Angela Brand) and focusing on the translation of genome-based knowledge and technologies into public health, health policies and healthcare as a whole. This partnership not only provides GMA members with a highly respected forum to publish their original research findings but also with discounts on the journal's annual subscription, Open Access fees and Karger books.

In addition, and in order to support the trans-national mobility of students and junior researchers, the GMA plans to launch short- and long-term research fellowships for early-stage researchers from developing countries to pursue research in Centers of Excellence in developed countries. The GMA envisages doing this in collaboration with the Golden Helix Foundation and other charities. Last but not least, the GMA will continue to endorse conferences and educational activities in the field of Genomic Medicine in Europe, the Middle East, Latin America and Southeast Asia. Indeed, since 2014, the GMA has established, in conjunction with Golden the Helix Foundation, the Golden Helix Summer Schools (http://summerschools.goldenhelix.org; see also next Chapter). This international initiative in the field of Genomic Medicine and Genome informatics aims to provide researchers around the world with the opportunity to expand their knowledge in these rapidly evolving disciplines.

In essence, the GMA aspires to become a focal point for harmonizing research activities in the field of genomic medicine between developed and developing countries while helping to pave the way for a smoother transition from genomics research to genomic medicine.

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Figure 15.1

Graphical depiction of the GMA research activities that aim to translate Genomics Research and Pharmacogenomics into Genomic Medicine (see text for details). Research disciplines are listed in alphabetical order and (this order does not imply any prioritization of research activity).

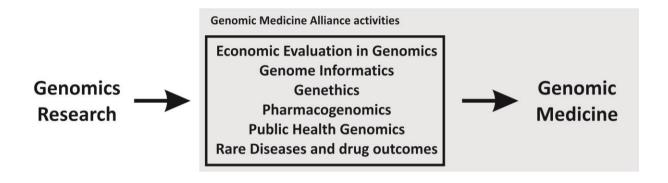


Table 15.1.

Members of the GMA International Scientific Advisory Committee (in alphabetical order per by continent).

Continent	No	Member	Country
Asia/Middle East	1	Fahd Al-Mulla	Kuwait
	2	Ming Ta Michael Lee	Japan
Americas	3	Paolo Fortina	USA
	4	Federico Innocenti	USA
	5	Marc S. Williams	USA
Europe	6	Angela Brand	The Netherlands
	7	David N. Cooper	<u>United</u>
			Kingdom Ireland
	8	Vita Dolzan	Slovenia
	9	Milan Macek Jr	Czech Republic
	10	George P. Patrinos	Greece
	11	Barbara Prainsack	United Kingdom
	12	Ron H. van Schaik	The Netherlands
	13	Alessio Squassina	Italy
	14	Domenica Taruscio	Italy
	15	Effy Vayena	Switzerland
	16	Athanassios Vozikis	Greece
	17	Bauke Ylstra	The Netherlands