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Article

Pulling the Strands Together: MEGA Steps to Drive European Genomics and Personalised Medicine

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Abstract
The increasing understanding of the genome is recognised as being one of the main determinants of future improvement in healthcare. The availability of genetic data from a large number of individuals increases the ability to investigate questions across many rare and common diseases and in different populations, and also provides more information for understanding clinical care outcomes for an individual. A number of large scale genome sequencing initiatives have been launched in the last few years to try and capitalise on this potential. Within Europe, the UK has led the way with the 100,000 Genomes Project. This project looks at the genome sequences of patients with rare diseases or cancer. More recently France announced plans to invest EUR 670 million in a genomics and personalised medicine programme. In the US, the Precision Medicine Initiative aims at large-scale research by gathering one million or more volunteers to extend precision medicine to all diseases. Meanwhile, China has announced plans to invest nearly USD 10 billion in its own precision medicine initiative. These projects demonstrate the commitment at a national level and raise the question "What benefits would be realised by undertaking a million genome initiative in a coordinated effort across European countries?" A coordinated, pan-European MEGA project would garner crucial genetic information that could have an immeasurable benefit when it comes to the health of current and future EU citizens.

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Maximising Genomics

Seeking the key to concrete action to channel Europe's wealth of expertise in genomics is long overdue. Europe not only has formidable potential, but has already yielded world-beating insights in the short history of the science.

But the expertise is widely scattered, Europe's actions in the field are frequently uncoordinated and even disjointed. And the infrastructure necessary for full development of the potential is conspicuously patchy. For all the brilliance of its researchers, the enterprise of its companies, and the foresight of its authorities, perceptions and understanding of this treasure-house of opportunity vary widely, and Europe displays only the most tenuous shared purpose as to how to maximise its undoubted strengths in contributing to the health of Europeans and of their health systems [1].

Genomics is increasingly ready to be used to improve health and it can provide a treasure-house of opportunity. It is now beginning to move on from specialist areas such as diagnosis of rare diseases and the selection of appropriate cancer therapies, towards the fuller integration of genomics across healthcare systems that will permit wide use of personalised medicine to improve health care and reduce costs [2].

Improved Health Outcomes

Genomics has transformed diagnosis, treatment and management of Bardet-Biedl syndrome, a rare ciliopathic human genetic disorder leading to renal disease, obesity and diabetes. Until recently, its rarity meant a long journey to diagnosis and fragmented and costly care. But UK health service collaboration with patient supporters and research groups created a next-generation genetic testing service that has proved so successful the model is being replicated across the spectrum of ciliopathies.

Whole genome sequencing has allowed clinicians to rapidly identify Brown-Vialetto-Van Laere syndrome, a rare degenerative disorder that leads to progressive sensorineural deafness. Diagnosis is difficult – misdiagnosis can often lead to multiple ineffective treatments and unnecessary surgery without delivering patient benefit. But now it is possible to treat the disease simply – and cheaply – with vitamin B_2.

Genomics is allowing clinicians to prevent – or identify and treat – serious adverse drug reactions to medicines such a warfarin and carbamazepine. Ensuring that the right drugs are targeted to the right patients is eliminating unintended patient harm and life-threatening emergency medical admissions.

Using genomics, clinicians are now able to far more accurately assess each individual's personal risk of breast cancer, reducing the need for regular imaging and sometimes invasive procedures that deliver imperfect results. This allows a move away from a reactive approach to long-term management plans that combine targeted screening and non-invasive options such as tamoxifen to prevent breast cancer developing.

Genomics is aiding understanding of genetic change in tumours, and new, highly personalised and effective medications are now being used that target the genetically different subtypes of lung cancer.

Prostate cancer researchers are discovering genetic hallmarks that allow them to use olaparib – a drug originally developed for ovarian cancer treatment – to treat patients who have ceased to respond to more traditional prostate cancer approaches.

Research into Stage II (Dukes) colon cancer has developed a genetic blood test that allows clinicians to identify high-risk patients who are likely to experience recurrence after surgery and will benefit from chemotherapy.

Genomics has revealed that colorectal cancer is a heterogeneous disease and that traditional one-size-fits-all approaches are ineffective. Now it is identifying patients who will benefit from novel treatments – sparing many the trauma of chemotherapy [3].

Cytotoxic therapy – costly and ineffective in 80 percent of patients – is being transformed by genomics, which can predict and measure responses before treatment by using genetic biomarkers, sparing non-responsive patients.

Sequencing can help diagnosis by identifying relevant mutations causing disease, so reducing the use of interventions in patients who will gain little or no benefit, and consequently realising significant savings [4].

A More Efficient Europe

With so much opportunity, but with so much current dispersal of Europe's steps to take advantage of it, there is an obvious need to bring the many strands closer together. It does not help to advance genomics in Europe that there is so little interconnection between those who should be partners.

Europe needs agreement on standards for genomic data generation, analysis, privacy and sharing of genomic and associated clinical and other phenotype data, including self-reported data, data from wearables, omics, and imaging. It needs more effective clinical informatics, with agreed standards for interoperability of health informatics systems. Coordinated national activity would ensure best practice emerging on clinical implementation. There are gaps that need filling with a European strategy on engaging the public in discussions around genomics and data use, and with a European training programme in genomics, informatics and personalised medicine for clinical staff. And discussion is needed with and among European regulators on the appropriate mechanisms for regulating clinical genomic testing [5].

Filling the Gaps

The Million European Genomes Alliance (MEGA) is intended to remedy these deficiencies. It aims to allow the wide scope of genomics to be realised – and to ensure that these findings can also feed effectively to reinforce the emergence of personalised medicine. The rationale for MEGA is that there are massive gains within easy reach for science, research, medicine, healthcare resources, and patient outcomes. But these gains are still to be grasped.

MEGA will provide the mechanisms to derive fuller benefits sooner from all this potential. It will make it possible to combine forces across disparate and separate activities, to accumulate and exploit research findings, to ensure that Europe's infrastructure meets the needs – and, as its name suggests, it will provide information on the genetic, molecular, clinical and social characteristics of a million participating European citizens.

Crucially, it will bring focus to European activity in this field, building links across Europe. It will bring together the key partners in genomics and personalised medicine in the public sector, academia, industry, policy makers and civil society. The aim is for it to be up and running by 2020, and delivering benefits to Europe through the next decade of discovery as genomics and personalised medicine come of age.

Why would MEGA be superior to the many existing initiatives? On the conceptual level, a united project will make it possible to ask questions that smaller studies could not answer, such as multi-gene interactions. In terms of economics and organisation, a larger scale and sharing of data allow better use of resources and deeper analysis. The impact will be to

provide results of a pan-European project that can produce benefits for patients faster; the MEGA infrastructure will also be useful to disseminate results in a more coordinated way, easing access for end users.

At the technology level, it could respond to the widening perception that genomics, while extremely useful, is limited in providing functional information. For instance, the correlation of genomics with drug responses overall is rather poor apart from some exceptions. Genomics can predict a risk, but not when the risk will hit, or how a disease will progress and change during therapy. For these dynamic features dynamic parameters need to be measured, such as metabolites and proteins.

Shared Efforts

Across Europe, as across the developed world, there is a hunger to penetrate the science of genomics, to harvest the understanding it can offer at the most esoteric level of human biology, of health and disease, and of individuals' predispositions and characteristics. The European Union and its member states are backing these efforts with research funding, and by sponsoring or promoting or hosting initiatives ranging from biobanks to disease-related groups and research consortia. Professional and scientific societies are driving investigations. And the healthcare industry is investing massively in everything from basic research to candidate personalised medicine products and companion diagnostics based on the evolving science [6]. The overall goals of all this activity overlap, more or less, but with significant divergences and frequent inconsistencies. MEGA will make it possible for multiple efforts to become shared efforts, with consequently improved chances of success, both in science, and in application of the science in improved healthcare. It will institute a central coordinating body to link across regions, member states, and European bodies and infrastructure.

Shared Focus

Clinical and research use of genomic technologies has until now largely concentrated on the one percent of the genome that are the instructions for cells to make proteins, the genes [7]. MEGA will look to provide maximal gain by concentrating on whole genome sequencing. It will concentrate on access to high-quality data to increase the power of genomic testing in current clinical indications and establish the foundations for future application of genomic medicine. The disease areas incorporated will respond to requests from the clinical, patient and life science community, assessed by a central expert advisory body. The focus is likely to encompass rare diseases (patient and relevant family members), cancer (with patient samples from blood and tumour), and a number of complex diseases (covering both physical and mental health). There will also be scope for incorporating "healthy" participants although the focus here will be on studies to understand role in disease prevention and risk assessment.

Shared Benefits

Genomics has been a game-changer for clinical and translational research over the past decade, and has improved success in drug discovery and development. Major genomics programmes are also recognised as having stimulated significant economic return. The economic impact of the Human Genome Project in the USA has been calculated as USD 796 billion. With a direct personalised medicine market that is predicted to grow to over EUR 150 billion in 2024 there are rewards available for leaders in this sector [8].

There are currently limitations and inefficiencies in national programmes aiming to secure these health and commercial benefits. A collaborative supra-national initiative such as MEGA can offer an answer, and help position Europe as the global leader in personalised medicine and genomics. MEGA can provide benefits to European countries of whatever size,

because even the biggest member states are unable to conduct all the aspects of this burgeoning discipline on their own.

However, across European countries taken together there is the critical mass and all the components needed to realise this vision. MEGA will bring together bodies, infrastructure and people with similar purpose but fragmented activity. It will leverage investments already made, particularly in sequencing, biobanking and data infrastructure, but also in the equally necessary realms research, health, and education systems.

Bringing together world-leading practice and expertise that exists in pockets across countries and sectors will make it possible to apply their collective knowledge and skills to address universal health challenges, and provide a network for sharing best practice [9]. The scope of MEGA will also provide sufficient scale to inform the significance of "signals" identified in genomic and associated data and make new clinically impactful associations, as well as to support cost rationalisation.

There will be benefits too for Europe's ambitions to provide its citizens with safe, cost-effective, sustainable health systems with equality of access. It will support initiatives on eHealth and cross-border healthcare. And it will help in developing high-value jobs and giving the healthcare industry additional vigour as part of a digital economy.

MEGA would be a realisation of the aims expressed in Article 35 of the Luxembourg EU Presidency's Council Conclusions on personalised medicine to "encourage dialogue with Member States' authorities and stakeholders to facilitate step-by-step implementation of the public health genomics approach both at European Union and national level… and facilitate ongoing initiatives" [10].

Shared Assets

Europe has attributes that give it the chance of being highly competitive in a world fighting for leadership in this promising sector. It is the home to a large and heterogenous population that also contains diverse ethnic populations and some genetic isolate populations. It boasts cohesive and predominantly social health systems, working to a high standard with the same values in comparable structures and under similar pressures, adhering to similar legislation and other influences. Its scientific and technology capabilities in genomics and in many broader fields are globally respected and envied. Public funding support is available for health research, and major national and multinational programmes have demonstrably delivered successful results. And there is some health data infrastructure [11]. With adequate investment and political will, the chances are good for successful cross-border collaboration, for enhancement of the data infrastructure, and even for that most elusive element of Europe's skill-set – translating its knowledge capital into innovation and into successful commercialisation.

Shared Opportunities

Even with Europe's advantageous background, to seize the opportunities of personalised medicine requires in-depth expertise across clinical, genomic, health informatic, bioinformatic, and social engagement and implementation fields. Many of the skills and experience needed are rare in individual nations, and difficult to harness. But the skills do exist taking Europe as a whole rather than as a collection of separate countries [12]. This is where MEGA will play a crucial role, bringing these skills together so as to further the plans of individual nations through deploying the sum of expertise derived from wide participation.

MEGA will provide a common vision and purpose, so that existing resources are best used, and related initiatives at member state and European level can be accelerated. It will develop a federated "knowledgebase" of genomic and health information, and surround this with platforms and networks for clinical discussion and training, collaborative research and

innovation and enterprise. It will set up a cross-border network of expertise, and create a platform for participant engagement to educate and involve citizens and patients in the use of their genomic and health data. And it will support the development of necessary infrastructure.

Genomic Medicine Initiatives

A catalogue of global genomic data initiatives (Table 1) is compiled by the Global Alliance for Genomics and Health (GA4GH). This demonstrates the great breadth and purpose of major initiatives, with many established for research purposes but a number with the intention of directly supporting clinical care or to generate data for commercial uses, most commonly for drug discovery.

Shared Infrastructure

Infrastructure is as vital as expertise to the successful exploitation of genomics and the development of personalised medicine – and in Europe it is just as scattered. Infrastructure encompasses a broad range of needs: health and research systems able to process samples and collect and transfer data; centralised biobanks that can efficiently manage and store samples; sequencers capable of performing whole genome sequencing at scale and supercomputers capable of processing large volumes of genetic information; and a skilled workforce and engaged population [13]. Some of this infrastructure is already in place in the member states (Table 2). MEGA will support further investment to ensure all participating countries can meet needs of shared development of personalised medicine, and bring experts in required areas from across countries to share knowledge and agree best practice.

Shared Engagement in Europe

Beyond specific initiatives and infrastructure directly related to genomics, MEGA will also support wider priorities at a European and member state level, in eHealth, cross-border clinical care, and networks of expertise such as the rare disease reference networks. It will also provide a platform to generate implementation evidence and to consider the wider implications of genomic and health data. Using MEGA as a real use case will help shape the implementation of recent major revisions of EU legislation, such as rules on data protection or in vitro diagnostics, and will support efforts at harmonisation of legal and ethical frameworks across European countries [14].

Shared Responsibilities

Advances in knowledge and technology, exemplified by the improvements in genomic sequencing, enable the shift to a personalised, predictive, preventive, and participatory health system. A system that can provide the right information and treatment to the right people at the right time.

But the rapid advances in technology have the potential to present a further challenge to sustainability of health systems. If they are applied in an indiscriminate and uncoordinated manner their results could destabilise the already fragile framework of national health budgets. Avalanches of expensive new products, perhaps insufficiently validated, or duplicating one another's effects, could raise the pressure on the strained finances of national authorities. However, with planned development and appropriate regulatory systems, personalised medicine holds out the prospect of more sustainable, efficient and effective health systems. Much depends on the quality of the arrangements for the development and funding of personalised medicine [15].

Table 1. National personalised and genomic medicine initiatives and strategies. A catalogue of global genomic data initiatives is compiled by the Global Alliance for Genomics and Health (GA4GH). This demonstrates the great breadth and purpose of major initiatives, with many established for research purposes but a number of them with the intention of directly supporting clinical care or to generate data for commercial uses, most commonly for drug discovery

Project	Country	Origin and funding	Purpose	Operations
100,000 Genomes Project	UK	UK government; funding in excess of GBP 300 million to date	Sequencing and analysis of 100,000 genomes to inform the diagnosis of patients with cancer and rare diseases. Its four main aims are to: (1) Create an ethical and transparent programme based on consent; (2) Bring benefit to patients and set up a genomic medicine service for the NHS; (3) Enable new scientific discovery and medical insights; (4) Kick-start the development of a UK genomics industry	Most ambitious and advanced national project encompassing clinical implementation, research and commercial aims. Operates through a government owned company, Genomics England.
Danish Government and Regions National Strategy for Personalised Medicine 2017–2020	DK	Danish Ministry of Health and Regions; initial funding of DKK 100 million	Strategic action areas: (1) Transparent governance structure with nationwide involvement (2) Clear legal framework addressing ethical principles and data privacy and security (3) Patients and citizens must be involved (4) A technological infrastructure with secure, efficient and equal access (5) Genomics research must be international and deeply integrated in the healthcare system (6) Tools and competencies to use genetic data (7) Attractive development in relation to personalised medicine	Established a national Genome Centre at the University of Tartu. Builds on previous investments in biobanking, sequencing and data infrastructure, and research.
Estonian Genome Project	EE	Estonian Government	The project was proposed as being of huge cultural value and leading in this area in global research. It has collected over 50,000 samples (5% of adult population) and links this to clinical and survey data to form a rich data set. Genotyping analysis has been performed on these samples, along with sequencing in a proportion, along with additional samples and investigations in many. There are ambitions to grow it further to cover a significant percentage of the population and embed genomics within the health system as part of clinical decision support. It has gathered significant awareness and support across a large proportion of the population.	Continues and develops the work over the past fifteen years in biobanking and eHealth. Established through legislation in the Human Genes Research Act. Operates through a government owned company, EGeen.
Finland's Genome Strategy	FI	Ministry of Social Affairs and Health, Finland	The aim of the strategy is to: (1) Make Finnish healthcare more effective through better and more targeted care, with integration of genomics in clinical care, individuals able to make use of their genomic data, and a containment of healthcare costs and better allocation of resources; (2) Researchers will have entirely new opportunities for utilizing genomic data; (3) Transform Finland into an internationally attractive environment for research and business in the field of genomics	Establishing a National Genome Centre to implement the strategy, including the development of a national genome reference database.
France Médecine Génomique 2025	FR	French Government; investment of EUR 670 million in public-private partnerships	Targets of the 2025 France Genomic Medicine Plan: (1) Position France among the leading big countries in the field of genomic medicine within the next ten years, with the aim of exporting expertise and developing a strong medical and industrial framework; (2) To establish a generic care pathway with access to genomic medicine for all French people affected by cancer, a rare disease or a common disease; (3) To be capable by 2020 of sequencing 235,000 genomes a year for rare diseases and cancer, with growth beyond 2020 to cover common diseases	Led by the National Alliance for Life Science and Health (Aviesan) consortium. Development of a hub and spoke model, with development of regional sequencing centres and a central reference centre for innovation, assessment and transfer (CReflX).
NHS England Personalised Medicine Strategy	UK	NHS England lead the National Health Service in England	Aims aligned to Five Year Forward View and health sustainability: (1) Improved prevention based on underlying predisposition; (2) Earlier diagnosis of disease as a result of identifying abnormality earlier; (3) More precise diagnosis based on cause; (4) Targeted interventions through the use of companion diagnostics to identify and stratify effective treatments	Builds on the strategy of the 100,000 Genomes Project, and NHS England as a partner in that.

Table 1 (continued)

Project	Country	Origin and funding	Purpose	Operations
Personalised Medicine – Action Plan	DE	Federal Ministry of Education and Research, Germany (BMBF); up to EUR 360 million funding	Strategic funding for research in personalised medicine. Targeted across R&D from biomarker validation through to therapies and service implementation. Main goal is for patients to benefit more quickly. Ethical, legal and economic challenges and engagement and information platforms are also included within this.	Predominantly operates through an open competitive research funding programme.
Precision Medicne Initiative	CN	Chinese Government; expected funding of CNY 60 billion (EUR 7.9 billion) by 2030	The Chinese government confirmed plans to make precision medicine part of its Five Year Plan for 2016–2020 as it works to prioritise genomics to drive better healthcare outcomes.	
Precision Medicne Inititative (All of Us)	US	US Government; initial funding of over USD 200m	Aim is to enrol one million or more volunteers to enable research for a wide range of diseases and increase our understanding of healthy states. Scientific opportunities presented by All of Us include the ability to: (1) Develop ways to measure disease risk based on environmental and genetic factors; (2) Pharmacogenomics; (3) Biomarker identification and validation; (4) Use mHealth technologies to correlate activity, physiological measures and environmental exposures with health outcomes; (5) Develop new disease classifications and relationships; (6) Empower study participants with information to improve their health; (7) Create a platform to enable trials of targeted therapies	Operated from within the structures of the National Institutes of Health (NIH). Committed to engaging multiple sectors and forging strong partnerships with researchers, patient groups, and the private sector. Setting the foundation for new ways of engaging research participants, sharing health data and information, and employing technology advances to mine the information for comprehensive results.

A Shared Shift in Healthcare

The proper use of personalised medicine implies a shift to a predictive, preventive, and participatory healthcare system that puts the citizen at the centre. By providing the right information and treatment to the right people at the right time, personalised medicine permits a move beyond merely reactive disease-centred systems, and opens the pathway to an approach planned and concentrated on prevention and health. The move away from a "one size fits all" approach is facilitated by using new technologies, and notably genome sequencing, to understand the fundamental biological basis of health and disease. By combining this information with a person's clinical information, circumstances, and values, personalised medicine allows doctors, patients, and citizens to develop and implement targeted prevention and treatment [16].

Shared Mechanics

At the heart of MEGA will be information on the genetic, molecular, clinical and social characteristics of a million participating European citizens. Genomic data produced by participating organisations will be stored in the database, and the linking of health data with genomic data will be made possible along with access to repositories of publicly available data. Working across country borders to link and develop the infrastructure to form a genome-phenome knowledgebase of scale will help address the understanding of genetic change in an individual setting by providing validated information on others with the same genetic change, as well linking to the appropriate clinician or relevant researcher [17].

Maximising the value of a knowledge-base of genomic information requires tools to support access and understanding, and interaction across different groups. So supporting platforms and networks will provide clinical application, through interpretation and report-

Table 2. Alignment with other European initiatives

Name	Summary of purpose	Potential synergies and relationship with MEGA
Biobanking and Biomolecular Resources Research Infrastructure-European Research Infrastructure Consortium (BBMRI-ERIC)	BBMRI-ERIC supports a pan-European distributed research infrastructure of biobanks and biomolecular resources to support high quality biomolecular and medical research. It consists of nineteen Member States and one International Organisation.	Obtaining, processing, and storing to standardised processes samples is a fundamental requirement of MEGA. Linking regional or national biobanking capabilities of participating Member States through BBMRI will support the MEGA project as well as giving a core shared purpose for standardisation of practice across contributing biobanks.
Coordinated Research Infrastructures Building Enduring Life-science (CORBEL) Services	CORBEL is an initiative of eleven new Biological and Medical Science Research Infrastructures, who together will create a platform for harmonized user access to biological and medical technologies, biological samples, and data services.	The aims and experience of CORBEL to facilitate access to data, samples and instrumentation, bringing in partners such as ELIXIR, BBMRI and ECRIN, will provide experience that can be utilised by MEGA.
ELIXIR	ELIXIR is a European intergovernmental organisation that brings together data and information technology life science resources. The goal is to coordinate these resources so that they form a single infrastructure to enable scientists to find and share data, exchange expertise, and agree on best practices to derive new insights.	Many of the primary requirements for MEGA, in terms of data infrastructure and tools, can be guided and supported by ELIXIR. In turn ELIXIR will be able to support the data exchange and training for genomics which is at the core of much of modern life sciences.
eTRIKS consortium platform	An EU-funded project through the Innovative Medicines Initiative (IMI). eTRIKS is the result of a collaboration between seventeen different partners to develop a platform and services for data staging, exploration and use in translational research.	The platform produced by eTriks for knowledge management to support data intensive translational research has the potential to be directly utilised by MEGA, or at least learnt from in supporting the same needs.
European Bioinformatics Institute (EBI or EMBL-EBI)	EMBL-EBI presents public biological data freely available to the scientific community via a range of services and tools, perform basic research, and provide professional training in bioinformatics.	The depth of bioinformatics and large genomic dataset expertise at EMBL-EBI will be invaluable in structuring and making available data from MEGA. EMBL-EBI will be able to use the MEGA database to further develop tools, pursue research aims, and support training in bioinformatics.
European Clinical Research Infrastructure Network (ECRIN)	ECRIN is a not-for-profit intergovernmental organisation that has the status of an ERIC. It supports the conduct of multinational clinical trials in Europe through the provision of tools and consultancy services.	Leverage the expertise in coordinating the many operational, legal, regulatory and administrative challenges of multinational research; and tools to support this. MEGA will in turn provide valuable infrastructure that builds the capability of genomic research in Europe.
European Molecular Biology Laboratory (EMBL)	EMBL is an intergovernmental organisation that provides a flagship laboratory for the life sciences with more than 80 independent research groups across six sites covering the spectrum of molecular biology.	EMBL can provide links in to genomics researchers across Europe as well as specific expertise in certain areas such as laboratory and sample processing protocols. The MEGA initiative will provide a core research and training resource for EMBL.
European Open Science Cloud	The European Open Science Cloud, created by the EC, will offer Europe's 1.7 million researchers and 70 million science and technology professionals a virtual environment to store, share, and re-use their data across disciplines and borders.	Although the use of the Open Science Cloud is not a dependency for MEGA partial or complete use of the cloud for data transfer, storage and analysis has many advantages, especially for cross-border projects utilising big data. Adherence to legislation, participant wishes, and data security measures will be fundamental to the decision on appropriateness of cloud, as well as timescales of development with regards to the Open Science Cloud specifically.
ICPerMed	ICPerMed brings together over 30 European and international partners representing ministries, funding agencies and the European Commission (EC). Together, they work on coordinating and fostering research to develop and evaluate personalised medicine approaches.	MEGA furthers all the ambitions of ICPerMed into a deliverable project to contextualise goals, address challenges, and give tangible outcomes with regards to genomics.
p-medicine	7th Framework funded project to develop new tools, IT infrastructure and VPH models to accelerate personalised medicine for the benefit of the patient. Involves nineteen partners from nine European countries and Japan to create support and sustain new knowledge and innovative technologies.	Many of the tools produced through the p-medicine project will have direct utility for MEGA, which will support the validation of p-medicine tools as well as providing data and aggregated expertise to develop further tools.

Summaries of relevant European initiatives and infrastructure and proposed alignment, benefits from, and coordination with MEGA. MEGA, Million European Genomes Alliance.

ing tools and integration into health records, health professional interaction, and access as a training resource. MEGA will also support collaborative multidisciplinary research, and commercial enterprise through the development of new analytical tools, integrating innovative technologies and providing a drug target discovery and trials interface.

MEGA will also support an evolving workforce to access information to guide cost-effective management at the point of care, by establishing appropriate quality standards for data, and providing an ecosystem to ensure the right information is provided to health professionals in the most intelligible format. It will also work alongside national eHealth programmes and clinical guidelines to ensure the right information is integrated into electronic health records of participants. New clinical decision support tools will help make information become part of daily practice. Clinical discussion networks across participating sites will aid interpretation and wide application of genomics, and collaborating with national and regional education programmes will make genomic and clinical data available for recognised training.

Although a number of European and national initiatives have improved large-scale collaborative working there are still barriers to multidisciplinary collaborative health research and much activity is within "siloes" of activity. MEGA will form research area groups to work together to answer clinically and socially pertinent questions.

Innovative approaches across sectors and disciplines will be pioneered to develop more effective medicines and diagnostic tests, as well as new models in health technology, data analytics and informatics that address key clinical and scientific challenges.

Sharing Partners

The likely partners include relevant European Commission directorates-general, such as Health and Food Safety, Research and Innovation, Digital Economy, and Enterprise and Industry. They will also feature initiatives such as ELIXIR, the European Bioinformatics Institute, the Biobanking and Biomolecular Resources Research Infrastructure, the European Open Science Cloud, and the international consortium on personalised medicine, ICPerMed. Member state ministries covering health, research, science, and business, regional health organisations, major healthcare providers or payers, and health data bodies are other obvious potential partners. Patient and support organisations such as the European Cancer Patient Coalition, European Patient Forum, European Organisation for Rare Diseases, Inspire2Live, International Diabetes Federation, European Brain Council would also find their place in MEGA. So too would academic, research and funding bodies such as the European Organisation for Research and Treatment of Cancer, Science Europe, European Association for Cancer Research, or clinical and scientific professional societies such as the European Societies of Human Genetics, Medical Oncology, Cardiology, and Pharmacogenomics and Personalised Therapy, European Respiratory Society, or the European Centre for Public Health Genomics. Industry bodies such as the European Federation of Pharmaceutical Industries and Associations or MedTech Europe would bring important perspectives, as would key companies in the field, such as Illumina, Roche Diagnostics, BC Platforms, or Sophia Genetics in genomic sequencing and analysis, Intel and SAP in IT infrastructure, and pharmaceutical firms heavily involved in personalised medicine such as AstraZeneca, or Roche.

The European Alliance for Personalised Medicine either incorporates or is linked in to all of these stakeholders and provides a platform to manage and coordinate stakeholders from an already advanced and educated position.

A Shared Future

Some of these technological and scientific advances are already being implemented in healthcare, and more are coming closer to turning opportunity into reality. Change is inevitable. The question that Europe faces now is not whether to pursue the development of personalised medicine, but how to support health systems so they can integrate personalised medicine into the efficient and effective transformation that it offers. MEGA puts participating Member States on an accelerated and realisable path to achieve this.

This might include a phased approach to areas of focus – such as tackling low hanging fruits, such as cancer and rare disease, in years 1–3; then midterm (years 3–6) diabetes and cardiovascular; and long term (years 6–10) neurodegeneration, immune response disorders, inflammation, arthritis.

The intention is to secure support for the proposal in 2017, so that core leadership and a project team can be set up to lead gap analysis in 2018 while winning broad stakeholder engagement. In 2019 pilot work should start, and core infrastructure and processes should be developed. In that way, MEGA can deliver benefit as from 2020.

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References

1 Horgan D, Paradiso A, McVie G, Banks I, Van der Wal T, et al: Is precision medicine the route to a healthy world? Lancet 2015;386:336–337.
2 Genomics England: The 100,000 Genomes Project. July 21, 2014. http://www.genomicsengland.co.uk/the-100000-genomes-project/ (cited March 13, 2016).
3 Vayena E, Gasser U: Between openness and privacy in genomics. PLoS Med 2016;13:e1001937.
4 Tabor HK, Berkman BE, Hull SC, Bamshad MJ: Genomics really gets personal: how exome and whole genome sequencing challenge the ethical framework of human genetics research. Am J Med Genet A 2011;155A:2916–2924.
5 Hervey T, Vanhercke B: Health care and the EU: the law and policy patchwork; in Mossialos E, et al (eds): Health Systems Governance in Europe: The Role of European Union Law and Policy. European Observatory on Health Systems and Policies. Cambridge, Cambridge University Press, 2010.
6 Rahimzadeh V, Dyke SO, Knoppers BM: An international framework for data sharing: moving forward with the Global Alliance for Genomics and Health. Biopreserv Biobank 2016;14:256–259.
7 National Human Genome Research Institute: All about the Human Genome Project. Updated October 1, 2015. https://www.genome.gov/10001772 (cited February 11, 2016).
8 European Medicines Agency: Publication and access to clinical-trial data (draft). June 24, 2013. http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/06/WC500144730.pdf (cited March 17, 2016).
9 Horgan D, Lawler M, Brand A: Getting personal: accelerating peronalised and precision medicine integration into clinical cancer research and care in clinical trials. Public Health Genomics 2015;18:325–328.
10 Council of the European Union: Council conclusions on Personalised medicine for patients. Brussels, December 7, 2015. http://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:52015XG1217(01)&from=EN (cited May 4, 2016).
11 European Alliance for Personalised Medicine: Conference Report: "STEPs in the Right Direction to a Brave New, Healthier and SMART Europe." University Foundation, Brussels. 2015. http://www.euapm.eu/pdf/EAPM_Presidency_Conference_Report_Personalised_Medicine_Smaller_Members_And_Regions_Together.pdf (cited May 5, 2016).
12 PerMed: Shaping Europe's Vision for Personalised Medicine: Strategic Research and Innovation Agenda (SRIA). 2015. http://www.permed2020.eu/_media/PerMed_SRIA.pdf.
13 Global Alliance for Genomics and Health. http://genomicsandhealth.org/.
14 OECD; European Commission: Cancer Care: Assuring Quality to Improve Survival. Paris, OECD Publishing, 2013.
15 Powers M, Faden R: Social Justice: The Moral Foundations of Public Health and Health Policy. New York, Oxford University Press, 2006.
16 World Health Organization Europe: Access to new medicines in Europe: technical review of policy initiatives and opportunities for collaboration and research. March 2015. http://apps.who.int/medicinedocs/documents/s21793en/s21793en.pdf.
17 European Commission: Regulatory framework applicable in the field of personalised medicine: Agenda item 7. March 10, 2016. http://ec.europa.eu/health/files/committee/stamp/2016-03_stamp4/7_personalised_medicine_regulatory_framework_paper.pdf (cited 2016 March 12).