Genes Nutr (2010) 5:285–296
DOI 10.1007/s12263-010-0192-8

REVIEW

The Micronutrient Genomics Project: a community-driven knowledge base for micronutrient research

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Received: 17 July 2010 / Accepted: 13 October 2010 / Published online: 30 October 2010

Abstract Micronutrients influence multiple metabolic pathways including oxidative and inflammatory processes. Optimum micronutrient supply is important for the maintenance of homeostasis in metabolism and, ultimately, for maintaining good health. With advances in systems biology and genomics technologies, it is becoming feasible to assess the activity of single and multiple micronutrients in their complete biological context. Existing research collects fragments of information, which are not stored systematically and are thus not optimally disseminated. The Micronutrient Genomics Project (MGP) was established as a community-driven project to facilitate the development of systematic capture, storage, management, analyses, and dissemination of data and knowledge generated by biological studies focused on micronutrient–genome interactions. Specifically, the MGP creates a public portal and open-source bioinformatics toolbox for all "omics" information and evaluation of micronutrient and health studies. The core of the project focuses on access to, and visualization of, genetic/genomic, transcriptomic, proteomic and metabolomic information related to micronutrients. For each micronutrient, an expert

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group is or will be established combining the various relevant areas (including genetics, nutrition, biochemistry, and epidemiology). Each expert group will (1) collect all available knowledge, (2) collaborate with bioinformatics teams towards constructing the pathways and biological networks, and (3) publish their findings on a regular basis. The project is coordinated in a transparent manner, regular meetings are organized and dissemination is arranged through tools, a toolbox web portal, a communications website and dedicated publications.

Keywords Micronutrient · Bioinformatics · Database · Genomics

The introduction of genomics in micronutrient research

Micronutrients are essential regulators of important metabolic and physiological processes in humans. Micronutrient deficiencies cause specific illnesses. Suboptimal intakes may contribute to the development and severity of chronic diseases. An increasing number of studies also demonstrates the undesirability of high micronutrient doses (by supplements intake for example) in favour of optimal doses (e.g. [17]). Based on these observations, a continuous process of re-assessing dietary requirements and upper safety limits for micronutrients is taking place in the context of public health nutrition [1]. These new reviews are based on best available science, including considerations on differential recommendations for subgroups (e.g., elderly, children, pregnant women).

With recent advances in systems biology and genomics technologies, it is becoming feasible to assess the biological action of a micronutrient in its complete biological context, that is, in relation to its effects on multiple metabolic pathways, including interactions with other nutrients in context of genetic make-up. These mechanistic and integrated ('systems') approaches in the micronutrient and health relationship may complement the pubic health recommendation approaches and provide refinements in specific cases. Three major developments in the area of genomics now allow us to further study the molecular mechanisms involved in the (optimal) health relationship with micronutrients. These are

- the ability to inexpensively analyse genetic variation in human genes related to micronutrient uptake and metabolism;
- the unravelling of the molecular complexity of the modes of action of micronutrients using omics technologies
- the generation of multiple inter-related biomarkers and diagnostics that accurately define optimal micronutrient intake for health at the molecular level.

The Micronutrient Genomics Project (MGP) described in this paper is a research community project to stimulate and facilitate the most recent developments by providing the required knowledge-based infrastructure for nutritional recommendations at the genetic subgroup and individual level. Four observations that necessitate integrating micronutrient research and genomics are particularly relevant.

Micronutrients have complex biological actions

The effects of micronutrients depend on a series of physical, chemical, and physiological processes, including amount ingested, meal matrix, digestion, absorption, distribution, metabolism (biotransformation), excretion (last four collectively known as ADME), genetic factors in all of the above processes, and last, but not least, cellular mechanisms of action (e.g., [26, 38]). Each of these processes involves a complex interaction among genes, gene products, and environmental factors. For example, the core one-carbon pathway that produces *S*-adenosylmethionine for methylation and other reactions utilize folate and three other vitamins (B12, B2, and B6) in conjunction with at

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least eight enzymes or transporters to perform the core reactions. Furthermore, metabolites in this pathway are used in multiple critical cell functions such as DNA synthesis, maintenance methylation of DNA sequences and neurotransmitter synthesis.

Micronutrients have overlapping biological action

The above example also demonstrates that micronutrients do not act independently. The need to consider the impact of micronutrient combinations on biological processes is becoming increasingly evident, since micronutrients have overlapping or complementing actions, or even act in concert (e.g. 5-methyltetrahydrofolate as substrate and vitamin B12 as cofactor for methionine synthase). Selenium, zinc, folate, vitamins D, E, B2, B6, and B12 are all involved directly or indirectly in the innate immune response, oxidative stress response, and DNA metabolism [25]. Many micronutrients play a role in oxidative stress defence. From a reductionist viewpoint, it makes sense to study each pathway and reaction in an isolated manner, as this provides insight into mechanisms. However, from a physiological and a systemic (= systems biology) view, the best approach is to study the role of *all* actors.

Micronutrients and genetic variations

Until recently, micronutrient research was usually conducted under the assumption that the underlying mechanisms are the same in all humans. About 600 enzymes for which micronutrients are cofactors are known in the human proteome, and the genetic diversity of most has not been extensively characterized. A significant effort is now being made to characterize alleles of "micronutrient" genes within the human population. A widely studied example is methylene tetrahydrofolate reductase (*MTHFR*). The most studied genetic variants are c.677C > T (p.A222V) and c.1298A > C (p.E429A). The allele frequency of the homozygous TT genotype varies from 0% in sub-Saharan African populations to 25.3% in Colombians [6]. Although much research focused on these variants, the full range of human genetic variation in *MTHFR* and their allele frequencies in various populations have not been studied. For example, Marini et al. [30] re-sequenced 564 individuals of diverse genetic ancestry and discovered 14 non-synonymous changes including 11 alleles with frequencies <1% along with the common alleles p.A222V, p.E429A, and p.R594Q. Increased levels of folate restored MTHFR activity to the normal range in 4 of the 5 variants and riboflavin, the cofactor of MTHFR, can normalize the activity of the C677T variant of the enzyme indicating the feasibility of corrective nutritional intervention for specific genotypes [34]. One specific example is the observation that riboflavin supplementation improves blood pressure specifically in cardiovascular disease patients with the *MTHFR 677* C > T polymorphism [18]. Other genes involved in vitamin metabolism also show population differences. Another example is the p.379A > V (SNP rs7501331) in the β-carotene 15,15′-monoxygenase (*BCMO1*) gene which has a high frequency in the individuals of European ancestry, but much lower frequency in ethnic groups from China and Japan and is absent in Yoruba Nigerians [26]. This genetic variation is not considered in developing recommended intakes for vitamin A which were based on pro-vitamin A conversion factors of either 1:6 or 1:12, irrespective of the observed large inter-individual variation in conversion efficiency [5, 16, 26, 47]. Variation in genes involved in metabolism or interactions of micronutrient genes are likely to generate differing intake requirements for optimal health in population subgroups and individuals.

Genotype to phenotype translations

The relationships between genetic variation and health outcomes for almost all micronutrient metabolism genes are under intense investigation and discussion. Recent examples are studies on the relationship of vitamin D, selenium, and carotenoids with cancer [28, 32]. Over 1,600 studies associating polymorphisms in *MTHFR* with various disease or physiological conditions have been published (check "MTHFR" in the Genopedia of http://hugenavigator.net). In many cases, these studies analyse single micronutrients and one or several variants in a gene or pathway. A systems biology approach will add to these studies by integrating analyses and data from multiple systems and technologies.

The Micronutrient Genomics Project

Although the amount of results from gene–nutrient interaction studies is growing rapidly, the available information is often disconnected and generated by diverse experimental designs that do not allow data comparison or consolidation. To fully tap into the potential of data mining, published data as well as organizing data from research in the micronutrient genomics field, a systematic, searchable, central repository or portal of genetic and phenotypic information related to micronutrients are needed. Such a systematic portal would provide a bioinformatics resource that can be used to build a global view of micronutrient biological activity, to drive new studies, and to identify gene-micronutrient interactions with significant effects on health. A consortium of micronutrient researchers was formed to create a new set of bioinformatics resources and to exploit these in research activities and to disseminate them to the entire micronutrient research community. This

effort is named the Micronutrient Genomics Project (MGP).

The MGP considers itself an integrative and iterative project, combining expert knowledge with standard bioinformatics resources. It thus explicitly does not replicate but rather exploits and integrates the invaluable bioinformatics tools and omics databases that are already available, such as the Human Variome Project [41], the National Center for Biotechnology Information (NCBI), The Human Genome Epidemiology Network (HuGENet) [24], the European Bioinformatics Institute (EBI), and the Human Metabolome Database HMDB [49]. Dedicated databases such as the selenoprotein genetics database [8] will be linked or integrated into the MGP portals.

An online portal has been created at http://www.micronutrientgenomics.org. This portal allows access to all information and tools collected and structured by the Micronutrient Genomics Project. Three basic bioinformatics resources form the backbone of the micronutrient genomics portal:

1. The nutritional phenotype database
2. The micronutrient pathway portal
3. The micronutrient genetic variation portal

Additional tools are accessible via the main portal or will be integrated into the three resources mentioned. Newly emerging tools and data resources will be continuously added, maintaining the micronutrient genomics portal as the central point of access for this type of research. An important activity of the MGP will also be to continually critically review the information in these portals and databases for accuracy and relevance as they evolve and become more complex.

The nutritional phenotype database

The nutritional phenotype database (dbNP) is a infrastructural project which allows storage, processing, and meaningful queries of information on (micro)nutrient-oriented human and animal model intervention studies with all omics components included (genetics, transcriptomics, proteomics, metabolomics, biomarkers a.o.), together with a detailed description of the study design. This resource is described in a separate paper [45]. The dbNP also allows additional analyses of existing samples from nutritional intervention studies and encourages the future collection and analysis of samples for this purpose.

dbNP is complementing the existing publically available databases. The data in these valuable resources come from unconnected studies and populations. dbNP facilitates comparison of data from harmonized studies where proper reporting standards are used and metadata describing the experimental design are captured. Thus, in addition to its function to utilize existing data from publically available databases, MGP supports a data repository for ongoing and new studies of micronutrient–genome interactions. Standards for incorporating new data and results are being developed as more complete datasets are obtained from members of the MGP team.

The development of dbNP is performed as an open-source modular project (see http://www.dbnp.org), with clearly described data formats, data communication standards, and software plugin interfaces. This allows collaboration with other initiatives to build the necessary modules of systems biology databases which is already taking off. It also allows the dbNP analysis tools to work on external data using the same kind of webservices approaches that are used internally or alternatively to offer data from dbNP for analysis in other pipelines in an automated way.

The micronutrient pathway portal

The micronutrient pathway portal is implemented at http://micronutrients.wikipathways.org and offers all the functionality available in Wikipathways [40] including a search option for pathways, genes and metabolites, a pathway editor, download options in formats relevant for a number of tools and webservices for programmatic access [23]. The portal presents micronutrient-related pathways and biological networks (Fig. 1). For many micronutrients, knowledge of their biological functions is still fragmented. Thus, the portal is both a permanent interface for established pathways and biological networks, and a flexible wiki-editable interface for the parts that are being newly developed. Although the wiki tool allows access to anyone who registers, professional help and curation is offered by a core pathway team that also actively constructs and maintains pathways and biological networks.

The phenotypic expression of the gene–micronutrient interaction is visualized at the level of transcripts, proteins and metabolites. Pathways or biological networks are best shown in a graphical manner. This allows an integrated view on related parameters and visualization of experimental data. The micronutrient pathway portal features pathways that combine gene product (transcriptome and proteome) and metabolome entities (Fig. 1).

The selenium biological network (http://www.wikipathways.org/index.php/Pathway:WP15) is presented as an example (Fig. 1). The relationships in this biological network include molecular interactions, but also established relationships where the molecular basis is yet not fully understood. In the selenium network for instance, ‘negative effects’ are indicated as dotted lines. The visualization also includes regulation, compartmentalization, and organ specificity. An important feature is the visualization of the

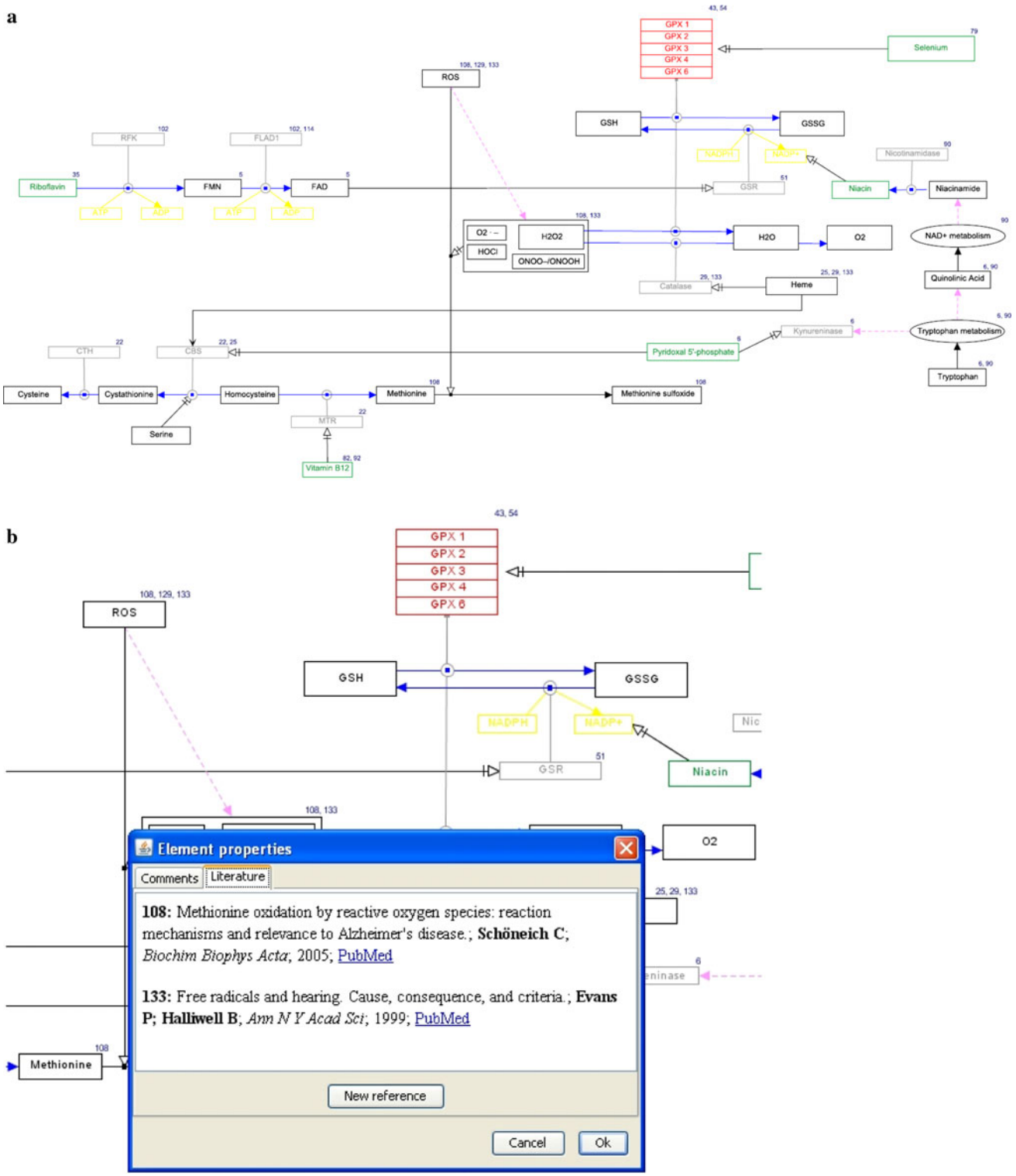

Fig. 1 Example of a WikiPathways visualization of micronutrient biological activity. The selenium pathway provided in Fig. 1a can be found at http://www.wikipathways.org/index.php/Pathway:WP15. All reactions are manually curated, with references available as demonstrated in Fig. 1b

relationship between intracellular processes and plasma components (including transport information). This allows for analysing and quantifying intracellular micronutrient mechanisms from a plasma-oriented perspective. This is essential for human applications where plasma is the prime source of biomaterial for biomarker analysis. Moreover,

the relationship between molecules in the selenium pathway and overarching processes (metabolism, oxidation, inflammation) is indicated.

Detailed biological networks are available for selenium and folate/B12. Biological networks for iron, carotenoids/vitamin A, and others are under construction. Straightforward pathways are available for almost all micronutrients.

Using pathways for analysis

While pathway representations alone can already be very useful to understand the biological process represented, the most interesting aspect of pathways is that they can be used in the analysis of actual study data.

Gene expression Transcriptomics, gene expression regulation (e.g. ChIP and DNA methylation), and proteomics analyses of the mechanisms of action of micronutrients are increasing [2, 11, 14, 37]. The construction and optimization of the needed pathways and related biological networks for micronutrients are performed as part of the MGP. Available tools allow the statistical evaluation and visualization of this type of information directly on the pathways.

Metabolomics Traditionally, plasma biomarkers are used to quantify micronutrient status. With the advent of metabolomics, the application of the measurement of the "complete" set of metabolites in an integrated evaluation of biological activity [43], a broader use of plasma biomarkers is proposed, linking status biomarkers to health quantification [46]. MGP constructs micronutrient centred pathway-based biological networks. In these pathways, intracellular mechanisms related to micronutrient activity are linked to plasma and blood cell membrane concentrations of all relevant metabolites and (in a later stage) proteins. Relevant information on the incorporated metabolites is available via the pathway (Fig. 2).

Analysing genetic variation To allow integration of genetic data into pathway analyses, the genetic variation data need to be linked to the available genes in the pathway. As an example, for MTHFR the gene in the pathway needs to be linked to the 14 alleles discovered by Marini et al. [31]. Each gene can show variations that may affect enzyme or protein properties, influence protein–protein interactions, alter gene expression, intron splicing, or RNA stability and may have copy number variants (CNVs) and small indels. Visualization tools are being developed to show subsets of these variations on the pathways. Where available, this type of information will be linked to the entities in the pathways using data integration options offered by BridgeDB [44]. Much of the information about epistatic combinations that lead to differences in phenotype is currently not available and thus will be made available as part of the third resource that MGP is offering: the micronutrient genetic variation portal. This information will then be linked to the pathways in the same way that we previously added information about the micronutrients themselves through links to the Nugowiki (http://www.nugowiki.org). This allows making information about the biological functionality available during pathway analysis. For example, genes known to have CNVs and those with SNPs known to alter enzymatic properties may be highlighted via colour changes in the pathways. Alternatively, one might highlight coding variants with associated biochemical data or indicate that transcription factor bindings are expected to be influenced by motif variations.

The micronutrient genetic variation portal

The MGP aims at identifying all relevant genetic variations related to the biological activity of micronutrients and to make those available for usage in micronutrient genomics research. While the US National Center for Biotechnology Information (http://www.ncbi.nlm.nih.gov/) catalogues sequence variants of all human genes and two new databases store CNV data (http://projects.tcag.ca/variation and http://cnv.chop.edu), these genetic variations are typically still unlinked to phenotypes or to nutritional effects. The MGP portal will not duplicate the many resources available for genes, variants, or genomes, but will rather provide the ability to extract specific information from these resources for interpreting data or developing experimental strategies. Molecular data are typically gene centric in these databases, that is, each gene has its own page of information. SNP data are summarized for a gene although each SNP has a separate page of information, including allele frequencies. Genome browsers are designed to show the gene in the context of its chromosomal location. While each of these "views" is of value, integrating information for a set of genes or pathways is time consuming and error prone. In addition, none of the publically available datasets provides information associating a gene or variant with a nutrient or phenotype. The standards and database models for linking genetic variation to phenotype are being developed by the HVP [21], and these will be used by the MGP.

Hence, the MGP portal will create tools to dynamically create tables of gene, variant, and other genomic data for a pathway or network of genes involved in micronutrient metabolism. As an example, filters and search tools will allow genes in a pathway to be listed with all coding SNPs (cSNPs) that are non-synonymous or which map to a chromosomal position associated with a phenotype such as obesity or diabetes (e.g. [48]). The resultant data will be shown in tables with an export function for off-line uses

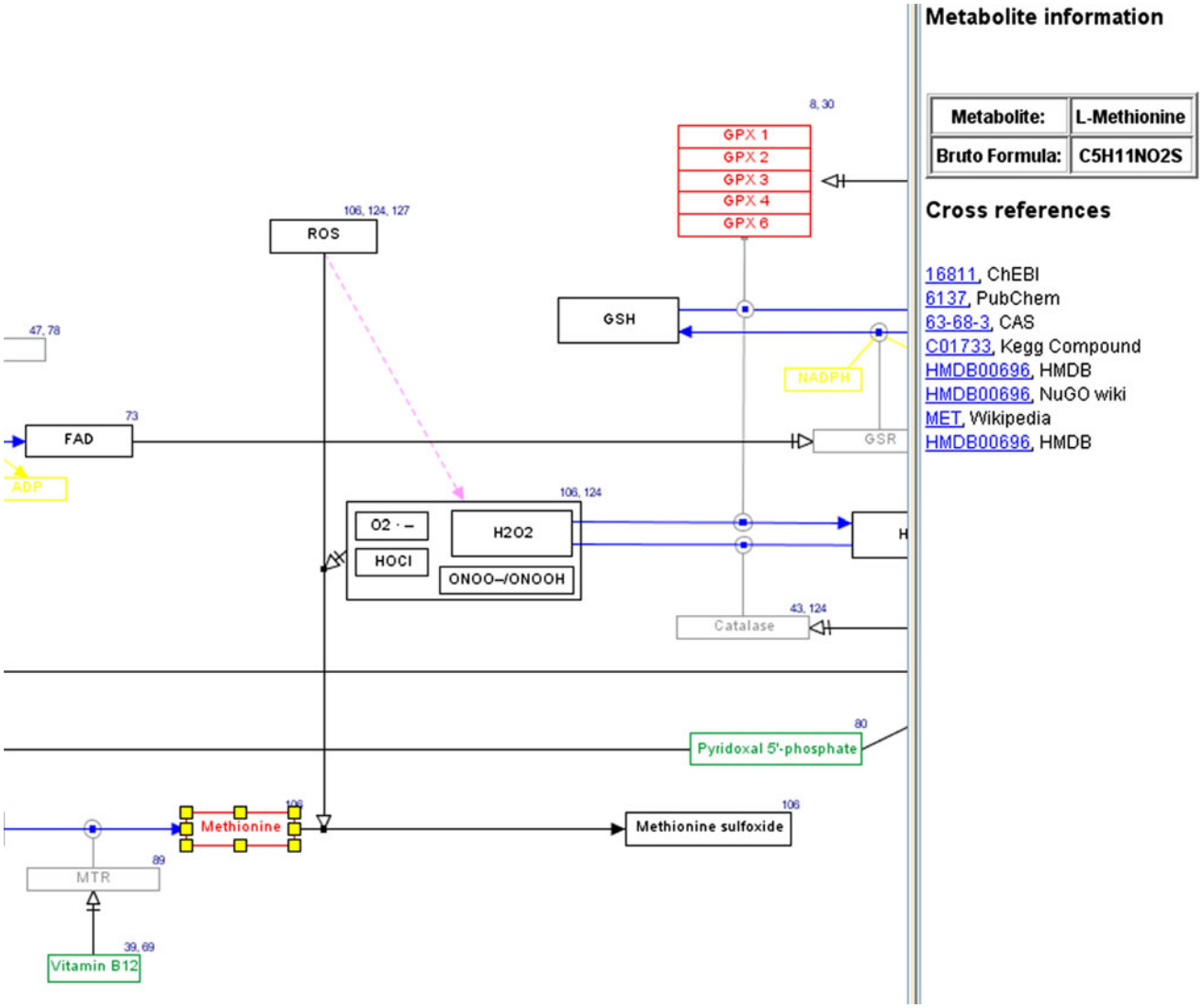

Fig. 2 The pathways on WikiPathways are linked to relevant information about the entities present. By clicking on an entity (in this case methionine), the *right panel* (backpage) appears with aggregated information and links to external databases. In this way, the pathways can provide access to information on genetic variation in dbSNP which will be extended with information from the genetic variation portal

such as designing primers or probes or importing results into statistical packages.

Based on the above the micronutrient genetic variation portal will contain

1. Lists of (links to) the relevant genes (which will preferably part of GeneOntology [3]) and the pathways they occur in. These pathways will then be on the micronutrient pathway portal. Literature references describing the genes and why they are part of the pathways will be added to the pathways themselves. Genes, gene-sets, and literature collections will also be made available on the genetic variation portal to assist analysis for instance to allow corpus extension in text-mining exercises.
2. List of relevant genetic variations in those genes (preferably linking to database produced by the HVP initiative) plus links to the original publications or datasets (where possible uploaded in dbNP) that describe the relevance of these variations for nutritional phenotype. Each of these variations will be supplemented with links to other relevant sources about the genetic variation itself (like dbSNP and Hapmap) and its implications (like SNPedia and OMIM).

Technical solutions that allow these links, for a large part based on BridgeDB [44], have already been developed and tested.

Other applications of the Micronutrient Genomics Portal

The Micronutrient Genomics Portal provides readily accessible information on, for example:

- The metabolic pathways and genes that code for the receptors, transport proteins required for uptake, transport, storage, metabolism and excretion (for example, the zinc transporters [27]).
- The genes that code for enzymes that use the micronutrient as substrate to convert it into its biologically active form.
- The genes that code for enzymes that require the micronutrient as a cofactor and whose activity is therefore modifiable by the micronutrient concentration (as example, the zinc-binding proteins involved in immune function [15]).
- The genes that code for enzymes that require the micronutrient as an integral part of their structure (e.g. seleno-enzymes and zinc finger proteins) and whose activity is therefore modifiable by the micronutrient concentration.
- Predictive in silico models of the interactive impact of micronutrient and genotype (for example, the Nijhout model of folate metabolism [35]).
- Rare mutations [9] and common single nucleotide polymorphisms in the genes that affect molecular regulation (transcription, splicing, and RNA turnover) involved in uptake, transport, metabolism, and excretion of the micronutrient.
- Rare and common single nucleotide polymorphisms in the enzyme for which the micronutrient is a cofactor.
- Effect of life-stage and life-style factors on the expression and activity of the enzymes required for the micronutrient's uptake and activation, and which require it as a cofactor, and how this affects requirements.
- Current knowledge on the measureable health effects of insufficiency (i.e., subclinical effects), deficiency, and excess and determination of the "window of benefit" [22] or developmental window in early life stages [13, 20, 33].
- The impact of micronutrients on DNA damage and gene expression. For example, moderate deficiencies or excesses in micronutrients and their interactive effects (e.g. folate and riboflavin or calcium) can cause as much DNA damage as significant doses of known carcinogens and can alter the gene expression profile in tissues [7, 12, 29].
- Integrate knowledge from model systems, such as transgenic mice and appropriate cell culture systems (e.g. stem cells), into the human knowledge base.

A special future feature is the creation of a harmonized research protocol that will generate data for local populations, but which produce data that can be combined to study the full range of human micronutrient metabolism. A central database is essential for creating the ability to compare results from such studies.

Finally, a database with all published intervention studies on genetics and micronutrients is being created by the EU Network of Excellence EURRECA and made available via the MGP portal.

The central point of access for the MGP is created at http://www.micronutrientgenomics.org. This website provides information on all project activities, meetings, members, expert groups, and a scientific networking structure.

The above-mentioned bioinformatics databases, tools, and resources will facilitate the identification of the mechanism of action for each micronutrient depending on genotype and environmental factors. These are

- Kinetic modelling of micronutrient bioavailability and efficacy. Physiologically based pharmacokinetic models are routinely used for such pharmaceutical (e.g., [19]) and nutrient analyses [35, 42].
- Metagenomic analyses in response to changing nutrient intakes [4, 10].
- Systems biology modelling of specific parts of the biological networks.
- Flux modelling using stable isotope methodologies [10, 36, 39, 50].
- Predictive modelling of micronutrient interactive effects on genome and epigenome stability.

The MGP operational pipeline

For each micronutrient, a MGP expert group is being formed. The group then acts according to an established information pipeline. As illustrated schematically in Fig. 3, each pipeline starts with acquiring the information needed to construct the biological network, centred around the micronutrient pathways, and cataloguing of SNPs in genes that code for the components of metabolic and regulatory pathways linked to that particular micronutrient. This initial information provides the basis for the micronutrient genetic variation portal. Both efforts are assisted by the bioinformatics team, which incorporates the obtained information in the relevant portals. The expert teams continuously evaluate the available data and information, and identifying those SNPs that have functional consequences.

An embedded goal is also to generate a standardized review describing all the evidence linking genes with a specific micronutrient's metabolism, clinical significance and toxicity in ethno-culturally diverse populations. Each review summarizes existing results on feeding trials and depletion/repletion studies and evaluates all metabolomics, transcriptomics, proteomics, and genetics/genomics data

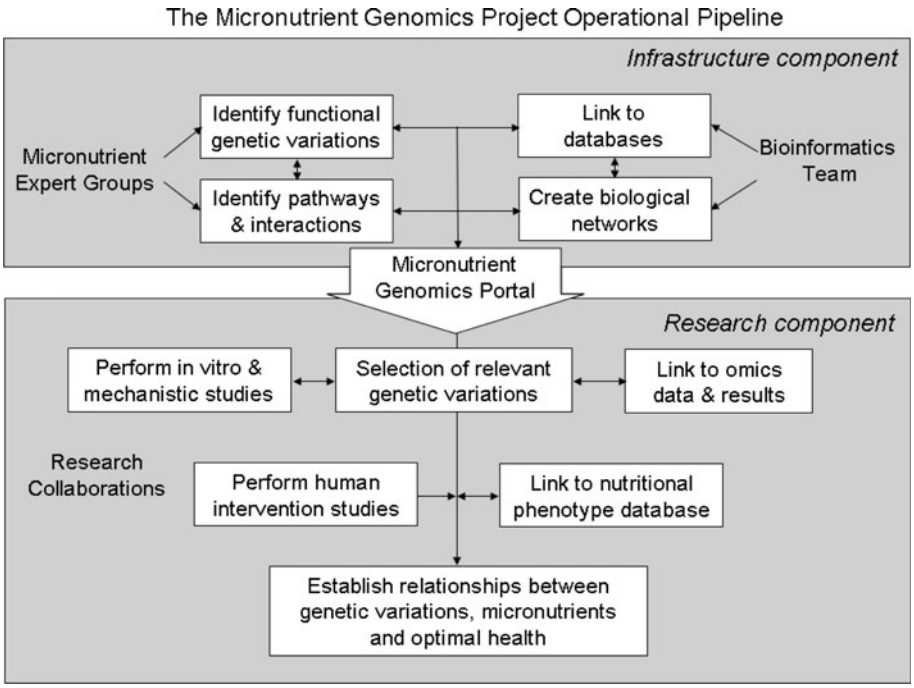

Fig. 3 The Micronutrient Genomics Project operational pipeline demonstrates how the workflow of expert teams and bioinformaticians produces the 'Micronutrient Genomics Portal'. This Portal provides all basic 'omics' information on micronutrients and thus becomes a valuable tool for in vitro and in vivo research projects, ultimately leading to relationships between (individual) genetic variations, micronutrients, and optimal health

for a specific micronutrient. Information on data collection, measurement units and sample preparation and analytical methods will be included so as to better enable comparisons between studies. Micronutrient intervention studies will be encouraged to be entered into the nutritional phenotype database. A systematic methodology for assembling the reviews has been developed to ensure consistent coverage of available information for each micronutrient. These reviews will also identify gaps in knowledge.

The MGP organization

The MGP was initiated in May 2008 at the Nutrigenomics 2008 conference (Melbourne, Australia). Subsequent progress meetings were held during NuGOweek 2008 (the annual European Nutrigenomics Organisation conference) in Potsdam, Germany, at a special workshop in February 2009 in Vancouver, Canada, during NuGOweek 2009 in Montecatini, Italy, and as a satellite of the HVP conference, May 2010. The presentations and meeting minutes are available at http://www.micronutrientgenomics.org. Further information can be obtained from the chair of the MGP advisory committee via the website mentioned above. MGP is collaborating closely with the EURRECA Network of Excellence which has parallel goals for making recommendations for micronutrient intakes for the European populations.

Testing the community effort model

The MGP is primarily based on the contribution of researchers with an interest in its objectives. As mentioned above, the chosen method to accomplish this community effort is to shape micronutrient working teams for each micronutrient. Our current approach is to focus on one specific micronutrient to provide tangible proof-of-concept and guide the development of the informational architecture and web interface necessary to connect users with the available and emerging data. To date, the focus has been the micronutrient selenium, because the many genes, metabolic pathways, and biological processes involved in are reasonably well understood, and some of the interactions have been mapped by several groups. A bioinformatician, a WikiPathways building expert, and a web designer are connected to this team. Again, detailed information on this pilot project can be found on http://www.micronutrientgenomics.org. Once the lessons of this pilot expert team are learned, the MGP will proceed and shape expert teams and further support for all micronutrients.

Managing a community effort: setting rules on how to grow

A community project is owned by the community, so any imposition of ownership impedes its shaping and progress. Managing the MGP should thus be completely transparent, democratic, and facilitating. During the first year of its shaping, this has been a "volunteer-only" model, with decisions made via e-mail consensus and meetings. After this initial phase, the participants proposed a next level of management structure consisting of a governing body. This governing body has an expert advisory group (currently consisting of 6 members) with a chairperson and supported

by a secretariat which assumes responsibility for the website and communication between members. The governing body determines the timeframe for the work output. The codes of conduct on intellectual property, collaboration, and data sharing will be developed at future workshops. The composition of the governing body will be reviewed annually, to be decided during progress meetings, which will occur at least once annually. Progress meetings will be organized as satellites of relevant symposia and conferences (HVP, NuGO, Eurreca and various nutrigenomics conferences and workshops). Location and dates can be found at the MGP website. For the portal to become a community effort, active participation is vital. Researchers, experts, and stake holders are encouraged to enquire about the progress of the work output and when new micronutrient teams will be needed and assembled (for contact details, see the MGP website).

Conclusion

The establishment of a systematic, centralized repository of micronutrient-genomic information will provide the research community and health care practitioners with comprehensive, one-of-a-kind access to current and future advances in all aspects of micronutrient genomics research. Our goal is to create an unparalleled, comprehensive understanding of gene–micronutrient interactions, biomarkers of status, micronutrient requirements, and upper safety limits for individuals in ethno-culturally diverse subgroups of populations. The database will allow for the in-depth exploration of the relationship between micronutrients and chronic diseases in diverse cohorts. Ultimately, the MGP online portal seeks to facilitate the kinds of research advances that will enable informed intake recommendations for specific micronutrients for both individuals and subpopulations, in order to prevent acute illness and chronic disease.

Acknowledgments Funding for the Vancouver planning workshop was provided by a Meetings, Planning and Dissemination Grant from the Canadian Institutes of Health Research (CIHR), as well as contributions from the Office of Biotechnology, Genomics and Population Health of the Public Health Agency of Canada (BGPH/PHAC), the United States Food and Drug Administration (FDA), the European Nutrigenomics Organisation (http://www.nugo.org), Eurreca (http://www.eurreca.org) and the Advanced Foods and Materials Network (AFMNet). This work has been approved for publication by the FDA but it does not necessarily reflect official agency policy.

Conflict of interest The views presented in this article do not necessarily reflect those of the Food and Drug Administration.

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