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From metabolism to metabolomics: Conceptual and applicative aspects related to food science, pharmacology and agrobiology review

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Abstract

In living organisms complex vital processes take place having at their origin biochemical interactions based on physico-chemical transformations which are going on in a continuous, interrelational, reversible or non-reversible way.

The paper presents conceptual data on the new domain of "omic sciences" limited to metabolomics. In this framework, references are made to applicational aspects integrating general principles regarding the methods of separation and detection of metabolites with small molecules

Distinctly, there are presented applications in biochemistry and molecular biology, in genomics, in agrobiology and food science, in pharmacology (medicine). The metabolomics-bioinformatics relationship is highlighted in obtaining "databases" of applicative interest.

Keywords: metabolomics, biomarkers, food science, pharmacology, agrobiology

Introduction

The biochemical interactions in the organism define metabolism, taking into account, mainly, compounds of exogenous origin (nutrients) and compounds of endogeneous origin (metabolites from the internal environment) - originating from the renewal of bioconstituents.

The development of metabolic processes (catabolic/anabolic) specific to nutrients takes place on „native biochemical pathways". According to systems theory, in this way the continuous exchange of substances, energy and information between the organism and the environment is assured. Nutrients metabolism is integrated into the so called „genetic programme" that exists in the genes originating from the parental forms (maternal and paternal).

Progresses achieved in the last decades made possible to open new conceptual and applicative horizons by the development of «life sciences» in connection with various domains of technology/biotechnology and informatics/bioinformatics. Towards the end of the XXth century some new domains of «life sciences» resulted and called as „omic sciences" [1,2].

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«Metabolomics» developed in the framework of «omic sciences», as a subsequent domain of these.

1. General conceptual aspects

The conceptual aspects regarding metabolomics were accredited over time, together with the advances of the investigations in analytical / bioanalytical chemistry [3,4].

The term of „metabolomics" was used for the first time in the literature by Tweeddale et al. [5] in some studies on Escherichia coli metabolism.

Gradually, distinct directions were constituted, that study the chemical compounds derived from interactions specific to different "biochemical pathways". Among these representative are the metabolites with small molecules resulting from the catabolism of nutrients. Some of these small molecules are precursors in the anabolism of the bioconstituents of one's own body.

There are a number of "small molecules" which will become - by expanding research - biomarkers in biochemistry / pathobiochemistry and in physiology / pathophysiology.

From an evolution standpoint one can mention the fact that the first book refering to metabolomics (integrating the approach of the concept of „metabolic profile") was writen in the first decade of the XXIst century [6].

Gradually metabolomics was also integrated into the „computational strategies" and thus came to the attention of bioinformatics [7].

Various attempts to define and explain the theoretical and applicative specific of metabolomics existed.

„Metabolomics can be defined as a study regarding the identification and quantification of the small molecules present in the organism through the analysis of biological samples, based on «specific technologies» with the purpose of determining the metabolic profile" [8]. In the view of the authors, by applying software based methods the analysis, characterisation and interpretation of data, information regarding the work flow, the resulting meta data, standards in metabolomics, statistic analysis methods, the specific of „data bases", etc. become possible.

Thus, metabolomics was estimated as an „instrument" that defines the composition of certain specific molecules, representing the so-called „molecular phenotypes" associated with metabolism. These are often called „metabolic phenotypes" as well.

It is also stated that „Metabolomics combines strategies for the identification and quantification of cellular metabolites, based on performant analytical methods and multivariable statistical procedures for the interpretation of biological data" [9].

2. General applicative aspects

„Metabolomics is a domain of «life sciences» that involves a rapid uses of advanced chemical analytic methods, combined with valuable statistical procedures for a rapid characterisation of the metabolome [10]. Generally, the metabolome is defined as a complete collection of information regarding the metabolites represented by the „small molecules" present in the cells and biofluids of the organism. Characteristic for such metabolites is their molecular mass which is less than 1500 Da."

A presentation which allows to "evaluate the applications of metabolomics" in a global framework given by Gomez et al. [11] is made in Figure 1. This evaluation offers data on the aspects regarding food technologies, human diseases, pharmacology, toxicology, plant biotechnologies, microbial biotechnologies, systems biology, catalytical activity of enzymes, and generally on biological systems. The listed applications advocate for a wide analytical spectrum provided by the samples that constitute the "metabolomic tests" and offer a comprehensive biochemical measurement method ".

According to Clish, 2015, metabolomics represent a comprehensive analysis of the metabolites from various biological samples and constitutes an «emerging technology» that promises a practical, precise way of obtaining information in the domain of medicine as well. In the author's perception „metabolomics offer a detailed characterisation of the «metabolic phenotype» from normal to pathological and my allow precision in the medical domain especially to the characterisation of metabolic disorders [12]. Thus, the following are facilitated: a) discovery of diseases; b) evaluation of new therapeutical targets; c) determination of certain biomarkers suitable for the diagnosis of diseases; d) monitoring therapeutical procedures".

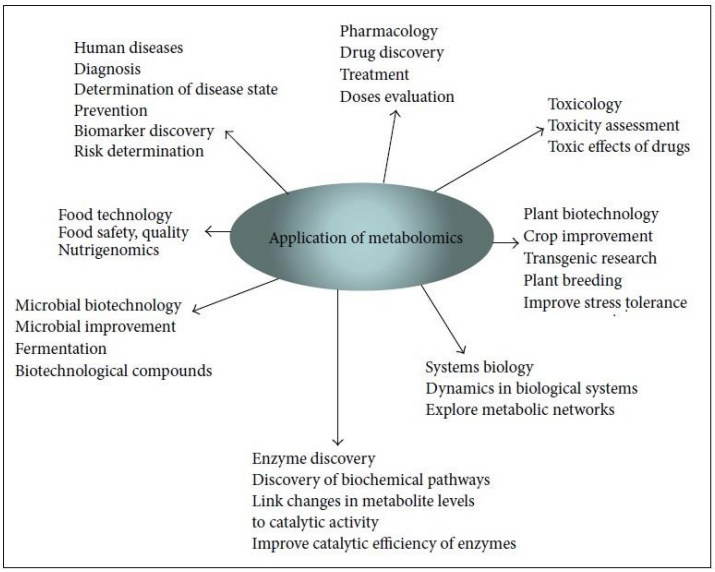

Figure 1. Applications of metabolomics (according to Gomez-Casati et al., 2013)

3. Investigation methods in omics sciences

3.1. General aspects

In omic sciences, generally, and in metabolomics, especially, the perfecting of research regarding the identification and comparative evaluation of certain analytical data based on investigations that use accurate physico-chemical methods (instrumental) is considered. The priority of such methods are the "primary metabolites" represented by "small molecules".

The metabolites represented by "small molecules" include biochemical compounds with a molecular mass ranging from 50-1500 Da. These are in a continuous transformation, ensuring the morphofunctional status of the organism, conditioned by the nutritional input (the digestive pathway - enteral), by the inhalation/exhalation of gases (the respiratory pathway), by the presence of xenobiotics of food and pharmaceutical interest (the enteral/parenteral pathway).

Also, „secondary metabolites" are taken into consideration, partly represented by the „chemical xenobiotics" (food contaminants, drugs a.o.), as well as by the xenobioderivatives resulted from their biotransformation. In this group of metabolites are also included the extraction compunds originating from the "intestinal microbiome".

In metabolomics, metabolites can be evaluated by so-called multiple reaction monitoring (MRM). This type of monitoring starts from the idea of evaluating metabolites from a complex mixture in which various chemical compounds can appear, e.g .: carbohydrates, lipids, proteins, etc. Subsequently, this information on metabolites can be constituted as "standard databases" for metabolomics.

In molecular biology there are also specific applications in which metabolomics (considered as a subsequent field of "omics sciences") makes it possible to perform qualitative and quantitative analyzes of metabolites in various biological samples.

3.2. Analysis of biological samples-specific methods

For the analysis of samples it is considered that there is a flow of stages with metabolomic specificity that include successively: α) collection of samples - from cells and tissues, from plasma, saliva, urine, etc.; β) preparation of samples - concerns certain preliminary standards; γ) analysis of samples - is performed by accurate physico-chemical methods (separation and detection); δ) data acquisition - resides in the registration of analytical results provided by the devices; ε) evaluation and interpretation of data - is made on the basis of various biostatistical analyzes through which are pursued significant correlations having known aspects in physiology / pathophysiology, etc.

An approach to analytical aspects from the point of view of metabolomics involves the use of some methods such as: a) separation; b) detection. Summary data are presented below.

a) Separation methods

For the preliminary evaluation of the metabolites, various separation methods can be used: α) gas-chromatography (GC) - which is suitable especially for the study of small volatile molecules; β) high performance liquid chromatogaphy (HPLC) - with a lower resolution, but with the possibility of detecting polar molecules. The method makes possible the separation in liquid phase and allows the investigation of a wider range of compounds; γ) capillary electrophoresis (CE) - has superior efficiency to previous methods by the fact that it extends the methodological framework by electrophoretic specificity.

b) Detection methods

Among these methods are used, more frequently: α) mass spectrometry (MS) - which is suitable for the identification and quantification of metabolites after their separation by GC, HPLC or CE.

Sometimes there are used "coupled methodological systems" called "tandem methodological systems". The following are exemplified: the GC-MS system; HPLC-MS system (or simply LC-MS). β) electronic ionization (EI) - is a common method applied in tandem with separation by GC (so the GC-EI system; γ) electrospray ionization (ESI) - is a method frequently used for polar molecules with ionizable functional groups; δ) nuclear magnetic resonance (^{1}H-NMR, ^{13}C-NMR, ^{31}P-NMR) - is a spectroscopic method that has the advantage of having high analytical reproducibility. Also, in this case the preparation of samples is easier.

Other more complex physico-chemical methods are mentioned in the specialized treatises on instrumental analyzes.

4. Biomarkers in metabolomics

Biomarkers have been / are used efficiently in various fields of metabolomics. Over time, certain phases have been established for the discovery of biomarkers. Thus, the idea of two distinct phases was outlined: a) in phase I - differentiation of metabolites, is proceeding to: α) identification of biomarkers; β) validation of analyzes; γ) confirmation of the study undertaken; b) in phase II - in which the deepening of the investigations is pursued, is proceeding to: α) studies on accuracy; β) confirmation of the reproducibility of the study; γ) the possible limits of the study; δ) testing of biomarkers on a more extensive case study [13].

The human metabolom is represented by food-derived compounds (nutrients and probiotics from the microbiome) and non-food-derived compounds (represented by chemical xenobiotics of food and / or pharmaceutical interest).

4.1. Types of biomarkers - specifics of investigations

In the case of the human organism, "native biochemical pathways" - defining for nutrient metabolism and "specific biochemical pathways" dependent on the presence of chemical xenobiotics can be evaluated by using biomarkers [14-17].

The experimental data obtained following the laboratory investigations, allowed the establishment of more rigorous criteria for the selection of biomarkers and their classification, distinguishing:

a) Exposure biomarkers. It results from the metabolization of nutrients or the biotransformation of xenobiotics. Structurally, biomarkers are "small molecule" compounds that can be taken from a compartment (cells / biofluid) of the organism and are suitable for analytical quantification.

b) Effect biomarkers. They allow the evaluation of biochemical, morpho-physiological, behavioral or other changes that have occurred in an organism. Depending on the magnitude of the biomarkers, the effects may be directly recognized or may be associated with possible changes in health.

c) Susceptibility biomarkers. They look like as indicators of an organism's innate or acquired ability to respond to the challenge of exposure to a particular substance (eg, excess nutrients, chemical xenobiotics). These biomarkers allow the elucidation of the individual degree of response.

Ideal biomarkers - according to Grandjean et al. [18] - must meet several distinct characteristics: α) a simple collection and analysis of samples; β) the specificity of the biomarker in relation to a distinct type of exposure; γ) the reflection (by the biomarker) only of a reversible subclinical change; δ) application (based on analytical results) of relevant preventive interventions; ε) the use of the biomarker is ethically acceptable.

From the exposed data it can be concluded that, in the domain of food science, biomarkers allow the

detection of contaminants (used deliberately – as food additives) and pollutants (which acced in foods accidentally or deliberately involved in pathobiochemical effects.

4.2. Biomarkers in metabolome reprogramming

Justification of the interest in the discovery of biomarkers was / is also explained by the concern for their use in "metabolome reprogramming" [19].

The strategy in metabolomics, conceived in the acceptance of the possibility of reprogramming, is based on the existence of the similarity of the metabolic pathways and of the chemical compounds with structural and functional identity in different species.

This explains the fact that in pathobiochemistry certain substances can be affected, targeted. This situation leads initially to "molecular injury" and then to "cell damage".

Starting from the "molecular basis" of biochemistry and molecular biology, it was possible to approcah the problems regarding the "metabolome reprogramming ". In such situations, the molecular mechanisms following the beneficial / harmful action of the modified internal or external environmental factors can be elucidated.

These observations have inherently led to the idea of possible strategies that can change environmental factors with application in food science, pharmacology, agrobiology.

In food science - nutrients from both natural foods (plant and animal products) and processed foods (containing certain contaminants and / or food pollutants) are of interest.

In pharmacology - the situation is more complex because it concerns both prophylaxis and metaphylaxis in relation to certain xenobiotics (chemical, physical, biological agents) and therapy in connection with the increase of immunity of the host organism.

This vision, tributary to the last two decades, reveals the trends of metabolomics and the approach of a subsidiary field of it with the generic name of "metabolome reprogramming".

5. Applications of metabolomics

In biochemistry / xenobiochemistry, but also in the domain of food chemistry, clinical chemistry, pharmacology, toxicology, etc. a correlation can be made between the investigations carried out in the "omic sciences" and the appropriate biomarker.

5.1. Applications in biochemistry and molecular biology

5.1.1. Molecular associations in biochemistry and classical biology

The study of genotype and phenotype in biochemistry and classical biology was limited in the first half of the twentieth century due to more modest means of investigation, based only on biochemical analysis and optical microscopy. Thus, gradually (over several decades), it became possible to know chromosomes and genes.

The concept of genome was defined more clearly with the characterization of the morphophysiological and topobiochemical peculiarities of genes in viruses, prokaryotes and eukaryotes.

From this fundamental knowledge more elaborate evaluation of the concept of genotype and, further, to that of genofond was reached. The concept of genotype - defines the totality of the genes of the organism under study in the case of an individual. The concept of genofond - extended to biochemistry, cell biology and genetics - has made it possible to move from individuals to populations. So, it refers to the genotypes of all individuals in a population - called for this reason "innate heritage" of a particular population.

In human biology – largo sensu - the problem of the genofond can be seen in a biological, sociological, economic context, etc.

In agrobiology - the genofond refers to the totality of the genetic information of the plant varieties - in the vegetal kingdom, respectively the totality of the genetic information of the animal races - within the animal kingdom.

Within certain limits, the environment - viewed in its complexity - can influence the phenotypic expression of the genotype. There is, therefore, a possible environmental determinant of the phenotype. This also explains various bioincompatible changes, which can lead to:

mutagenesis, teratogenesis, autoimmune diseases, oncogenesis, etc.

Advances in nucleic acid research initially led to the idea of the formation of so-called "molecular associations" of DNA with small molecules (.eg: polycyclic aromatic hydrocarbons, acridines, metal ions, some cytostatics, etc.) and even with metal ions - chelated forms [20].

With the evolution of knowledge over time, one came to the idea of replacing the old name of "molecular associations" with that of "adducts" and to make the association with "adduction reactions" [21].

5.1.2. Adducts in biochemistry and molecular biology

Biomarkers of major interest for specific investigations in molecular biology include also the adducts of deoxyribonucleic acid (DNA) described in biochemistry and xenobiochemistry.

In this sense, methods for the exploration of nucleic acids were initially developed: i.e. molecule sequencing (e.g. Sanger-Gilbert method), nucleic acid hybridization (homotypic and heterotypic), molecular probe detection (e.g. radiolabeled and chemolabeled), nucleic acid fragmentation methods (e.g. Southern method, Northern method, etc.), amplification method by Polymerase Chain Reaction - PCR; Restriction Fragment Length Polymorphism - RFLP evaluation method; Amplified Fragment Length Polymorphism – AFLP method, etc. - for details see Gârban [22].

There are used currently various analytical methods for detecting DNA adducts [23]. Systematized data on the main methods of detecting DNA adducts are presented in Table 1.

In food science - from the point of view of xenobiochemistry – DNA adducts biomonitoring can highlight exposure to certain xenobiotics, such as carcinogens in food, following their processing (e.g. polycyclic aromatic hydrocarbons, heterocyclic amines, etc.).

In pharmacology, the determination of DNA adducts can be used to diagnose neoplastic diseases, but also for the biomonitoring of the effectiveness of cytostatic chemotherapeutics (e.g. cisplatin, cyclophosphamide.

In the field of toxicology, DNA biomarkers allow the detection of toxics represented by organic compounds (aflatoxins, nitrosamines, polycyclic hydrocarbons) and inorganic (biocides with various heavy metals).

Table 1. Detection methods for DNA adducts applicable for biomonitoring in man (after Phillips and Arlt, 2009)*

General methods	Analytical techniques	Amount of necessary DNA (μg)	Aproximativ detection limits
^{32}P post-marking (isotope marking)	Treatment with nuclease, extraction with buthanol, HPLC and isotope determinations	1-10	1 adduct per 10^{9}-10^{10} nucleotides
Quantitative immunological	ELISA; CIA, IHC	20	1 adduct per 10^{9} nucleotides
Fluorescence	HPLC fluorescence, SFS	100-1000	1 adduct per 10^{9} nucleotides
Mass spectrometry	MS	up to 100	1 adduct per 10^{8} nucleotides
Accelerated mass spectrometry	AMS	up to 100	1 adduct per 10^{11}-10^{12} nucleotides

* Various physico-chemical methods can be used for detection such as: isotopic labeling with 32P (i.e. 32P postlabeling); high performance liquid chromatography - HPLC; enzyme-linked immunosorbent assay - ELISA; chemoluminescence immunoassay - CIA; immunohistochemistry - IHC; synchronous fluorescence spectroscopy – SFS;, mass spectrometry - MS; accelerator mass spectroscopy – AMS, etc.

5.2. Applications in genomics

5.2.1. Evolutionary aspects

Genomics, as a subsequent branch of biochemistry and molecular biology, appeared and developed thanks to the accurate researches in which physico-chemical (instrumental) methods are used. The study of the genome has in view all the genes of an organism, under a natural aspect, as well as the possible changes that occur through time [24-26].

In humans, for example, the genome includes about 30,000 genes. With the help of genomics the following can be studied: the structure of an individual gene, the interactions between genes and the interactions of genes with chemical, physical and biological agents from the environment.

The evolution of genomics was favoured by the genome sequencing possibilities together with the development of knowledge regarding the fragmentation of DNA and the applications of bioinformatics in the analysis of multiple variables. Initially, it was though that it will be used with good performaces only in the discovery of drugs.

The comparison between genetics and genomics is interesting. Genetics, in the classical view, followed the detection of the locus of a gene on the chromosome, then cloning the gene and then determining the DNA from it.

Genomics follows the sequencing of DNA from the chromosomes, then the identification of all genes. This is followed by the maping of genes (going to defining the loci) from the chromosomes and the atempt to establish the characteristics and functions of all genes from the chromosomes.

The applications in genomics also involve the evaluation by biomarkers. The exposure biomarkers have a special importance. These can offer information with a predictive character [27, 28].

In the investigation of the genome, based on molecular biology, from a bioanalytical point of view, two important groups of so called ,,genome technologies" are distinguished: structural genomics and functional genomics. These have applicative consequences. In Figure 2 the interrelationships between the mentioned genome technologies are presented - see Karahalil [29].

A. Functional genomics

Has in view the maping of the genome, the sequencing, the organisation of genes and genome, manipulation of the genome, determining the 3D structure and functions of all proteins, the study of networks (of genes, of proteins). In this genomics numerous applications exist and various parameters are evaluated.

B. Structural genomics

Includes three distinct investigation directions: a) transcriptomics; b) proteomics and c) metabolomics [1]. Brief mentions are given in the following section.

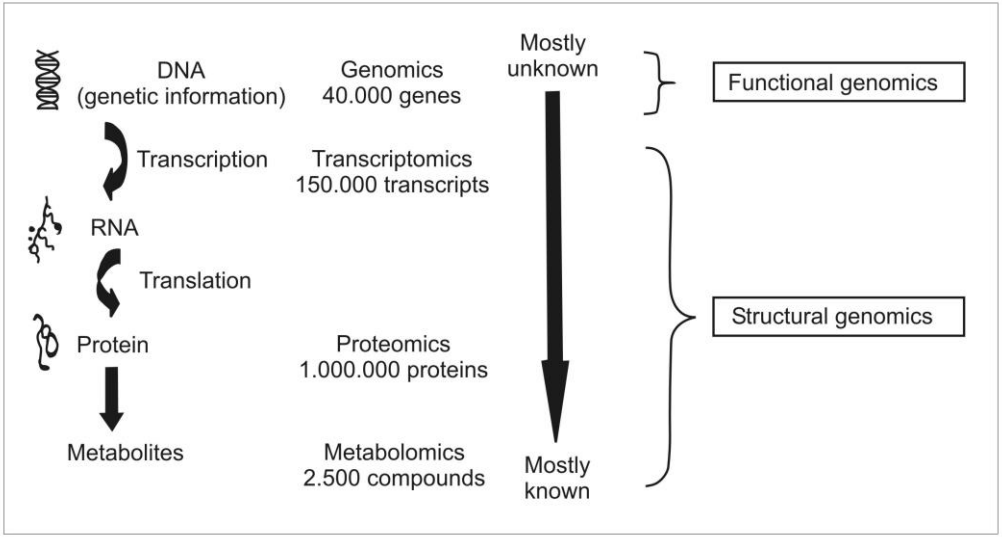

Figure 2. Interrelation between tehnologies of structural and functional genomics (according to Karahalil, 2010)

a) Transcriptomics. Follows the stage of transcription between DNA and RNA. In this situation the susceptibility of the organism to genetic diseases (congenital) and/or to acquired diseases (e.g. the response of the organism to xenobiotics) can be revealed. Transcriptomics has in view the complete set of ribonucleic acids (RNA) that can be produced by the genome. About 150.000 transcriptions can be followed.

b) Proteomics. Is considered the most important direction of structural genomics for the reason that it is involved in the translation of biological information. From this direction of investigation (due to the identification and characterisation of proteins) there were many expectations regarding biomarkers that can offer information for diagnosis and prognosis. Proteomics takes into account about one million proteins.

c) Metabolomics. Constitutes the final direction that can offer information on the concentrations, flows and molecular mechanisms of the metabolites transport. From this perspective the data offered by metabolomics is changing in a detectable way after the ingestion of food, due to the action of nutrients (sometimes accompanied by xenobiotics), as well as after the consumption of drugs. In these situations, for example, parameters such as blood sugar level, cholesterol level, triglyceride levels, creatinine level, uric acid level etc. may be modified.

Therefore, metabolomics pursues the study of the mechanisms that contribute to the modification of metabolic levels and their flux in order to understand in the organism the action of foods and its response to drugs. At the same time, metabolomics make possible to identify new biomarkers that can characterise foods (especially those containing xenobiotics) and of importance for public health.

5.2.2. Gene typing and phenotyping at the present time

Scientific research based on biochemistry and molecular biology has brought back to attention the classical concepts of "genotype" and "phenotype" and the very current applications based on "genotyping" and "phenotyping". These applications proved to be very current from a biomedical (diagnosis), agrobiological (agriculture, zooculture, foods) and pharmacological point of view.

A. Genotyping

In metabolomics, in order to highlight the aspects related to the individual genotype, the determining of DNA sequences from a certain biological sample is carried out, that is later compared to other individual samples [30].

Genotyping - is important in the research of natural genes and that of the variations of genes associated with gene changes. Specific determinations of genotyping are, however, limited to a relatively small number of fractions because of the complexity of the investigation technologies.

In addition to these classic methods, others are also used, such as: random amplified polymorphic detection (RAPD) of DNA genome; testing of allele specific oligonucleotide (ASO).

A mention is made regarding transgenic organisms whose genotyping involves the investigation of a single genome region, considering that this reflects the determination of the genotype. For example, in the case of the transgenic mouse a single PCR evaluation can offer typical information for the transgenic genome (this mention is made because the transgenic mouse in considered, at the present time, the model mammal, representative for numerous medical researches).

Genotyping is also possible in humans (even necessary in certain limit cases). In this situation, for example, paternity or maternity can be tested, the examination of only 10-20 genome regions being necessary, using the method of single nucleotide polymorphisms (SNP).

B. Phenotyping

Phenotyping - by definition, was circuscribed to a sum of investigations by which it was possible to pursue the specific processes and activities having as oal the determination, analysis and prediction (whole or in part) of the visible (external) aspects of an organism.

From a methodological point of view the knowledge of the phenotype benefited of specific analytical methods through which the individual external characteristics were determined/evaluated, at whose origin lie the structural and functional peculiarities of the genomic DNA.

In classical agrobiology the evaluation of the phenotype (a term that today was replaced by that of phenotyping) required a huge amount of work for

the evaluation of agricultural crops in order to record the biological characteristics of the plants, e.g. height, their characteristic traits (e.g. inflorescence, the weight of the grain, the stage of ripening etc.).

In fact, the phenotyping of plants pursued their characterisation by describing their anatomical, physiological, ontological and biochemical properties [31].

In modern agrobiology phenotyping of plants allowed to highlighti of changes that have at their origin peculiarities of the genome represented by DNA. For this purpose the so called ,,cascade" of modifications through which the genetic information starting from DNA is transcribed into RNA (transcriptomics) and later, leads to the formation of proteins (proteomics) is pursued.

Thanks to the applications of phenotyping the selection of desired genotypes depending on a certain interest became possible, e.g. drought tolerance, salinity tolerance, possibilities of production of various agricultural plants [32]. The effects of phenotyping were, of course, encountered in the domain of metabolomics and through this they raised interest for agriculture and food science.

5.3. Applications in food science

Metabolomics can contribute to the development of some efficient analytical methods in food science and food technology, e.g.: a) food quality control; b) identification of ingredients with commercial and nutritional value from unprocessed or processed foods intended for human consumption; c) selective use of certain physiologicaly active chemical compounds in food supplements; d) investigation of the interactions between nutrients and the intestinal microbiome, focusing on pro- and prebiotics [33-36].

An explanation of the relationship between genotype and phenotype in which the environment plays the background role was attempted. Knowing that the resources of the environment vary from one area to another, Walter et al. [32] tried to explain the part of the limited resources of the environment, offering a comparative example between two environments, noted as environment A and environment B (Figure 3).

In the diagram conceived by the authors the link between transcriptome-proteome-metabolome and even ionome (i.e. the role of the metabolism of hydro-electrolytes) is shown. In this diagram one can find mentions about the phenotype in the post-transcription stages, pursuing the morphological and physiological evolution in relation with the genotype.

Although the discussion of the authors refers mainly to the plant kingdom, the mentioned problems, as they result from structural and functional genomics are valid both for plants and animals.

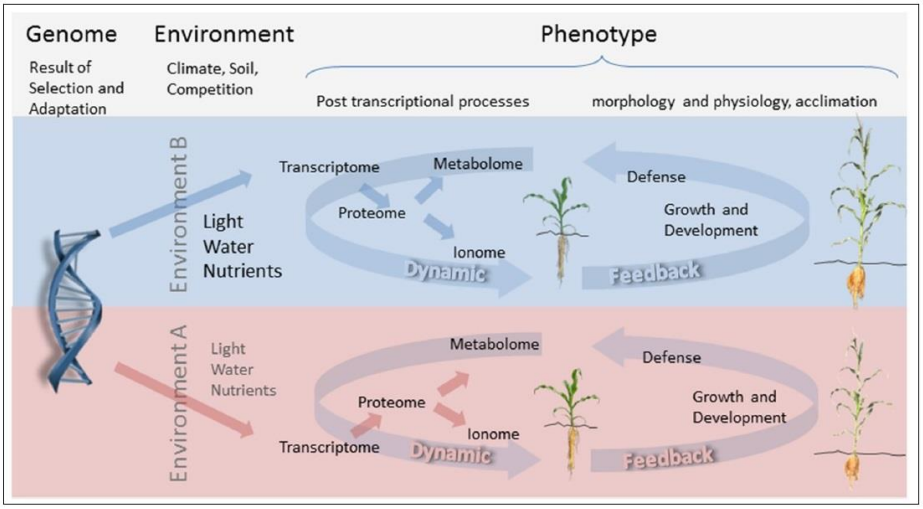

Figure 3. Genotype-fenotype relation between plants in different environmental conditions (environment A vs. environment B) with phenotype post-translational differences (according toWalter et al., 2015)

Evidently, the problem of the resulted metabolites becomes important for food science, being of interest both for the nutrients of plant and animal origin. Moreover, among the formed metabolites chemical compounds that are of interest for metabolomics from a biomedical standpoint can also be present.

Peculiar aspects of metabolomics are found at the frontier between genoyping and phenotyping, both in plants and animals.

In the past, in order to collect data referring to phenotype, days and weeks of field work was necessary. Manual plant measurements were carried out.

In the present, in order to evaluate the phenotype (phenotyping) non-distructive methods are used, allowing us to obtain data in short time - limited sometimes to a few hours. The technology of data aquisition is based on high-performance equipment (e.g. drones, satelites, various portable devices etc.) and specialized staff.

In plant biology phenotyping is considered a distinctive scientific domain that allows nowadays to take certain decisions in agricultural practice [32]. These decisions, with priceless economic consequences (e.g. food industry, light industry), actually reffer to the selection of certain superior genotypes for the cultivars of cultivated plants.

Approaching the problem in animal biology involves the investigation of the metabolome by extinding knowledge on various metabolites in the animal organism. Regarding the ,,metabolic phenotype", in the case of animal organisms references are made in relation with animal biology (growth, development, etc.) but also with their production technologies (e.g. milk, meat, fat a.o.).

In food analysis the chemical compounds originating from deliberate contamination (use of food additives) or accidental contamination, sometimes illicit contamination (food polution) can be detected.

5.4. Applications in medical sciences

In human medicine metabolomics, by investigating lipids, carbohydrates, proteins and chemical mediators with the help of methods specific to clinical chemistry and molecular biology can help us better understand the role of nutrition errors in the prevention of degenerative diseases, autoimmune diseases and even certain neoplasms, as well as the late effects of nutrition errors on health [11,37,38].

One of the subsequent domains of metabolomics has relevance through its applicative nature in personalized medicine. Among its objectives is the identification of pharmaceutical products intended for personalized therapies [39-41].

It is mentioned that at present, in clinical medicine the prognosis, diagnosis and treatment of different diseases is pursued by using metabolomics ,,data bases" that highlights a certain pathological specificity by investigating various cohorts/populations [39].

In medical sciences it is often mentioned that the metabolites analysis offer a wide spectrum of knowledge. Metabolomics, in turn, involves the simultaneous investigation (multiparallel) of a large number of metabolites, in the order of hundreds. Many of these still remain unidentified.

In Figure 4 a general diagram is given according to Patil [42], regarding genomics and proteomics, evolving towards metabolomics.

Metabolomics can lead to the discovery of the factors that influence the biosynthesis of phytochemicals and zoochemicals from which extracts of nutritional interest (physiologically active used in food supplements) and of medical interest (pharmacologically active substances) can be obtained.

It is reiterated that related investigations on metabolomics, ethnonutrition and ethnopharmacology are based on numerous preliminary studies in which accurate physico-chemical methods were used, that allowed the accumulation of information referring to the ,,metabolic profile". This information, sumarised in the so called ,,data bases" contributed efficiently to applications of nutritional and therapeutical interest.

A general characteristic of ethnopharmacology (applying in ethnonutrition as well) resides in the fact that the action of plant extracts was known long before knowing their mechanism of action, as well as the kwon biologically active specificity.

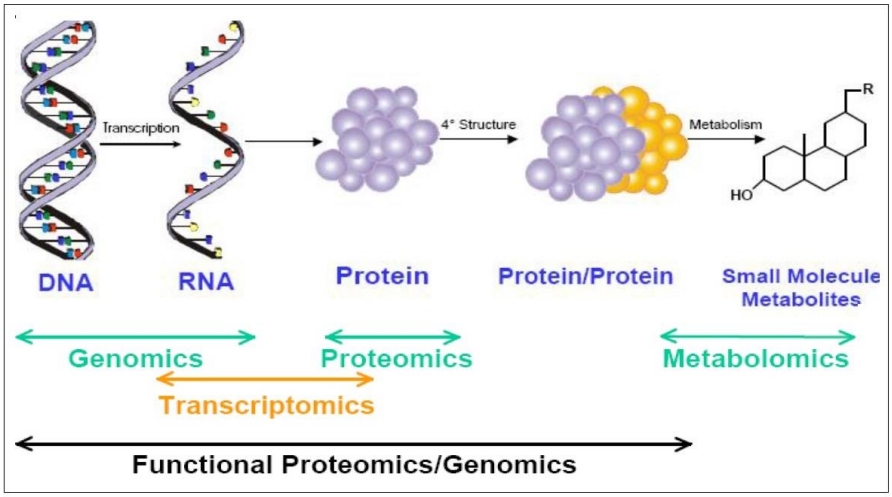

Figure 4. The dinamics of the simulataneous evolution of the interactions from genomics to metabolomics (according to Patil, 2015)

6. Conclusion

Concepts conveyed over time in the study of metabolism offered particularly, ways of qualitative asssement of the ,,metabolic profile" based on the study of the composition of samples taken from tissues and biological fluids. Those data represented the ,,first steps" towards metabolomics.

Towards the middle of the XXth century the physico-chemical (instrumental) methods and especialy their applications were greatly extended. Among these the researches on DNA (oriented towards genomics) had a great importance. Thusly the quantitative evaluation of the ,,metabolic profile" became feasible.

More conclusive concepts regarding the ,,omics sciences" were elaborated, using the terminology of ,,omics technologies". The interpretation and contextual derivation through biostatistics lead to the creation of certain ,,data bases" made possible by the analytical investigations. These present an important applicative area in metabolomics and bioinformatics.

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