Placenta 36 (2015) 329–340

Contents lists available at ScienceDirect

Placenta

journal homepage: www.elsevier.com/locate/placenta

Current topic

Morphomics: An integral part of systems biology of the human placenta

T.M. Mayhew

School of Life Sciences, Queen's Medical Centre, University of Nottingham, E Floor, Nottingham NG7 2UH, UK

ARTICLE INFO

Article history:
Accepted 7 January 2015

Keywords:
Placenta
Systems biology
Morphomics
Nanomorphomics
Quantification

ABSTRACT

Introduction: The placenta is a transient organ the functioning of which has health consequences far beyond the embryo/fetus. Understanding the biology of any system (organ, organism, single cell, etc) requires a comprehensive and inclusive approach which embraces all the biomedical disciplines and 'omic' technologies and then integrates information obtained from all of them. Among the latest 'omics' is morphomics. The terms morphome and morphomics have been applied incoherently in biology and biomedicine but, recently, they have been given clear and widescale definitions.
Methods: Morphomics is placed in the context of other 'omics' and its pertinent technologies and tools for sampling and quantitation are reviewed. Emphasis is accorded to the importance of random sampling principles in systems biology and the value of combining 3D quantification with alternative imaging techniques to advance knowledge and understanding of the human placental morphome.
Results and conclusions: By analogy to other 'omes', the morphome is the totality of morphological features within a system and morphomics is the systematic study of those structures. Information about structure is required at multiple levels of resolution in order to understand better the processes by which a given system alters with time, experimental treatment or environmental insult. Therefore, morphomics research includes all imaging techniques at all levels of achievable resolution from gross anatomy and medical imaging, via optical and electron microscopy, to molecular characterisation. Quantification is an important element of all 'omics' studies and, because biological systems exist and operate in 3-dimensional (3D) space, precise descriptions of form, content and spatial relationships require the quantification of structure in 3D. These considerations are relevant to future study contributions to the Human Placenta Project.

1. Introduction

Biological research has proceeded in two distinct multidisciplinary phases. The analytical or reductionist phase has established the principal building blocks (nucleic acids, proteins, lipids, carbohydrates, etc) of biological systems and revealed that they are organized in 3D space into distinct compartments (division of labour) each of which performs a limited range of activities (division of function). The compartments exist at one or more levels of structural organization ranging from the molecular or supramolecular assemblage to the organelle, cell, tissue, organ and organism. The synthetic, holistic or integrative phase (latterly referred to as systems biology) attempts to describe, quantify and understand the complex and regulated interactions that operate within biological systems at all levels of organization. Systems biology requires a considerable investment in technology and is a daunting task because large amounts of data must be collected, stored, analyzed and interpreted with speed and accuracy. High throughput can be improved in various ways including automation, computation, various forms of statistical and network modelling as well as the development of new technologies.

The placenta is a transient structure that serves the needs of the growing embryo/fetus but its functioning has impacts on health and wellbeing that stretch far beyond its own lifespan [1,2]. Understanding the biology of the human placenta demands the same approach as that for any other biological system (e.g., see Ref. [3]). The Human Placenta Project [4,5] aims to (i) improve existing technologies and develop new ones for examining normal and abnormal placentas in real time, (ii) identify prognostic and diagnostic biomarkers for abnormal pregnancy states, (iii) understand better the association between the placenta and future adult health

E-mail address: terry.mayhew@nottingham.ac.uk.

http://dx.doi.org/10.1016/j.placenta.2015.01.001
0143-4004/

status and (iv) devise therapies to treat outcomes resulting from abnormal placental functioning. Meeting these aims will involve applying a comprehensive and inclusive set of qualitative and quantitative techniques developed by all the biomedical disciplines and all the 'omics research' fields including genomics, transcriptomics, proteomics and metabolomics. It also requires that real-time information is integrated with 'frozen-time' (e.g. fixed tissue) information about placental structure obtained at multiple levels of resolution. This general field of study has been termed morphomics [6]. By this integrated approach, we will be able to appreciate more fully the processes by which the human placenta alters with time, experimental manipulation or environmental insult.

2. The morphome and macroscopic to nanoscale morphomics

Clear definitions have been given recently to terms which refer to the total contents of structures at successive levels of biological organization and to the field of study which describes and quantifies them [6]. The terms morphome and morphomics are more appropriate than anatome and anatomics because, etymologically, the term anatomy refers to the activity of cutting up [7]. By analogy to other 'omes', the morphome refers to the total complement of morphological features within a biological system and morphomics to the systematic study of the qualitative and quantitative characteristics of those structures. Morphomics involves applying appropriate tools and techniques spanning all attainable levels of resolution from the macroscopic (e.g. dissection/prosection, surgery, surface anatomy, medical imaging) to the microscopic and nanoscopic (micro-CT and all forms of optical and electron microscopy). Each level of biological organization contributes a subset to the complete morphome. For instance, qualitative and quantitative analysis of structure at the nanoscale (e.g. using the electron microscope) has been termed nanomorphomics [6].

Quantification is an important part of the field of morphomics. Indeed, since biological systems exist and operate within 3D space, precise descriptions of form and content require the estimation of global and/or individual volumes, surface areas, lengths and numbers of interesting features and the spatial relationships between them. However, in order to reveal the internal structure of a system, we usually apply some form of sectioning or slicing (whether physical/mechanical, optical, tomographic or medical). These various types of slice image must be sampled carefully and properly. Currently, the quickest, cheapest, most precise and least biased way of obtaining quantitative 3D structural information from non-exhaustive slice images is to apply the principles and tools of stereology [8]. An additional benefit is that these tools are applicable across the spectrum of biological organization from the molecule to the organ or organism.

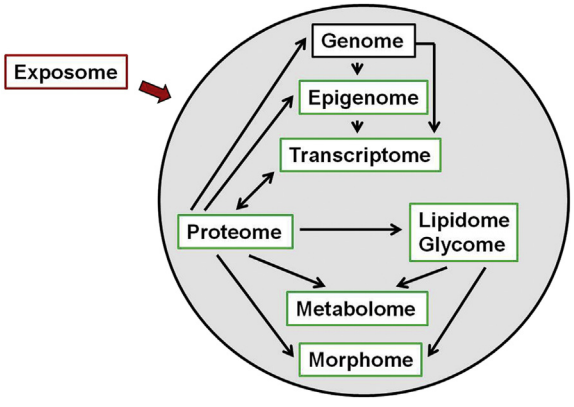

Fig. 1. Morphomics is an integral part of systems biology of the human placenta. The genome is essentially constant but the epigenome is more variable and, with the genome, changes the transcriptome, proteome, lipidome, glycome, metabolome and morphome. The different elements are multiply interconnected and the arrows in this simplistic illustration do not convey all the possible interconnections. All these 'omic' fields of study, together with others not mentioned, contribute to our understanding of the human placenta and how it is affected by the exposome (the varying and various conditions to which it is exposed).

3. Some 'omics technologies' applied to the human placenta

The adoption of 'omics' technologies (Fig. 1) to study the human placenta is relatively recent and published applications are comparatively few. The following is not intended to be comprehensive but serves merely to illustrate the point that 'omics research' on human placenta and its subcompartments in normal and abnormal pregnancies has been initiated by different groups.

3.1. Genomics

The genome represents to the total complement of genes and genetic material within a biological system and genomics applies DNA technology (recombination and sequencing) and bioinformatics to identify genome structure and function. DNA microarrays for studying the genomics of trophoblast invasion have been reviewed [9] and changes have been noted during labour [10].

3.2. Epigenomics

This is concerned with chemical changes to DNA and histones which alter genome function and gene expression without altering DNA sequences. Changes include DNA methylation and histone methylation, acetylation and phosphorylation. The study of epigenetic changes has been facilitated by genomic high-throughput assays [11]. For a review of placental epigenetics, see Ref. [12]. It has been shown that DNA methylation varies widely within the placenta [13] but not for the mitochondrial–telomere axis [14].

3.3. Transcriptomics

The transcriptome is the totality of RNA species synthesized by a system. It is influenced by the genes that are being expressed. Transcriptomics embraces the quantitative study of the expression levels of mRNAs utilizing microarray and RNA-seq technologies. The transcriptome of placentas from normal pregnancies has been characterized [15] and significant changes occur in pregnancies compromised by antiphospholipid antibodies [16] and by maternal cigarette smoking [17].

3.4. Proteomics

The ultimate aim is to identify all proteins (and their modifications) expressed in the system. Proteins may be detected by mass spectrometry (MS) and immunoassays and their post-translational modifications (e.g. phosphorylation, glycosylation) by gel electrophoresis. Protein complexes can be detected by matrix-assisted laser desorption/ionization (MALDI) and electrospray ionization. Interactions between different proteins and other molecules form the basis of interactomics. There have been various applications to human placenta in normal and compromised pregnancies [18–23].

3.5. Glycomics

The glycome is the complete set of carbohydrates (whether present or not in more complex molecules) within a system.