Scientific Research Publishing

Health, 2021, 13, 766-776
https://www.scirp.org/journal/health
ISSN Online: 1949-5005
ISSN Print: 1949-4998

Understanding Human Body Maintenance, Protection, and Modification: Antibodies, Genetics, Stem Cells and Connected Artificial Intelligence Applications—Where Are We?

Raphael R. Ciuman

Mülheim an der Ruhr, Germany
Email: ciuman.raphael@cityweb.de

How to cite this paper: Ciuman, R.R. (2021) Understanding Human Body Maintenance, Protection, and Modification: Antibodies, Genetics, Stem Cells and Connected Artificial Intelligence Applications—Where Are We?. *Health*, **13**, 766-776.
https://doi.org/10.4236/health.2021.137059

Received: June 16, 2021
Accepted: July 18, 2021
Published: July 21, 2021

Abstract

Research in antibody reaction, genetics, stem cells together with advances in imaging techniques and connected referenced-based applications led to a deeper understanding of the physiological mechanisms of functioning and fine regulation of tissue maintenance, protection, and modification in recent years. Meanwhile, the past major research milestones are up to date more than ever. The article comprehensively breaks down these scientific fields in molecular biology, describes the current knowledge, recent advancements and challenges in antibody, genetics, regulation of gene expression respectively, and stem cell research, and gives an overview of the research supporting the areas of artificial intelligence and its connected reference-based applications, which enable the handling of huge genetic and biochemical data amounts.

Keywords

Antibody, Genetics, Imaging, Immunology, Navigation, Artificial Intelligence, Stem Cell

1. Background

It has become common knowledge that the molecules providing stability and flexibility for modification of genetic coding are deoxy- and ribonucleic acids (DNA, RNA) [1] and that specific immunity is ensured by alterations of foreign molecule targeting antibodies, molecules consisting of steady and variable regions. Regulation of gene expression is the key mechanism for cell function and tissue development in toti- or pluripotent cells. For example, a cell cannot ex-

press epithelial, mesenchymal, and endothelial characteristics at the same time. Organogenesis takes part at certain early time points in body differentiation with ongoing genetic expression regulation together with the possibilities and necessities of epigenetic influences. Consequently, there are mechanisms necessary for fine regulation additionally to the current substrate situation [2] and aerobic state [3] or general growth needs by cell and tissue polarity characteristics [4]. At the same time adult stem cells in the various tissues, adult means the reference to the cell lineage they are originated from, contain the original genetic information. For handling this huge amount of biochemical data computational systems were introduced. And according to the huge amount of genetic data, the underlying mechanisms of physiological modification are numerous as well.

2. Immunology/Antibodies

Nowadays, the use term "antibody" reflects the finest way of molecule recognition and elimination by the very intra- and interindividual diverse antibody molecules having the responsibility to recognize foreign molecules and protect their molecules. Paul Ehrlich concluded after animal studies that the organism reacts specifically to foreign proteins with the production of matching anti-protein [5] [6]. The discovery of the ABO system by Karl Landsteiner showed that the human immune system recognizes and targets by few major characteristics, whenever the answer of the immune system has to be fast or immediately [7] [8]. Targeting tissue differences and signaling pathways become more complex according to allowed timelines for organic reaction, e.g. slow and fast regenerative tissue or the various epitopes of the Human leukocyte antigen (HLA) system. Polyclonal antibodies make the immunological answer more precise, whereas polyvalent antibodies broaden the immunological answer. Neutralizing antibodies inhibit the molecule action completely, whereas non-neutralizing antibodies inhibit the target molecule only to some degree. Recognizing multiple epitopes, or cross-reactivity respectively can be depending on current tissue characteristics, e.g. pH or state of the tissue. Besides, the human body works with overlapping mechanisms to guarantee functioning, e.g. from various pain signaling cascades to various nerval receptors. Consequently, there is a step from just recognizing and eliminating to tolerating foreign tissue or to steadily accepting and integrating it, e.g. Graft Versus Host Disease (GvHD).

The reservoir of current existing antibodies represents the preferred design for potential future antibodies in the human body with the generation of a unique antibody variable region. In general, a priming antigen exposure and an exposure in childhood provide a more robust and stable antibody response than a boosting event [9] [10]. Attributable to the fact that slight modifications in one pathway may conserve the concerted properties of the immune system and avoid mesenteric cross-hindrance of proteins and cells. Besides, universal structural elements shorten the time until immunoreactivity [11]. Recombination mechanisms include class switches and somatic hypermutation (maturation of the anti-

body response) of plasma cells as well as cell differentiation of daughter plasma cells [12]. The latter can be divided into transcriptional and cellular events [13] and can be follicular and extrafollicular located [14]. In addition, the plasticity of the immune system includes conformational heterogeneity and the use of cofactor molecules [15] [16], but always allowing immune cell fate determination by affinity and antibody recall [17]. Not to forget, that cell receptor editing is part of the immune response as well [18]. Antibody folding or conformational organization might define the function of the molecule, although the molecular composition is completely different, e.g. hemoglobin and further molecules for oxygen transport in other species [19]. Besides, molecule folding is rearranged after binding, and flexibility in conformation contributes to a stronger antigen-antibody binding following the molecular function [20].

Immunity implies lifelong memory and learning processes in the diversity and variability of the antibody repertoire according to intra- and interindividual, respectively species-specific limits. The extent and predetermination of repertoires driven by genetic factors on the one hand or antigen exposure, on the other hand, remain unclear, as well as individual differences in antibody formation [21] [22]. Although, it is clear whenever illness occurs the body pays currently more attention to antigen exposure. Precise prediction of antibody formation within its superstructure due to conformation variability because of e.g. somatic hypermutation remains a challenge. In summary, intraindividual antibody formation reflects the principles of diversity, variability, conformation and timing.

3. Genetics

All various mechanisms, steady and temporary characteristics and differences of body function are filed in genetics, subsequently regulated by genetic expression and influenced by epigenetics which is by definition inheritable. Regulation extends overall steps in genetic expression, from transcription, over RNA splicing, and transport to translation and posttranslational modification. We are definitely at the beginning of epigenetics and understanding gene expression and epigenetic fine regulation for coding and expression stability in development, survival, and function with already identified examples, like methylation and mutagenesis of methylated bases, chromatin remodeling and histone protein modification, and their importance for RNA editing, genomic imprinting, genomic editing and its crosstalk in the human body [23]. In addition to RNAs responsible for mRNA (messenger RNA) synthesis non-coding RNAs like rRNA (ribosomal RNA), which form together with proteins the two complementary ribosomes, snRNA (small nuclear RNA), which is responsible for transcription splicing mechanisms of pre-mRNA, tRNA (transport RNA), and RNAs like small nucleolar RNAs (snoRNA) which guide chemical modifications of other RNAs, regulate the transcription and translation process to the protein product. Various posttranscriptional RNA modification mechanisms have been studied, e.g. like commonly known polyadenylation at the 3' end [24] and RNA capping on the 5'

end [25], determine RNA stability and degradation [26], ensuring a finely balanced protein production.

The important interaction between epigenetic factors like nutrition, smoking, alcohol consumption, chronic stress, inflammation, microbiota, climate pollution, physical activity and other environmental factors is already well known [27] [28]. Genetics overcomes the time limits of, e.g. immunology and antibody reaction by constant integrating procedures, with every processing and cell division having a necessary time of memory. In addition to identifying the adequate target, challenges of genetic research consist in recognizing the underlying details in the techniques for genetic transcription and translation. Expression stimulation is characterized by the quantity and duration of gene expression regulation. The functionality can either be genetically controlled or by controlling the gene product itself.

The importance of noncoding RNA for regulation is underlined by its various forms. Mechanisms for co- and posttranslational genetic modifications include RNA interference by microRNA (miRNAs), small interfering RNAs (siRNAs), long non-coding RNA or non-coding circular RNA, that alternate quantity of gene expression [29] [30] [31] [32]. It seems that the barriers between DNA repair and modification mechanisms are fluent, just reflecting the general structural principles [33]. Transposons are genetic elements that can relocate between DNA or RNA genomic sites using a "cut and paste" mechanism or a "copy and paste" mechanism to achieve a high replication or transcription rate [34]. In addition, the term retrograde signaling does not only include the impact that proteins and various nucleic acids have on translation and genomics but includes communication of cell organelles as well. The extent and limits of retrograde signaling are an interesting topic of current research. It seems to have important implications, in epigenetics as well and for cell survival in young and old age, e.g., in communication between mitochondrion and cell nucleus and regulation of radical oxygen species (ROS), chromatin and histone formation, and for adjustments in metabolic and stress responses [35] [36]. In contrast, the term anterograde signaling is used for nuclear-encoded factors.

4. Stem Cells

Regeneration with the need for perfect alignment as a precondition for function characterizes the capability of stem cells. Regeneration of blood and immune function by hematopoietic stem cells, which consist of a surprisingly heterogeneous population of multipotent stem cells which collectively possess the potential to form all blood cell types, has lead the way to discoveries and understanding of the gradual differences in the regeneration of organic function in the human body [37] [38] [39]. Autologous hematologic stem cells like megakaryocytes or platelets respectively are becoming the first cells overcoming the hurdles of laboratory reproduction in feeder cell-free settings [40]. For recapitulation, stem cells are by definition undifferentiated cells and totipotent or pluripotent. Adult

stem cells are multipotent, meaning they refer to the cell lineage they are originated from. In contrast, progenitor cells cannot divide indefinitely, and precursor cells differentiate into one specific cell type. Induced pluripotent stem cells are converted mature body cells.

Stem cells can replicate by all possible types of cell division, either symmetric, intrinsic asymmetrical division, and extrinsic asymmetrical division. The latter depends on the signaling of the surrounding cells. Equal for all stem cell-stimulating pathways, either for induced pluripotent stem cells [41] [42], or resident stem cells, by nonmitotic cell transdifferentiation, the mitotic proliferation of a subset of cells or differentiation of resident stem cells, either of epithelial origin (derived from the oral mucosa, amniotic membrane, epidermis, hair follicle), mesenchymal origin (bone marrow, adipose-derived, amniotic membrane, placenta, umbilical cord), neural crest origin (dental pulp stem cells) or by introducing of exogenous pluripotent precursors, e.g. human fibroblasts or adipocytes, is that the challenges consist in controlled cell growth with fully functional and organized cells, variable human response to resorption, recellularization, regeneration, and potentially disastrous consequences, e.g., tissue transformation [43] [44].

Cell or tissue growth and regeneration are always under the control and fine regulation by intracellular, regional, and distant molecules, namely, cytokines, growth factors, or hormones. Regulation is either performed by direct molecule stimulation or by indirect molecule modification before allowing the target molecule its action to unfold. Regulation of intra- or extracellular receptors in quantity or quality, molecule modification respectively, is the precondition before action is allowed to unfold on the genetic level. In contrast to cytokines, which can represent growth factors as well, growth factors have always stimulating properties [45]. Besides, cell communication, often summarized with non-autonomous regulation, with its various molecules, e.g., growth hormones or via neurons with retrograde neuronal signaling up to brain structures like the hypothalamus and for example, the subsequent metabolic rearrangements in mitochondria, has a crucial role for environment adjustments and aging [35] [46].

5. Connected Artificial Intelligence Applications

Acquired data quantities connected with reference-based individualized applications, e.g., in antibody designing, genetics, radiology, navigation, [47] [48], and general reference-based applications in all kinds of analytics and science have become ubiquitous (**Table 1**). The more precise the target or reference data the more successful the match. Consequently, database design, development, and long-term management of specific databases and database collections are crucial. Fast item identification and comparison, data extraction, as well as calculation algorithms in acquired data amounts are the domains of these applications. Further, the applied algorithms help to analyze large databases, either by logic,

Table 1. Glossary of the scientific fields for general and individualized artificial intelligence applications.

Scientific field	Definition
artificial intelligence	general term as summarization for all computational benefits based on data gathering, collection and analysis
bioinformatics	general term for data gathering, collection and analysis in biology with its subdivisions genomics, proteomics, etc., synonymous use with computational biology
computational biology	general term for data collection and analysis in biology with its subdivisions genomics, proteomics, etc., synonymous use with bioinformatics
cloud technology	superimposed computational organization for data resources, extraction and interchange limited to a single organization or available to multiple organizations (public could) previously to peripheral server and customer usage; composed of its subdivisions computing, network, identity, storage, database, content, communication, collaboration, monitoring, queue organization, financial resources
computer assisted medicine	computational assistance and its applications for calculation, decision making and signaling in medicine
cybernetics	organization of regulation and information transfer their structures, constraints and possibilities in systems, e.g. biology, computation, etc.
data analysis	logic: conclusional analytics according to predefined algorithms and margins mathematical optimization: algorithms to overcome data gaps and selection of the best choice based on classification, correlation, regression, probability analysis or reference data network analysis: organization and analysis of item relations, interactions, sequences and consequences statistics: mathematical algorithms for data collection, summarization and extraction probability analysis: mathematical algorithms after executed statistical or network analysis for decision making
database organization	data organized for extraction and presentation in specific or superimposed database collections, synonymous use with data mining
deep learning	algorithms for self-modification based on predefined principles; term mostly used for complicated network settings, synonymous use with representation learning
genomics	sequencing and analysing of the complete genetic material and its structure, function, mapping and evolution of one individuum or species
genetics	analysis of the characteristics of the specific genes in one individuum or species
internet of things	superimposed computational organization for data extraction and interchange on the internet
machine learning	predefined algorithms criteria for data analysis and algorithm modification to optimize its function, e.g. feature detection, classification and usage in feature or representation learning
mechatronics	general term for interdisciplinary engineering of controlled mechanical devices for human assistance with its subdivisions computer, electronics, robotics, telecommunications, synonymous use with automation, electromechanical engineering, robotics
navigation	assisting applications for feedback and signaling of the current or predefined location

Continued

proteomics	one field of bioinformatics analysing the composition, structure, function, interaction and evolution of proteins
radionics	data collection, analysis, presentation and assisting decision making systems in radiology
robotics	general term for interdisciplinary engineering of controlled mechanical devices for human assistance with its subdivisions, computer, electronics, mechanics, telecommunications, synonymous use with automation, electromechanical engineering, mechatronics

artificial neural networks, statistics, probability analysis, or mathematical optimization, with or without machine learning.

Different steps of data analysis might be distinguished, like data acquisition, the definition of target, data (pre) processing like reconstruction and denoising, feature extraction, selection of the relevant features, classification, and interpretation [49]. The validity, reliability, effectiveness, and applicability of the applications have to be clarified for the specific setting [50]. Every step of analysis might be subject to great variability. Therefore, responsible, comprehensible handling of the submitted data and applied analysis methods is an indispensable requirement [51], what will lead to an increased usage of artificial intelligence due to the needs for fast idem identification and comparison, data extraction and calculation in growing data sets in the future. Besides, the value of assisting systems consists in the higher achievable resolutions of the acquired data compared with the human senses, like visuality or haptic perception.

6. Conclusion

Research in antibody reaction, genetics, and stem cells opened the understanding of the resources and mechanisms of human body maintenance, protection, and modification, based on and in continuation with the major discoveries of the past. The handling of huge genetic and biochemical data amounts, particularly in the regulation of gene expression and antibody recombination mechanisms, is supported by the various areas of artificial intelligence.

Funding

The author has no funding to announce.

Conflicts of Interest

The author has no relevant financial or non-financial interests to disclose. The author has no conflicts of interest to declare that are relevant to the content of this article. The author certifies that he has no affiliations with or involvement in any organizations or entity with a financial interest in the subject or materials discussed in this manuscript. The author has no financial or proprietary interest in any material discussed in this article.

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