

OPINION

Mother Genetics

Enrique Daniel Austin-Ward^{1,2,3}

1) Institute for Advanced Scientific Research and High Technology Services - INDICASAT; 2) Hospital Pacifica Salud; 3) Institute of Medical Genetics and Genomics, Caja de Seguro Social, Panama, Rep. of Panama.

Received: 12 de de 2023 / Accepted: December 12th, 2023 / Published: December 31th, 2023.

© The Author(s) 2024. Article published with Open Access.



Abstract

While I was thinking about how to write this brief article, I was looking for the most appropriate sequence of arguments to make my way to justification and acceptance in the consciences, but I ended up deciding to go to the point and simply say: "everything starts from Genetics". And, "Genetics is at the starting point of all intelligent and well-reasoned clinical practice" or at least, it should be. And I am convinced that it certainly will be. Although this is not a need for affirmation and self-convincement, and a statement of this caliber might at first be misplaced because of its possible self-centeredness and apparent lack of humility, nothing could be further from our real intention. The purpose of this paper is to show that we have been witnessing, for a couple of decades now, an unavoidable and urgent paradigm shift in the understanding of the health-disease balance, and that this is not an arbitrary statement, but is based on the robust logic of the literature and scientific evidence. Therefore, this paradigm shift requires special attention so that changes in the understanding of the origin of diseases occur more effectively, as we know that modern science advances rapidly, testing our ability to adapt quickly to all these changes. Along with technical changes, which are the easiest to perceive, there are changes in paradigms or models of thought, which often occur more silently and require changes in health care structures and models that are more difficult to implement, due to the complexity of daily life, and the need for re-education. This means that changes in habits and ways of thinking are required.

While I was thinking about how to write this brief article, I was looking for the most appropriate sequence of arguments to make my way to justification and acceptance in the consciences, but I ended up deciding to go to the point and simply say: "everything starts from Genetics". And, "Genetics is at the starting point of all intelligent and well-reasoned clinical practice" or at least, it should be. And I am convinced that it certainly will be.

Corresponding author Enrique D Austin Ward Email

austin_ward@yahoo.com

Keywords: genetics, health-disease paradigm, changes in health care models.

Bioethical aspects: The author(s) declare that they have no competing interests, and have obtained informed consent from the patients. This work was approved by the institutional ethics committee.

Funding: The authors declare that they have not received external funding associated with this work.

Licence and Distribution: Published by Infomedic International under the Creative Commons Attribution 4.0 International License.

DOI: 10.37980/im.journal.ggcl.20232288

Although this is not a need for affirmation and self-convincement, and a statement of this caliber might at first be misplaced because of its possible self-centeredness and apparent lack of humility, nothing could be further from our real intention.

The purpose of this paper is to show that we have been witnessing, for a couple of decades now, an unavoidable and urgent paradigm shift in the understanding of the health-disease balance, and that this is not an arbitrary statement, but is based on the robust logic of the literature and scientific evidence. Therefore, this paradigm shift requires special attention so that the changes in the understanding of the origin of diseases occur more effectively, as we know that modern science advances rapidly, testing our ability to adapt quickly to all these changes.

Along with changes in technique, which are the easiest to perceive, there are changes in paradigms or models of thinking, which often occur more silently and require changes in the structures and models of health care that are more difficult to implement, due to the complexity of daily life and the need for reeducation. This means that changes in habits and ways of thinking are required.





Figure 1. Graphic representation of the influence of genetics in the Medical Specialties.

We also know that human beings are "creatures of habit". Changing them is not so easy, since, even when this "realization" that the most scientific possible analysis of the mechanisms of health-disease should start precisely from the knowledge of the individual genetic and molecular basis is produced, it is not possible to couple and internalize this form of analysis to our thought processes, even though we perceive that these are already obsolete, due to "force of habit". However much we may wish it, there is often a lack of clarity as to what changes to implement that will bear fruit as desired in order to be at the forefront on firm foundations and that merit the evolution of previous operating schemes. But the old must give way to the new and so we must be willing to let go or to "wipe the slate clean", willing to sweep away what is on the table and... start from scratch.

A clear example of this situation is related to the role of Genetics in daily clinical activity, which is moving towards the vision of a near future in practices such as Translational Medicine, Precision Medicine and self-care processes guided by Artificial Intelligence.

Translational Medicine (TM) can be defined as the interdisciplinary application of biomedical research for the improvement of the health of patients and society [1]. On the other hand, Precision Medicine (PM) consists of identifying which approaches/treatments will be effective for which patients according to the group to which they belong based on genetic factors. The overall goal of PM is to offer patients a treatment tailored to their biological and clinical characteristics on an individualized basis. The notion of Precision Medicine remains focused on the use of large volumes of data (e.g., genomics, transcriptomics, epigenomics, proteomics, metabolomics, and pharmacogenomics) and for individual-centered purposes and applications [2].

In this context of large volumes of information, Artificial Intelligence (AI) accompanies the historical moment to support this circumstance. AI is a broad branch of computer science that deals with the construction of intelligent machines capable of performing tasks that normally require human intelligence, and which human intelligence cannot easily handle due to their volume and complexity. Although the imminent replacement of physicians by these systems is not foreseen, AI can also help patients with follow-up care and the availability of alternatives to prescription drugs [3].

It is not easy to change the "chip" or functional programming of a Medical Science based on solid bulwarks of centuries of clinical practice carried forward in an exceptional way by physicians in their role represented by countless personalities of the clinical environment, and in general by the professionals of Medicine who have always put all their talent and their best gifts of observation, deduction and decisions in favor of the health and welfare of the sick.

Although the figure of this clinician with invaluable gifts, rigorously trained and polished by years of experience, we could anticipate that it will never disappear because it is an essential part of what Medicine is. It is convenient that we realize that we are witnessing this paradigmatic change, where Genetics plays a basic role in this daily practice and where it is perceived



more and more every day in the need for it that clinicians in general have to exercise their medical criteria and their decision making, by requiring genetic and molecular information to carry out an adequate and updated management of their patients.

This really has to do with the way in which Genetics has evolved as a Science and the integration of its advances in medical practice, when Mendel's work was rediscovered only at the beginning of the 20th century by Hugo de Vries, Carl Correns and Erich von Tschermak [4].

Everything starts from Geneticslt is increasingly clear that the individual is basically, and without being reductionist, genetic information that is expressed and modulated by the environment in which he/she is immersed. In this context, what the individual develops as a "disease process" in the circumstances of intrinsic conditions or the way in which the organism responds to both extrinsic and intrinsic conditions and which constitute a defined clinical entity, has a pathophysiological basis related to the genetic profile of the individual, either by how the disorder evolves per se or by the mechanisms at the molecular level that are part of the individual itself and which result in expressions that are often unique in the clinical manifestations and in how the organism defends itself or responds to a particular condition.

Much of what used to make medicine an art (although in my opinion, it will never cease to be so), where interventions were

based on a delicate intuition, part personal talent, and part product of experience, which in the end always ended up being empirical due to the issue of unique and unrepeatable individualities, now does not have to be based on subjective conjectures.

The concepts of "idiopathic", "idiosyncratic" and "random" for example, when confronted with the patient's clinic and which rather alluded to our ignorance of information on individual aspects which until some time ago were impossible to determine, are fading away in the face of the magnitude of information available, which removes the veil on that unknown abyss which was "the individual" and which is determined by its genetic base and its molecular constitution.

Medical specialties have much to advance and to contribute in the fight against diseases if they can start from the solid base of knowledge of the individualities provided by genetic information and all the other areas included in multiomics, such as functional genomics, transcriptomics, proteomics, metabolomics and "interactomics". So, Genetics, which started as the Cinderella among the branches of Biology and Medical Specialties, still ignored, unknown or considered as "rare things", has turned out to be the epicenter of most of the clinical phenomena faced by modern medical practice. To deny this reality is to stubbornly turn one's back on reality, a denial that the future will slowly take care of dismissing.

REFERENCES

[1] Liu Y, Jesus AA, Marrero B, Yang D, Ramsey SE, Sanchez GAM, Tenbrock K, Wittkowski H, Jones OY, Kuehn HS, Lee CR, DiMattia MA, Cowen EW, Gonzalez B, Palmer I, DiGiovanna JJ, Biancotto A, Kim H, Tsai WL, Trier AM, Huang Y, Stone DL, Hill S, Kim HJ, St Hilaire C, Gurprasad S, Plass N, Chapelle D, Horkayne-Szakaly I, Foell D, Barysenka A, Candotti F, Holland SM, Hughes JD, Mehmet H, Issekutz AC, Raffeld M, McElwee J, Fontana JR, Minniti CP, Moir S, Kastner DL, Gadina M, Steven AC, Wingfield PT, Brooks SR, Rosenzweig SD, Fleisher TA, Deng Z, Boehm M, Paller AS, Goldbach-Mansky R. Activated STING in a vascular and pulmonary syndrome. N Engl J Med. 2014 Aug 7;371(6):507-518. doi: 10.1056/NEJMoa1312625. Epub 2014 Jul 16. PMID: 25029335; PMCID: PMC4174543

[2] Jeremiah N, Neven B, Gentili M, Callebaut I, Maschalidi S, Stolzenberg MC, Goudin N, Frémond ML, Nitschke P, Molina TJ, Blanche S, Picard C, Rice GI, Crow YJ, Manel N, Fischer A, Bader-Meunier B, Rieux-Laucat F. Inherited STING-activating mutation underlies a familial inflammatory syndrome with lupus-like manifestations. J Clin Invest. 2014 Dec;124(12):5516-20. doi: 10.1172/JCI79100. Epub 2014 Nov 17. PMID: 25401470; PMCID: PMC4348945.



- [3] Suckale, J., Sim, R.B. and Dodds, A.W. (2005), Evolution of innate immune systems. Biochem. Mol. Biol. Educ., 33: 177-183. https://doi.org/10.1002/bmb. 2005.494033032466.
- [4] Diamond, M.S., Kanneganti, TD. Innate immunity: the first line of defense against SARS-CoV-2. Nat Immunol 23, 165– 176 (2022). https://doi.org/10.1038/s41590-021-01091-0
- [5] Medzhitov, R, Janeway, C. Innate Immunity. N Engl J Med 2000; 343:338-344
- [6] Handly LN, Yao J, Wollman R. Signal Transduction at the Single-Cell Level: Approaches to Study the Dynamic Nature of Signaling Networks. J Mol Biol. 2016 Sep 25;428(19):3669-82. doi: 10.1016/j.jmb.2016.07.009. Epub 2016 Jul 16. PMID: 27430597; PMCID: PMC5023475.
- [7] STING1 stimulator of interferon response cGAMP interactor
 1 [Homo sapiens (human)] Gene NCBI [Internet].
 Nih.gov. [citado el 26 de diciembre de 2023]. Disponible
 en: https://www.ncbi.nlm.nih.gov/gene/340061
- [8] Zhang S, Zheng R, Pan Y, Sun H. Potential Therapeutic
 Value of the STING Inhibitors. Molecules. 2023 Mar
 31;28(7):3127. doi: 10.3390/molecules 2807 3127. PMID:
 37049889; PMCID: PMC10096477.
- [9] Mair B, Konopka T, Kerzendorfer C, Sleiman K, Salic S, et al. (2016) Gain- and Loss-of-Function Mutations in the Breast Cancer Gene GATA3 Result in Differential Drug Sensitivity. PLOS Genetics 12(9): e1006279. https://doi.org/10.1371/ journal.pgen.1006279
- [10] d'Angelo DM, Di Filippo P, Breda L, Chiarelli F. Type I
 Interferonopathies in Children: An Overview. Front Pediatr.
 2021 Mar 31;9:631329. doi: 10.3389/fped.2021.631329.
 PMID: 33869112; PMCID: PMC8044321.
- [11] Entry search OMIM 615934 OMIM [Internet]. Omim.org.
 [citado el 26 de diciembre de 2023]. Disponible en: https://www.omim.org/search?search=615934

- [12] Elvan Tokgun P, Karagenc N, Karasu U, Tokgun O, Turel S, Demiray A, et al. Treatment of STING-associated vasculopathy with onset in infancy in patients carrying a novel mutation in the TMEM173 gene with the JAK3inhibitor tofacitinib. Arch Rheumatol 2023;38(3):461-467.
- [13] Wang Y, Wang F, Zhang X. STING-associated vasculopathy with onset in infancy: a familial case series report and literature review. Ann Transl Med 2021;9(2):176. doi: 10.21037/atm-20-
- [14] Li W, Wang W, Wang W, Zhong L, Gou L, Wang C, Ma J,
 Quan M, Jian S, Tang X, Zhang Y, Wang L, Ma M, Song H.
 Janus Kinase Inhibitors in the Treatment of Type I
 Interferonopathies: A Case Series From a Single Center in
 China. Front Immunol. 2022 Mar 28;13:825367. doi:
 10.3389/fimmu.2022.825367. PMID: 35418997; PMCID:
 PMC8995420.
- [15] Ganeva M, Petrova G, Mihailova S, Gesheva N, Nedevska
 M, Boyadzhiev M, Shivachev P, Stefanov S (2022) STINGassociated vasculopathy with onset in infancy: the first case in Bulgaria and review of the literature,
 Biotechnology & Biotechnological Equipment, 36:1, 773-781, DOI: 10.1080/13102818.2022.2112909
- [16] Fathy M, Saad Eldin SM, Naseem M, Dandekar T, Othman EM. Cytokinins: Wide-Spread Signaling Hormones from Plants to Humans with High Medical Potential. Nutrients. 2022 Apr 2;14(7):1495. doi: 10.3390/nu14071495. PMID: 35406107; PMCID: PMC9003334.
- [17] Zhang J, Zhang L, Chen Y, Fang X, Li B and Mo C (2023)
 The role of cGAS-STING signaling in pulmonary fibrosis and its therapeutic potential. Front. Immunol.
 14:1273248. doi: 10.3389/fimmu.2023.1273248

