Autoimmunity Reviews 15 (2016) 833–842

Contents lists available at ScienceDirect

Autoimmunity Reviews

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

Review

# Personalized medicine. Closing the gap between knowledge and clinical practice

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ARTICLE INFO

*Article history:*
Received 3 June 2016
Accepted 7 June 2016
Available online 11 June 2016

*Keywords:*
Precision medicine
Pharmacogenomics
Autoimmune ecology
Rheumatoid arthritis
Type 1 diabetes
Developing countries

ABSTRACT

Personalized medicine encompasses a broad and evolving field informed by a patient distinctive information and biomarker profile. Although terminology is evolving and some semantic interpretations exist (e.g., personalized, individualized, precision), in a broad sense personalized medicine can be coined as: "To practice medicine as it once used to be in the past using the current biotechnological tools." A humanized approach to personalized medicine would offer the possibility of exploiting systems biology and its concept of P5 medicine, where predictive factors for developing a disease should be examined within populations in order to establish preventive measures on at-risk individuals, for whom healthcare should be personalized and participatory. Herein, the process of personalized medicine is presented together with the options that can be offered in health care systems with limited resources for diseases like rheumatoid arthritis and type 1 diabetes.



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## 1. Introduction

Personalized medicine (PM) encompasses a broad and evolving field informed by a patient distinctive information and biomarkers profile (i.e., clinical, genetic, genomic, and epigenetic/environmental) [1]. Thus, PM is committed to survey, monitor and diagnose risk to provide and present patients with specific treatments spanning from their molecular and particular outline. Though, PM jargon is evolving and some semantic interpretations exist (e.g., personalized, individualized, precision), its main underlying premise is to approach and overhaul medicine by employing integrative biomarkers (short for biological

*Abbreviations:* PM, Personalized medicine; AD, Autoimmune disease; RA, Rheumatoid Arthritis; T1D, Type 1 Diabetes Mellitus; ACPA, anti-citrullinated peptides antibodies; RF, rheumatoid factor; DMARD, disease-modifying antirheumatic drug; HAQ, Health Assessment Questionnaire; DAS28, high disease activity score.

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http://dx.doi.org/10.1016/j.autrev.2016.06.005
1568-9972/

markers) to treat patients not diseases (Fig. 1). In addition, the convergence of the digital revolution and systems approaches to wellness and disease is beginning to lead a proactive P5 medicine, that is predictive, preventive, personalized and participatory medicine, at the population level [2].

The ideal setting of any health care system is to maintain and avoid disease costs in disease prone unaffected individuals, a concept seemingly far from the current reality seen in developing countries, also called third-world countries. The optimal expenditure of loss-prevention activities was outlined as "self-protection" by Ehrlich and Becker [3]. Further, they also showed that insurance and prevention could either substitute or complement each other. According to their premises, primary prevention regroups all the actions, which reduce the likelihood of falling ill [3]. On the contrary, secondary prevention refers to actions that decrease the consequences of an illness (i.e., screening strategies) [3]. A tertiary prevention activity focuses on managing rehabilitation strategies and programs to recover functionality, in order to facilitate incorporation back into society.

Struggling with their economical capabilities developing countries offer health care services to an ill and undiagnosed population; thus making preventive medicine feel as a delicacy that only organized and well established health care systems are able to offer. Nevertheless, a generalized preventive screening strategy, will not save health care costs unless it is targeted to selected individuals within a population [4,5].

Optimal drug selection and dosage for disease are limited by the unawareness of the unique genetic and environmental/epigenetic burden each individual pertains. The role of PM in this scenario entails the usage of systemic information of an individual, by using his medical and familial history, environmental/epigenetic expositions and genetic/genomic factors, to envisage the likelihood and possible disease outcome [6]. Environmental exposures to exogenous agents arise from both external and internal sources. The exposome [7] represents the combined environmental exposures from all sources that reach the internal chemical environment involving the totality of exposures from conception onwards, as a matter of critical interest for understanding the environmental causes of disease.

First world countries are optimizing health care and changing disease burden by introducing PM and focusing on costly pathologies such as autoimmune diseases (ADs), but can this apparently costly approach be introduced in developing nations? [6]. This document is aimed to connect and describe the gap between PM in developing countries and the processes of PM that can be offered in health care systems with limited resources in diseases like rheumatoid arthritis (RA) and type 1 diabetes (T1D).

## 2. From personalized to precision medicine

PM aims to recognize which interventions will be most effective on the disease outcome of an affected individual based on environmental/epigenetic ecology, and their genetic and molecular landscape. This encompasses the measurement of disease predisposition, screening and early diagnosis, prognosis assessment, pharmacogenomic measurements, and disease course monitoring. All of these interventions might be able to target given populations limiting the burden of the disease, and in some cases avoiding it [8]. Recently developed high-throughput omic technologies (i.e., genomics, transcriptomics, proteomics and metabolomics) have led to rapid progress in data input on healthy and affected individuals, however, the silver lining for association studies coming from this approaches is distant of general acceptance given the current scarcity of clinical utility [6]. Thus, genetic testing consideration for a specific pathology should be supported when: 1) existence of a high risk of developing disease, 2) disease considerable morbidity and mortality rates and 3) the possibility of a tangible intervention.

In lieu of a proof-of-principle, clinical pathologies lead us to consider disease as either an independent entity or a diverse set of traits governed by common physio-pathological mechanisms that are prompted by environmental assaults throughout life. This had led the field to focus on individuals that share a clinical course of disease, respond similarly to treatment, and/or present a higher mortality or a

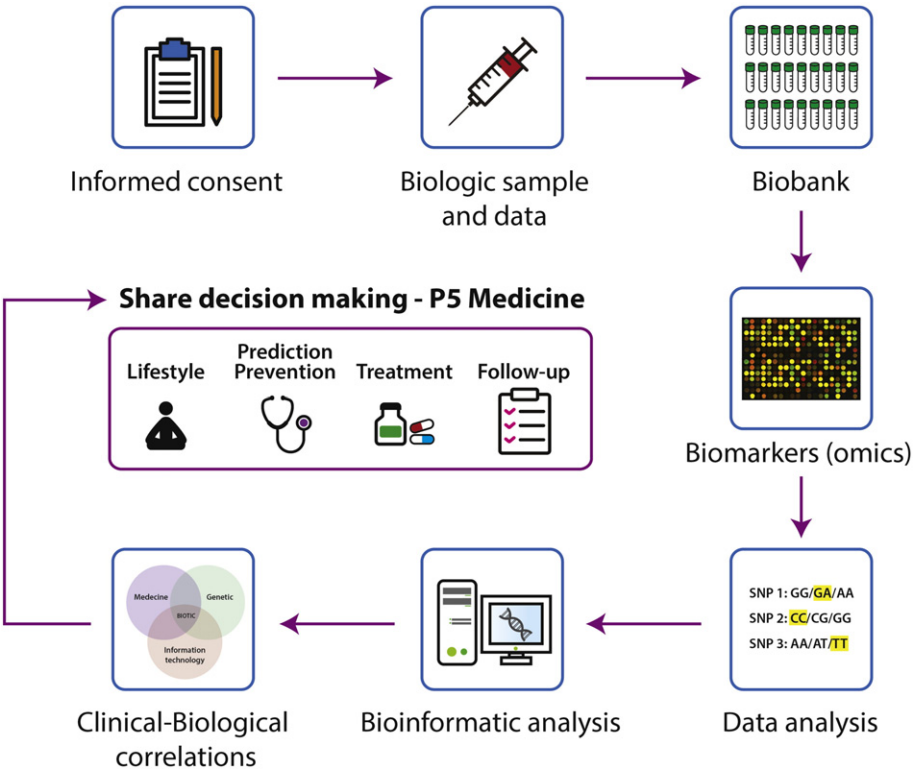


**Fig. 1.** Steps on the road to personalized medicine.