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# Perspective: Personalized and Precision Medicine (PPM) hold the Hi-Tech Future for Healthcare via Biodesign to Secure the Human Healthcare and Biosafety

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Healthcare is undergoing a transformation, and it is imperative to leverage new technologies to support the advent of Personalized and Precision Medicine (PPM) (Fig 1),

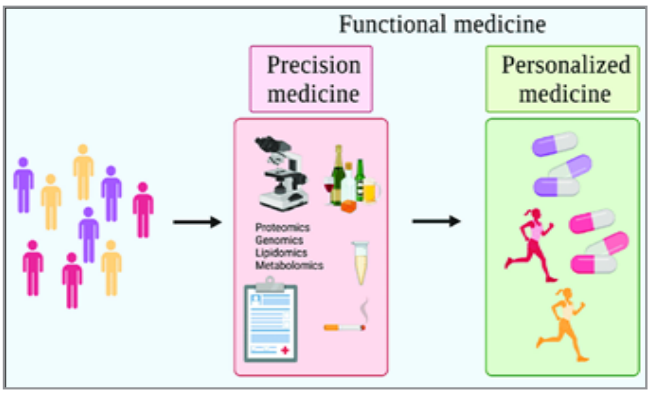


**Figure 1:** Schematic Model of Precision and Personalized Medicine (PPM)

Precision vs. personalized vs. functional medicine. Precision medicine identifies differences in individuals, categorizing based on environmental, biological, and psychosocial factors. Personalized medicine takes these differences and implements preven-tions/treatments tailored to the individual. Functional medicine is an overarching term that seeks to encompass both precision and personalized medicine.

which, in turn, has being the grand challenge to forecast, to personalize, to predict and to prevent is rooted in a big and a new science generated by the achievements of Biodesign-related impacts whilst integrating OMICS platforms and Bioinformatics as well.

It is necessary to create a fundamentally new strategy based upon the biomarkers and targets to have a unique impact for the implementation of PPM model into the daily practice, biotech and pharma. It would be extremely useful to integrate data harvesting from different datasets for ap-plications to thus provide more tailored measures for the patients and persons-at-risk resulting in improved outcomes including diagnostic, preventive and therapeutic tools based on the latest achievements of engineering and design.

The development and application of systems strategies to biology and disease are transforming medical research and clinical practice in an unprecedented rate. Biodesign is a kind of the innovative applied science that aims at making scientific discoveries available for application in relation to life sciences, medicine and healthcare services. Biodesign is thus an area of research and applications that aims to improve human health and longevity by determining the relevance to human disease of novel discoveries as applicable to PPM.

This tremendous revolution being driven by the impact of PPM and aimed to unveil the global secrecy of the Hi Tech has come in the late 20th and then continued in the 21st century, with smart cross- and transdisciplinary technologies and PPM has witnessed interdisciplinary technology innovations in healthcare with a continuous growth in life expectancy across the globe.

As PPM becomes a greater focus in healthcare, biotechnology, biomanufacturing and bioindustry continues to play a big role in its future. PPM holds tremendous potential to remake the healthcare industry. By applying a deeper understanding of diseases with richer patient data and advanced analytics and then modeling the pathologies, PPM can help physicians tailor medicines and nutriceutics to the needs of individual patients, rather than by broader populations, leading to better outcomes at potentially lower costs [1-4].

So, the goals of PPM and Biodesign as a tandem in academia and bio-industry are complementary. Thus, a balanced approach that encourages partnership between those entities could establish a positive feedback loop in which benefits raised in academia would lead to the development of new products in biotechnology, biomanufacturing and bio-industry and then to be implemented in clinical practice.

To really understand PPM, we would have to understand the various fields of Biodesign-based translational applications that provide Systems Biology-related and OMICS tools to exploit and practice PPM (Fig. 2A, B)!

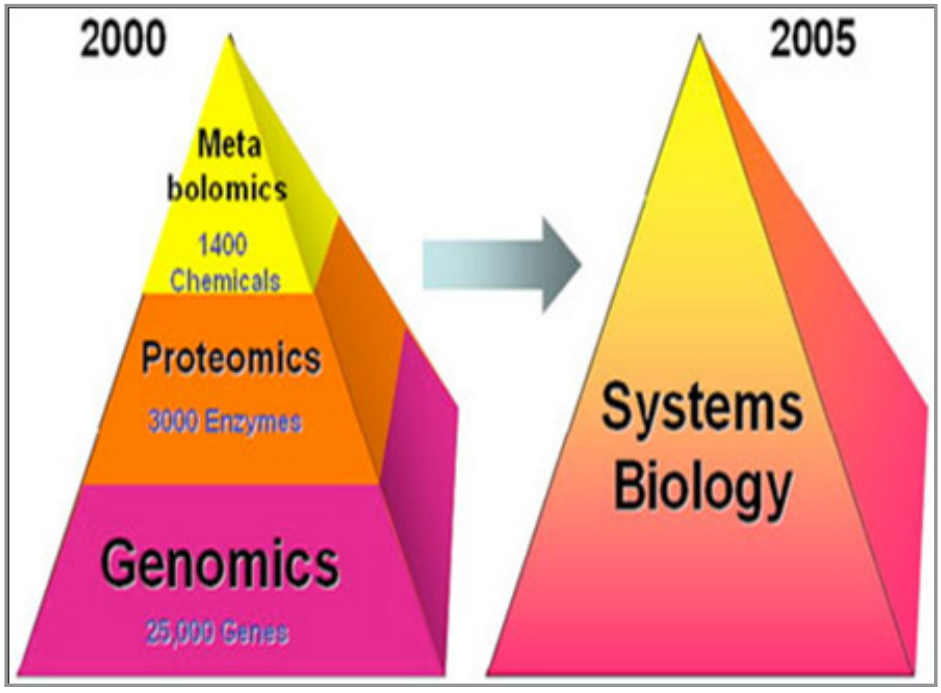


**Figure 2A:** Systems Biology-Related and OMICS Tools to Exploit and Practice PPM

Systems biology incorporates the whole workflow from experimental design and data management through data acquisition, processing and modelling to visualization and interpretation of the experimental findings. The goal of systems biology is to discover new emergent properties in order to better understand the entirety of processes that happen in a biological system. Some of the areas of study are listed below, along with the associated OMICS-technologies being integrated into OMICS portfolio

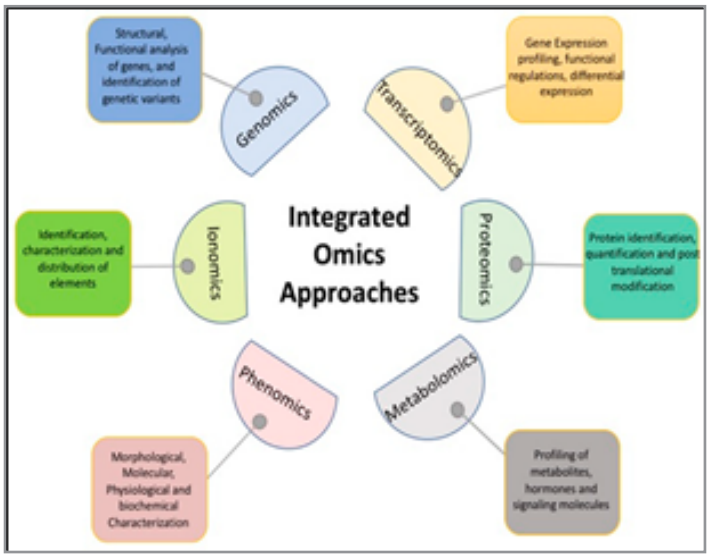


**Figure 2B:** Different OMICS Branches as an Inte-grated Portfolio being used Individually or in an Integrated Manner in Design-Driven Biotech (Build-ing Blocks of OMICS Approach in PPM-Related Areas)

OMICS refers to collective and high-throughput analyses including genomics, transcriptomics, proteomics, and metabolomics and others that integrated through systems biology, bioinformatics, and computational tools to study the mechanism, interaction, and to assess function of cell populations' tissues, organs, and the whole organism in a non-targeted and non-biased manner. Therefore, identification and OMICS-based profiling of multiple biomarker profiles possess the greatest statistical power and reliability for future screening/diagnosis/monitoring/treatment strategies. Development of OMICS-based discriminatory biomarkers for sub-clinical (pre-early) and predictive detection, as well as novel targeted interventional and therapeutic strategies are crucial for an individualized healthy life as well as disease management.

The human genome holds the clues to diverse diseases and improved quality of life. Provocatively, one can raise a question whether in the genome resides a signature for healthy disease-free life? What would it take to approach wellness of human beings from a health rather than disease perspective? So, Genomics is considered to be a set of the unique biomarkers and thus the molecular tools to probe genome for its quality and now even be tested to secure genome profiling (Fig. 3).

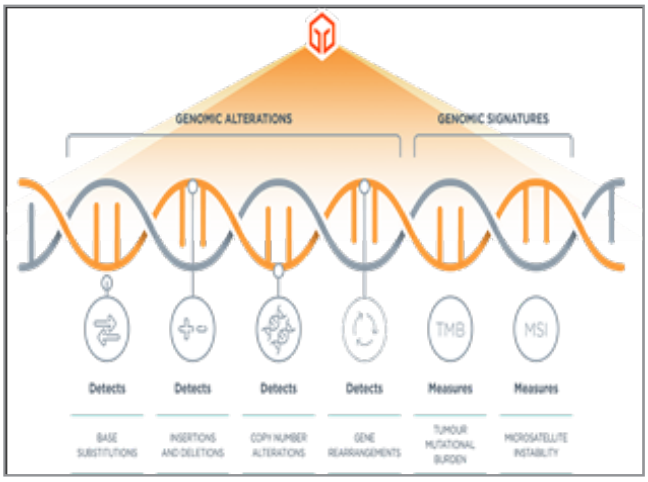


**Figure 3:** Principles of Genome Profiling

Genomic profiling (CGP) is a next-generation sequencing (NGS) approach that uses a single assay to assess hundreds of genes including relevant biomarkers, as established in guidelines, for therapy guidance. The ability to profile has launched a worldwide trend known as personalized & precision medicine (PPM), and the fusion of genomic profiling and pharmacogenomics is paving the way for PPM for cancer. The profiling is coupled with information about targeted therapies available to patients with specific genotypes. For instance, investigations into the genomic profiles of tumors have enabled clinical labs to identify mutations driving can-cers, which provides labs and clinicians with actionable in-sights for a better-informed course of targeted treatment. There are several methods available for genomic profile investigations including single-marker methods, sequencing of hot spot panels and comprehensive genomic profiling, with each method offering its own advantages.

Currently, particular attention is being paid to the development of pathological genomics, which allows not only for molecular genetic diagnostics, but is also an important step to determining the intensity of RNA transcription and protein translation in relation to the onset and development of diseases. Designed genetic tests can help to:

- Diagnose disease
- Identify gene changes that are responsible for an already diagnosed disease
- Determine the severity and aggressiveness of cancer
- Guide doctors in deciding on the best medicine or treatment to use for
- certain individuals
- Identify gene changes that may increase the risk to develop a disease.

Pharmacogenomics-Related Testing is aimed at tailoring drug therapy at a dosage that is most appropriate for an individual patient, with the potential benefits of increasing the clinical efficacy and individualized safety and identifies individual differences in how well or badly people re-spond to particular drugs [2,6].

Pharmacogenetic tests can be used to predict and to target medicines to good responders or to identify whether an individual has an increased risk of a specific adverse drug reaction from a particular medicine (Fig. 3)

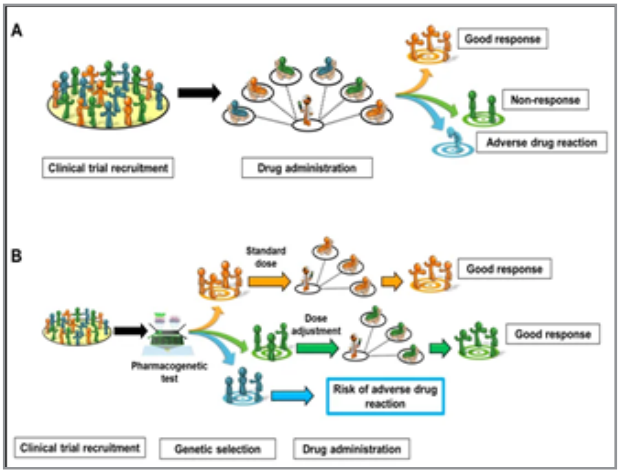


**Figure 3A:** Comparison of two Drug Prescribing Strategies

A: traditional treatment plan without additional genetic testing. B: considering the genetic characteristics of patients when prescribing a drug, including the genetically determined response of the body to the drug in order to adjust the dose

If genomics is rooted in the development of DNA and RNA sequencing techniques, Biodesign-related methods for the identification of individual proteins and antigenic determinants contained therein play a fundamental role in proteomics.

Proteomics relies fundamentally on the use of kits, including immunochemical tests, protein micro-sequencing techniques, high performance liquid chromatography (HPLC) with mass-spectrometry, and on protein microchips for high throughput screening.

A combination of genomic and proteomic/metabolic biomarkers and tools to reflect the complexity of all network pathways in cells at given points in time, are becoming of great significance to be applied in PPM, and need to be translated into the daily practice to predict risks of the chronification and thus of disabling [7].

Molecular Imaging (Fig 4A, B) is defined as the ability to visualize and quantitatively measure the function of biological and cellular processes in vivo and has enormous relevance for patient care: it reveals the clinical biology of the disease process and has the potential to personalize a patient's care. PPM and molecular imaging will enable us to accelerate and improve cancer management in future medicine.

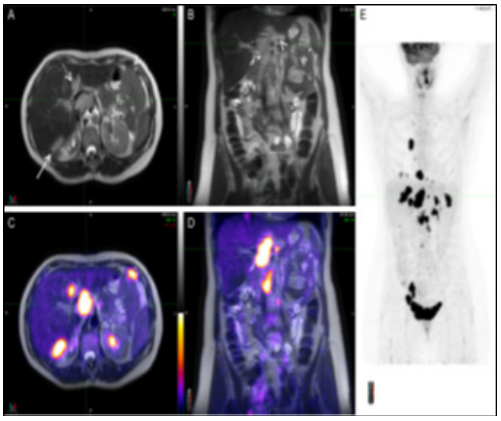

**Figure 4A:** A Typical Representative of the PET/MRI Molecular Imaging Benefits in PPM-Related PPO Cancer Care

Staging PET/MRI scan of a 56-year-old woman with ovarian cancer. The MRI images (A and B) show multiple lesions abutting the liver posteriorly (long arrow), involving the porta hepatis (short arrow) and seeding the peritoneum (arrowheads). A round, well defined lesion with same features is also visualized in segment IV of the liver (dotted arrow). On PET/MRI images (C and D) the lesions earlier described, and others not so evident, are depicted by high FDG uptake confirming their malignant nature. Maximum intensity projection of the whole body (E) reveals several lesions both in the chest and abdomen.

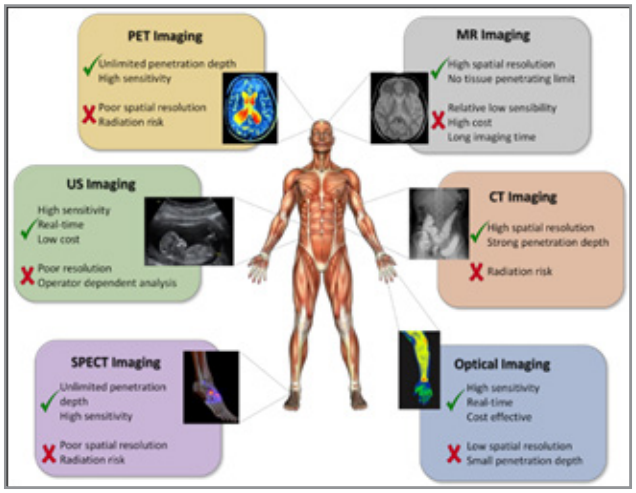


**Figure 4B:** Molecular Imaging Techniques through the View of Biodesign

Molecular imaging techniques allow an individualization and optimization of therapy on a patient basis noninvasively. The availability of new hybrid scanners, like PET-computed tomography and PET-MRI allow the combined assessment of changes in morphology and function and are a unique tool for personalized cancer treatment.

The development of new specific tracers will enable a more accurate assessment of a therapeutic result.

In this context, the designed magnetic nanoparticles have been positioned as strong candidates for diagnostic agents as they provide very good imaging performance. Furthermore, thanks to their high versatility, when combined with other molecular agents (for example, fluorescent molecules or radioisotopes), they highlight the advantages of several imaging techniques at the same time. These hybrid nanosystems as a product of biodesign can be also used as multifunctional and/or theranostic systems as they can provide images of the tumor area while they administer drugs and act as therapeutic agents [8].

Advances in multimodality imaging, integrating anatomical and functional features of tumors, have allowed guiding clinicians in a prompt decision of the effectiveness of treatments in individual patients, thus reducing therapeutic failures. Indeed, molecular imaging methods allowing in vivo characterization and measurement of biological processes at the cellular and molecular level can detect mechanisms of drug resistance and avoid the use of an ineffective treatment in nonresponding patients. In addition, this approach can identify specific molecular targets, allowing the selection of patients for novel therapies (9).

The emergence of a large amount of unstructured information as a result of research is inconvenient. Such information overload is now being resolved by means of two unique technological platforms - BI and Artificial Intelligence (AI) for the analysis of Big Data being harvested from screen-ing, scanning and assessment procedures (Fig. 5A, B)


**Figure 5A, B:** Bioinformatics and Artificial Intelligence and their Contents as Applicable to PPM and PPM-Related Biodesign Innovations

Those two platforms are expected to provide professional communities with the means to mine, integrate, store, process and interpret large quantities of data, as done never before (Fig 6A, B) [10].

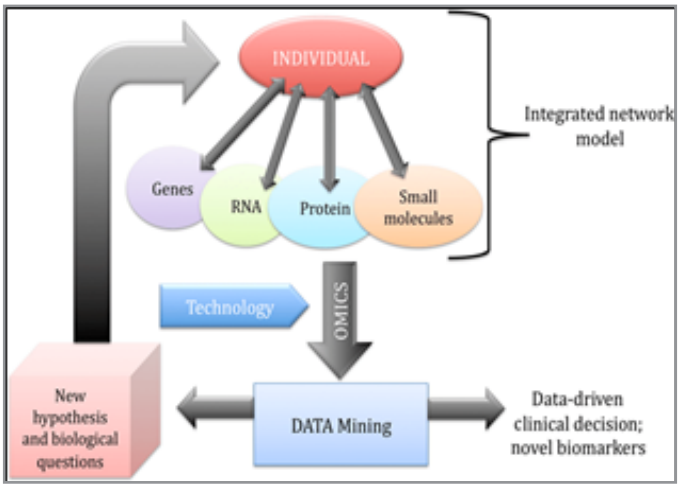


**Figure 6A:** Systems Biology & OMICS data Towards Data Driven Clinical Decision Sup-port

Systems biology integrated network OMICS data contribute to find biomarkers of the disease that contribute to clinical decision-making and may induce new hypothesis and biological questions to be tested.

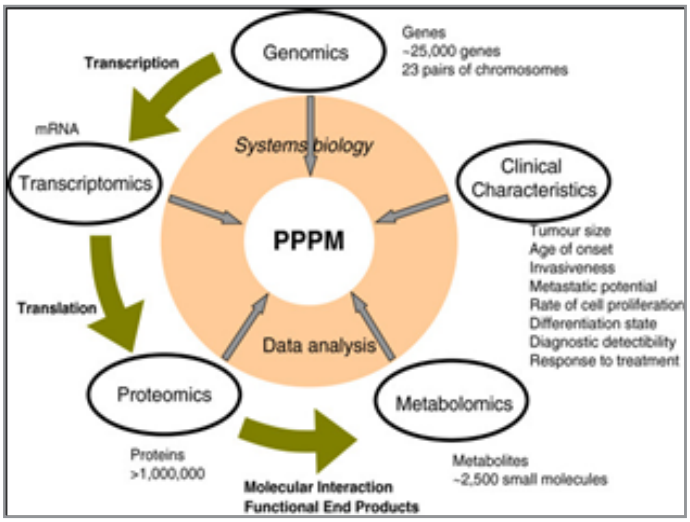


**Figure 6B:** The Contributions of 'OMICS' and Systems Biology to the Practice of PPM

A real bioinformatics challenge has been interpretation of data resulting from the sequencing of the human genome. Furthermore, with the most recent advances in DNA sequencing this field moves rapidly to integrate sequence information from individual patients in real time and to understand the latter through the view of digitalization. Thus, the BI-related armamentarium is be-coming open and thus able to provide the newest technological support for the PPM health care model being implemented into the daily practice.

So, Biodesign-driven BI is a growing domain of PPM. And we believe that BI will help fuel the disruptive innovation needed to advance PPM to standard of care. Manufacturers compose drug labeling to market their product and to inform consumers of the associated risks, thus, information in its current form may not be appropriate or accessible for use by prescribing physicians. BI research can help facilitate personalized medicine practices such as biomarker-informed pre-scribing by designing, implementing and evaluating new and creative techniques and technologies.

In this sense, Biodesign seeks to coordinate the use of new knowledge in clinical practice, bio-tech and biopharma and to incorporate clinical observations and questions into scientific hypotheses in the laboratory. Thus, it is a bidirectional concept, encompassing so called bench-to-bedside factors, which aim to increase the efficiency by which new diagnostic, predictive, prognostic & therapeutic strategies developed through basic research are tested clinically, and bed-side-to-bench factors, which provide feedback about the applications of new treatments and how they can be improved.

The global main goal of Biodesign is to bring together disciplines, resources, experience, and armamentarium within this niche in order to prompt laboratory designed innovations ahead to reach the practice and to thus improve PPM-related practice, including prevention, prophylaxis, diagnosis, treatment and rehabilitation. So, Biodesign is considered today as interdisciplinary field of scientific and medical endeavor, linked with a deep knowledge of drug development, intellectual property, and regulatory issues, all to define optimal mechanisms for translation

of the latest science and healthcare concepts from bench to bedside, and often involving the formation of spin-out biopharma and biotech companies along the way. This is giving rise to a new philosophy and definition of a term of interdisciplinarity and communications to underpin an explosion of healthcare innovations in the very near future to come.

In this sense, Biodesign integrates living organisms into designed solutions and can offer opportunities for new kinds of technologies to facilitate a transition to the home of the future. Many families have had to learn to work alongside each other, and technology has mediated a transition from standard models of operation for bioindustries. These are the challenges of the 21st century that mandate careful thinking around interactive systems and innovations that support new ways of living and working at home to discuss the issues of mutual interest. The outcome will generate an understanding of the role of interactive biodesign systems at home, as a place with extended functionalities.

Biodesigners, Chemical designers and Bio-manufacturers are beginning to realize the promise of PPM, translating to direct benefit to practice. So, partnering and forming strategic alliances be-tween researchers, designers, engineers, clinicians, business, regulatory bodies and government can help ensure an optimal development program that leverages the Academia and industry expe-rience and FDA's new and evolving toolkit to speed our way to getting new chemical tools into the innovative markets.

Currently, the principal priority of Biodesign and Biodesign-related applications are to find potential and highly informative biomarkers with their subsequent selection (Fig. 7).

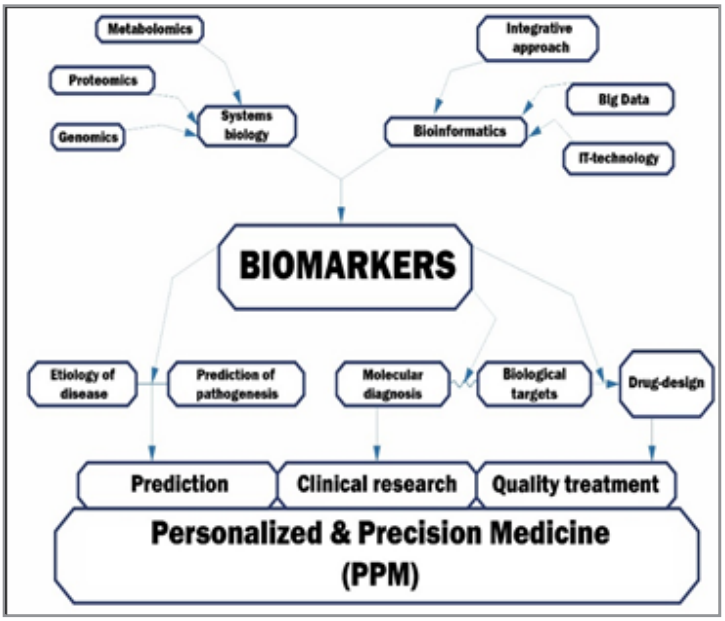


**Figure 7:** Biomarkers through the Integration of Multi-OMICS Datasets are Unique Achievement of Personalized & Precision Medicine (PPM)

A number of applications of PPM (e.g., a growing number of genomic markers of efficacy, adverse events and dosing of therapeutics) have been proposed and have contributed to oncology practice and healthcare as a whole at many points in an individual's (including patient's and person-at-risk') lifespan. So, we might stress that the translation of PPM into clinical care and health policy has lagged behind the pace of basic science discoveries.

Multi-omics data are initially collected from patients and integrated to create their individual molecular profiles, which are then matched to previously defined disease profiles that can guide the selection of treatment. This is achieved either through a match to known biomarkers, OMICS signatures or network/pathway signatures. The appropriate drug is then selected based on this match, to improve the chance of successful treatment and reduce the probability of side effects.

According to the trend-affiliated data, future challenges illustrating the biomarkers world would also include the development of combinatorial mathematical algorithms to handle simultaneous analysis of many parameters (perhaps up to thousands even) illustrating the functional architecture of the interactome-based networks to aid the diagnosis be confirmed. In this sense, it is worth noting that the most import ant achievement of Biodesign is the identification of biomarkers pathogenic pathway [12].

As a strategic product of the applications, biomarkers, that gave impulse to the development of the concept of the precise diagnostic and targeted therapy, provide an opportunity to create pre-cise tools belonging to the fundamentally new generation. And a comprehensive understanding of the relevance and validity of each (regardless to being simple or combinatorial ones) biomarker will be very important to efficiently diagnose the cancer condition and provide appropriate direction in the multiple therapeutic alternatives.

Each unit of PPM is such an independent qualified segment, as a separate «specific brick» of a multidisciplinary functional system. Consequently, PPM-model can permanently work only with interaction between all segments. Creating a damage-proof base, these «bricks» piece together into unified whole, and a completely new technological model can be created, working for the benefit of society.

As you might see from the above-mentioned, PPM has drastically changed and is keeping on changing the landscape of healthcare. In this sense, due to our viewpoint, all healthcare professionals of the future should be educated to deliver patient-centric care as members of interdisciplinary teams, emphasizing evidence-based practice, quality improvement approaches and bioinformatics.

Based on an interdisciplinary Biodesign-driven basis, PPM is developing and producing scientific yield, that can be effectively used in daily clinical practice in the future. No less important is that such a multi-disciplinary alliance should be properly and correctly structured and adopt-ed under real real-world environment.

In this sense, Biodesign, Biotech and Biomanufacturing TRIO, is an example of a dual-use technology: it promises numerous beneficial applications, but it can also cause harm humans or dam-age the environment. For example, there is huge value in our ability to engineer viruses to be more effective and specific shuttles for gene therapies of devastating inherited disorders; however, engineering viruses may also lead to the creation of more deadly pathogens by those intent on harm.

Exchange of ideas and information is vital in promoting and sustaining research and develop-ment. It helps in innovation and in finding newer solutions to long battled challenges. The col-laboration and strategic partnerships to be included would also include private players for attaining competitive advantage.

In the fast advancing era of PPM and PPM-related innovations based on Biodesign-driven suc-cess, stakeholders are inevitably inclining to specificity in the practice of medicine. Pharmaceutical and biotechnology companies are advancing in drug development pathways, which are quick-er with much predictive outcomes in order to save time and money. Regulatory authorities are being pressured to approve drug therapies with minimum adverse reactions and increase efficacy. Government agencies and healthcare agencies have also developed an interest in more precise treatments in order to prevent expenditure on ineffective dugs which will lengthen patients' morbidity span and incur more health bills.

Yet, to this point, the biomedical incumbents have remained unthreatened in the delivery of healthcare; while there have been interesting partnerships, acquisitions, and enabling technology development, there have been no at-scale examples of healthcare disruption by a major tech play-er to date. An important open question is whether one set of players will ultimately win the day, or whether the coming years will see greater collaboration and joint product development that will ultimately transform how most patients interact with the healthcare system.

In this sense, Biodesign is a tool of R&D for unlocking the interdisciplinary barriers and translating rules of nature for solving complex societal challenges to be applied in PPM and PPM-related areas. The major solutions could be translated as high value-added products when biodesign intersects with entrepreneurship which is described generally as the capacity and willingness to develop, organize and manage a business venture to create a societal added value, along with any of its risks in order to make a profit. It entails recognizing the right opportunity, finding resources to pursue the opportunity and creating the right team of biodesigners to do so.

In the conclusion, we would to note that a number of Biodesign-driven applications of PPM (e.g., a growing number of biomarkers of efficacy, adverse events and dosing of therapeutics, or theranosticums, etc) have been proposed and have contributed to clinical practice and healthcare as a whole at many points in an individual's (including patient's and person-at-risk') lifespan.

The next important step in the direction of the PPM approach should be its early adoption in clinics for future medical interventions! To achieve this goal, PPM needs to rely on Biodesign-related data-driven sources of fundamentals, analytical tools and services that draw from the rapidly evolving Hi-Tech areas & healthcare-IT infrastructure.

PPM is shaping the Biodesign-based future of medicine and stands a promising chance of over-taking conventional medicine in the future. So, consequently, in coming year's next generation biotechnologies will reorient medical practice more towards disease prediction and prevention approaches rather than curing them at later stages of their development and progression, even at wider population level(s) for general public healthcare system.

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## Conflict of Interest
The authors declare no conflict of interest.

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