

PERSONALIZED MEDICINE: AN INNOVATION IN HEALTH-CARE SYSTEMPIYALI KHAMKAT¹, VIVEK BARIK¹, BHAKTI BHUSAN BARIK¹, SNEHAMOYEE MOHAPATRA^{2*}, RAJAT KAR³¹Department of Pharmaceutical Technology, Brainware University, 398, Ramkrishnapur Road, Barasat, Kolkata, India. ²Department of Pharmaceutics, Shiksha 'O' Anusandhan, J-15, KhandagiriMarg, DharamVihar, Jagamara, Bhubaneswar, Odisha, India. ³Department of Pharmaceutics, Dadhichi College of Pharmacy, Vidya-Vihar, Sundargram, Odisha, India. Email: snehamayeemohapatra@soa.ac.in*Received: 08 June 2022, Revised and Accepted: 16 July 2022***ABSTRACT**

Personalized medication (PM) is a wide and progressed field of medical science with more accuracy of medication to educate every individual's clinical data. This model categorizes individuals within discrete subject groups with medical accountability, utility, or products being customized to each group based on their expected response. It is an emergent and rapidly developing method of clinical practice which utilizes advanced technologies that give a conclusion concerning to the prognosis, prevention, recognition, and treatment of diseases. The advantages is to improve the usefulness of PM over traditionally approved drugs due to less toxicity and side effect with therapeutic efficacy, which leads to patient stratification, proactive treatment regimens resulting in reduced health-care costs, and ultimately enhanced the quality of life. This review focused to an extensive understanding of personalized medicines as a major therapeutic approach to overpass the health-care problems and highlights the challenges, current strategies, and future prospective.

Keywords: Personalized medicine, Theranostics, Autoimmune diseases, Imaging protocols, Proteomics.

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INTRODUCTION

The vision of medication in the 21st century is all about "the right drug at right dose with right time for right patient." Since the past two decades after the accomplishment of the human genome first project (the concept of personalized medicine), there is a proliferation of pharmaceuticals and scientific promises of the health-care system and revolution [1-3]. With the ability to generate, examine, and interpret genomic-determined information in a useful and economical way, genomics and the logical research of genomes, DNA groupings, and the functional interaction of their genes have flourished to fast drive emerging breakthrough [4]. PM approach is a completed increase of standard technique (one-size-fits-all) to extend our ability to predict which clinical prescriptions which will be secured and strong for the individual patients, and which ones will not be, on account of the patient's, and which ones won't be, because of the patient's one of a kind hereditary profile. Information on PM works with prior infection recognition by employing improved utilization of existing biomarkers and recognition of ahead of schedule genomic and epigenetic occasions in infection advancement, especially carcinogenesis or chronic diseases. This review focused on an extensive understanding of personalized medicines, current strategies their challenges, and prospects.

WHAT IS PERSONALIZED MEDICINE?

Personalized medicine (PM) incorporates an expansive and developing field in health care concerned with patient distinctive data and biological indicators such as clinical, hereditary, genomic, and environmental information [5]. Along these lines, PM is resolved to review, screen, and analyze hazards to give furthermore, present patients with explicit medicines crossing from their subatomic and specific diagram. However, PM develops the understandings that exist (e.g., personalized and accuracy), its main goal is to propose and redesign medication by combining biomarkers to treat patients rather than diseases (Fig. 1).

PERSONALIZED TO PRECISION MEDICINE

PM expects on affected individuals dependent on epigenetic nature and their hereditary and subatomic groups. This incorporates the estimation of ailment predisposition, screening furthermore,

preliminary determination, pharmacogenomics estimations, and disease course monitoring [6].

High-throughput omic advancements (genomics, transcriptomics, proteomics, and metabolomics) have recently caused an increase in data input on sound and impacted persons [7]. PM, covering terms, for example, personalized and accuracy may be termed as an outcome of translational medication, characterized as research to further develop well-being and life span by deciding the significance to human illness of novel revolutions in the biological sciences. Translational medication is a bidirectional idea, which incorporates seat-to-bedside factors that seek to expand the effectiveness of therapeutic methodologies tried in people and bedside-to-seat factors that give feedback about the impacts of treatment. Assessments rely on technologies for diagnosing the disorders and generating innovative hypotheses that based on direct human perception [8].

PERSONALIZED MEDICINE AND FAMILY HEALTH HISTORY (FHH)

FHH is crucial for the conveyance of individual well-being hazard data. A potent FHH can enhance hereditary-based hazard data and connect it into patient consideration because it is a combination of common hereditary, medical problems, and life sciences components. FHH evaluations along with PM would assist with distinguishing people at higher danger for illness, empowering protective and preventive advances, well-being screening, testing, and preliminary treatment as necessary [9,10].

PERSONALIZED MEDICINE AND THE HUMAN GENOME

The consolidation of data from genomes, their sequences, and their ancillary components is currently strengthening the PM (namely, ribonucleotides, nucleic acids, and metabolites) into clinical dynamics: Genome-based well-being measures can be utilized to foresee hazards, screen for transporters, set up clinical diagnosis and prognoses for people, and direct clinical management [11]. Subsequently, human genomic data currently permit suppliers to make streamlined consideration plans at each phase of an illness, moving the concentration from reactive to preventive well-being care [5,12]. At

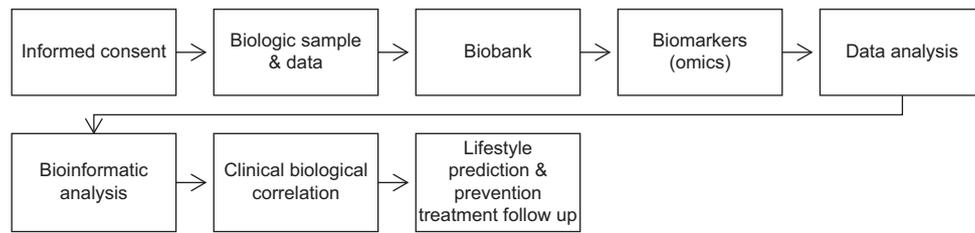


Fig. 1: Process for the development of personalized medicine

present, treatment for chronic disease (red line) happens at the stage in the disease process represented by “typical contemporary intervention” – a phase in the disease process where treatment is most expensive and reversibility prospects are slim. Professionals can use novel genome-based biomarkers to determine the risks and events of a disease [5].

STRATEGIES OF PM

PM used on autoimmune disease

If medical services providers can forecast the course of infection at that point in time as an internal (genome and epigenome) and external (autoimmune ecology) element, medication can be administered in a tailored manner from the primary patient’s encounter. When an infection has fully developed, using secondary and tertiary prophylaxis tailored to each group of patients is a must [13].

Alzheimer’s disease is a complex genetic disease that appears to accumulate disease burden, a condition known as autoimmune tautology. The long-term clinical expression of a specific AD or an aggregate of ADs is dependent on the interaction of normal and explicit HLA, non-HLA alleles with certain epigenetic and environmental factors [14]. Risk scores have been established using unique numerical models and methodologies; in any event, these are better applied to patients that share infectious pathways that determine phenotypes [15].

In-between the diseases, proposals centered toward the development of PM models, there are hopeful and sceptical suppositions. The primary intention is to input additional data accessible which will continue research nearer to the subatomic starting points of infection, therapeutic targets, and making of exceptionally viable medications [16]. Despite the high cost of ADs, intervention on ecological intermediates is based on a main avoidance strategy; they cannot be totally avoided or healed.

EXEMPLARY ILLUSTRATIONS OF PERSONALIZED MEDICINE

There have been a considerable number of instances of medication customized for each patient profile, essentially every one of them dependent on hereditary profiles. Before giving a couple of exemplary models, it ought to be underlined that customized medication can be rehearsed for the treatment of ailment, yet additionally for the early discovery and counteraction of infection.

Numerous early instances of personalized medicines were related to hereditary interceded pharmacokinetic parts of medications. This was expected to some extent to the comprehension of medication utilizing proteins and the task they are performing inside the body in response to drugs. An amazing introduction to the pharmacogenetic properties of drugs as well as hereditary variations in factors that affect the viability of drugs (especially with respect to hereditary variations in drugs utilizing catalysts) [17]. Warfarin is generally utilized as an anticoagulant drug that, if not taken as expected, could cause perilous ADRs. Warfarin focuses on a specific quality, VKORC1, and its metabolism happens to an extent by gene CYP2C9. Normally, it is heredity assortment in both the VKORC1 and CYP2C9 characteristics prompts variety in the pharmacodynamics and pharmacokinetic parameters of warfarin among people, eventually showing variation in people’s reactions to warfarin. The US Food and Drug Organization has hence suggested that dosing for warfarin should be dependent upon a person’s genotype (i.e.,

the portion should be customized for individuals dependent on explicit hereditary variations they have in the VKORC1 and CYP2C9 genes).

Primaquine is yet another excellent example of a drug that should be administered to persons with a certain hereditary condition (PQ). PQ has been utilized to treat malaria effectively in a few regions in the world where malaria is indigenous. In any case, armed forced medical practitioners working previously detected that some of the troopers’ diagnosed by them for malaria were given the medication that became icteric and lethargic. When symptoms finally emerged, “acute hemolytic anaemia” was given a name (AHA). Subsequently, it was being shown that the people displaying AHA after primaquine conveyed variations in the G-6PD gene [18]. At present, the medical practice with PQ, therefore, requires the genotyping of each and every patient to check whether they convey applicable variations in the G-6PD quality which may debilitate primaquine usage for them.

CURRENT EXEMPLARY ILLUSTRATION OF PERSONALIZED MEDICINE

When a patient has a specific hereditary indicator, medications like warfarin, PQ, and imatinib appear to just work without adverse reactions. This has made a significant impact on identifying factors, like hereditary variations, that affect a person’s reaction to many medications and interventions. This goal in developing personalized pharmaceuticals to treat disease and disorder has expanded to include tailored disease surveillance (i.e., early detection shows) and personalized infection prevention techniques.

MUTATION-SPECIFIC THERAPIES

Rather than promoting medication and then identifying characteristics that reduce its viability through observational studies on people who have received it, as is the case with warfarin, PQ, and imatinib, there are now efforts to identify, namely, hereditary profiles of patients and afterward provide treatments that remarkably focus on the profiles. The medication ivacaftor was developed to treat cystic fibrosis (CF) patients who have extremely particular pathogenic abnormalities in the nature of CFTR [19]. An “entryway-like” structure in the CFTR quality’s encoded protein that can open and control the advancement of salts throughout cells coordinates with another structure in the protein that is also encoded for the CFTR quality. On the off chance that the CFTR quality is useless, the gate is shut, causing the development of body fluid and constituents in the lungs. Various changes in the CFTR quality lead to various kinds of dysfunction. Different transformations prompt the gate mechanism to dysfunctional. Ivacaftor is intended to open the entryway for longer timeframes within the sight of specific changes that will in general leading the entryway to be closed. As a result, ivacaftor is only important for the small proportion of CF patients whose CFTR mutations cause this specific gating problem.

Another example includes the arising cancer treatments such as immune therapy. Although there are many sorts of immune therapy, every one of them tries to prime or trigger a person’s safe framework to attack a malignancy. One type of immune therapy makes use of “neo-antigens,” which are frequently equipped for raising a safe reaction when perceived appropriately by the host’s immunity cells, and which emerge in a malignant growth patient’s cancer cells,

and which are regularly equipped for raising a safe reaction when perceived appropriately by the host's immunity cells. Ultimately, this type of immunotherapy works by extracting cells from a patient that intervene in that patient's immune response, similar to T cells, and then directing those cells to expressly see and spotlight on the neo-antigens found in the patient's malignancy. These altered cells are then reintroduced to the patient's body to attack the cancer development cells that are conveying the neo-antigen signals. This type of cytotoxic T-cell medication, like most immunotherapy, has had some success, although it can be quite tolerable for two reasons. To begin with, a patient's neo-antigen profile may be exceedingly unique, to the point where cytotoxic T cells are induced to recognize and attack a specific set of antigens. Second, if "autologous" forms are utilized, the patient's T cells are adjusted and so are not compelled to fill in for another patient, despite efforts to generate "allogeneic" forms in which one individual's T cells are modified and transplanted into the body of another patient [20].

CUSTOMIZING EARLY DETECTION STRATEGIES

If a person is predisposed to an illness or a return of a sickness, that person should be monitored. To make claims concerning verification or indicators of sickness or a pathogenic process, it is now understood that such study should be sought using an "individual threshold" rather than a "population threshold" [21]. Population thresholds are generated from epidemiologic data and population research, such as cholesterol levels >200 being a sign for the risk of coronary artery disease, or a systolic heartbeat >140 being a marker for hypertension, stroke risk, or coronary artery disease. Critical deviations from historical and average legacy are considered indicators of a shift in welfare status, regardless of whether or not those traits are over a population threshold [22].

CUSTOMIZING DISEASE PREVENTION

The use of hereditary data to support personalized disease prevention approaches is based on standard analyses, but it has not yet been widely used in clinical practice. There have been numerous remarkable examples of how the use of genetic information can result in both a reduced risk of infection and lower burdens from routine treatment and screening approaches. A great representation identifies with colorectal disease, which stays the third driving reason for malignancy deaths regardless of being a profoundly preventable ailment.

For instance, in 2018, Jeon et al. described the precise application of extended hazard forecast models for determining when to begin looking for colorectal disease. The guidelines utilize age and family parentage as variables. Jeon *et al.* have shown that by utilizing data relative to a person's environmental factors and hereditary profile, explicitly the presence of colorectal cancer is related to hereditary variations [23]. The region under the curve (AUC), an incentive for a model including normal and hereditary components, where an AUC of 1.0 would suggest a model with ideal prescient precision, was 0.63 for men and 0.62 for women, according to the accuracy of relative predictions about an individual's probability for colorectal harmful development that has appeared differently in relation to an AUC worth of 0.53 (men) and 0.54 (ladies) when just family ancestry information was taken into account. Despite the fact that there is still room for improvement, given that the AUCs for the model incorporating the patient's environmental exposure and genetic information were only 0.62, the improvement over models that excluded inherent or biological information legitimizes its usage.

Challenges associated with PM

As personalized medication is rehearsed all the more generally, various difficulties emerge. The momentum ways to deal with protected innovation rights, repayment strategies, patient security, information inclinations, and classification just as administrative oversight should be reclassified and rebuilt to oblige the progressions of customized medication will have an impact on health care [24]. As an example, a

review acted within the UK inferred that 63% of the UK grown-ups are not pleased with their own info being utilized for AI in the clinical field [25,26]. For example, hereditary info acquired from cutting-edge sequencing requires PC concentrated information preparing preceding its analysis. Later on, sufficient instruments will be needed to speed up the reception of customized medication to additional fields of medication, which necessitates interdisciplinary collaboration of specialists from explicit sectors of exploration, such as medication, clinical oncology, and AI.

Intellectual property rights related to PM

Likewise, with any advancement in medication, speculation and interest in customized medication are impacted by licensed innovation rights [27]. There has been a great deal of discussion in regard to patent insurance for indicative devices, qualities, and biomarkers. The United States Supreme Court ruled in June 2013 decided that normal happening qualities can't be protected, while "Synthetic DNA" that is altered or misleading in any case be protected. The Patent Office is currently looking into a number of questions concerning patent laws for personalized drugs, such as whether "confirmatory" assistant hereditary testing performed after an initial diagnosis is exempt from patent restrictions. The person who goes against licenses contends that licenses on DNA groupings are a hindrance to continuous exploration while defenders highlight research exceptions and stress that licenses are important to allure and ensure the monetary speculations needed for business research and the turn of events and progression of administrations offered [28].

Individual confidentiality

The confirmation of patients is, in some ways, the most important issue with the commercialization of modified prescriptions. The worry and potential end for people who are prone to hereditary experimental outcomes or who are unaffected by specific treatments are probably the most serious issues. It influences the psychological research of patients in view of genetic experimental outcomes. The right of a family who doesn't straight forwardly being counseled turns into another issue, taking into account the genetic inclinations and risks that are inherited.

FUTURE PROSPECTIVE OF PERSONALIZED MEDICINES

Patient-derived cellular avatars

Without a direct biopsy of the afflicted tissue, it is now possible to collect cells from humans and employ pluripotency enlistment (that is, induced pluripotent foundational microorganism or "iPSC") procedures on those cells to produce extra cells of significance to a patient's disease. It enables examiners to connect the cell model of a patient's condition to the patient's condition in a fundamental way [29-31]. These *in vitro* cell "avatars" can be concentrated to recognize essential sub-nuclear pathologies that might offer a hint concerning how to treat a person in the most effective way. The utilization of iPSC advances as such can be stretched, as of late created, advances to make shockingly better models of a patient condition. For example, in the event that the patient has an acknowledged change causing their condition, it is advisable to use estimates subject to, for example, Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) and moderately creates to make isogenic cells in which a few cells undergo changes. The correlation of these cells permits direct understanding regarding the impacts of the transformation while controlling all significant hereditary foundation factors relative to the patient's genome [32,33]. Furthermore, it is achievable to make inadequate organs or "organoids" from cells gained from an individual [34]. Organoids can give more noticeable information into atomic pathologies related to an individual patient's condition since they can show cell: cell connections and all the more wide tissue work [35].

Intensive personalized health monitoring

The accessibility of modest genotyping and sequencing developments is allowing individuals and their clinical consideration providers to

overview their innately mediated peril for sickness and additionally make a genetic assurance in the event that they are unhealthy. Moreover, given the accessibility of well-being checking gadgets, online requested blood-based clinical tests, economical imaging gadgets, etc. [36,37]. Given, consolidating hereditary danger or demonstrative evaluation with exceptional health monitoring makes sense. Various people with specific diseases and health conditions have profited from a hereditary analysis, as it explained the potential hereditarily intervened pathogenic systems or uncovered expected focuses for pharmacotherapy for them [38,39].

Digital therapeutics and personalized app content

The omnipresence of advanced mobile phones has drawn in light of a legitimate concern for some scientists in the well-being callings as a vehicle for gathering well-being information through different “applications” as well as to give exhortation, criticism, training, symbolism, music, instant messages, or associations with different assets that could help a person with a specific condition or infection. This has provoked the improvement of the possibility of a “computerized remedial:” An advanced level cell application expected to get and convey easing an individual affected by a clinical or state of mind [40]. The data given by a modernized application could be useful to an individual could change on what is discovered with respect to that individual and their response to content given in the application. Thusly, the application can be customized. Many progressed therapeutics have gone through an appraisal for their ability to interface with customers and give advantages to them [41]. The US Food and Drug Administration (FDA) has made guidelines for enrolling automated therapeutics as evident insurance reimbursable, upheld prosperity advancements, and has begun evaluating and supporting enormous quantities of them. The initial support upheld progressed therapeutics – an application for substance abuse – was embraced by the FDA in 2017. How viably automated therapeutics will be accustomed into the thought stream is an open inquiry [42].

Customized medications strategies and approaches can be applied to drugs for benefits, as various experts have proposed. For example, it has been suggested that one could utilize “genuine world” data accumulated consistently on patients visiting regenerative medicine and productivity offices (from, e.g., electronic medical record (EMR) systems set up at various clinics and centers), and use this data to in assessments examining plans, patient assortments and every patient profile that could reveal knowledge into assortment in progress rates, responses to interventions to update wealth, and so on. The eventual outcomes of these examinations could then guide the future thoughts for patients with fertility issues [43]. With respect to the usage of advanced medication, recommendations to encourage PDA applications that could give altered educating substance to further develop pregnancy have been suggested [44]. Hereditary varieties known to affect richness have similarly been perceived and could be used to investigate or modify intervention objectives [45,46].

Notwithstanding more ordinary ways of managing modifying richness intervention, there are different emerging strategies to ad lib ripeness among women that go past set up technique of invigorating ovaries [47]. For example, it is as of now possible to cryopreserve a bunch of oocytes and ovarian tissue tests from a woman a while later install them in her soon that may suit her yearning to become pregnant [48]. Such a strategy would be significantly modified, since it would work with an individual’s own cells and oblige her tendencies for becoming pregnant. Regardless, this procedure would perhaps work in the event that the defended tissues were sensible and not hurt, disregarding the way that fitting cells in those tissues could on a fundamental level be changed for innate imperfections using quality modifying techniques. A more futuristic and questionable customized fruitfulness intercession incorporates the possibility that one could use cell rethinking advances to make sperm and egg cells from various cells got from an individual (e.g., skin cells) that could be adjusted

to deliver new gametes for readiness – a thought named as “*in vitro* gametogenesis” [49].

Theranostics

Theranostics is a customized way to deal with treating cancer, utilizing comparative molecules for both imaging (diagnose) and treatment. The word theranostics is a combination of the words therapeutics and diagnostics. It is currently most applied to the field of nuclear medication where radioactive particles are fixed to gamma or positron producers for SPECT or PET imaging, and to beta, alpha, or Auger electrons for treatment. Perhaps, the earlier model is the utilization of radioactive iodine for therapy of patients with thyroid malignancy. Different models incorporate radio-named hostile to CD20 antibodies (for example, Bexxar) for treating lymphoma, Radium-223 for treating bone metastases, Lutetium-177 DOTATATE for treating neuroendocrine tumors, and Lutetium-177 PSMA for treating prostate cancer. The most regularly utilized reagent is fluorodeoxyglucose, utilizing the isotope fluorine-18.

Respiratory proteomics

Respiratory contaminations impact mankind universally, with industrious lung sicknesses (e.g., asthma, progressing obstructive aspiratory illness, and idiopathic pneumonic fibrosis, among others) and cell breakdown in the lungs causing broad harm and mortality. These conditions are profoundly heterogeneous and require early detection. In the course of the most recent couple of years, customized medication has arisen as a clinical consideration approach that utilizes novel innovation expecting to customize therapies as per the specific patient’s clinical requirements. In explicit, proteomics is utilized to investigate a progression of protein articulations, rather than a solitary biomarker. Respiratory proteomics has gained huge headway in the advancement of personalized medication for supporting medical services as of late. For instance, in an investigation led by Lazzari *et al.* in 2012, the proteomics-based methodology has made significant improvement in recognizing numerous biomarkers of cellular breakdown in the lungs that can be utilized in fitting personalized medicines for individual patients. More and more investigations have shown the convenience of proteomics to give designated treatments to respiratory disease [46].

NOVEL APPROACHES: 3D PRINTING AND PERSONALIZED MEDICINE

3D printing is the process of creating a three-dimensional item with the use of computer software. 3D printing has a wide range of applications in pharmaceutical dosage forms of various shapes and medication combinations. Inkjet printing, binder jetting, fused filament fabrication, selective laser sintering, stereolithography, and pressure-assisted microsyringe are some of the key 3D printing platforms studied in the pharmaceutical industry. This technique could have a future application in a clinical context, where prescriptions could be distributed based on individual needs (Fig. 2).

CONCLUSION

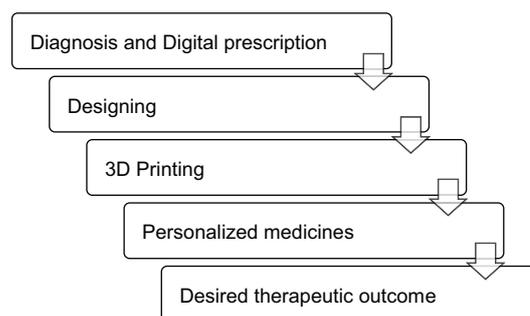


Fig. 2: Novel aspects of personalized medicine with 3D printing

Personalized medicine holds promise and provides medical aid in evaluating disease risk and prevention. It can involve case studies and genomic data. Genomic research laid the groundwork for genomic medicine products, and a patient's genomic data can be used to determine important clinical outcomes. The integration of genetic research and clinical practice must be uniform and efficient. Personalized medicine is already being used in clinics, and the use of genomic techniques has improved patient treatment, particularly in oncology and cardiology patients. To fully integrate personalized medicine into the clinical workflow, many challenges in education, accessibility, legislation, and reimbursement must be overcome. These PM models are used in theranostics, DNA sequencing, proteomics, imaging procedures, and health monitoring systems, among other things.

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An "entryway-like" structure in the CFTR quality's encoded protein that can open and control the advancement of salts throughout cells coordinates with another structure in the protein that is also encoded for the CFTR quality.

AUTHORS' CONTRIBUTION

The study was designed by Rajat Kar and Snehamoyee Mohapatra. The data were gathered by Piyali Khamkat and Vivek Barik who also created the figures and assessed the study. The final version of the manuscript was authorized for submission by Bhakti Bhusan Barik.

CONFLICTS OF INTEREST

There are no conflicts of interest associated to this article, according to the authors.

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REFERENCES

- Baltimore D. Our genome unveiled. *Nature* 2001;409:814-6. doi: 10.1038/35057267.
- Lander ES, Linton LM, Birren B, Nusbaum C, Zody MC, Baldwin J, et al. Initial sequencing and analysis of the human genome. *Nature* 2001;409:860-921. doi: 10.1038/35057062
- Peltonen L, McKusick VA. Dissecting human disease in the postgenomic era. *Science* 2001;291:1224-9. doi: 10.1126/science.291.5507.1224
- Kumari PV, Rao YS. Personalized medicine-a review. *Res J Pharm Technol* 2019;12:3989-92. doi: 10.5958/0974-360X.2019.00687.5
- Ginsburg GS, Willard HF. Genomic and personalized medicine: Foundations and applications. *Transl Res* 2009;154:277-87. doi: 10.1016/j.trsl.2009.09.005
- Ross JS, Ginsburg GS. The integration of molecular diagnostics with therapeutics implications for drug development and pathology practice. *Am J Clin Pathol* 2003;119:26-36. doi: 10.1309/VMLL-66Y5-KHQ3-5KUE
- Akhmetov I, Bubnov RV. Assessing value of innovative molecular diagnostic tests in the concept of predictive, preventive, and personalized medicine. *EPMA J* 2015;6:19. doi: 10.1186/s13167-015-0041-3
- Marincola FM, Sheikh JJ. A road map to translational medicine in Qatar and a model for the world. *J Transl Med* 2012;10:1-15. doi: 10.1186/1479-5876-10-177
- Guttmacher AE, Collins FS, Carmona RH. The family history: More important than ever. *N Engl J Med* 2004;351:2333-6. doi: 10.1056/NEJMs042979
- Rich EC, Burke W, Heaton CJ, Haga S, Pinsky L, Short MP, et al. Reconsidering the family history in primary care. *J Gen Intern Med* 2004;19:273-80. doi: 10.1111/j.1525-1497.2004.30401.x
- Collins FS. Shattuck lecture-medical and societal consequences of the human genome project. *N Eng J Med* 1999;341:28-37. doi: 10.1056/NEJM199907013410106
- Abrahams E, Silver M. The case for personalized medicine. *J Diabetes Sci Technol* 2009;3:680-4. doi: 10.1177/1932296809000300411
- Maciosek MV, Coffield AB, Edwards NM, Flottesmesch TJ, Goodman MJ, Solberg LI. Priorities among effective clinical preventive services results of a systematic review and analysis. *Am J Prev Med* 2006;31:52-61. doi: 10.1016/j.amepre.2006.03.012
- Swapna B, Kumar VS. Personalized medicine-a novel approach in cancer therapy. *Res J Pharm Technol* 2017;10:341-5. doi: 10.5958/0974-360X.2017.00069.5
- Huizinga TW. Personalized medicine in rheumatoid arthritis: Is the glass half full or half empty? *J Intern Med* 2015;277:178-87. doi: 10.1111/joim.12319
- Murali M, Kothandan S, Chandrasekaran M, Singh SK, Kuppasamy G, Radhakrishnan A. Fluticasone and Cyclophosphamide towards the track of personalized medicine. *Res J Pharm Technol* 2021;14:179-84. doi: 10.5958/0974-360X.2021.00031.7
- Lee MT, Klein TE. Pharmacogenetics of warfarin: Challenges and opportunities. *J Hum Genet* 2013;58:334-8. doi: 10.1038/jhg.2013.40
- Luzzatto L, Seneca E. G6PD deficiency: A classic example of pharmacogenetics with on-going clinical implications. *Br J Haematol* 2014;164:469-80. doi: 10.1111/bjh.12665
- Davis PB, Yasothan U, Kirkpatrick P. Ivacaftor. *Nat Rev Drug Discov* 2012;11:349-50. doi: 10.1038/nrd3723
- Farkona S, Diamandis EP, Blasutig IM. Cancer immunotherapy: The beginning of the end of cancer? *BMC Med* 2016;14:73. doi: 10.1186/s12916-016-0623-5
- Drescher CW, Shah C, Thorpe J, O'Briant K, Anderson GL, Berg CD, et al. Longitudinal screening algorithm that incorporates change over time in CA125 levels identifies ovarian cancer earlier than a single-threshold rule. *J Clin Oncol* 2013;31:387-92. doi: 10.1200/JCO.2012.43.6691
- Schork NJ, Goetz LH. Single-subject studies in translational nutrition research. *Ann Rev Nutr* 2017;37:395-422. doi: 10.1146/annurev-nutr-071816-064717
- Jeon J, Du M, Schoen RE, Hoffmeister M, Newcomb PA, Berndt SI, et al. Determining risk of colorectal cancer and starting age of screening based on lifestyle, environmental, and genetic factors. *Gastroenterology* 2018;154:2152-64.e19. doi: 10.1053/j.gastro.2018.02.021
- Williams MS. Early lessons from the implementation of genomic medicine programs. *Annu Rev Genomics Hum Genet* 2019;20:389-411. doi: 10.1146/annurev-genom-083118-014924
- Vayena E, Blasimme A, Cohen IG. Machine learning in medicine: Addressing ethical challenges. *PLoS Med* 2018;15:e1002689. doi: 10.1371/journal.pmed.1002689
- Huser V, Sincan M, Cimino JJ. Developing genomic knowledge bases and databases to support clinical management: Current perspectives. *Pharmacogenomics Pers Med* 2014;7:275-83. doi: 10.2147/PGPM.S49904
- Goetz LH, Schork NJ. Personalized medicine: Motivation, challenges and progress. *Fertil Steril* 2018;109:952-63. doi: 10.1016/j.fertnstert.2018.05.006
- Anaya JM, Rojas-Villarraga A, Garcia-Carrasco M. The autoimmune tautology: From polyautoimmunity and familial autoimmunity to the autoimmune genes. *Autoimmune Dis* 2012;2012:297193. doi: 10.1155/2012/297193
- Beltrao-Braga PC, Pignatari GC, Russo FB, Fernandes IR, Muotri AR. In-a-dish: Induced pluripotent stem cells as a novel model for human diseases. *Cytometry A* 2013;83:11-7. doi: 10.1002/cyto.a.22231
- Sayed N, Liu C, Wu JC. Translation of human-induced pluripotent stem cells: From clinical trial in a dish to precision medicine. *J Am Coll Cardiol* 2016;67:2161-76. doi: 10.1016/j.jacc.2016.01.083
- Wu J, Belmonte JC. Stem cells: A renaissance in human biology research. *Cell* 2016;165:1572-85. doi: 10.1016/j.cell.2016.05.043
- Song M, Ramakrishna S. Genome editing in stem cells for disease therapeutics. *Mol Biotechnol* 2018;60:329-38. doi: 10.1007/s12033-018-0072-9
- Uppada V, Gokara M, Rasineni GK. Diagnosis and therapy with CRISPR advanced CRISPR based tools for point of care diagnostics and early therapies. *Gene* 2018;656:22-9. doi: 10.1016/j.gene.2018.02.066
- Ho BX, Pek NM, Soh BS. Disease modeling using 3D organoids derived from human induced pluripotent stem cells. *Int J Mol Sci* 2018;19:936. doi: 10.3390/ijms19040936
- Es HA, Montazeri L, Aref AM, Vosough M, Baharvand H. Personalized cancer medicine: An organoid approach. *Trends Biotechnol* 2018;36:358-71. doi: 10.1016/j.tibtech.2017.12.005
- Appelboom G, Camacho E, Abraham ME, Bruce SS, Dumont EL, Zacharia BE, et al. Smart wearable body sensors for patient self-assessment and monitoring. *Arch Public Health* 2014;72:28. doi: 10.1186/2049-3258-72-28
- Swan M. The quantified self: Fundamental disruption in big data science and biological discovery. *Big Data* 2013;1:85-99. doi: 10.1089/big.2012.0002
- Schork NJ, Nazor K. Integrated genomic medicine: A paradigm for

- rare diseases and beyond. *Adv Genet* 2017;97:81-113. doi: 10.1016/bs.adgen.2017.06.001
39. Bai J, Shen L, Sun H, Shen B. Physiological informatics: Collection and analyses of data from wearable sensors and smartphone for healthcare. *Adv Exp Med Biol* 2017;1028:17-37. doi: 10.1007/978-981-10-6041-0_2
40. Sverdlov O, Dam JV, Hannesdottir K, Thornton-Wells T. Digital therapeutics: An integral component of digital innovation in drug development. *Clin Pharmacol Ther* 2018;104:72-80. doi: 10.1002/cpt.1036
41. Jamal A, King BA, Neff LJ, Whitmill J, Babb SD, Graffunder CM. Current cigarette smoking among adults-United States. *Morb Mortal Wkly Rep* 2016;67:53-9. doi: 10.15585/mmwr.mm6544a2
42. Phillips KA, Douglas MP, Trosman JR, Marshall DA. What goes around comes around: Lessons learned from economic evaluations of personalized medicine applied to digital medicine. *Value Health* 2017;20:47-53. doi: 10.1016/j.jval.2016.08.736
43. Jungheim ES, Carson KR. Leveraging real-world data to move toward more personalized fertility treatment. *Fertil Steril* 2018;109:608-9. doi: 10.1016/j.fertnstert.2018.01.036
44. Dijk MR, Koster MP, Willemsen SP, Huijgen NA, Laven JS, Steegers-Theunissen RP. Healthy preconception nutrition and lifestyle using personalized mobile health coaching is associated with enhanced pregnancy chance. *Reprod Biomed Online* 2017;35:453-60. doi: 10.1016/j.rbmo.2017.06.014
45. DeAngelis AM, Roy-O'Reilly M, Rodriguez A. Genetic alterations affecting cholesterol metabolism and human fertility. *Biol Reprod* 2014;91:117. doi: 10.1095/biolreprod.114.119883
46. Laber EB, Zhao YQ, Regh T, Davidian M, Tsiatis A, Stanford JB, et al. Using pilot data to size a two-arm randomized trial to find a nearly optimal personalized treatment strategy. *Stat Med* 2016;35:1245-56. doi: 10.1002/sim.6783
47. Jungheim ES, Meyer MF, Broughton DE. Best practices for controlled ovarian stimulation in *in vitro* fertilization. *Semin Reprod Med* 2015;33:77-82. doi: 10.1055/s-0035-1546424
48. Tao T, Del Valle A. Human oocyte and ovarian tissue cryopreservation and its application. *J Assist Reprod Genet* 2008;25:287-96. doi: 10.1007/s10815-008-9236-z
49. Nagamatsu G, Hayashi K. Stem cells, *in vitro* gametogenesis and male fertility. *Reproduction* 2017;154:F79-91. doi: 10.1530/REP-17-0510