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Towards the use of nanotechnology and pharmacogenomics in personalized medicine

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ABSTRACT—An erroneous concept in drug delivery is that "One size fit all". This is due to side effects or adverse effects and variability observed in drug response. The variability is a result of genotypic variations which is studied in the branch of science called Pharmacogenomics. The variability in drug response is studied by multigene analysis or profiling of whole-genome single nucleotide polymorphism and is recorded in terms of the pharmacokinetic (absorption, distribution, metabolism, and elimination) and pharmacodynamic (drug-receptor interaction, immune response, etc.) response of the drug. Therefore, a foray into this research area can provide valuable information for designing of drug therapies, identifying disease etiology, therapeutic targets, and biomarkers for application in treatment and diagnosis of all types of diseases, especially cancer. Lately, with the integration of pharmacogenomics and nanotechnology, a new understanding for the diagnosis and treatment of diseases has opened, and the prescription pattern of drugs has moved to pharmaco-typing (individualized dose and dosage-form adjusted therapy) using nanoplatforms like nanotheranostics.

Keywords— Pharmacogenomics, Nanomedicine, Nanotechnology, Nanotheranostics.

INTRODUCTION

Nanotechnology has many applications in sciences of life including diagnostics, drug delivery, and nanomedicine development. Nanotechnology, molecular pharmacology, and pharmacogenomics are enhancing the clinical results by advancing the outcome of drug delivery, improving clinical diagnosis capacity, and highlighting the pathogenesis pathway (1). Combining nanotechnology with personalized medicine created a unique opportunity to evaluate complex diseases, and to use target guided nanodevices to incorporate the genomic information into clinical practice (2). Nanoparticles offer unique properties in designing nanomedicine such as tininess, flexibility, enhanced surface-to-volume ratio, and multi-purpose surface modification using ligands to obtain targeting of cells. Nanomedicine holds potential to improve anticancer therapy (3). To reduce the risk of disease initiation, progression and drug toxicity, nanotechnology-based drug delivery systems have developed specialized technical frameworks for the exploitation of genomic knowledge (4).

Pharmacogenomics underlines the relationship of the genesrole in the etiology of a disease, disease pathophysiology, disease biomarkers, medication target, medication effect, and the destiny of medication inside the body. The integrated application of pharmacogenomics and nanotechnology provides better therapeutic outcomes with minimized side effects and adverse drug reactions during therapy (5). Pharmacogenomics is emerging as a science highlighting differences in the drug response to differences in genetic makeup in particular groups.

Differences in genes are responsible for the difference in specific functional process inside the body by changes in protein synthesized. Any disorder or deformity may also result due to these functional changes. Both the structural and the functional pharmacogenomics are effective in predicting, recognizing genetic markers of disease, and planning and optimizing drug therapy in the treatment of that disease (6).

The field where pharmacogenomics is used in the delivery of drugs for tailored medicines is called nanotheranostics. It is a combination between drug therapy and diagnosis. Using Pharmacogenomics is an excellent method to

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quantify parameters related to the disorder and its severity, together with treatment and personalizing the medicine based on an individual's genotype. Using Nanotechnology makes it possible to develop and design therapeutic strategies, which are capable of concurrently detecting genetic biomarkers for disease along with drug therapy. Nanotechnological materials such as gold-based nanomaterials, magnetic nanomaterials, polymeric nanomaterials, carbon-based nanomaterials, silica-based nanomaterials, composite nanomaterials, and quantum dots may be used to build such drug delivery systems (7,8).

Pharmacogenomics and drug selection

Structural Pharmacogenomics aims to recognize and verify disease-relevant targets for therapeutic activity or biomarkers like the EGFR signaling system, PI3K, RAF, MAPK, KRAS AKT markers for various forms of cancers. Pharmacogenomics compares the biomarkers targeted with disease processes to create a connection between the disease and the biomarker of the experiment, which then helps in defining the drug molecule for such a target (9,10). Specific genome targets like enzymes, drug carriers, proteins, nucleic acids, chromosomes, cell surface proteins, ion channels, and other biomolecules contributing to the pathophysiology of the disease have been provided by human genome sequencing. Such possible causes to the pathophysiology of the disease can serve as target sites for drug action. Thus, the pharmacogenomics concept can be used in target recognition, genotyping, structural elucidation, and target confirmation that improve safety and efficacy of medicines. Sequencing of the target genes can be used in the discovery and validation of lead compounds (11,12).

For cancer nanomedicines to succeed clinically and commercially, rational drug selection is essential. All clinically approved cancer nanomedicines (besides antibody-drug conjugates) are based on cytostatic drugs, such as doxorubicin, daunorubicin, paclitaxel, vincristine and irinotecan (13). The re-formulation of nanomedicine in all these agents improves the therapeutic index, but mostly by attenuating side effects rather than by improving therapeutic responses significantly. To maximize nanomedicine's impact on the therapeutic index, specific side effects of nanomedicine, such as complement-mediated infusion reactions (14), have to be considered, and a better mechanistic understanding of these effects and identification of efficient approaches are crucial (15). Moreover, future efforts in cancer nanomedicine drug development should focus more on the use of nanocarrier materials for the delivery of non-standard drugs, such as biologics, and on smarter approaches including drug derivatization, modular nanocarrier design, and library screening.

Nanoparticles in personalized medicine

Because of their exploratory features, nanoparticles facilitate the molecular targeting of medicines. Recent studies offered detailed information on the relationship of NPs with biological processes to promote their use for nanotheranostics diagnosis, imaging, and drug delivery. Today, nanotheranostics have been developed to monitor transcription and translation of genes, recognize cancer cells, control the proliferation of T cells, and manage blood sugar levels. Moreover, blood urea levels can be detected by an implant and normal levels can be restored. Another implant was created for artificial insemination that injects bull spermatocytes into the bovine ovary by identifying luteinizing hormone levels, especially during ovulation. Any disorder can be treated at the cellular and molecular level by detecting particular biochemical parameters (16).

While several experiments have been performed, relatively few pharmaceutical drug products have been developed as nanotherapeutics in the pharmaceutical market, indicating the uncertainty of formulating active compounds in these formulations. A PEGylated liposome doxorubicin medication called Doxil, approved for therapeutic use by the FDA, is the most popular example of nanoparticle technology for clinical use. The principle of PEGylation was first developed as a means for recombinant protein drugs to improve their circulation and stability. Another FDA approved effective nanoparticle application is Abraxane, which is albumin functionalized paclitaxel. In an attempt to merge nanoscale therapeutic and diagnostic modalities, separate nanotheranostic agents have been designed to provide flexible platforms for the simultaneous delivery of diagnostics and therapeutics (6).

However, many new materials have arisen as theranostic agents such as gold nanoparticles, carbon nanotubes, metal organic frameworks and iron oxide nanoparticles; problems of safety and bio - compatibility and unspecified tolerance and toxicity need to be evaluated in the clinic. Regardless of these drawbacks, nanotheranostics seem very optimistic to develop personalized medicine (16).

Personalized nanomedicines

Personalized nanomedicine may be described as the management of a patient's disease or drug response using nanomedicine in combination with clinical and molecular expertise

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(for example genomics, proteomics, epigenomics and metabolomics) as well as bioinformatics techniques to produce the best possible medical treatment for that person. In addition, by integrating nanotechnology and genomics expertise, personalized nanomedicine may create enhanced profiles for demographics and particular patients for prognosis, diagnosis, and drug therapy, as well as surveillance through medical science and clinical management. Advantages of using personalized medicine include (17):

I. Personalized nanomedicine is in nano-scale size range
II. Personalized nanomedicine offers tunability and flexibility
III. Offers possibility of using labile substances such as siRNA
IV. The active concepts of personalized nanomedicine: encapsulation and safety
V. Targeted delivery to organs/ tissues/ cell compartments
VI. Probability of responding to a need of specific patient group
VII. Adapting patterns of treatment to each patient (e.g., dosage, frequency, etc.)

Personalized nanomedicine in the treatment of cancer

The advancement of personalized nanomedicine is a useful technique in the cancer therapy. Personalized oncology is raising new prospects for the elimination of cancer incidence by specifically targeting anticancer medicines to cancerous cells, target areas on the cell surface and inside the tumor microenvironment.

Nano oncology has succeeded in improving the specificity and efficiency of cancer therapies, both by promoting the development and distribution of medications and by reducing clinical toxicity and serious incidents (18). Personalization of cancer treatment is focused on a deeper knowledge of the pathogenesis at the molecular scale and nanomedicine can play a significant role in this direction (19). Nanobiotechnology can enhance early cancer diagnosis and enhance personalized cancer treatment. Molecular diagnostics is the most important aspect of personalized medicine, and nanobiotechnology can play a significant role in its refinement (20).

Dendrimers are a class of nanoscale, core-shell, three-dimensional structures that can be synthesized precisely for a variety of uses. Specialized methods in chemistry allow detailed control over the dendrimer's physical and chemical properties. They are most effective in the delivery of drugs, but they can also be used to produce new pharmaceuticals with emerging technologies. With several therapeutic target, polyvalent dendrimers interact simultaneously. They can be transformed into new-targeted therapeutics for cancer. Using complementary DNA oligonucleotide primers, dendrimers may be covalently linked to various bio-functional groups, such as folic acid, to create clustered molecules attacking cancer cells that overexpress the high affinity folate receptor (20). Endothelial αvβ3-Integrintargeted paramagnetic nanoparticles are being used to identify very limited angiogenesis area linked with tumors of nascent melanoma (21).

Nanobodies (Ablynx) are the smallest intact antigen binding fragments that have the full antigen binding capacity of natural heavy-chain antibodies. Nanobodies are prospective era of antibody-based treatments as well as diagnostic tools for diseases like cancer. Nanobodies have a relatively high specificity and low endogenous toxicity. They can tackle therapeutic targets that are not readily detected by traditional antibodies such as enzyme active sites. Nanobodies have the ability to be produced as personalized cancer therapies (22). Nanotechnology is revolutionizing the treatment of cancer as it can alter its diagnosis, clinical path, and prognosis. Before treatment, cancer molecular profiling may be extremely prognostic and predictive of clinical responses or recurrence, encouraging the most effective treatment to be prescribed with each specific cancer.

CONCLUSION

Pharmacogenomics is progressing in the form of personalized medicines in the world today. The main purpose of personalized therapies is to improve healthcare through the application of emerging technology. In these advances, nanotechnology plays a key role with integration of pharmacogenomics to improve diagnosis and therapeutics at the individual level treatment. With this approach the introduction of personalized nanomedicine, has provided a major stimulus to the medicine and pharmacy disciplines to include advanced clinical therapies, disease management, diagnosis, and delivery of drugs.

REFERENCES

[1]. Vizirianakis IS, Miliotou AN, Mystridis GA, Andriotis EG, Andreadis II, Papadopoulou LC, et al. Tackling pharmacological response heterogeneity by PBPK modeling to advance precision medicine productivity of nanotechnology and genomics therapeutics precision medicine productivity

of nanotechnology and genomics therapeutics. Expert Rev Precis Med Drug Dev [Internet]. 2019;4(3):139–51. Available from: https://doi.org/10.1080/23808993.2019.1605828

[2]. Vizirianakis IS, Amanatiadou EP. Pharmacogenomics and Nanotechnology Toward Advancing Personalized Medicine. :115–34.

[3]. Peer D, Karp JM, Hong S, Farokhzad OC, Margalit R, Langer R. Nanocarriers as an emerging platform for cancer therapy. 2007;751–60.

[4]. Alharbi KK, Al-sheikh YA. Role and implications of nanodiagnostics in the changing trends of clinical diagnosis. Saudi J Biol Sci [Internet]. 2014;21(2):109–17. Available from: http://dx.doi.org/10.1016/j.sjbs.2013.11.001

[5]. Jhawat V, Gulia M, Gupta S, Maddiboyina B, Dutt R. Integration of pharmacogenomics and theranostics with nanotechnology as quality by design (QbD) approach for formulation development of novel dosage forms for effective drug therapy. J Control Release [Internet]. 2020;327(August):500–11. Available from: https://doi.org/10.1016/j.jconrel.2020.08.039

[6]. Gupta S. SC. J Control Release [Internet]. 2016; Available from: http://dx.doi.org/10.1016/j.jconrel.2016.11.018

[7]. Wang L. Nanotheranostics – a review of recent publications. 2012;4679–95.

[8]. Mura S, Couvreur P. Nanotheranostics for personalized medicine ☆. Adv Drug Deliv Rev [Internet]. 2012;64(13):1394–416. Available from: http://dx.doi.org/10.1016/j.addr.2012.06.006

[9]. Mäbert K, Cojoc M, Peitzsch C, Kurth I, Souchelnytskyi S, Dubrovska A. and future perspectives PT. 2014;

[10]. Date A. Correspondence : 2014;

[11]. Cichonska A, Rousu J, Aittokallio T, Cichonska A, Rousu J, Aittokallio T. Expert Opinion on Drug Discovery Identification of drug candidates and repurposing opportunities through compound – target interaction networks Identification of drug candidates and repurposing opportunities through compound -- target interaction networks. 2015;0441(October).

[12]. Verma S, Prabhakar YS. Target Based Drug Design - A Reality in Virtual Sphere Target Based Drug Design - A Reality in Virtual Sphere. 2015;(February).

[13]. Hare JI, Lammers T, Ashford MB, Puri S, Storm G, Barry ST. SC. Adv Drug Deliv Rev [Internet]. 2016; Available from: http://dx.doi.org/10.1016/j.addr.2016.04.025

[14]. Szebeni J, Simberg D, González-fernández Á, Barenholz Y, Dobrovolskaia MA. reactions to nanomedicines. Nat Nanotechnol [Internet]. 2018;13(December). Available from: http://dx.doi.org/10.1038/s41565-018-0273-1

[15]. Dobrovolskaia MA, Farhangrazi ZS, Farrell D. HHS Public Access. 2018;11(1):12–8.

[16]. Treatment I, Versus E, Treatment A. Precision Medicine Versus Evidence-Based. 2019;1236–8.

[17]. Sciencedirect S, Ehrlich P, Feynman R. Personalized nanomedicine : paving the way to the practical clinical utility of genomics and nanotechnology advancements ☆ Multidisciplinary experimental approaches Nanomedicine. 2012;64:1359–62.

[18]. Fruscella M, Ponzetto A, Crema A, Carloni G. The Extraordinary Progress in Very Early Cancer Diagnosis and Personalized Therapy : The Role of Oncomarkers and Nanotechnology. 2016;2016.

[19]. Pharmabiotech J. Role of Nanobiotechnology in Developing Personalized Medicine for Cancer. 2005;4(6).

[20]. Atkinson SP, Andreu Z, Vicent J. Polymer Therapeutics : Biomarkers and New Approaches for Personalized Cancer Treatment. 2018;

[21]. Schmieder AH, Winter PM, Caruthers SD, Harris TD, Williams TA, Allen JS, et al. Molecular MR Imaging of Melanoma Angiogenesis With ␣ □ ␍ 3 -Targeted Paramagnetic Nanoparticles. 2005;627:621–7.

[22]. Micro-ct S, Olive L, Gainkam T, Huang L, Caveliers V, Keyaerts M, et al. Comparison of the Biodistribution and Tumor Targeting of Two 99m Tc-Labeled Anti-EGFR Nanobodies in Mice , Using Pinhole. 2008;49(5):5–7.