

Precision Drugs Development Needs Artificial Intelligence

Karel Petrak*

**Chief Scientific Officer, Nangio Tx, Inc., 50 Rector St., Suite 1403, Newark NJ 07102, USA.*

Received May 24, 2023; Revised May 27, 2023; Accepted May 30, 2023

The concept of precision medicine is to use genetic, environmental, and lifestyle data for optimal treatment of patients. However, corresponding precision drugs have not been developed to implement this concept. Targeting the existing drugs to deliver therapeutic doses and avoiding undesirable effects on healthy tissues does not address the aims of precision medicine.

The pivotal concept of precision medicine is to use genetic, environmental, and lifestyle data in developing an optimal treatment strategy for treating patients. According to Manzari [1] precision medicine can be implemented by appropriately designed and improved drug delivery. However, it can be argued that delivering therapeutic doses and avoiding undesirable effects on healthy tissues does not address the aims of precision medicine. For example, while minor improvements may be implemented, encapsulating and delivering small-molecule chemotherapeutic drugs using nanoparticles does not address the requirement of precision medicine to consider the patients' "genetic, environmental, and lifestyle data".

While passive targeting of nanoparticles to tumor sites may reduce undesirable drug activity in normal tissues and organs [2] it does not act on the molecular targets of diseases. Further, the existing drug targeting methods are ineffective for delivering large, fragile, and negatively charged macromolecules such as proteins, DNAs, and RNAs. In particular, the existing drug targeting methods are ineffective for delivering large, fragile, and negatively charged macromolecules such as proteins, DNAs, and RNAs. Several systems have been developed to deliver nucleic acids to cells in vitro efficiently, but few have been successfully developed for clinical use [3-6].

PubMed searches conducted on 5/4/23 (cancer mechanism of action, 1 year, reviews; cancer initiation, 5 years, reviews) showed 6,483 and 925 hits, respectively. The majority of existing drugs act on symptoms and not on the cause of diseases. Drugs that act on targets loosely associated with the disease initiation and progression are delivered by non-specific systems.

Molecular targeted therapeutic agents used in cancer treatment utilize various functions and characteristics, acting on cell surface antigens, growth factors, receptors, or signal transduction pathways which regulate cell cycle progression, cell death, metastasis, and angiogenesis [7]. However, all these targets are likely only indirectly related to the molecular structures responsible for the disease initiation.

Drug-containing nanoparticles have been delivered using viral vectors that can be immunogenic, and patients may have pre-existing immunity to viral vehicles [8]. Putnam [9] reviewed the lower efficiency of nonviral vectors for delivering large molecules. Raguram [10] reviewed approaches to therapeutic in vivo gene editing, including viral vectors, lipid nanoparticles, and virus-like particles, compared the benefits and drawbacks of each method and suggested future improvements.

Unlike the delivery to targets of diseases caused by external agents (bacteria, viruses, etc.), disease targets of internal diseases (e.g., cancer) have not been fully defined. According to Mendelsohn [11] "Molecularly targeted therapy uses an agent (or combination of agents) that acts with a high degree of specificity on a well-defined target or biologic pathway that drives the cancer phenotype". Cancer cells treated with such agents are to be destroyed with minimal harm to normal cells. However, at best, the existing delivery system transport drugs to the disease's approximate location and targets presumed to be associated with the disease's initiation and progression. The target definition could be as broad as cancer immunotherapy, which employs a patient's immune response against cancer [12].

Although the current approaches might improve the overall survival of some patients, they are effective in only a

Corresponding author: Karel Petrak, NangioTx, Inc., 50 Rector St., Suite 1403, Newark NJ 07102, USA, Tel: +1 2818868529; E-mail: klpetrak@gmail.com

Citation: Petrak K. (2023) Precision Drugs Development Needs Artificial Intelligence. BioMed Res J, 7(3): 630-633.

Copyright: ©2023 Petrak K. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

fraction of cancer patient cohorts [13] and produce immune-related adverse events. Limitations of immunotherapies using nanoparticle systems to deliver therapies to the target tissues, protect the drugs from degradation, and increase bioavailability have been reviewed by Manzari [1] Liu [14] and others.

The use of drug delivery strategies to improve targeted therapies has reached the clinic in a few cases [1]. However, tumor immunotherapy's overall clinical response rate still needs improvement [15].

Raza [16] argued that "it is time to discard the outmoded way of viewing, researching, and talking about cancer." Further, "there is a misconception that we are just around the bend from winning the war on cancer." Statistics have been used to support that cancer deaths have declined by 20 percent since 1980. However, Raza explains that the "decrease is not due to improved treatments but mostly to early diagnosis and a decline in smoking." Further, "recent advances relate primarily to improvement in cancer mortality due to early detection, not meaningful advances in the treatment of metastatic cancers".

The existing personalized therapies are very diverse. Delivery systems act by altering the drugs' pharmacokinetics and biodistribution and may reduce drugs' toxicities and improve efficacy. In preclinical research, mechanism of action studies supported the selection of therapeutic agents, appropriate models of efficacy, experimental design, and rational characterization and prediction of nontumor (host) effects. In clinical research, mechanism of action studies supported the identification of surrogate markers of efficacy (critical for determining the adequacy of dose and latency of response) and the selection of patient subpopulations and tumor subtypes most likely to exhibit clinical responses. Finally, information on the mechanism of action may suggest strategies for combination therapies and predict potential mechanisms of disease resistance to therapy [17].

According to Koeffler [18] cancer is caused by DNA damage. Generated by several common mechanisms such as translocations and point mutations, including the functional loss of "tumor suppressor genes." The authors recognized that targeting these abnormalities at the molecular level would significantly enhance cancer diagnosis, classification, and treatment. The reported multiple molecular targets and signaling pathways related to the action of the existing targeted treatment [19] exerted anticancer effects through multiple mechanisms, including proliferation inhibition, apoptosis induction, metastasis suppression, immune function regulation, and multidrug resistance reversal.

As discussed earlier [20] Artificial Intelligence (AI) will be needed to incorporate all the existing disease data, current assumptions, and disease initiation and progression theories.

Ultimately, based on all the information, it will need to have the capacity to generate new knowledge and know-how to

define the unique molecular structures involved in the disease initiation. There are concerns that the "use of new AI technologies could harm others" and that the tools it helps to create could "spell the end of humanity" [21]. Such concerns do not apply when AI investigates human diseases. AI will need to generate new knowledge and know-how. It will need to reason and answer the "what if" questions, imagine, be intuitive, predict, and make decisions.

REFERENCES

1. Manzari MT, Shamay Y, Kiguchi H, Rosen N, Scaltriti M, et al. (2021) Targeted drug delivery strategies for precision medicines. *Nat Rev Mater* 6(4): 351-370.
2. Ibrahim YH, Garcia GC, Serra V, He L, Lockhart KT, et al. (2012) PI3K inhibition impairs BRCA1/2 expression and sensitizes BRCA-proficient triple-negative breast cancer to PARP inhibition. *Cancer Discov* 2(11): 1036-1047.
3. Mendes BB, Connot J, Avital A, Yao D, Jiang X, et al. (2022) Nanodelivery of nucleic acids. *Nat Rev Methods Primers* 2: 24.
4. Huang YW, Lee HJ, Tolliver LM, Aronstam RS (2015) Delivery of nucleic acids and nanomaterials by cell-penetrating peptides: Opportunities and challenges. *Biomed Res Int* 2015: 834079.
5. Zhang Y, Liu Q, Zhang X, Huang H, Tang S, et al. (2022) Recent advances in exosome-mediated nucleic acid delivery for cancer therapy. *J Nanobiotechnol* 20(1): 279.
6. Reschke M, Piotrowski-Daspit AS, Pober JS, Saltzman WM (2022) Nucleic Acid Delivery to the Vascular Endothelium. *Mol Pharm* 19(12): 4466-4486.
7. Saijo N, Kenmotsu H (2010) Recent development of molecular-targeted drugs in lung cancer. *Intern Med* 49(18): 1923-1934.
8. Mintzer MA, Simanek EE (2009) Nonviral Vectors for Gene Delivery. *Chem Rev* 109: 259-302.
9. Putnam D (2006) Polymers for gene delivery across length scales. *Nat Mater* 5: 439-451.
10. Raguram A, Banskota S, Liu DR (2022) Therapeutic *in vivo* delivery of gene editing agents. *Cell* 185(15): 2806-2827.
11. Mendelsohn J, Powis G (2008) From Bench to Bedside with Targeted Therapies. *The Molecular Basis of Cancer* (Third Edition), pp: 521-530.
12. Hu Q, Sun W, Wang J, Ruan H, Zhang X, et al. (2018) Conjugation of haematopoietic stem cells and platelets decorated with anti-PD-1 antibodies augments anti-leukaemia efficacy. *Nat Biomed Eng* 2: 831-840.

13. Menon S, Shin S, Dy G (2016) Advances in Cancer Immunotherapy in Solid Tumors. *Cancers (Basel)* 8(12): 106.
14. Liu Z, Jiang W, Nam J, Moon JJ, Kim BYS (2018) Immunomodulating Nanomedicine for Cancer Therapy. *Nano Lett* 18(11): 6655-6659.
15. Wang DR, Wu XL, Sun YL (2022) Therapeutic targets and biomarkers of tumor immunotherapy: response versus non-response. *Signal Transduct Target Ther* 7(1): 331.
16. Raza A (2019) The First Cell: And the Human Costs of Pursuing Cancer to the Last.
17. Cattley RC, Radinsky RR (2004) Cancer therapeutics: Understanding the mechanism of action. *Toxicol Pathol* 32 Suppl 1: 116-121.
18. Koeffler HP, McCormick F, Denny C (1991) Molecular mechanisms of cancer. *West J Med* 155(5): 505-514.
19. Ke X, Shen L (2017) Molecular targeted therapy of cancer: The progress and future prospect. *Front Laborat Med* 1(2): 69-75.
20. Petrak K (2020) A Challenge to Artificial Intelligence: Find Molecular Structures Uniquely and Functionally Connected to the Initiation and Progression of Diseases. *Acta Sci Cancer Biol* 4(2): 01-04.
21. BBC (2017) AI godfather Geoffrey Hinton warns of dangers as he quits Google in Cancer Patients. *Clin Pharmacokinet* 56: 293-303.