ACTA SCIENTIFIC CANCER BIOLOGY (ISSN: 2582-4473)

Volume 4 Issue 2 February 2020

Mini Review

A Challenge to Artificial Intelligence: Find Molecular Structures Uniquely and Functionally Connected to the Initiation and Progression of Diseases

Karel Petrak D Phil*

Matrx Pharmaceuticals, Inc, USA.

***Corresponding Author:** Karel Petrak D Phil, Matrx Pharmaceuticals, Inc, USA.

DOI: 10.31080/ASCB.2020.04.0196

Received: December 09, 2019

Published: January 07, 2020

Abstract

Artificial Intelligence (AI) could make a major contribution to the development of disease-targeted drug delivery by elucidating what drives diseases at the molecular level, and in particular what unique molecular structures are involved that are not shared by non-disease cells. To this end, AI will need to acquire the manner of processing information in human-thinking terms such as perception, abstraction and memories, apply critical analysis of the information and then remember and recall outcomes as and when needed to synthesize a new, more complex whole. Ultimately, it will need to have the capacity to generate new knowledge and know-how.

Keywords: Molecular Structures; Progression

Introduction

The fact

The current FDA drug-product approval process has a 97% failure rate of clinical trials for oncology, mainly due to drug-efficacy or toxicity goals not being met [1]. The key failing is the lack of understanding of the disease mechanisms and hence the lack of identification of disease-relevant molecular targets. A common problem in many cancer trials appears to be that off-target interactions are de facto the actual mechanism of drug action [2].

The most recent SEER Cancer Statistics Review [3], released in April 2018, reports that cancer death rates in the United States decreased from 2006 to 2015 by 1.4% and 1.8% among women and men, respectively. So perhaps some progress is being made to treat cancer, if not through better therapies but through changes in lifestyle (such as giving up smoking) and prevention. Still, the burden of cancer in the United States remains high, with some 1,735,350 new cases of cancer diagnosed in 2018. The Expert Opinion review by Austreid., *et al*. [4] can be taken as a good illustration of a number of mechanistic pathways and biological compounds that have been identified as playing a role in (breast) cancer. Developing drugs to inhibit the action of individual components of the overall scheme of cancer development and progression has been found not to be productive. It is likely that current drugs aim, in a "hit or miss fashion", to alter the disease far too late in the chain of events that lead to cancer.

On an intelligent approach to cancer targeting

To a scientist, intelligence is a tool that is to be used at all times. Out of the features of "intelligence", the capacity to acquire knowledge and retain it, understand it, use it for logical reasoning, evaluate it critically, create new ideas and concepts, and plan to solve emerging problems are perhaps most important to employ. Taking "Artificial intelligence" as the ability of computer systems to perform tasks needing human intelligence, it will need to have all the above features effectively to perform all the decision-making involved in solving problems encountered in the process of curing diseases. Efforts it takes to read and understand the constantly growing medical-science information has become excessive for medical professionals and researchers. Artificial Intelligence needs to become a routine tool to process knowledge resources and move forward in an informed and rational manner.

The possibility of delivering drugs to site of diseases without causing off-site undesirable effects has been considered for more than a century; effective disease-targeted drug delivery (with the exception of targeting agents of infection) has not been realized. A PubMed search on 10/24/2016 on (((drug) AND delivery) AND target) AND disease) listed 15097 publications. Many of the publications promise to "deliver" but fail to enable generation of therapeutic products [5-7]. Apart from our still incomplete understanding of diseases, one of the main reasons for the lack of progress is that researchers do not know, recognize, or choose to ignore what are the necessary conditions for effective drug delivery. For example, a recent publication describing composite particulates with targeting, chemotherapeutic, and magnetothermal functionalities suggested that the material had "therapeutic potential in treating breast cancer" [8]. The publication presented fine work in the area of material science, however its conclusion based solely on data showing killing of breast cancer cells *in vitro* is nothing more than speculation.

Research has clearly established the essential requirements that need to be met for drug delivery to be efficacious and free of side effects [9-12]. Further, it has become clear that there is an essential need to identify unique molecular targets involved in disease initiation and progression [13]. I argue here that to achieve this, a form of Artificial Intelligence will need to be employed.

Several pharmaceutical companies have now started to use a form of AI – "machine learning" [14]. Buvailo and Ajami [15] reported a rapidly growing use of AI in drug discovery and development that is being applied to tasks such as "mining" of data, target identification, and divining properties and risks of new drug candidates. AI has been able to assist with data-rich areas such as designing chemical syntheses, planning complex activities such as pre-clinical and clinical research and in evaluating resulting data. While AI is being applied in matching drugs to existing targets, it is clear that identifying molecular structures uniquely associated with diseases continues to be an unmet need [16], recognizing that claims made about AI may be "overhyped".

In 2015, the FDA approved a number of drugs described as being "targeted": Uptravi, Cosentyx, Cotellic, Odomzo, Xifaxan, Darzalex, Praxbind, Technivie, Opdivo, Alecensa, Empliciti, Keytruda, Ninlaro, Tagrisso and Orkambi. Most of these drugs have been designed to act on the pathways that are presumed to influence the disease but not the actual disease target. DARZALEX® provides a prime example [17]. This therapeutic agent is a monoclonal antibody that attaches to CD38 protein present on the surface of certain types of cells (e.g., red blood cells) and is also present in high numbers on multiple myeloma cells. Since DARZALEX® targets the CD38 protein, it may also affect other cells with this protein on their surface. This is very characteristic of all the drugs listed above. In consequence, all these drugs exhibit side effects. This clearly illustrates that targeting ubiquitous cellular pathways that function in both the disease and healthy cells is responsible for generating many, and often severe side effects.

In developing disease-targeted drugs therapies it is critical to make the task very clear and define it in terms of unique molecular structures present at a specific disease-associated cells [10-13].

A key question does remain: "Can this be done using the approaches employed so far?" [18]. And further - can Artificial Intelligence be employed to answer this question? Machine learning is capable to process large amounts of data; hence, it might be very useful to process all the existing information and, based on all the negative data, determine what should not be done.

However, a major positive step forward could be made by adopting a more proactive, rational approach based on understanding of what drives diseases at the molecular level, and in particular what unique molecular structures are involved that are not shared by non-disease cells. This approach has been very effective for curing bacterial and recently even viral infections in which molecular features of organisms foreign to human body were identified. When applied to other diseases, such knowledge would enable development of truly disease-targeted drugs. To this end, it is very likely that Artificial Intelligence will need to be employed [19].

In a way of Conclusion; a new paradigm needs to be adopted

The first step might be to develop approaches to identify any unique molecular structures present on narrowly defined population of cells in order to evaluate whether finding such features associated with disease might be at all realistic. Provided this first step is successful, setting up a full effective algorithm for identifying such unique structures relevant to diseases will need a major input into Artificial Intelligence from human "brain power". The input will need to provide guidance on how to get and curate rel-

evant data (published and perhaps even unpublished; regardless, all should be validated); on how to test to show that the algorithm is performing as is needed; and how to improve the approach to answer the initial question that is being asked.

All this will require solid guidance from human-level intelligence. It will require for the AI to assimilate all the existing data on the topic, all the current assumptions and theories about how disease originates and progresses, and how it could be cured. It will need to go beyond extracting information, and draw novel conclusions and recommendations on what steps need to be taken to reach the ultimate goal – understanding the disease and defining unique molecular structures. It will need to foresee ways of making use of this information. To this end, it will need to be fully competent in intelligence of the given topic. In other words, it will need to acquire full capabilities in all aspects of human intelligence such as being able to perceive the real world beyond the information given to it by its programmers. It will need to have the ability to determine the significance of various parts of the overall task and decide on which to focus. It will need to acquire the manner of processing information in human-thinking terms such as perception, abstraction and memories, apply critical analysis of the information and then remember and recall outcomes as and when needed to synthesize a new, more complex whole. Ultimately, it will need to have the capacity to generate new knowledge and know-how. Will AI be able to speculate and imagine? It will need to. Will it be able to reason? It will have to. Will it be logical where humans often cannot be? Will it be able to handle the "what if" questions and predict, and make decisions? All that and more. It would better be. But very likely an intelligent input from humans will be needed all along the way to solve the challenging task at hand.

Bibliography

1. Wong C., *et al*. "Corrigendum: Estimation of clinical trial success rates and related parameters". *Biostatistics* 20.2 (2018): 273-286.

2. Lin A., *et al*. "Off-target toxicity is a common mechanism of action of cancer drugs undergoing clinical trials". *Science Translational Medicine* 11.509 (2019).

3. SEER Cancer Statistics Review (2015).

4. Austreid E., *et al*. "The emergence of targeted drugs in breast cancer to prevent resistance to endocrine treatment and chemotherapy". *Expert Opinion on Pharmacotherapy* 15.5 (2014): 681-700.

5. Petrak K. "Visions but Not False Promises Should Be Funded". *Developing Drugs Journals* 5 (2016): 154.

6. Petrak K. "Targeting Drug-Delivery Systems: Promises, Promises, and More Promises". Let's Change the Paradigm in Recent Advances in Drug Delivery Research (2013): 167-180.

7. Petrak K. "A New Paradigm for Developing Effective Anti-Cancer Therapeutics". *Cancer Therapy and Oncology International Journal* 4.5 (2017): 555649.

8. Pramanik N., *et al.* "A Composite of Hyaluronic Acid-Modified Graphene Oxide and Iron Oxide Nanoparticles for Targeted Drug Delivery and Magnetothermal Therapy". *ACS Omega* 4.5 (2019): 9284-9293.

9. Petrak K. "Essential properties of drug-targeting delivery systems". *Drug Discovery Today* 10.23-24 (2005): 1667-1673.

10. Boddy A., *et al.* "Efficiency of drug targeting: steady-state considerations using a three-compartment model". *Pharmaceutical Research* 6 (1989): 367-372.

11. Petrak K. "Disease-Target Drug Delivery - Science or Fiction?" *Journal of Cancer Science and Treatment* 1.1 (2018): 101.

12. Petrak K. "The difference between targeted drug therapies and targeted-drug therapies". *Medical and Clinical Research Reports* 1.1 (2018).

13. Petrak K. "The Complex Challenge of Targeted Therapy in Cancer". *Acta Scientific Cancer Biology* 3.6 (2019): 08-13.

14. Walker J. Machine Learning Drug Discovery Applications – Pfizer, Roche, GSK, and More (2019). https://emerj.com/ai-sector-overviews/machine-learning-drug-discovery-applications-pfizer-roche-gsk/

15. Buvailo A and Ajami A. Top 7 Trends in Pharmaceutical Research In (2018).

16. Buvailo A. "Brings A Surge of Activity in the "AI for Drug Discovery" *Space* (2018).

17. Darzalex® (Daratumumab) Is Now Approved Across Newly Diagnosed Patients with Multiple Myeloma (2019).

18. Petrak K. "The difference between targeted drug therapies and targeted-drug therapies". *Medical and Clinical Research Reports* 1.1 (2018): 5-8.

19. Krupansky J. How Close Is AI to Human-level Intelligence Here in (2018).