ORIGINAL ARTICLE

USING ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING APPROACHES TO ENHANCE CANCER THERAPY AND DRUG DISCOVERY

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Background: In normal pharmacological effect screening protocols, natural substances that were thoroughly diluted and without their active components separated are employed. Over the last two decades, strong active isomeric compounds have been identified and isolated. The notion of multi-target treatment was novel in the mid-2000s, but it will be one of the most significant advancements in drug development by 2021. Instead, then relying on organically generated mixtures, researchers are looking at target-based drug development based on precisely specified fragments for effective organic anticancer medicines. This study emphasizes the breakdown of structures utilizing computer aids or fragments, as well as a process for applying natural anticancer medications. The use of computer-assisted drug development (CADD) is becoming more frequent. The major areas of this study were the development of computer-aided pharmaceuticals and anticancer agents. The discovery of effective all-natural cancer treatments will be accelerated. Multitarget drug development methodologies have enabled the development of cancer medicines with fewer negative side effects. Cutting-edge analytical and bioinformatics approaches, particularly machine learning, will be employed to uncover natural anticancer therapies.

Keywords: Cancer; Machine learning; Artificial intelligence

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INTRODUCTION

Those cancerous cells may spread to other parts of body via the lymphatic system or circulation. 2020 [Vesteghem C] Big data's emergence in biomedical research has altered cancer research. Handling complex biological concerns and acquiring knowledge from several sources seems easy to scientists. It is well accepted that research institutes do not have enough data to effectively create prognostic and predictive models. Thus, data integration is critical for precision oncology. [Wise, J., and A. G. de Barron, 2019]. COVID-19 and specific cancer programs face several challenges today. Data recording, storage, and reuse are all difficult tasks. Combining information from many sources is also challenging, costly, and time-consuming due to the diverse data required and poor data management in various healthcare systems. Numerous European cancer efforts attempted to standardise and simplify data pipelines before the coronavirus pandemic [Wilkinson M. D., Dumontier M., Aalbersberg 2016]. Many cancer study groups use one of the FAIR data ideas to promote data interoperability and versatility through the use of guidelines, commonly used metadata formats and ontologies. [Vesteghem C., Brndum R., 2020] Cancer researchers and clinicians rely on good data management This is critical to make data easily shared, to decrease duplication, and to enhance machine discovery. As a result of COVID-19, cancer researchers could soon be able to apply their expertise to prevent future healthcare and societal tragedies.

Many programmes, notably VODAN BR, are collecting semantic (meta) data from COVID-19. [Zong N., Wen A., D.J. Stone, 2020] The researchers desire to utilize machine learning, artificial intelligence, and other data science approaches to connect personal patient data to a range of other distant information. [Douzas, G., and F. Bacao, 2018] Adherence to the FAIR principles will improve global genomic research and progress. Sarcoma (cancer of the immune system cells) is another (cancer of the muscle, blood vessels, cartilage, fat, bone, fat, or other connective tissues or supporting tissues). 2015 [Konstantina Kourou] Cancerous cells can grow

through a variety of pathways, such as genetic characteristics and environmental factors. Malignancies of the stomach, skin, prostate, rectal, colon, lung, and breast will be the most common by 2020 (figure 1). [WHO 2020] Every year, one out of every six people dies from cancer. consisting BMI, alcohol consumption, poor diets consisting in processed foods, and insufficient exercise account for almost one-third of all cancer-related fatalities. G. Douzas, F. Bacao, and F. Last (2018) Early-stage patients with no access to diagnosis and therapy are widespread in underdeveloped and emerging nations. Only 15% of low-income countries receive complete treatment, compared to 90% of high-income nations. Cancer has a huge and escalating financial toll. Rather than eliminating risk variables, our technology may assist in sorting out the complicated web of relationships between them. Researchers employed data-driven variable selection and professional clinical judgement to minimize overfitting and bias. In addition, we performed research to address two real-world challenges with COVID-19 patient care. [MK and S Gupta, 2021] Our model only incorporated data that was available at or before the time of COVID-19 diagnosis (time zero) to correctly reflect clinicians' knowledge at time of treatment. As the result, medical factors consisted of the model can be inconsistent. 2020 [S Gupta, M K Gupta] Nonetheless, only 56/348 of our COVID-19 patients (or 16.1%) were needed to undergo D-dimer testing. Individuals at varying stages of illness progression were not taken into account. This paradox would require to be included in a realistic model. [2020] S. S. Patel, A. Acharya, and R. S. Ray

Machine learning offers both advantages and disadvantages. When contrasted to traditional modelling techniques, automated models allow for the assessment of a significantly broader range of clinical variables as indicators for the extent of illness [Wang C., Yu Y., et al. 2020]. Cross-validation checks the model's prediction capability while minimizing overfitting. However, the method reveals characteristics related with medical outcomes but not certainly those that induce illness. 2020 [W. J. Mulder, J. Ochando, and J. Joosten] We examined integrating data-driven methodologies with professional clinical judgement to solve the challenge. 2020 [B. Norgeot, G. Quer, and B. Beaulieu-Jones] It's still difficult to tell the difference among the relative value of healthcare practice and quantitative data. Cancer will have killed 10 million individuals by 2020, making it main cause of death among newly diagnosed cancer patients.

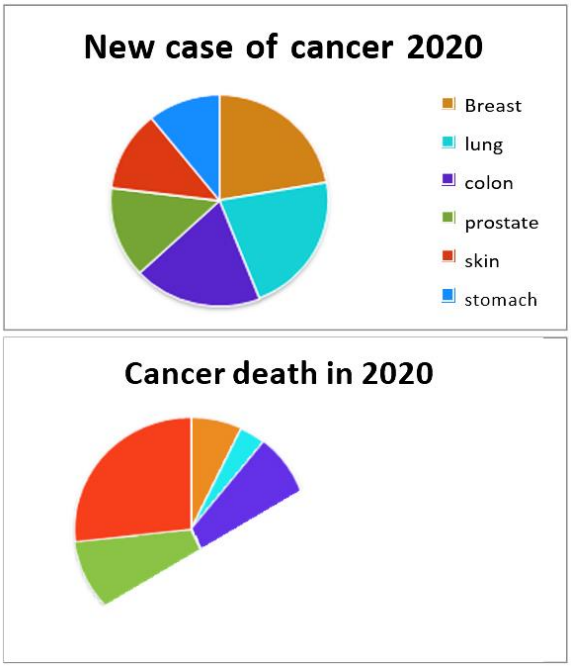

Figure-1: 2020 reports on new cancer cases and deaths worldwide

Drugs that target cancerous cells whereas leaving healthy cells alone are used in targeted treatment. Gene mutations that distinguish cancer cells from healthy ones are rather common. E. R. Flores and M. Napoli, 2020. A cell's DNA includes genes that instruct it on how to conduct several activities. Gene-modified cells behave significantly than healthy ones. When the cancer cell's genes are changed, it may reproduce and develop fast. [2020] G. Quer, B. K. Beaulieu-Jones, and B. Norgeot There nonetheless are several types of cancer, each with its unique group of cancer cells. Differences in gene expression, for instance, make breast and colon cancer cells more likely to form and spread. Although two people both have colon cancer, their particular cases of the illness (e.g., colorectal cancer) may differ. A. Gonçalves, P. J. Ballester, and A. Bomane, 2019. The settings that allow a tumor to form, prosper, or spread are not always the same. Enzymes or proteins that guide cell proliferation and expansion are found in some kinds of cancer. Targeted drugs can stop or turn off signals that tell cancer cells to grow or self-destruct. [F. Vafaee and S. Ebrahimkhani, 2018] As scientists understand more about the abnormalities in cancer cells, they will develop more tailored cancer treatments. This medicine is now routinely used to treat a small number of malignancies. Patients undergoing targeted therapy may need surgery or chemotherapy. [Tschandl, P.; Rinner, C., Apalla 2020] Proposals for drug repurposing and network pharmacology have been made in response to the greater accessibility of FDA-

approved medications and statistical genomic samples from the human genome project. To destroy rapidly dividing cells, cytotoxic drugs target specific mitosis or DNA recompilation pathways. [Setlow R. B., 2001] By engaging with the molecular targets that are involved in cancer growth, progression, and dissemination, targeted therapies halt the development and spread of cancer. [NIH 2021] These effective treatments and their data may aid researchers in discovering novel therapeutic targets, repurposing existing pharmaceuticals, and understanding computational pharmacology. The research of drug-disease/target networks will assist us in updating FDA-approved anticancer drugs and understanding the molecular processes behind therapeutic benefits. 6,000-8,000 of the 30,000 genes in the human genome are thought to represent pharmacological targets. [WHO 2021b] Despite this, only a tiny portion of these proteins is beneficial in the development of medications. Unlike many other human disorders, cancer has a diverse set of molecular targets for therapeutic intervention. Traditional drug research emphasises on drug-protein interactions rather than the "one molecule, one target, one illness" paradigm. Several target proteins have been linked to a range of illnesses, which has gone unreported. Felton, S. S. Hecht, and G. N. Wogan (2004)

Furthermore, certain drugs' "poly-pharmacological" properties may result in unfavourable side effects. Cancer drugs have the most negative side effects. One example of an advantage is the fact that a single molecule may affect many routes. Protein-drug interactions have also been explored using computational techniques by S. Forli, R. Huey, and M. E. Pique (2016). Models based on networks and machine learning are increasingly required. Those are some of the well-recognized computational models that were investigated. [Popova, M.; Isayev, O. 2018]

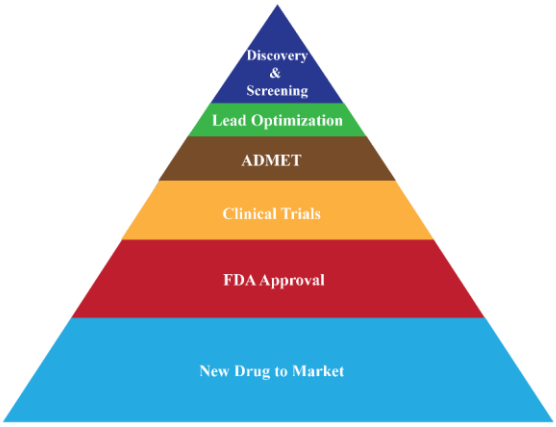

Figure 2: Discovery of drug and its development

Organizations are gradually adopting "best practice" recommendations for creating and deploying AI solutions that help patients. New checklists were established to standardize and promote ML-based therapy. [Ekins, S., and S. Kortagere, 2010] For AI systems to be utilized efficiently, medical personnel and clients must respect their suggestions. D. P. Bottaro and J. S. Rubin 1991 Human-computer cooperation is possible with well-designed and proven human-computer interfaces. [A. Markham, 2019] According to [Lennerz, J. K., and Kwak, 2011], precision oncology may be produced with the help of AI in the coming years, benefiting patients worldwide.

In precise oncology, drugs are used to target genetic anomalies in patients' cancers. In recent years, molecular profiling has become more common in medical oncology, and numerous drugs with molecular targets were approved authorized to enhance results for patients. Immune checkpoint inhibitors have recently been approved for the management of cancer patients who show symptoms of microsatellite instability. [Lam, M. Colombet, J. Ferlay, M. Ervik, 2021] Because to personalized cancer therapy, more anti-tumor drugs and diagnostic test options are accessible than ever before. Personalized oncology can improve clinical phenotype forecasting while simultaneously lowering test costs and improving patient care. They are competent. It must be acknowledged by all stakeholders that these objectives face significant challenges. With big, heterogeneous data sets, it is possible to use AI and ML to find medically meaningful patterns. [Machine Learning Instrument 2021] Hence, machine learning (ML) may enhance individual care. Digital pathology and computer vision pioneers have exposed how ML models may enhance diagnostic processes with a minimum of human participation. to help generalist pathologists speed up clinical diagnosis while doing clinical procedures. The field of diagnostic radiography also aids in the early diagnosis of cancer. [DeMartel, C., Georges, D., and Bray, 2020] Random fore methods may effectively detect circulating microRNAs, and several machine learning experiments using tA methylation patterns collected in plasma cell-free nucleic acids have shown strong performance9. [WHO 2020] Cancer patients are increasingly utilizing AI-driven decision assistance tools. The most effective course of therapy for cancer patients may be predicted using machine learning (ML) models that integrate tumor growth kinetics, genetic profile, and pharmacological characteristics. [Wild CP, Weiderpass E, 2020.] Accessing population-scale sets of data with molecular and clinical classifications is necessary for this. By selecting the ideal patient feature mix, which can include non-genetic tumor features, ML models can

also be utilized to improve prediction accuracy. [Z. T. Al-Salama, Keam, & 2019] To predict clinical aspects, ML models have been trained on responses from patient-derived xenograft experimental systems or large-scale in vitro drug response studies. Preclinical models are unquestionably helpful for developing new drugs, but it is unknown how well they work for precision oncology. Considering substantial efforts, anticipating the appropriate treatment approaches and trends remains challenging. [H. A. Blair, 2018] However, this developing market may alter precision. Despite several attempts, it is expected that merging digital technology into medical procedures would allow AI systems to thrive in the area of medicine. S. Anthony, C. Masuyer, G., and D Sturrock (2012) Those "best practises" have enabled the development and implementation of artificial intelligence systems that best benefit patients. New checklists were established to standardise and promote ML-based therapeutic techniques. [Butrynski J. E. and D. A. D'Adamo, 2010] AI systems need to be acknowledged by both patients and healthcare providers to be successful in clinics. Collaborative interfaces must be properly designed and tested, and users must standardize on AIpublicize operating principles and interpretability. [Yean, D., and Chao W. R., 2007] Artificial intelligence is currently being used in precision oncology. The current increase of proof-of-concept research reveals what precision oncology may look like in the future. [A. Markham, 2017] Many challenges must be solved before AI can have a meaningful impact on medicine. Regardless of the realistic aspirations raised by this exploratory inquiry, productive practises require a greater knowledge of the previously addressed limitations. In coming years, AI may help to improve precision oncology, helping individuals all around the world. [WHO 2019]

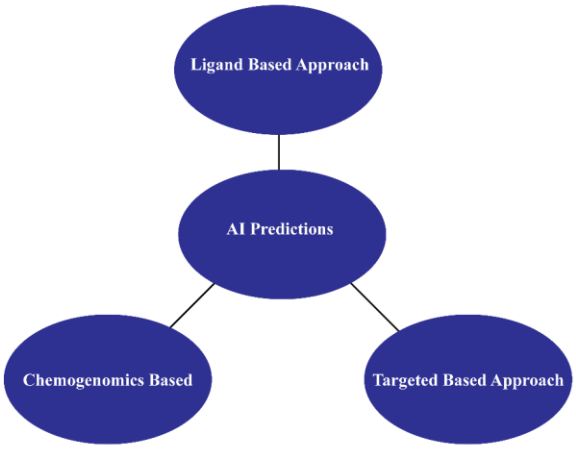

Figure 3: Predictions of artificial intelligence about natural product:

The massive development of chemical bioactivity databases has raised the importance of computational approaches for discovering new DTIs for natural compounds. P. Mathi and M. V. V. Prasad (2018) Several articles have been written on the topic of in silico target prediction. Figure 3 depicts the use of network-based, chemogenomics-based, ligand-based, target-based, and lastly omics-based systems biology techniques to uncover new organic material targets.

To create effective targets for targeted therapies, one must first identify factors that affect the survival and proliferation of cancer cells. [Drews, J., 2000] The term "rational" pharmaceutical design is often used to describe targeted medicines. Comparing the protein levels in cancerous cells and healthy cells might help researchers identify possible targets. [Moro, S., and V. Salmaso, V., 2018] A protein associated with cell survival or proliferation could assist oncogenic cells. The receptor for human development factor epidermal is one example of a destination that is produced to varying degrees in different tissues. On the surface of some cancer cells, HER-2 is highly expressed. Trastuzumab (Herceptin), one of many HER-2-targeted therapies, is agreed for the therapy of certain breast and gastric cancers that overexpress HER-2. [G. G. Eskiler 2019]

Mutant proteins are created by additional cancer cells (altered). BRAF V600E, a mutant form of this protein that signals cell proliferation, is present in many melanomas. Vemurafenib (Zelboraf), an FDA-approved drug, is available to patients with metastatic or incurable carcinoma whose BRAF protein has been changed. [Hollon, T. C. et al., 2020] They also look for chromosomal abnormalities that are exclusive to cancer cells. [Campanella, G., and M. G. Hanna, 2019] Fusion genes—genes that incorporate parts of two separate genes—can develop as a result of chromosomal abnormalities that result in fusion proteins. Fusion proteins might help with personalized cancer therapy. Imatinib mesylate (Gleevec) targets a protein produced by the fusion of two genes in some leukaemia cells. [Rydzewski, J., Nowak, 2018]

Precision medicine, as opposed to the traditional "one pill, fits all" concept, permits healthcare to be personalized to each patient's genetic composition. Large-scale multi-omics investigations generated a list of physiologically intriguing proteins and genes. [P.J. Ballester, 2019] Drug repurposing may uncover proteins associated to cancer that can be targeted by new treatments. Cancer medicine research seeks to increase likelihood that drugs exposed by biochemical or phenotypic approaches will improve medical effectiveness and disease management. Cancer is more expensive than other therapy. N. Coudray and Ocampo (2018) Signature-targeting drugs can be more suitable for therapeutic repurposing

than cell-based models. Several signaling pathways have been linked to the formation of cancer. Mono- or multi-hallmark medications, on the other hand [Forli, S.; Huey, R.; Pique 2016], may pharmaceutically attack a variety of supporting systems, avoiding adaptive resistance. There are various cancer-prevention monotherapies and combinations of non-oncology drugs. [Rosales, A.R., Wahlers 2019]

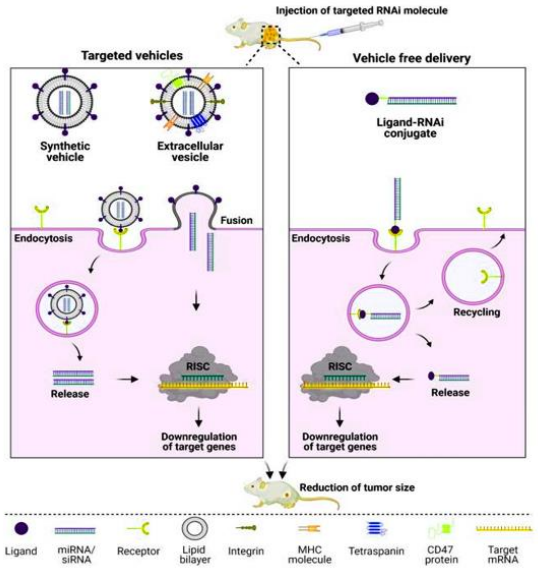

Figure-4: The internalization procedures of the siRNA or miRNA that is ligand-targeted

CONCLUSION

Our initial research included 348 cancer patients. Models should assist doctors in allocating real-time diagnostic test services based on a patient's predicted discriminating capacity. A new drug costs $2.7 billion and takes 12 years to develop. A lack of understanding of molecular pharmacology complicates the development of cancer medicines. As a result, discovering and developing novel medicines requires time and money. This includes virtual screening, drug target prediction, binding site prediction, and protein-interaction network analysis. Some of the innovative strategies that may assist in the identification of anticancer drugs include pharmaceutical binding affinity prediction, drug scaffold assembly, and retro-synthetic routine designs. It uses previously known drug discovery building blocks to create novel therapeutic molecules. The application of machine learning (ML) improves the effectiveness and precision of drug screening and design. It is frequently emphasized the need of combination models or employing efficient procedures (such as dimensionality reduction). To find breakthrough natural product leads, scientists from numerous disciplines must collaborate. Chemicals through various structures and mechanisms of action are identified in natural materials by means of nanotechnology and analytical approaches. Chemistry is required for biodiversity. RNAi-specific delivery strategies were developed to target cancers. Packing the RNAi molecules inside a carefully designed delivery vehicle is one of these approaches, as is indirect target-ligand-RNAi molecule conjugation. The discovery of effective all-natural cancer treatments will be accelerated. Multitarget drug development methodologies have enabled the development of cancer medicines with fewer adverse effects. Cutting-edge analytical and bioinformatics methods, with machine learning, will be employed to uncover natural anticancer therapies.

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