Global Scientific JOURNALS

GSJ: Volume 14, Issue 1, January 2026, Online: ISSN 2320-9186

www.globalscientificjournal.com

Why Cancer Drugs Fail: Resistance Mechanisms and Weaknesses in Preclinical Models

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Abstract

Cancer drug resistance remains a major obstacle to effective cancer therapy. This is because it significantly limits treatment efficacy. This leads to cancer relapse and poor patient outcomes. Cancer develops resistance through a range of intrinsic and acquired mechanisms, including mutations, drug efflux and DNA repair. By explaining the main characteristics of cancer and their resistance mechanisms, this paper aims to examine and identify why drugs often fail to completely cure cancer in patients. The research has pinpointed that limitations to preclinical models, including two-dimensional cell lines and animal models, can also lead to poor clinical translation. Finally, improved experimental models, combination therapeutics, adopting the help of artificial intelligence and other ways to improve clinical outcome are evaluated. An in-depth and accurate understanding of resistance and limitations of research models is essential for steps forward in oncology.

Keywords: Cancer; Resistance mechanisms; Cancer research models; 2D cell lines; Mice models; Organoids; Combination therapy

Introduction

Problem Associated with Drugs Being Ineffective in the Body

Cancer research has progressed tremendously throughout the past decade, as it is providing far more treatment options for cancer patients. Notably, between the years 2013 and 2022, there was a 1.7% annual reduction in cancer mortality rates, attributable to enhancements which have been made in treatment approaches (American Cancer Society, 2025). Despite these improvements, many cancer cases continue to present significant challenges for both patients and healthcare providers. This is primarily due to a prevalent issue in oncology: drug resistance. This is

when some cancer cells manage to overcome the effects of cancer drugs that are administered into a patient's body (Houseman et al., 2014).

Tumours may reemerge in a process referred to as recurrence or relapse, which can occur at any point during a patient's treatment, and may even arise several years after the conclusion of that treatment (Li et al., 2015). Therefore, combating drug resistance is a crucial area of research that strives to improve the efficacy of drugs to completely eradicate cancer cells with one treatment method and prevent recurrence. This research study examines and explains why cancer drugs lose efficacy, by using Photodynamic Therapy (PDT), Imatinib and Programmed Death Protein 1 (PD-1) blockade as case studies. Additionally, it outlines strategies to overcome resistance and the preclinical-to-clinical gap.

Understanding the Concept of Drug Resistance

Drug resistance could be in the form of intrinsic resistance or acquired resistance (Wang et al., 2019). Intrinsic resistance refers to cancer cells within the same tumour that can exhibit a variety of molecular changes. This phenomenon is known as tumour heterogeneity. Tumour heterogeneity allows subclones of cells with a growth advantage to persist and ultimately proliferate (Lüönd et al., 2021). This causes the drug to only be effective to certain parts of the tumours, while some parts remain resistant (Dagogo-Jack & Shaw, 2018). As a result, some cancer cells in the tumour continue to proliferate, causing relapse after treatment. On the other hand, acquired resistance refers to new changes that occur to cancer cells under treatment pressure, such as mutations, epigenetic rewiring and pathway bypass (Hamilton et al., 2009; Niederst & Engelman, 2013). The cancer cells possess the capability to adapt to the drug administered and acquire the molecular changes, which allow them to fully evade the intended effect of the drugs.

Whether it is intrinsic or acquired resistance, these traits of cancer cells remain as some of the most challenging problems that oncology is facing. Although some treatment plans are tested to be effective against eradicating certain cancer cells in the laboratory, they can often have low clinical efficacy due to drug resistance.

What is Cancer?

Cancer is a disease in which abnormal cells divide in an uncontrolled fashion, invade and colonise areas that are normally reserved for other cells. Even though cancer can refer to a wide array of diseases, researchers have defined cancer by using certain hallmarks which are common in all cancer types (Hanahan, 2022). The 6 main characteristics are explained below:

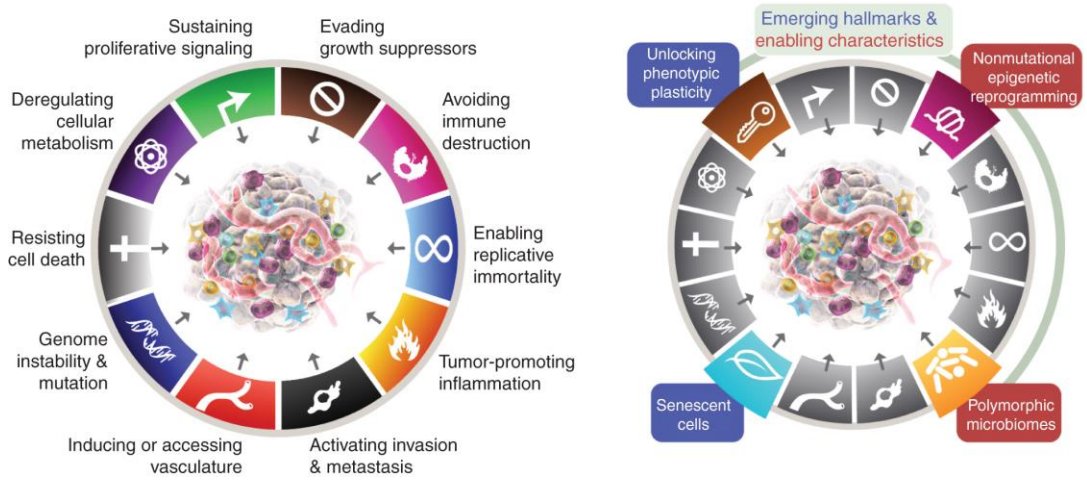

Figure 1. Capabilities of Cancer Cells - This figure illustrates the various characteristics of cancer that researchers have identified over the years. It began with just 6 main characteristics in 2000. The advances in our understanding of cancer have expanded the framework to include 14 characteristics.

1. Self-sufficiency in growth signals

Cancer cells gain the ability to continuously signal themselves to divide, bypassing the strict control present in normal cells. Even without external cues, cancer cells behave as if the body is constantly signalling them to proliferate. Thus, leading to uncontrolled expansion.

2. Insensitivity to anti-growth signals

Normal tissues rely on tumour suppressor genes to stop cell division when conditions are unsafe or unnecessary. Cancer cells disable these brakes. Without growth suppressors, cancer cells can divide uncontrollably.

3. Evading apoptosis

Apoptosis eliminates damaged or dangerous cells. Cancer cells acquire mutations that disable apoptosis, so they survive despite severe abnormalities. As these abnormal cancer cells survive, there is a greater chance for them to mutate and resist therapy methods.

4. Metastasis

Metastasis is the process where cancer cells spread from the primary tumour to distant organs and form new tumours. It is considered one of the most critical hallmarks because 90% of cancer-related deaths result from metastatic disease and not the primary tumour itself.

5. Sustained angiogenesis

Tumours cannot grow beyond 1-2 mm without blood vessels. Cancer cells induce the formation of new blood vessels to supply oxygen, nutrients and remove waste to ensure their survival.

6. Limitless replicative potential

Most normal cells can divide only 50-70 times due to telomere shortening. Cancer cells bypass this limit and become 'immortal'. Thus, cancer cells can proliferate indefinitely. This allows tumour masses to become large and persistent.

Additionally, the wide variety of cancer types can be grouped into 5 main groups according to where they originate in the body (as shown in Figure 2) (Cancer Research UK, n.d.).

Type of cancer	Area of origin	Occurrence rate (%)
Carcinoma	Skin or tissues that cover internal organs	80
Sarcoma	Connective or supportive tissues	1
Leukemia	Tissues that produce blood cells	3
Lymphoma and Myeloma	Immune system	7
Brain and Spinal cord	Brain or spinal cord	3

Figure 2. Table showing types of cancers and their respective occurrence rates

The Significance of the Paper

According to the World Health Organisation (WHO), approximately 1 in every 5 people develop cancer in their lifetime. 1 in 9 men and 1 in 12 women die from the disease (World Health Organisation, 2024). Therefore, this

means that with such a high cancer incidence and death rate, it is crucial to constantly improve treatment methods and tackle the challenges that drugs face in terms of treating cancer.

Studies have demonstrated that drug resistance proves to be one of the principal limiting factors to finding cures in cancer cases (Vasen et al., 2019). In addition to the emotional impact on cancer patients and their family members, the cost of cancer treatment is a burden. Research highlighted that the drugs which were developed between 2009 and 2014 cost more than $100,000 USD per year (Natasha & Leighl, 2021). Drug resistance means the patient will have to receive multiple forms of treatment. Therefore, further exacerbating the cost of treatment. As cancer cells are discovered to be resistant to available drugs, new drugs will have to be made. Additionally, high mortality rates from cancer places stress on the healthcare systems and governments to emphasise on conducting ongoing research towards tackling cancer drug resistance.

Aims and Goals of the Paper

This research investigates why some drugs look promising in the pre-clinical phase and fail in translation. In addition, the study will provide certain strategies to overcome drug resistance in cancer.

Literature Review

Mechanisms of Resistance

Target Alteration

Target alteration refers to mutations that are present in areas of cancer cells which a cancer drug is designed to target. One of the most common examples of drug resistance is due to secondary mutations. It causes a change in drug targets, evident in imatinib resistance in chronic myeloid leukaemia (CML). Mutations in the proteins of the cancer cells cause imatinib to be unable to perform proper binding. Therefore, losing the drug effectiveness (Mansoori et al., 2017).

Bypass Signalling

Target alteration allows cancer cells to develop resistance to the specific drug that is administered into the body. On the other hand, bypass signalling activates an alternative or parallel molecular pathway to maintain their growth and

survival when a drug inhibits its primary pathway. Therefore, it creates another route leading to the same goal, allowing the tumour to 'bypass' the drug's intended effect (Niederst & Engelman, 2013).

Drug Efflux

Adenosine triphosphate - binding cassette (ABC) transporters are known to help cancer cells develop drug resistance by pumping drugs out of cancer cells to reduce their effectiveness. Cancer cells overexpress specific membrane proteins known as efflux pumps to bind to the drugs. The pumps use cellular energy to actively transport the drugs out of the cell. This process lowers the drug concentration inside the cancer cell. Thus, preventing it from killing the cancer cells (Kurimchak et al., 2022).

DNA Repair

Chemotherapeutic agents damage the cancer cells DNA directly and/or indirectly. Cancer cells can recover from such damages by repairing the damage to the DNA. DNA repair mechanisms help to maintain genomic stability in normal cells. However, the dysregulation of this mechanism in cancer leads to resistance against therapies, such as chemotherapy and radiotherapy. Cancers often upregulate repair pathways to survive DNA damage from treatments, diminishing the efficacy of treatment (Mansoori et al., 2017).

Tumour Microenvironment (TME)

The TME consists of many structures and cells that work together to protect the tumour. Cancer-associated fibroblasts (CAFs) can secrete cytokines which cause cancer cells to enter a drug-tolerant state. Additionally, CAFs can remodel the extracellular matrix (ECM). This creates a stiff barrier that blocks drug penetration. Immune-suppressive cells present in the TME, such as tumour-associated macrophages and regulatory T-cells can weaken the ability of the immune system in damaging cancer cells. A combination of CAFs, ECM, immune-suppressive cells and many other factors in the TME help to improve cancer cell survivability and resistance against cancer drugs (Senthebane et al., 2017).

Phenotypic Plasticity

Phenotypic plasticity allows cancer cells to dynamically switch to drug-resistant states through non-genetic changes under therapeutic stress. Thus, enabling survival by adopting different cell functions. Cancer cells can bypass drug

actions, which can lead to treatment failure. One example is the epithelial-mesenchymal transition (EMT). During EMT, cancer cells lose their epithelial features and gain mesenchymal, migratory and invasive traits. This normally leads to metastasis and increased drug resistance. EMT cancer cells are less proliferative. Thus, reducing the efficacy of chemotherapy that usually targets cell division. In addition, EMT cancer cells carry out drug efflux more efficiently. They cause cancer cells to be more stem-like with features, such as strong DNA repairing capabilities and greater resistance to apoptosis (Gupta et al., 2019).

Common Resistance Mutations

An example of common resistance mutations is related to an enzyme - tyrosine kinase. It requires energy from adenosine triphosphate (ATP) to trigger growth signals. This enzyme exhibits abnormal activity in cancer cells, which leads to uncontrolled cell growth. Hence, many cancer drugs named as tyrosine kinase inhibitors (TKIs) aim to target these malfunctioning enzymes in order to control cancer growth.

Furthermore, mutations can cause certain TKIs to lose their efficacy on cancer cells. For example, the T315I gatekeeper mutation in tyrosine kinase causes resistance to drugs, such as imatinib, dasatinib and nilotinib. This mutation is known to be the cause for 20% of CML patients. Another mutation is the T790M gatekeeper mutation in epidermal growth factor receptor (EGFR). Approximately 60% of patients developing drug resistance have this mutation in non-small cell lung cancer (NSCLC). These mutations are known as gatekeepers because they physically regulate the size and shape of the binding site where other molecules, including ATP or inhibitor drugs bind. Thus, the ‘gatekeepers can prevent drugs from binding to the active site and decrease the efficacy of the drugs (Kim et al., 2021).

Current Cancer Treatment Methods that are Effective

Photodynamic therapy (PDT) is identified as a promising treatment method for cancer, as it has fewer side effects for the patients and it can stimulate the immune system. PDT is commonly used to treat actinic keratoses and certain superficial basal cell carcinomas (Wachowska et al., 2011). These are diseases that can develop after prolonged exposure to ultraviolet light. Actinic keratoses are precancerous lesions on the skin which have the potential to develop into cancer if left untreated, while superficial basal cell carcinoma is a common skin cancer and it is slow-growing.

PDT works by first introducing a photosensitiser, such as aminolaevulinic acid. This is taken up by the body and accumulates in abnormal cells. Upon exposure to light of a specific wavelength, photosensitisers are activated to

produce reactive oxygen species (ROS) within the cell that can trigger apoptosis or necrosis**.** Thus, PDT helps to kill cancer cells with the help of photosensitisers and the exposure of light. It is important to note that PDT efficacy is limited by light penetration and it is best for superficial lesions (Wachowska et al., 2011).

Additionally, Gleevec was recognised globally and given the 2009 Lasker-DeBakey Clinical Medical Research Award by the Lasker Foundation for being a major advance in medical research that improves the lives of thousands of people. Gleevec was awarded due to its ability to treat chronic myeloid leukemia. It turned a fatal cancer into a manageable disease. Chronic myeloid leukemia is a type of cancer of the bone marrow. The bone marrow is the tissue within bones where blood cells are made. This cancer causes an increased number of abnormal white blood cells in the body.

Dysregulation of tyrosine kinases contributes to malignancy, as it allows for uncontrolled proliferation of cells. This process requires the binding of adenosine triphosphate (ATP) to the active site of tyrosine kinase. The drug imatinib competitively binds to the ATP site. With imatinib bonded to the active site, it prevents ATP molecules from binding to tyrosine kinase. This effectively blocks abnormal growth signals from the malfunctioning tyrosine kinase enzymes in cancer cells (Iqbal & Iqbal, 2014).

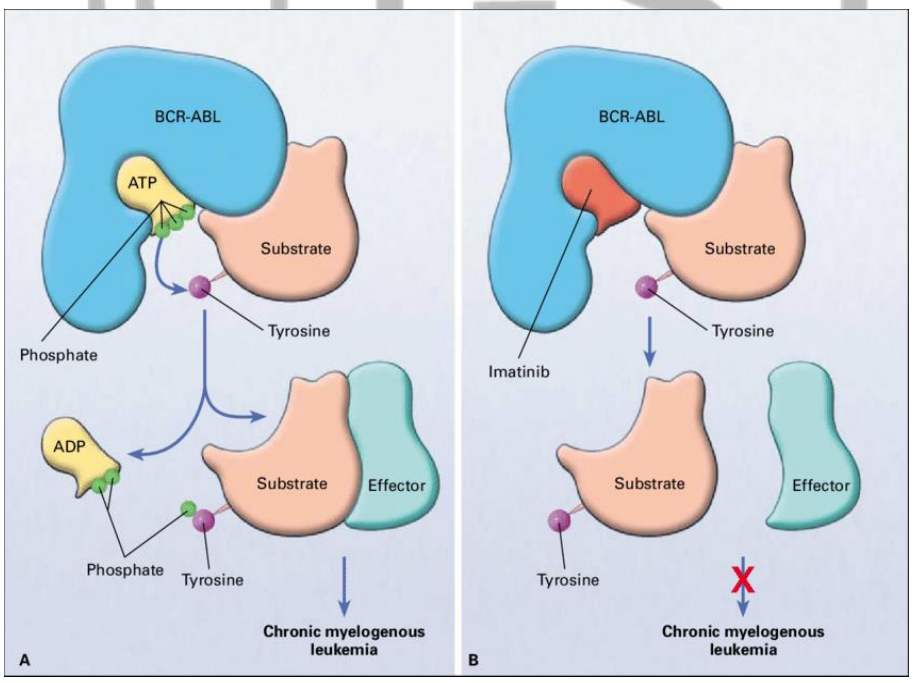

Figure 3. (Savage & Antman, 2002). Imatinib binding to BCR-ABL. As illustrated, imatinib functions by competitively binding to the active site on BCR-ABL so that tyrosine kinase cannot function as intended. Thus, preventing the uncontrolled proliferation of cancer cells.

Keytruda is an immunotherapy that studies have shown to be relatively effective to advanced melanoma that are unresectable and metastatic. Melanoma is an aggressive skin cancer that causes metastatic melanoma patients to have an overall survival period of <12 months (Kwok et al., 2016). Some cancer cells can evade the host's immune system by engaging the PD-1/PD-L1 inhibitory pathway (Patsoukis et al., 2020). These cancer cells overexpress a protein called PD-L1 on their surface, which then binds to the PD-1 receptors on T-cells. T-cells normally identify and destroy infected, cancerous or foreign cells.

However, PD-L1 deactivates the T-cells. Thus, preventing the immune cells from attacking them (Han et al., 2020). The main ingredient in Keytruda is pembrolizumab. It blocks PD-1 on T cells and prevents PD-L1/PD-1 inhibitory signalling and restores T-cell activity. Thus, the immune system is assisted by pembrolizumab in identifying cancer cells, and allowing T cells to attack.

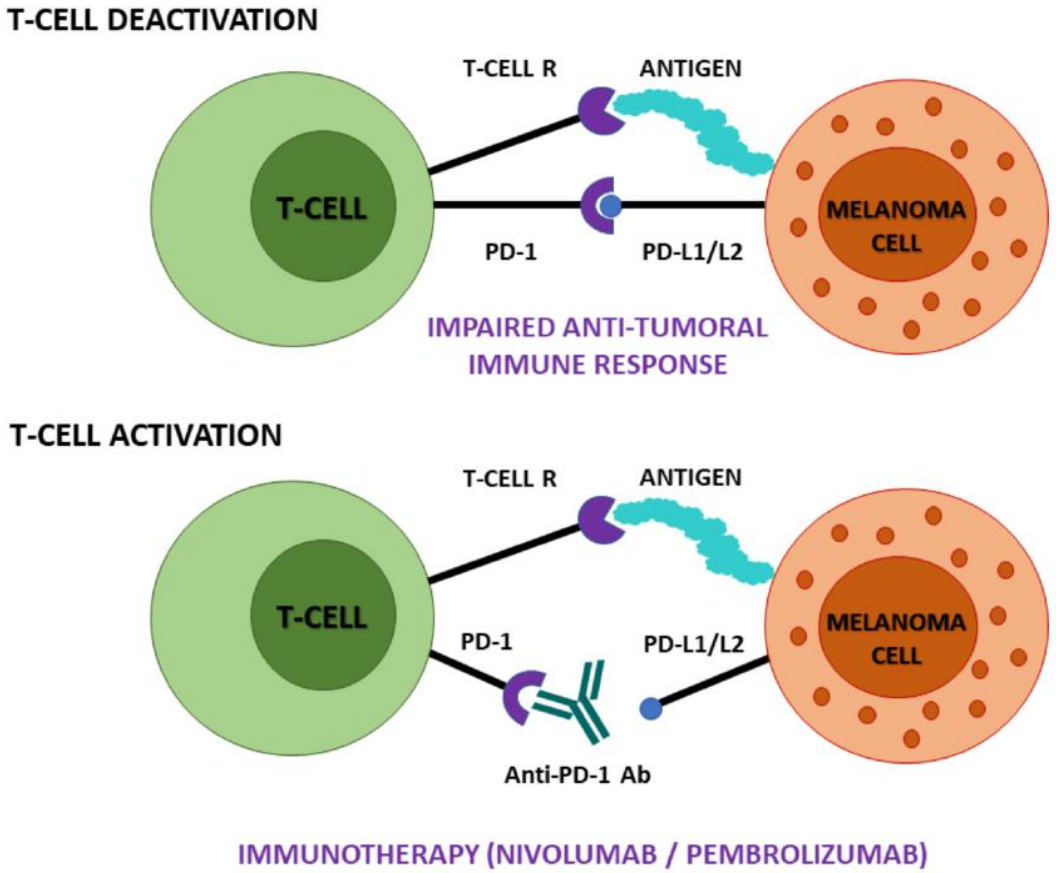

Figure 4. (Kamińska et al., 2021). Pembrolizumab mechanism - as demonstrated, T cells can be deactivated when PD-L1 on cancer cells bind with PD-1 on T cells. Pembrolizumab functions by competitively binding with PD-1 on T cells to ensure they continue to attack cancer cells.

Drug Resistance in Case Studies

Research has proven that cancer stem cells (CSCs) can develop resistance to PDT. This involves the photosensitiser aminolaevulinic acid (5-ALA-PDT). CSCs upregulate ATP-binding cassette (ABC) transporters that influence 5-ALA by reducing their accumulation in cancer cells. Upon treatment with light, the photosensitisers do not trigger the intended effect of killing the cancer cells, as they are removed by the ABC transporters. This results in the development of 5-ALA resistant cancer cells that continue to proliferate (Rice et al., 2025). The drug will not be effective against the resistant cancer cells in the patient anymore.

Studies have pinpointed that drugs can be used to inhibit ABC transporters. This includes, lapatinib, as it binds well into the binding site of ABC transporters. Thus, blocking the transporter and preventing drug efflux. These drugs can be used to block the effect of efflux pumps in cancer cells, ensuring the intended effect of 5-ALA (Mansi et al., 2022).

Imatinib functions as a tyrosine kinase inhibitor in combating cancer cell proliferation. However, kinase mutations as a form of acquired resistance to imatinib occur in around 30-50 % of cases. The mutations can cause the ATP binding site on tyrosine kinase to change shape, which directly prevents imatinib from competitively binding. Thus, this limits the efficacy of imatinib in curing cancer (Srivastava & Dutt, 2013). With imatinib resistance becoming well-known, second generation and even third generation TKIs with higher potency are being released. These second and third generation TKIs are more selective and can demonstrate better ability to counter the mutations in cancer cells. Overall, imatinib is still the first line of defense against CML. In saying that, when resistance against imatinib is observed, other drugs such as, dasatinib, nilotinib and bosutinib are administered to provide assistance (Jabbour et al., 2015).

The tumour microenvironment can pose a challenge to immunotherapy, such as Keytruda. Regulatory T cells that are present in the tumour microenvironment can secrete immunosuppressive cytokines which inhibit the proliferation and activity of effector T cells. As Keytruda functions by helping effector T cells identify cancer cells, its efficacy is significantly reduced when cytokines can prevent the action of effector T cells on the tumour. In other words, certain tumour microenvironments prevent effector T cells from killing cancer cells even if Keytruda helps to identify them (Rodriguez-Pascual et al., 2019). As mentioned above, CAFs release cytokines, which in turn inhibit the activity of effector T cells. As a result, new studies aim to produce substances that block cytokine signalling

pathways. With decreased cytokine concentration, T-cell infiltration and anti-tumour immune response are enhanced. Thus, this improves the efficacy of PD-1 blockade mechanism (Hou, 2015).

The Reasons for Translation Gap

2D Cell Lines

Although 2D cell lines are used for their simplicity and low costs, they can cause great translation gaps in terms of testing cancer drugs. Firstly, a 2D experiment lacks the TME which is present around human tumours. Without the TME, there will be no CAFs that can produce cytokines that target the host's immune system, and there will be no ECM acting as a barrier that blocks drug penetration. Thus, immune cells will face little to no challenge in approaching cancer cells in dish experiments.

Secondly, cancer cells in 2D cell lines often lack tumour heterogeneity. They have equal access to nutrients, oxygen and signalling molecules. By being exposed to similar environments, the cancer cells can rarely mutate to form various cell lines. In the human body, differing environments, such as low oxygen levels can motivate the cancer cells to mutate. Therefore, resulting in different phenotypes of cancer cells coexisting in the same tumour. Therefore, drugs may be tested to be effective against a single type of cancer cells in dishes. However, they fail to work in the human body when a variety of cell types exist.

Lastly, it is important to note that 2D environments are unable to simulate metastasis in cancer cells. Additionally, this means that EMT is unlikely to happen. As explained above, mesenchymal traits cause cancer cells to be more drug tolerant as they have the capability to efflux drugs more efficiently and a stronger DNA repair response. As such, drugs might prove to work on non-metastasised cancer cells in dishes but lose effectiveness when combating stronger EMT cancer cells in vivo (Abuwatfa et al., 2024).

Researchers have identified the issues with 2D models and are improving research methods by introducing 3D models that better simulate the environment in the body. This includes factors like the TME and the presence of different phenotypes of cancer cells in the same environment.

Mice Models

The average rate of successful translation from animal models to clinical cancer trials is less than 8%. Animal models are limited in their ability to mimic the extremely complex environment in a human tumour (Mak, 2014). The low translation rate from mice models can be attributed to several factors. This incorporates the fact that the TME in mice is very different compared to those in humans. For instance, the PD-1 in mice is weaker than in humans. Thus, causing implications for immunotherapy. Therefore, weaker immunotherapy working in mice might not function effectively in humans.

Additionally, some mice models, such as the patient-derived xenographs (PDX), involve injecting human tumour samples into mice. These mice are usually immunocompromised to prevent tissue rejection. They lack a fully functional immune system. As a result, these mice models cannot accurately simulate key interactions which suppress or facilitate metastasis. This is similar to the limitation of 2D models: if metastasis does not occur, more drug tolerant cancer phenotypes do not present themselves in the drug experiments. Even if the drugs successfully eradicate cancer in these mice models, they might fail to translate clinically when tested against highly metastatic cancers. Furthermore, without a functional immune system, common immunotherapy drugs cannot be tested on mice models.

Lastly, mice generally have a higher metabolic rate compared to humans. This means that their liver is able to clear drugs much faster from their bloodstream. This explains the difference in drug intoxication between mice and humans. Drugs that worked on mice models might face the challenge of intoxicating human patients when the required dosage is administered (Ireson et al., 2019).

Methodology

A comprehensive literature review research approach was conducted to examine the reasons why developed cancer drugs fail and potential advancements to overcome therapeutic failure. Research papers have been collected from reliable academic sources, such as PubMed and Google Scholar. In order to ensure that the information obtained was relevant in the rapidly-changing field of cancer research, the years of publicity of the research papers was placed between 2015-2025. The search terms included combinations of keywords, such as cancer drug resistance, cancer resistance mechanisms, reasons for resistance to treatment and problems with cancer models.

Inclusion and Exclusion Criteria

Only peer-reviewed original research papers that were published in English were included. Studies which examined the specific reasons about why cancer drugs might not be effective in the human body were prioritised. These included cancer resistance mechanisms that cause drugs to lose efficacy and issues with models which were used to test cancer drugs that cause poor translational success.

On another level, articles which were unrelated to therapeutic resistance or did not provide relevant explanations about reasons for poor cancer drug translation are excluded. In addition, studies that were biased in their experimental data or did not contain a clear description of their methodology were excluded.

1. **Patient-derived lung cancer organoids as in vitro cancer models for therapeutic screening by Kim et al., 2019, published by Nature Communications**

This research paper found a new and effective method of using lung cancer organoids (LCOs) to imitate the lung cancer environment in patients. Many limitations of 2D and mice models are tackled by using this new method. LCOs are 3D mini-tumours grown in labs from a patient's cancer cells, mimicking the original tumour's structures, genetics and behaviours. This paper highlighted primary research, where the researchers took lung cancer tissue samples from patients. These samples were prepared into different preclinical research models to compare their similarities to the actual cancer environment. The limitation of the method was that the LCOs were derived from only epithelial cells. Therefore, they lacked a microenvironment involving stromal and immune cells. Despite this limitation, the LCOs proved to be much better than 2D or mice models.

2. **Combination therapies for cancer: challenges and opportunities by Zhou et al., 2023, published by BMC Medicine**

In the case of pancreatic cancer, it is the most lethal cancer as most patients are not able to receive resection surgery upon diagnosis. This research studied and explained why a new combination therapy approach provided the best chance to patients with pancreatic cancer compared to single-agent therapies. The approach involves using chemotherapy to shrink the size of the tumour first before performing surgery. As a secondary research paper, the research investigates various case studies involving the combination therapy to assess its efficacy on patients. Although this new combination therapy promises better outcomes for patients, it is important to note that the drug that they are administering, Folfirinox, can have adverse side effects on certain patients. For example, people who are diagnosed with neutropenia and neuropathy. A limitation included that the research paper did not provide sufficient evidence to substantiate the efficacy of the combination therapy as they had claimed.

3. The utilisation of artificial intelligence applications to improve breast cancer detection and prognosis by Alsharif, 2023, published by Saudi Medical Journal

The study examines the understanding that Artificial intelligence is being incorporated in many areas of cancer diagnosis, such as breast cancer detection. AI can be used to read mammograms, ultrasounds and magnetic resonance images. This secondary research paper reviews the different areas where artificial intelligence is used in aid of treating breast cancer. However, the papers had a small dataset. This raises questions about the actual accuracy and credibility of their system of recording the information. Nonetheless, the research shows potential for these tools to be used in clinics worldwide to aid physicians in their detection of cancer.

Findings and Discussion

This narrative review examined the fundamental reasons about why cancer drugs fail to cure cancer. This could be either due to the strong capabilities of cancer to resist against drugs by using various different mechanisms, or due to the limitations in experimental models which significantly reduce translational success. This places stress on researchers to develop new drugs and treatment methods to better combat cancer resistance and to improve research models to better represent cancers in the human body.

Research models are critical in cancer research as it sets the foundation on which researchers conduct preclinical tests. A poor research model means that drugs tested on them are unlikely to succeed when actually introduced to the more complex cancer environment present in the human body. In recent years, researchers have committed resources towards improving research models and introduced new models, such as organoids that aim to fill the gaps of 2D and mice models. Researchers have been able to establish lung cancer organoids (LCO) that could retain the histological and genetic features of the five most common subtypes of lung cancer. LCOs can maintain up to 77% consistency with the mutations that were present in original cancer cells. With a 3D structure and a greater similarity to actual in vivo cancer cells, the researchers proposed that this new model can be an improved platform for drug screening and clinical trials (Kim et al., 2019).

Patient variability is an important factor to consider in prescribing drugs to cancer patients. Even the same type of cancer can have different characteristics in different patients. There is no ‘one size fits all’ treatment plan for cancer cases. Instead, each patient should be accessed as a separate case and personalised treatment plan should be given to ensure successful treatments. Giving a non-tailored treatment approach will just waste precious time as the cancer

cells can effectively bypass the treatment methods. The organoid models mentioned above can tackle this problem, as they have demonstrated potential in assisting in vitro trials for predicting individual patient drug responses (Kim et al., 2019). With the help of these models, truly individualised cancer treatment plans can be prescribed to enhance the chances of successful treatment.

Due to the many resistance mechanisms that cancer has, single-agent therapies are less likely to work once cancer cells develop resistance to the drug used and resistance cell lines start to proliferate. This brings about the importance of combination therapies, targeting multiple survival mechanisms at once, lowering the chances of cancer cells surviving. Pancreatic cancer is one of the most lethal cancer cases. Instead of single-agent therapy, researchers are exploring combination therapies to combat this cancer. One of the main reasons pancreatic cancer is deadly is because the tumour wraps around vital blood vessels. This can complicate surgery, and cause resection of the tumour to be discouraged in many cases. This gives time for the cancer to become malignant and metastatic. However, neoadjuvant chemotherapy can be used as a first resource to shrink tumours before surgery is attempted to remove the tumour. This combination therapy approach has highlighted the potential to provide the best care to patients with pancreatic cancer (Zhou et al., 2023).

With the development of artificial intelligence (AI) in multiple fields, it is undeniable that AI has tremendous benefits to the oncology field as well. Machine learning can enable AI to be very accurate and precise with tasks that human beings might not be able to. Large amounts of imaging data can be fed to AI machines to teach them how to identify tumours. Although they cannot fully replace physicians yet, they do provide substantial assistance in early detection of cancer. Early detection in cancer is important as it prevents cancer from reaching more dangerous stages. Early detection and early treatment can significantly increase survival rate. Later stages of cancer can cause them to be more drug resistant. In the case of breast cancers, mammograms are used to detect and diagnose early stages of cancer. AI has proven to be beneficial in assisting doctors in identifying breast lesions, flagging out subtle abnormalities that may be missed (Alsharif, 2023).

Finally, the complexity of cancer treatment cannot be perfected by a singular department. Multidisciplinary collaboration is needed. This includes clinicians, biologists, chemists and data scientists to fully understand the complexities of the tumour microenvironment and the evolutionary pressures driving the development of durable cures.

Conclusion

In conclusion, cancer drugs fail mainly due to 2 reasons: cancer drug resistance and shortcomings in preclinical models. To tackle these problems, the healthcare sector can use the help of AI, delve deeper into combination therapies and improve preclinical models to better approximate tumour environments in the human body. Breakthroughs in these areas will prove of significant help to cancer treatment, ensuring more drugs are effective towards different types of cancer.

Acknowledgements

The author thanks Mentor Farah and Mentor Gift for their guidance and constructive feedback throughout the course of this paper.

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