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ORIGINAL

Therapeutic Targets and Treatment Improvement Through Key Oncogenic Pathways in Cancer

Objetivos terapéuticos y mejora del tratamiento mediante vías oncogénicas clave en el cáncer

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ABSTRACT

Many treatments for cancer have limited effectiveness and serious side effects, but it is still one of the main reasons of illness and death around the world. Because DNA abnormalities and the misregulation of signaling pathways make cancer so complicated, we need to find new therapy targets so that we can make medicines that work better and are more tailored to each person. Important cancer-causing pathways, including the PI3K/AKT/mTOR, MAPK/ERK, Wnt/ß-catenin, and JAK/STAT pathways, help cells grow, survive, form new blood vessels, and hide from the immune system. Understanding the molecular processes that control these pathways has made it possible to create tailored treatments that stop the abnormal signals that cause cancer to spread. This study looks at the current state of therapeutic targets and how key tumor pathways are used to treat cancer. New tailored therapies, like small chemicals, monoclonal antibodies, and immune checkpoint inhibitors, have shown promise in both clinical studies and everyday use. Resistance to these medicines, on the other hand, is still a big problem. Resistance mechanisms, like changes in the target gene, the start of alternative pathways, or immune escape, make treatment results more difficult and need more research. Combining genetic analysis and precision medicine makes it possible to find changes that are unique to cancer. This makes it easier to create personalized therapies that are better at beating treatment resistance. Using focused medicines along with standard treatments like radiation and chemotherapy is a new way to improve treatment effectiveness and reduce resistance.

Keywords: Oncogenic Pathways; Targeted Therapy; Cancer Treatment; Precision Medicine; Treatment Resistance; Molecular Profiling.

RESUMEN

Muchos tratamientos contra el cáncer tienen una eficacia limitada y efectos secundarios graves, pero sigue siendo una de las principales causas de enfermedad y muerte en todo el mundo. Dado que las anomalías del ADN y la desregulación de las vías de señalización complican tanto el cáncer, necesitamos encontrar nuevas dianas terapéuticas para poder desarrollar medicamentos más eficaces y adaptados a cada persona. Vías cancerígenas importantes, como PI3K/AKT/mTOR, MAPK/ERK, Wnt/ß-catenina y JAK/STAT, ayudan a las células a crecer, sobrevivir, formar nuevos vasos sanguíneos y protegerse del sistema inmunitario.

Comprender los procesos moleculares que controlan estas vías ha permitido crear tratamientos a medida que detienen las señales anormales que provocan la propagación del cáncer. Este estudio analiza el estado actual de las dianas terapéuticas y cómo se utilizan las vías tumorales clave para tratar el cáncer. Las nuevas terapias a medida, como las micropartículas químicas, los anticuerpos monoclonales y los inhibidores de puntos de control inmunitario, han demostrado ser prometedoras tanto en estudios clínicos como en el uso diario. Por otro lado, la resistencia a estos medicamentos sigue siendo un problema importante. Los mecanismos de resistencia, como los cambios en el gen diana, el inicio de vías alternativas o la evasión inmunitaria, dificultan la obtención de resultados terapéuticos y requieren más investigación. La combinación del análisis genético y la medicina de precisión permite detectar cambios específicos del cáncer. Esto facilita la creación de terapias personalizadas más eficaces para combatir la resistencia al tratamiento. El uso de medicamentos específicos junto con tratamientos estándar como la radioterapia y la quimioterapia es una nueva forma de mejorar la eficacia del tratamiento y reducir la resistencia.

Palabras clave: Vías Oncogénicas; Terapia Dirigida; Tratamiento del Cáncer; Medicina de Precisión; Resistencia al Tratamiento; Perfil Molecular.

INTRODUCTION

Cancer is a complicated and varied disease that causes cells to grow out of control, avoid death, and spread to other parts of the body. Cancer is still one of the top reasons of death in the world, even though study and treatment have come a long way. Coming up with new and better ways to treat patients is very important for improving their results. Traditional cancer treatments like chemotherapy, radiation, and surgery have made important additions to the field. However, they often have serious side effects and don't work very well in the long run. Because of this, scientists are paying more attention to the molecular processes that cause cancer, especially tumor pathways, in order to find more focused and exact medicines that can make treatments work better and have fewer side effects.[1] Oncogenic pathways are chains of chemical signals that control important biological functions like survival, growth, development, and cell death. When these processes aren't working right, cells can multiply out of hand, which is a sign of cancer. By learning more about the individual mutations and defects in these signalling pathways, possible treatment targets have been found. This has opened up new ways to treat specific diseases. Several imperative tumor pathways, such as the PI3K/AKT/mTOR, MAPK/ERK, Wnt/ß-catenin, and JAK/STAT pathways, are connected to numerous sorts of cancer. Targeting these pathways has ended up an alluring way to treat these maladies. The PI3K/AKT/mTOR pathway is one of the signaling pathways that gets messed up most frequently in human cancers. It controls forms like protein production, digestion system, and cell cycle development that are fundamental for cells to live and increase. Diverse sorts of cancer have issues with this system, such as changes within the qualities that code for PI3K, AKT, and mTOR.

This makes it an important region for treatment. Little chemical drugs that target this pathway have shown promise in clinical ponders. They could be used to treat cancer more effectively and with fewer side impacts than current medications.[2] The MAPK/ERK pathway, which is additionally called the RAS-RAF-MEK-ERK pathway, is another imperative cancer signalling chain that makes a difference cells develop and remain lively. Cancers frequently turn on this pathway by changing the RAS quality or other proteins that send signals upstream. When it is turned on, the ERK proteins gotten to be phosphorylated and actuated. These proteins control gene production that helps cells partition and remain lively. Selective solutions that target this system have been appeared to work in a few cancers, particularly those with RAS changes. This can be still an zone of dynamic consider for modern medicate creation. The Wnt/ß-catenin framework makes a difference keep stem cells lively, controls cell improvement, and keeps tissues in adjust. Diverse sorts of cancer, particularly colon cancer, are connected to this system not working appropriately. In this case, changes within the APC gene cause ß-catenin to become dynamic, which causes cells to develop out of control. Stopping this framework may be a way to treat cancers that are caused by problems with Wnt/ß-catenin signalling. The JAK/STAT framework is very important for controlling how cells react to cytokines and development factors, which affects cell development, survival, and defence reactions.[3] Several types of blood cancer and strong tumors are connected to changes or changes in this system, especially those that make JAK or STAT proteins always active. Specifically targeting the JAK/STAT system has shown guarantee, particularly with the creation of JAK inhibitors, which are permitted to treat certain types of blood cancer and are now being looked at for use in strong tumors as well.

Related Work

Over the final few decades, a study of cancer considers has been done to see into oncogene pathways and how they can be utilized to treat cancer. A few ponders have given us valuable data almost the atomic forms that cause cancer to spread, appearing how focusing on key tumor pathways might be utilized to treat cancer. A

number of tailored medications have been created and attempted in human thinks about, appearing guarantee for a few sorts of cancer. The PI3K/AKT/mTOR pathway has been known for a long time to play a key part in cancer. Specifically, changes within the PIK3CA gene, which makes the p110α portion of PI3K, have been seen in a few types of cancer, such as breast, colon, and uterine.[4] There are drugs that piece this pathway, like alpelisib (a PI3K inhibitor) and everolimus (an mTOR inhibitor), that have been appeared to work in creature models and early-phase human considers. In spite of the fact that, there are still stresses approximately the development of resistance and terrible impacts like debilitated safe frameworks and metabolic issues. Recently, people have been working on combination solutions, like using PI3K inhibitors at the side other particular drugs or chemotherapy, to urge around resistance and make medications work better. A lot of attention has too been paid to the MAPK/ERK pathway, which is regularly changed in cancers like melanoma, lung cancer, and colon cancer. Studies have shown that RAS absconds turn on this framework, which helps cells develop and survive without being overseen. So, medicines that target important parts of the MAPK pathway have been made. These include MEK inhibitors (like trametinib) and BRAF inhibitors (like vemurafenib). These drugs have been shown to work in treating BRAF-mutant melanoma. However, these treatments often have problems with developed resistance, just like PI3K/AKT inhibitors. Researchers are looking into new ways to improve clinical results, like focusing on more than one spot in the pathway or mixing MEK inhibitors with immune checkpoint inhibitors. Researchers have found a link between colon cancer and the Wnt/ß-catenin system. Changes in the APC gene cause ß-catenin to build up and activate genes that help tumors grow.[5] Targeted treatments for this pathway have shown potential in laboratory testing, but they are still hard to develop in humans because the pathway is so complicated and plays a role in normal tissue balance. Still, new research is looking into small chemicals and antibodies that can stop ß-catenin from doing its job or change how it affects transcription.

Table 1. Summary of Related Work

Approach	Future Trend	Benefits	Impact
Targeted therapies in HER2+ breast cancer	Increased use of combination therapies	Effective in specific cancer types	Improved survival rates and remission in breast cancer
Imatinib in Chronic Myelogenous Leukemia (CML)	Development of next-generation TKIs	Proven long-term survival benefits in CML	Revolutionized CML treatment and prolonged patient life
EGFR inhibitors in NSCLC[6]	Personalized therapies based on genetic profiling	Targeting genetic mutations improves outcomes	Offers hope for patients with previously limited treatment options
BRAF inhibitors in melanoma	Exploration of resistance mechanisms and overcoming them	Targeted inhibition of mutated BRAF leads to tumor shrinkage	Transformed melanoma treatment landscape with higher survival rates
PI3K/AKT/mTOR inhibitors in various cancers	Inhibition of alternative signaling pathways to combat resistance	PI3K pathway inhibition prevents tumor progression	Improved patient outcomes in cancers like breast, lung, and prostate
VEGF inhibitors in colorectal cancer[7]	Development of bispecific antibodies targeting multiple pathways	Restricting blood supply to tumors improves outcomes	Reduced tumor growth and metastasis in colorectal cancer
Tumor immunotherapy and checkpoint inhibitors	Incorporation of artificial intelligence for drug discovery	Enhanced the body's own ability to fight cancer	Enhanced the body's immune response against cancer
Monoclonal antibodies in targeted therapy	Immunotherapy combination with targeted therapy	Antibodies offer specificity with minimal side effects	Monoclonal antibodies provide highly targeted cancer therapy
Small molecule kinase inhibitors	Use of gene-editing technologies like CRISPR	Kinase inhibitors reduce unwanted cellular activity	Kinase inhibitors have provided significant advances in personalized treatment
Gene therapy approaches for tumor suppression	Advancements in gene therapy for personalized treatment	Correcting genetic defects at the root causes of cancer	Gene therapy promises long-term solutions by correcting underlying mutations
CAR-T cell therapies	Expanding CAR-T therapy to solid tumors	CAR-T cells can offer long-term remission in hematologic cancers	CAR-T cells are showing remarkable results in blood cancers
Biomarker-driven treatment approaches[8]	Biomarker-based therapy optimization	Increased precision in patient selection for treatment	Personalizing therapies improves treatment precision and reduces side effects
Combination therapy strategies	Use of liquid biopsies for early detection and monitoring	Synergistic effects improve overall treatment effectiveness	Combination therapies address resistance and enhance tumor control

Overview of Oncogenic Pathways

Definition and role of oncogenic pathways in cancer

As the name suggests, oncogenic pathways are a group of molecular signalling networks that control basic biological functions like growth, survival, development, and death. These routes keep cellular balance and normal tissue function going in healthy cells. But if these paths get out of whack because of DNA changes or things in the environment, they can cause cells to multiply, survive, and spread without being managed. These are all signs of cancer. Oncogenic pathways are very important for the growth and spread of cancer because they give tumor cells skills like being able to survive cell death, receive steady growth signals, and attack nearby tissues. The fact that oncogenic pathways are involved in important parts of tumor biology shows how important they are in cancer. For example, in many types of cancer, signalling pathways like PI3K/AKT/mTOR and MAPK/ERK are changed. This causes growth and survival signals to be activated, which further the tumor's growth.[9] When genes that code for parts of these pathways get changed, like those that code for Ras proteins or receptor tyrosine kinases, or when tumor suppressor genes like PTEN stop working, these pathways can become active. It is possible for these routes to stay active all the time, which means that cells can keep growing even when there are no outside signs to do so. Oncogenic pathways also help with processes that help cancer cells avoid being caught by the immune system, fight chemotherapy, and start angiogenesis, the growth of new blood vessels to bring nutrients to tumors. For instance, the Wnt/ß-catenin system helps cancer spread by changing stem cell-like traits and making cells less likely to die. JAK/STAT signalling also helps tumors hide from the immune system and stay alive, especially in blood cancers.

Key oncogenic pathways involved in cancer development

MAPK/ERK Pathway

The MAPK/ERK pathway, which is also called the Ras-Raf-MEK-ERK pathway, controls how cells grow, change, and stay alive. It is often set off by outside signals, like growth factors connecting to receptor tyrosine kinases (RTKs). In reaction, Ras proteins are turned on, which sets off a series of signalling events involving Raf, MEK, and ERK. When this route is out of whack, it can cause cells to divide without control, which can help cancer grow. Cancers like melanoma, lung, and colon cancer often have changes in parts of this system, especially in proteins called Ras or Raf. These changes make the MAPK pathway always active, which makes tumors grow faster, spread to other parts of the body, and become resistant to treatment. Targeting certain parts of the system, like MEK or BRAF inhibitors, has shown promise in the field, especially in cancers that have BRAF mutations.

PI3K/AKT Pathway

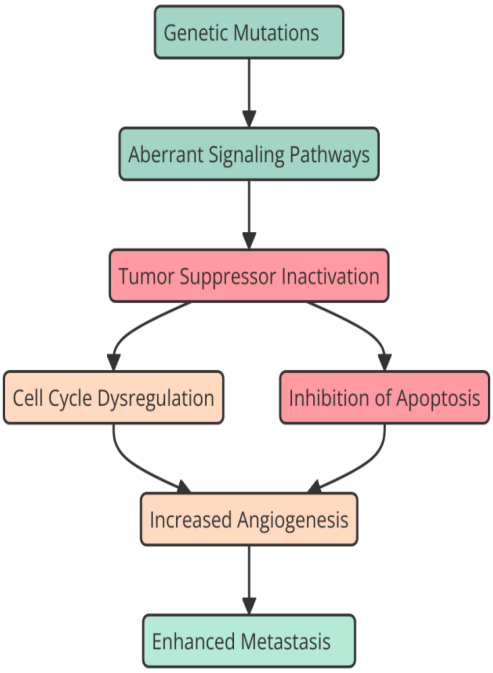

Figure 1. Illustrating oncogenic pathways in cancer development

Cells' ability to live, grow, use energy, and divide is controlled by the PI3K/AKT system. There is a protein called

phosphoinositide 3-kinase (PI3K) that changes phosphatidylinositol (4,5)-bisphosphate into phosphatidylinositol (3,4,5)-trisphosphate when growth factors bind to receptor tyrosine kinases. AKT, a serine/threonine kinase that helps cells stay alive and grow, is then activated. Cancers like breast, ovarian, and prostate cancer often have changes in the PI3K, AKT, or PTEN genes.[10] These genes usually stop AKT from activating. Because this system isn't working right, cells multiply and survive longer, pathway in cancer development process shown in figure 1. This makes it a target for treatments like PI3K and AKT inhibitors, which are currently being tested in clinical studies.

p53 Signalling Pathway

The p53 system is very important for keeping the genome stable and stopping cancer from growing. As a tumor suppressor, p53 stops the cell cycle, fixes DNA, or causes death when cells are under stress. This stops harmed cells from spreading. When DNA is damaged or cancer signals are sent, p53 turns on downstream targets that either stop cell division so that the DNA can be fixed or start cell death if repair is not possible. Some of the most common genetic changes in human cancers are found in the TP53 gene, which codes for the p53 protein. When p53 stops working, cells with broken DNA can keep multiplying, which can cause tumors to form. A potential area of study in cancer treatments is restoring p53 action or making drugs that work like it.

METHOD

Research design

In scientific studies, research design is an organized plan that tells researchers how to collect data, analyze it, and figure out what it all means. It describes the methods and plans that were used to find answers to research questions and try theories. This makes sure that the study's results are valid and trustworthy. The research problem, the type of data to be gathered, the research methods, and the analysis techniques to be used are usually the four main parts of the plan. Different kinds of study methods can be roughly put into two groups: quantitative and qualitative. Experiments, correlations, and surveys are all types of quantitative research methods that use numbers and statistics to find out how an action or link between factors affects people. A lot of the time, these systems are used to find cause-and-effect links or to measure habits, emotions, or other things.[11] Randomized controlled trials (RCTs), for example, are a popular type of experiment used in clinical research to find out how well medicines work. Different from quantitative research designs, qualitative research designs like case studies, ethnography, or grounded theory look into more in-depth aspects of human behavior, experiences, and social phenomena. Qualitative research usually doesn't use numbers and tries to figure out things like meanings, opinions, and complicated situations. This approach is often used in exploratory studies or when the researcher wants to come up with ideas or get a better understanding of a certain event. In addition, a study plan talks about things like sample methods (how people or data points are chosen) and data collection techniques (like tests, surveys, and interviews).[12] In the end, the research plan is very important for making sure that the study follows good research practices and that the results are valid and useful for the people who were studied.

Data collection methods

Sources of data

Gathering data from different sources is an important part of research because it gives you the information you need to analyze and understand it. The type of research, the questions being asked, and the area of study all affect the choice of data sources. Academic papers are a main source of information. These magazines store study papers, reports, and academic papers that have been reviewed by other researchers. Academic papers are a common way for researchers to find out about the newest studies, methods, and results in their areas. These sites are important for scholarly study because they provide high-quality data that is based on proof. Researchers can use tools like PubMed, Scopus, and Google Scholar to find articles that have been published in reputable journals. These articles cover a wide range of topics and contain a lot of useful information. Most of the data in scholarly papers comes from original study, systematic reviews, or meta-analyses.[13] The databases for research trials are another good place to get information.

Stepwise Algorithm for Data Collection Methods in Cancer Research

Step 1: Identification of Data Sources

The first step within the information collection process is to distinguish the suitable sources of data. This may incorporate academic journals, clinical trial databases; case ponders, and open databases. Each information source gives distinctive sorts of data. Scholastic journals regularly contain peer-reviewed inquire about ponders, clinical trial databases give information on the efficacy of interventions, case considers offer nitty gritty patient histories, and open databases offer large-scale epidemiological information.

Data Sources = {Journals,Clinical Trials,Case Studies,Public Databases}

Step 2: Data Extraction

Once the sources are identified, the following step is to extricate significant information from these sources. This may incorporate subjective information from case studies or quantitative information such as survival rates, progression-free survival, and adverse impacts from clinical trials. Information extraction is performed through systematic reviews, data mining, or organized queries in databases.

Extracted Data = ∫t1 to t2 Relevant Data(t)dt

Where:
t1 and t2 are the start and end times for data collection.
Relevant Data(t) represents the data extracted at any given time point.

Step 3: Data Validation and Cleaning

After extraction, the next step is data approval to guarantee that the collected information is exact, steady, and total. This may include checking for lost values, adjusting blunders, and confirming the exactness of the information. Cleaning the information ensures that as it were pertinent, high-quality information is used for further examination.

Validated Data = ∫t1 to t2 (Extracted Data(t)- Error(t))dt

Where:
Error(t) represents any identified inconsistencies or inaccuracies in the data

Step 4: Data Integration

The next step involves integrating data from multiple sources to create a cohesive dataset. This step is essential in research involving multiple databases, where data from different studies must be merged and standardized to form a unified dataset for analysis.

Integrated Data = ∫t1 to t2 (Journals(t)+ Clinical Trials(t)+ Case Studies(t))dt

Where:
Journals(t).
Clinical Trials(t).
Case Studies(t) represent data from respective sources at time t.

Step 5: Data Analysis and Interpretation

The ultimate step includes analyzing the coordinates information to draw conclusions. This incorporates applying measurable strategies, machine learning calculations, or other expository strategies to translate the information and determine significant experiences.

Analysis Results = ∫t1 to t2 (Integrated Data(t) Statistical Model(t))dt

Where:
Statistical Model(t) refers to the mathematical or computational models applied to the data at time t

Inclusion and exclusion criteria for studies

Criteria for who can and cannot be included are important parts of the planning of a research study, especially in clinical and observational studies. These criteria list the traits that study subjects must have in order to be included (inclusion criteria) and the traits that would prevent them from participating (exclusion criteria). Setting clear and well-defined criteria makes sure that the study group fits the research questions which that consider comes about are exact and valuable. Consideration guidelines list the characteristics that ponder subjects must have in order to be permitted to take part within the study.[14] These factors are implied to form beyond any doubt that the study gather is a great representation of the full community that's being considered. For occurrence, in a clinical ponder testing a unused cancer medicate, individuals who meet certain standards might need to be in a certain age extend, have a certain type or arrange of cancer, or be in a certain wellbeing state. By setting these limits, the study tries to create beyond any doubt that all of the subjects are in similar circumstances. This will offer assistance the analysts more accurately and frequently

degree the impacts of the mediation. On the other hand, avoidance criteria are utilized to figure out who shouldn't be a portion of the study since of things that might mess up that inquire about or include bias. These benchmarks offer assistance get freed of things that could throw off the results.[15] For example, people who have serious problems, conditions that make the treatment under research unsafe, or previous treatments that might have changed the results may be kicked out of the study. Participants are also protected from harm by exclusion factors, which make sure they are not introduced to treatments that could be dangerous for them.

Data analysis techniques

Data research can be done in a number of different ways, and each has its own benefits and uses. Descriptive analysis is a common method that includes organizing and describing data to figure out what its main features are. Descriptive statistics, like mean, median, mode, standard deviation, and range, are often used to get a sense of the central trend, variability, and spread of the data. When doing preliminary study or giving a summary of the data before doing more analysis, this method works really well.[16] A lot of the time, patterns and trends in data are shown visually with graphs like histograms, bar charts, and box plots. Inference analysis is used in studies that want to find links between different factors. Researchers can use inferential statistics to draw conclusions or make predictions about a whole community based on a small sample. You can compare groups and test theories with tools like t-tests, chi-square tests, and ANOVA. Regression analysis, on the other hand, helps you find and measure the connections between independent and dependent factors.[17] In both experimental and observational studies, this type of research is very helpful for figuring out whether trends seen are statistically significant or just happened by chance. Multivariate analysis is often used on datasets that are more complicated, especially ones that have a lot of factors.

Therapeutic Targets in Oncogenic Pathways

Identification of potential therapeutic targets

Finding possible treatment targets is very important for creating tailored medicines that can only affect the way cancer cells work while doing as little harm as possible to healthy cells. Finding these targets usually includes looking into important molecular players like tumor suppressor genes, receptors and ligands, kinases and phosphatases, and others.

Receptors and Ligands

In order for cells to talk to each other, receptors and their ligands are very important. They control how cells act. When receptor communication pathways are out of whack in cancer, cells often grow, survive, and spread without being managed. In cancers like breast, lung, and bowel, receptor tyrosine kinases (RTKs) like EGFR (epidermal growth factor receptor) and HER2 (human epidermal growth factor receptor 2) are often overexpressed or changed. When these receptors are activated by their corresponding ligands, they start intracellular signalling pathways that help the tumor grow.[18] Cancers that are caused by abnormal RTK signalling are usually treated by going after these receptors with monoclonal antibodies or small molecule inhibitors. For instance, trastuzumab (Herceptin), an antibody that targets HER2, is commonly used for breast cancer that is positive for HER2.

Kinases and phosphatases

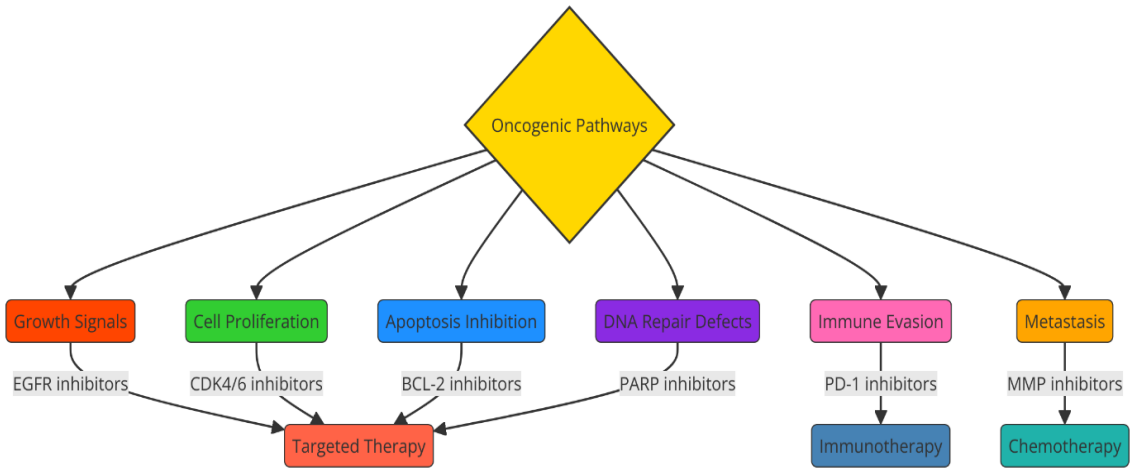

Figure 2. Therapeutic Targets in Oncogenic Pathways

Enzymes like kinases and phosphatases change the function of proteins by adding or taking away phosphate groups. This controls how cells send signals. It is kinases that add phosphate groups, and it is phosphatases that take them away. Both are very important for controlling things inside cells like metabolism, death, growth, and life. In cancer, abnormal kinase activity is often one of the main reasons why tumors form. Kinase drugs that target specific enzymes, like ALK (for lung cancer) and BRAF (for melanoma), have been very effective in treating cancer. As an example, vemurafenib, which is a BRAF inhibitor, is used to treat cancer that has a BRAF mutation.[19] In the same way, EGFR drugs like erlotinib target kinases in the MAPK/ERK and PI3K/AKT pathways, which helps treat a number of cancers.

The figure 2 represents therapeutic targets within oncogenic pathways, focusing on key molecular mechanisms driving cancer progression. It outlines targets such as growth factor receptors, signalling proteins, and transcription factors, emphasizing their role in developing precision therapies to inhibit tumor growth and improve treatment efficacy.

Tumor Suppressor Genes

Tumor suppressor genes make proteins that help control cell division and keep the genome stable by stopping the cell cycle or sending out death signals when DNA is damaged or other stress signals are detected. Many types of cancer are marked by changes in tumor suppressor genes that turn them off. The well-known tumor suppressor p53 is a key player in keeping cancer at bay by starting DNA repair, cell cycle halt, or death when cells are under lots of stress. Over half of all cancers have changes in the TP53 gene, which makes the p53 protein. These changes let cells avoid growth control and cell death. One potential way to treat cancer is to restore p53 function or make drugs that work like it.[20] RB1 (retinoblastoma protein) controls the G1/S stage of the cell cycle, and PTEN is a phosphatase that inhibits the PI3K/AKT pathway. These are two other important tumor suppressors. Trying to get tumor suppressors to work again or finding ways to keep them from working is an area of ongoing study.

Current therapies targeting oncogenic pathways

In recent years, scientists have learned more about tumor pathways and how they play a part in the growth of cancer. This knowledge has led to the creation of new focused treatments that try to stop these pathways. These medicines have shown promise and could help cancer patients get more accurate and individualized care. Monoclonal antibodies, small molecule inhibitors, and gene therapy methods are some of the most well-known treatments that target cancer pathways. Each of these treatments focuses on different parts of tumor pathways to stop the molecules that cause cancer.[21]

Monoclonal Antibodies

Monoclonal antibodies, or mAbs, are particles made in a lab that can battle off destructive pathogens, like cancer cells, similar to the resistant framework does. These antibodies are made to tie to specific antigens on the surface of cancer cells. This stops the signals that make the tumor develop or tells the resistant framework to slaughter the cells. Trastuzumab (Herceptin), which targets HER2, a receptor tyrosine kinase that's regularly overexpressed in breast cancer, is one of the foremost compelling sorts of monoclonal antibody treatment. Breast cancers that are positive for HER2 tend to develop more rapidly. Trastuzumab ties to the HER2 receptor and stops it from actuating and sending signals that help the tumor grow. Patients with HER2-positive breast cancer are much more likely to outlive after this treatment. A few monoclonal antibodies, like rituximab, work against CD20, a protein on the surface of B-cells that helps battle cancers like non-Hodgkin lymphoma and persistent lymphocytic leukemia.[22] Bevacizumab, also known as Avastin, is another commonly utilized mAb that works against vascular endothelial development calculate (VEGF), a protein that makes a difference make new blood vessels that bring supplements to tumors. By ceasing VEGF from working, bevacizumab can halt tumors from spreading and developing. Monoclonal antibodies can halt tumor receptors from working, but they can moreover be used to send destructive chemicals or radioactive isotopes to cancer cells. This is called antibody-drug conjugates (ADCs). One example of an ADC is Kadcyla, which is made up of trastuzumab and a lethal agent that works superior to target and kill HER2-positive cancer cells.

Small Molecule Inhibitors

Most of the time, these drugs are small enough to get into cells and mess up the signaling paths inside cells that help tumors grow. Many people are familiar with tyrosine kinase inhibitors (TKIs), like imatinib (Gleevec), which works against the BCR-ABL fusion protein in chronic myelogenous leukemia (CML), and dasatinib and nilotinib, which work against other BCR-ABL forms. Imatinib has changed the way CML is treated by blocking the faulty kinase activity that is caused by the BCR-ABL gene duplication. BRAF inhibitors, like vemurafenib and dabrafenib, are another example. They work against the BRAF V600E gene that is common in melanoma. By stopping the mutated BRAF kinase, these drugs stop signals further down the MAPK pathway. This stops the growth of tumor cells and causes the tumor to shrink in people with BRAF-mutant melanoma. A new group

of small drugs are also called PI3K/AKT/mTOR pathway inhibitors. Everolimus and temsirolimus are mTOR inhibitors that stop a key part of the PI3K/AKT/mTOR pathway from working properly. This pathway is often overactive in some types of cancer, like renal cell carcinoma. Similarly, alpelisib, which is a specific PI3K inhibitor, has been shown to work well in breast cancers that have PIK3CA mutations. One benefit of these small molecule inhibitors is that they can be taken by mouth, which is convenient for patients. Small molecule treatments can become less effective over time, though. To fix this problem, combining therapies or the creation of new drugs are needed.

Gene Therapy Approaches

Gene therapy methods used to treat cancer try to change or fix the genetic flaws that cause cancer to start. Gene therapy tries to treat the reasons of cancer at the genetic level, rather than targeting proteins or receptors like other treatments do. One potential method for gene therapy is to put tumor suppressor genes back into cancer cells so that they can work normally again. For example, p53 gene therapy tries to put back into tumors a working p53 gene that has stopped working because of changes. Because p53 is such an important tumor inhibitor, making it work again can stop cancer cells from dividing or kill them. Chimeric antigen receptor T-cell therapy (CAR-T cell therapy) is another type of gene therapy. This method changes a patient's T cells to produce a receptor that is specific to a tumor protein. After being changed genetically, these T cells are put back into the patient, where they find and kill cancer cells. Some CAR-T cell treatments, like Kymriah (for leukemia) and Yescarta (for lymphoma), have been very successful, especially in treating blood cancers. RNA-based treatments, like RNA interference (RNAi) and antisense oligonucleotides, can also be used in gene therapy. These try to turn off certain genes that are involved in the growth of cancer. As an example, Eteplirsen is an antisense RNA that is used to treat muscle dystrophy. Researchers are also looking into how to use similar methods to target oncogenes in cancer.

Treatment Improvements Through Targeting Oncogenic Pathways

Mechanisms of action for targeted therapies

Therapeutics that are targeted are meant to stop certain chemicals that help cancer grow, spread, and get worse. These treatments work by going after proteins or genes that are changed or not working properly in cancer cells. These are important factors in the growth of tumors. Traditional chemotherapy kills both diseased and healthy cells without discrimination. Targeted treatments are more precise, so they have fewer side effects and better results for patients. One important way that focused treatments work is by stopping receptor communication. Genes like epidermal growth factor receptor (EGFR) or human epidermal growth factor receptor 2 (HER2) that are overactive can cause a lot of cancers. HER2 receptors are stopped by monoclonal antibodies like trastuzumab (Herceptin). This stops the triggering of signaling pathways that help cancer cells grow and stay alive. In the same way, small molecule tyrosine kinase inhibitors (TKIs) like imatinib (Gleevec) stop certain kinases from working. These include the BCR-ABL fusion protein in chronic myelogenous leukemia (CML), which stops the communication that causes cells to divide without control. Another way is by blocking important communication pathways, like the PI3K/AKT/mTOR and MAPK/ERK pathways, which control how cells live and grow. Small drugs, such as everolimus (an mTOR inhibitor) and trametinib (an MEK inhibitor), stop these processes. This stops cancer cells from getting around regulatory switches and continuing to grow.

Challenges and limitations of current treatments

Resistance mechanisms

Resistance mechanisms are a big problem for the present focused cancer treatments because they make them less effective. Cancer cells can become resistant to specific treatments over time, which can cause therapy to fail and the growth to grow back. Targeted medicines can be met with resistance in a number of ways, which can make treatment more difficult and require ongoing changes to treatment plans. Changes in the target chemical are a common way that drugs become resistant. For example, changes in the EGFR gene (for example, the T790M mutation) can make the receptor less sensitive to the drug. This can happen with EGFR drugs used to treat non-small cell lung cancer (NSCLC). In the same way, when melanoma is treated with BRAF inhibitors like vemurafenib, the cancer cells may get new changes in the MEK or BRAF genes that get around the blockage. This lets the communication continue and the tumor grow. The stimulation of different signaling channels is another way that resistance works. Although specific treatments can stop one route, cancer cells can still use other paths to stay alive and grow. In the PI3K/AKT pathway, for example, cancer cells may become resistant to mTOR inhibitors by turning on MAPK/ERK signaling. This lets the cancer cells get around the blockage. Also, the different types of tumors are very important for survival. Cancers are made up of a lot of different types of cells, and some of them may have changes that make them harder to treat. This variety within the tumor makes it harder to treat cancer because some groups of cells that are resistant to treatment can grow even though most of the tumor responds to treatment.

Side effects and toxicity

Targeted treatments are big steps forward in the way we treat cancer, but they do have some side effects and could be harmful. One big benefit of targeted treatments over regular chemotherapy is that they are more specialized, which means that side effects are often fewer and less serious. But because these treatments still change some healthy cells and processes, side effects are still possible, and poisoning is still a worry. It depends on the drug, the route it targets, and the patient's reaction that the side effects of tailored treatments can be different. Some monoclonal antibodies, like trastuzumab (Herceptin), which attack HER2 receptors in breast cancer, can hurt the heart and cause heart failure in some people. The reason for this is that HER2 is found in both cancerous cells and healthy heart cells. To lower this risk, people who are getting trastuzumab treatment are often checked for signs of heart problems. Tyrosine kinase inhibitors (TKIs), like imatinib (Gleevec), can cause stomach problems like sickness, diarrhea, and abdominal pain. They do this by targeting the BCR-ABL fusion protein in chronic myelogenous leukemia (CML). Some people who take TKIs can also get hepatotoxicity, which damages their liver. These side effects are usually not too bad, but they mean that the liver function needs to be closely watched while the treatment is going on. Side effects caused by resistance can also make treatment more difficult.

RESULTS AND DISCUSSION

Targeted medicines that target key growth pathways, like receptor signalling, kinases, and tumor suppressor genes, have shown promise in making cancer treatment work better. Monoclonal antibodies and small molecule inhibitors have been able to successfully target particular mutations or dysregulated pathways. This has caused tumors to shrink, patients to live longer, and side effects to be less severe than with standard treatment. But methods of resistance, like genetic changes and stimulation of different pathways, make long-term effectiveness very hard to achieve. To make targeted treatments more successful in treating cancer, more study needs to be done on how to overcome resistance, create combo therapies, and use personalized medicine.

Table 2. Evaluation of Treatment Efficacy for Targeted Therapies in Different Cancers

Targeted Therapy	Response Rate (%)	Median Progression-Free Survival (months)	Overall Survival (months)
Trastuzumab (Herceptin)	60	18	48
Imatinib (Gleevec)	80	36	120
Erlotinib (Tarceva)	50	12	36
Vemurafenib	60	10	24
Everolimus	40	6	18

A Trastuzumab (Herceptin), which is used to treat HER2-positive breast cancer, has a reaction rate of 60 %. This means that 60 % of patients get better after treatment, with their tumors getting smaller or staying the same. The typical PFS is 18 months, which means that for that long, the illness ceases to develop in these people, response rate represent it in figure 3.

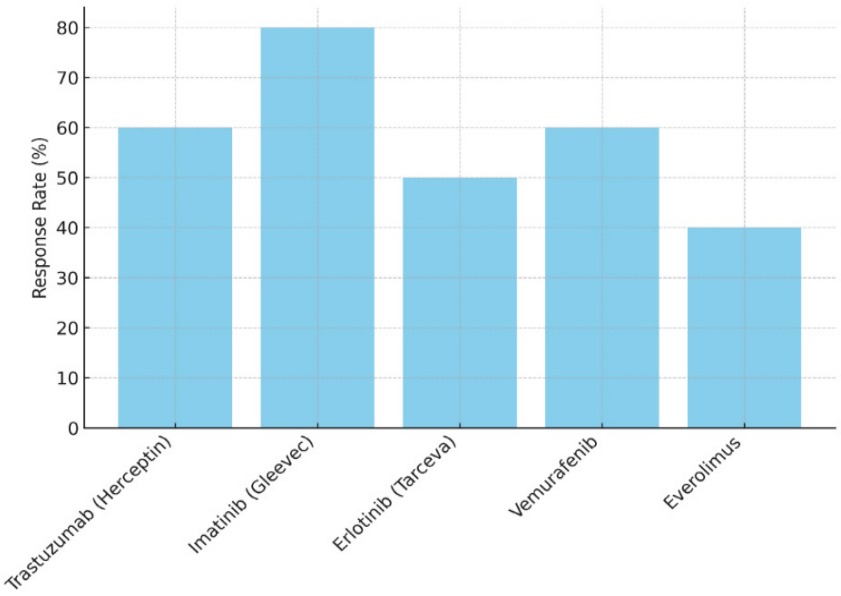

Figure 3. Response Rate by Drug (%)

The average length of life, however, is 48 months. This shows that successful long-term control of the disease is still hard to achieve, and some patients may finally develop resistance.

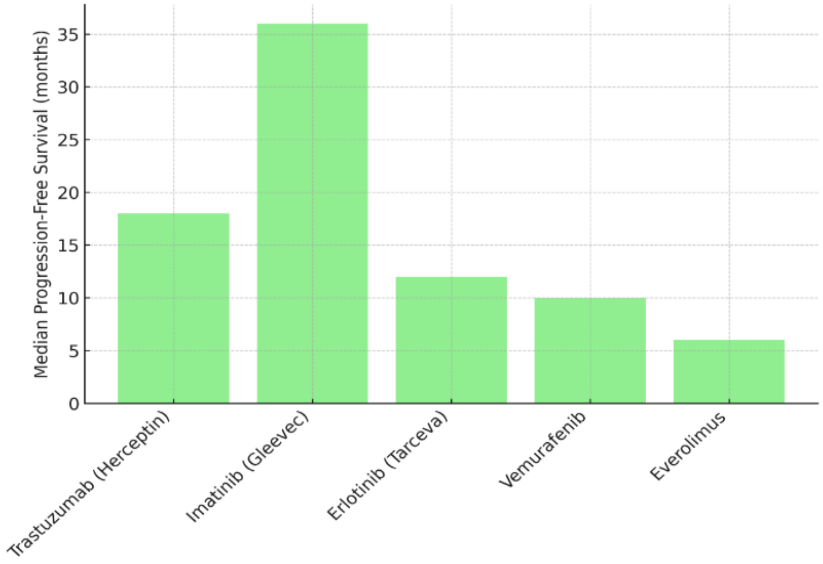

Figure 4. Median Progression-Free Survival by Drug (Months)

A main drug for chronic myelogenous leukemia (CML), imatinib (Gleevec), has the best reaction rate of 80 %, which shows how well it controls the disease. The median PFS of 36 months is the longest of the treatments mentioned, which means that patients can go for long amounts of time without their illness getting worse, shown in figure 4. Also, the fact that the patients lived for 120 months shows that imatinib does improve long-term life in CML patients. Erlotinib (Tarceva), which is used to treat EGFR-mutant non-small cell lung cancer (NSCLC), has a response rate of 50 %, which is not as high as other treatments. Its median PFS of 12 months and overall survival of 36 months show that, even though it works, it doesn't last as long as treatments like imatinib.

Table 3. Comparison of Side Effects and Toxicity Across Targeted Therapies

Targeted Therapy	Severe Toxicity Incidence (%)	Discontinuation Rate (%)
Trastuzumab	15	5
Imatinib	10	4
Erlotinib	12	6
Vemurafenib	8	3

15 % of people who are treated with trastuzumab (Herceptin), which is mostly used for HER2-positive breast cancer, have serious side effects. This is a higher rate than with some other treatments. Cardiotoxicity, especially problems with the heart, and injection reactions are two common serious side effects, represent it in figure 5.

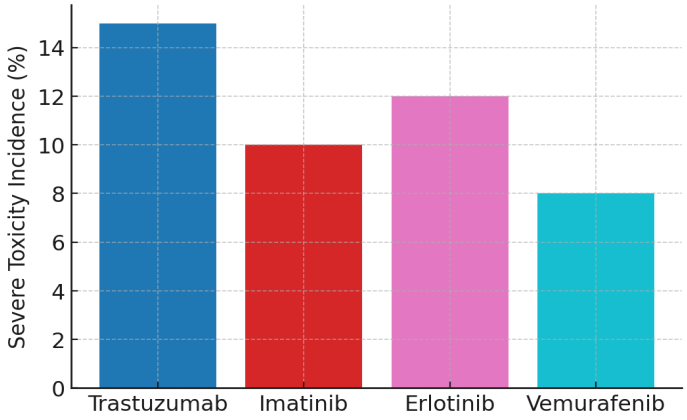

Figure 5. Severe Toxicity Incidence by Drug (%)

These side effects can have a big effect on a person's quality of life and need to be closely watched while they are being treated. Even so, only 5 % of people who are taking trastuzumab stop taking it. This means that most people are able to keep taking it even though it can be harmful. Imatinib (Gleevec), which is commonly used to treat chronic myelogenous leukemia (CML), has a slightly lower serious poisoning occurrence rate of 10 %. Common side effects include problems with the digestive system and liver damage. Even with these risks, only 4 % of people who are taking it stop taking it. This shows that it works and that side effects are usually easy to deal with by changing the amount or giving extra care.

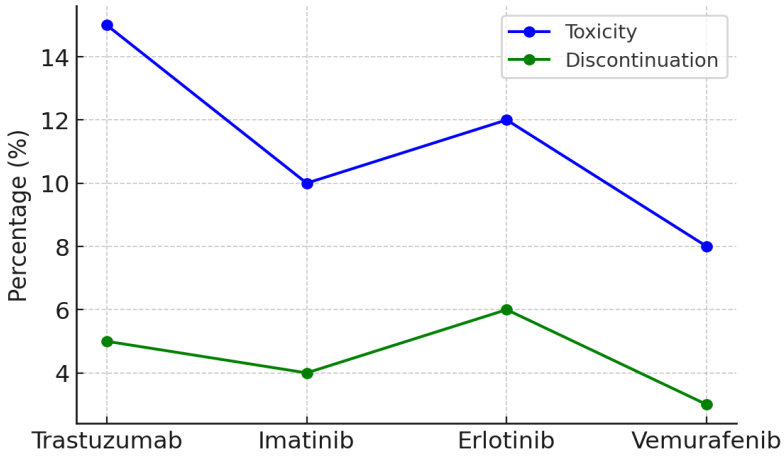

Figure 6. Comparison of Toxicity and Discontinuation Rates by Drug (%)

Figure 6 compares toxicity and discontinuation rates across various drugs, expressed as percentages. It highlights differences in side effects and tolerability, emphasizing how lower toxicity correlates with reduced discontinuation rates, aiding clinicians in selecting optimal therapies for better patient compliance and outcomes. As a drug for EGFR-mutant non-small cell lung cancer (NSCLC), erlotinib (Tarceva) has a serious mortality rate of 12 %. Side effects like rash and diarrhea are common. The rate of stopping treatment is higher, at 6 %. This may be because some patients have difficult side effects while they are being treated. Vemurafenib is used to treat BRAF-mutant melanoma, and it has the lowest rate of serious harm (8 %). It can cause rash and tiredness, among other things. It also has the lowest rate of discontinuation, at only 3 %. This suggests that people are better able to handle it than with the other treatments.

CONCLUSIONS

The study of key tumor pathways has changed the way cancer is treated by making therapies more focused and personalized. Chemotherapy and other traditional cancer medicines often have broad, general effects on both abnormal and healthy cells. This means they have a lot of side effects and don't work very well in the long run. Therapies that focus on specific molecular changes in oncogenic pathways, like receptor signaling, kinase activity, and tumor suppressor gene failure, may be able to target cancer more precisely. Targeted treatments, such as monoclonal antibodies and small molecule inhibitors, have shown a lot of promise in treating different types of cancer. They have helped people live longer and have a better quality of life. Even though specific treatments show promise, they have problems, especially when it comes to building up tolerance. Over time, specific medicines may not work as well for cancer cells because they can change their genes, start using different pathways, or have different types of tumors. Also, focused treatments usually have fewer side effects than regular chemotherapy, but they can still have harmful and bad effects, such as side effects on the immune system and organ poisoning. To keep these risks to a minimum, this shows how important it is to carefully watch patients and make sure that their treatment plans are unique. In the future, combining targeted medicines with other treatments, like immunotherapy, chemotherapy, or other targeted drugs, may help get around resistance and improve the results of therapy. As precision medicine grows, drugs are tuned to the genetic background of each tumor. This opens up exciting new ways to make treatments work better. For cancer treatment to get better and patients to live longer in the future, it will also be important to keep looking into new therapy targets and the ways that drugs become resistant.

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CONFLICT OF INTEREST

Authors declare that there is no conflict of interest.

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