Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 10, 2023

Cancer Biology and Therapeutics: A Contemporary Review

Dr. Aniketa Sharma[1], Gëzim Bara[2], Dr. Keshamma E[3], Bhawna Sharma[4], Shubham Singh[5], Surya Pratap Singh[6], Dr. Tarun Parashar[7], Dr. Hanumant Singh Rathore[8], Dr. Sai Koteswar Sarma[9], Sushama Rawat[10]*

[1]Assistant professor Department of medicine, Dr. YSP Govt. Medical College, Nahan H.P., India
[2]Associate Professor, Faculty of Natural Sciences. Department of Biology. University of Tirana, Albania.
[3]Associate Professor, Dept. of Biochemistry, Maharani Science College for Women, Maharani Cluster University, Palace Road, Bengaluru -560001
[4]PhD research scholar, Madhyanchal Professional University (Patel College of Pharmacy), Bhopal, M.P., 462044
[5]Assistant Professor, Sainath College of Pharmacy, Hinduwari, Sonebhadra, UP 231216
[6]Research Scientist-1, Uttar Pradesh University of Medical Sciences, Saifai Etawah, UP-206130
[7]Associate Professor, Uttaranchal Institute of Pharmaceutical Sciences, Uttaranchal University, Premnagar, Dehradun, Uttarakhand, 248007
[8]Assistant Professor, Department of Biotechnology, School of Engineering and Technology, Nagaland Central University, D.C Junction, Dimapur, Nagaland, India Pin: 797112
[9]Professor, Sri Padmavathi School of Pharmacy, Tiruchanoor, Tirupati, Andhra Pradesh affiliated to JNTUA
[10]Assistant Professor, NIRMA University, Institute of Pharmacy, Ahmedabad, Gujarat, Jaipur National University, School of Pharmaceutical Sciences, Jaipur, Rajasthan

***Corresponding Author:Sushama Rawat,**

Abstract

Since the second half of the 20th century, our knowledge about the biology of cancer has made extraordinary progress. Today, we understand cancer at the genomic and epigenomic levels, and we have identified the cell that starts neoplastic transformation and characterized the mechanisms for the invasion of other tissues. This knowledge has allowed novel drugs to be designed that act on specific molecular targets, the immune system to be trained and manipulated to increase its efficiency, and ever more effective therapeutic strategies to be developed. Nevertheless, we are still far from winning the war against cancer, and thus biomedical research in oncology must continue to be a global priority. Likewise, there is a need to reduce unequal access to medical services and improve prevention programs, especially in countries with a low human development index. Effective cancer therapy is still a great challenge for modern medical research due to the complex underlying mechanisms of tumorigenesis and tumor metastasis, and the limitations commonly associated with currently used cancer therapeutic options. Nanotechnology has been implemented in cancer therapeutics with immense potential for improving cancer treatment. Through information about the recent advances regarding cancer hallmarks, we could comprehensively understand the pharmacological effects and explore the

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 10, 2023

mechanisms of the interaction between the nanomaterials, which could provide opportunities to develop mechanism-based nanomedicine to treat human cancers.

Keywords: cancer, cell therapy, epigenomics, genomics, immunotherapy, metastasis, stem cells, targeted therapy

INTRODUCTION

As per world health organization (WHO), numbers of deaths caused by cancer are one among the highest after heart disease. Cancer is a major public health problem in most developed countries; however, there have been notable improvements in the survival rate of patients over the past three decades owing to early detection and progress in medical treatment(DeSantis et al. 2014)(Siegel et al. 2014). A substantial number of patients with cancer receive chemotherapy or chemo radiotherapy and benefit from treatment with anticancer drugs. However, because of their toxic effects on normal cells/tissues, anticancer drugs cause many side effects with a variety of symptoms, such as nausea, vomiting, anorexia, diarrhea, oral mucositis, and numbness. These side effects often compromise patients' quality of life (QOL) and sometimes make it difficult to continue chemotherapy or chemo radiotherapy(Gibson et al. 2013)(Jordan et al. 2014). Although many valuable strategies have been developed to treat or prevent these side effects, they are still insufficient. Rare abnormal growths inside the neuroendocrine system called neuroendocrine neoplasms (NENs) arise from widely dispersed cells. They produce peptide hormones and, depending on the hormone they produce, exhibit a wide range of symptoms. Their metastatic pattern's degree varies significantly amongst them(McClellan et al. 2022)(Gaudenzi et al. 2020). In addition to primary preventive measures and screening programs, early cancer detection is becoming a more important component of global cancer control strategy(World Health Organization 2017)(Ott, Ullrich, and Miller 2009).

When discussing health outcomes in oncology before to 1970, the fairly constrained end-points of survival and treatment toxicity were assumed to be being discussed(Gunz 1987)(Švajdová and Ondruš 2020)(Cella and Tulsky 1990)(Cella and Cherin 1988)(Fayers and Jones 1983). The use of diagnostic genetic analysis of tumor samples has significantly increased over the past several years, enabling the development of precision oncology by identifying an ever-increasing number of treatment targets and molecularly defined patient classification(Burkard et al. 2017)(Dalton et al. 2017)(Horak et al. 2017)(Zehir et al. 2017)(Hoefflin et al. 2018). One of the cornerstones of comprehensive cancer care is biomedical imaging, which offers numerous benefits such as real-time monitoring, accessibility without tissue destruction, minimal or no invasiveness, and the ability to operate over a broad range of time and size scales involved in biological and pathological processes. The time scales for chemical reactions and protein binding range from milliseconds to years for conditions like cancer. From molecular to cellular to organ to entire organism, size scales are used(Fass 2008).

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 10, 2023

The rate of all cancers as per the age group was 190 per 100,000 and it was higher in men than in women. With this growing burden almost in every country, it is a significant public health challenge to prevent cancer. In all cases, almost 40% of cancers could be prevented by effective and timely diagnosis and handling cancer-associated risks and factors to improve the survival rate in cancer patients. These factors are related to diet, nutrition, and physical activity, etc. Overall, the world is experiencing a growing burden of cancer incidence and deaths worldwide(Meyskens et al. 2016)(Schottenfeld and Beebe-Dimmer 2006). Cancer development starts when a normal cell is affected, and DNA is damaged followed by the pre-cancer stage finally leading to genome instability and loss of anti-oncogenes, etc. Until now, a lot of money and efforts have been diverted to finding an effective treatment for cancers but still, the etiology and pathogenesis of many cancers is poorly understood(Tran et al. 2022). Because of this cancer is still a deadly disease despite a lot of efforts being diverted already? Additionally, there are many computational frameworks developed so far to understand and explore cancer biology. The organism's biology is massive and contains the interconnection among various components such as molecules, proteins, and nucleic acids. Network-based methods are widely used to explore cancer biology. The working of biological systems is widely supported with proteins found interacting and working in disease related pathways and processes(Zhao et al. 2023)(McCloskey 1999).

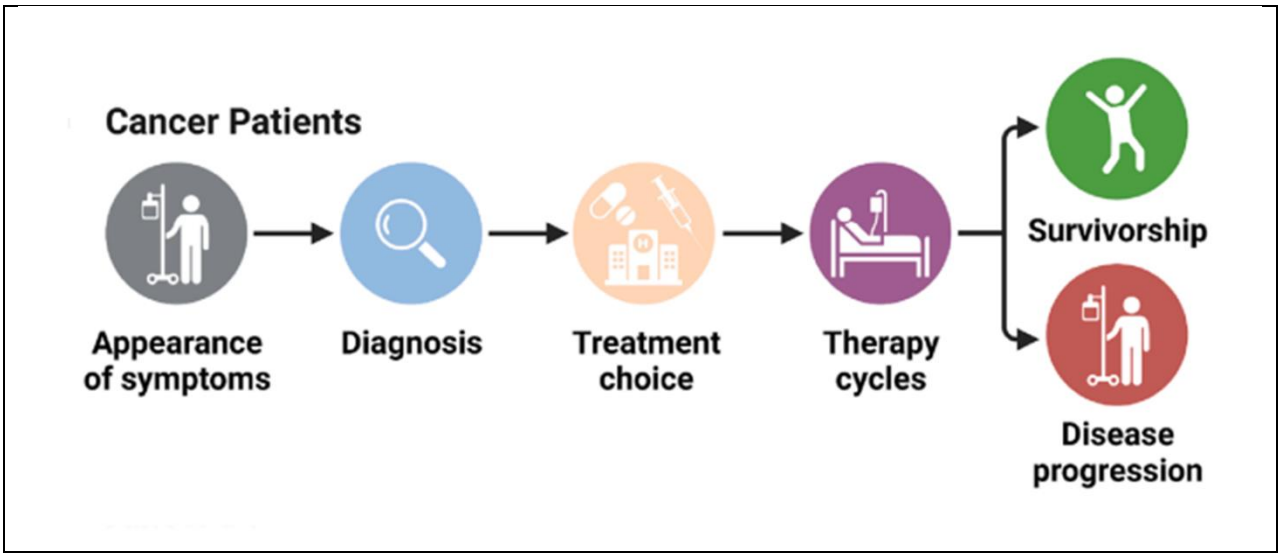

Figure 1: Lifestyle of cancer patients

Cancer is one of the leading causes of disease burden worldwide, with more than 14 million new cases and 8 million deaths estimated in 2012 alone. Approximately 57% of those new cancer cases and 65% of cancer deaths occurred in less developed regions of the world where resources to treat cancer are scarce. All cancer patients face challenges to treatment, but many of these issues are particularly stark in low- and middleincome countries, including diagnosis at late stages when treatment is generally less effective, lack of geographic access to cancer care facilities, a need for trained medical professionals, issues of affordability of care, stigmatization

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 10, 2023

of disease, and minimal access to palliative care (Ferlay et al. 2015)(Gelband et al. 2016). The integration of allopathic and traditional medicine may afford an opportunity to address some of the challenges in cancer control. Too often, we view traditional medicine and allopathic medicine as separate realms. We ignore the fact that cancer patients walk in both realms at the same time during their disease journey. A systematic review of studies performed in Europe, North America, Australia, and New Zealand found that the use of complementary medicines has been increasing over time, with almost half of cancer patients reporting use in the most recent time period. This prevalence is likely to be much higher in other parts of the world—for instance, an estimated 71% of the population in Chile and 65% of the population in rural India use traditional medicine to help meet their primary health care needs(Horneber et al. 2012)(World Health Organization 2003).

CANCER BIOLOGY

Cancer biology is the study of the abnormal growth, behavior, and characteristics of cancer cells and the mechanisms underlying the development and progression of cancer. It is a multidisciplinary field that combines elements of cell biology, genetics, molecular biology, biochemistry, and pathology to understand the complex processes involved in cancer(Ahmed et al. 2023).

Research on the biology of cancer starts with the simplest of questions: What is—and isn't—normal? To understand how cancer develops and progresses, researchers first need to investigate the biological differences between normal cells and cancer cells. This work focuses on the mechanisms that underlie fundamental processes such as cell growth, the transformation of normal cells to cancer cells, and the spread (metastasis) of cancer cells(Ahmed et al. 2023)(Errington et al. 2014). Virtually all major advances against cancer originated with discoveries in basic science. Basic research can reveal new ideas about the causes of cancer and how it develops, progresses, and responds to therapy. Knowledge gained from such studies deepens our understanding of cancer and produces insights that could lead to new clinical interventions. For example, studies of cell signaling pathways in normal cells and cancer cells have contributed greatly to our knowledge about the disease, revealing molecular alterations that are shared among different types of cancer and pointing to possible treatment strategies(Katti et al. 2022)(Brown et al. 2020).

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 10, 2023

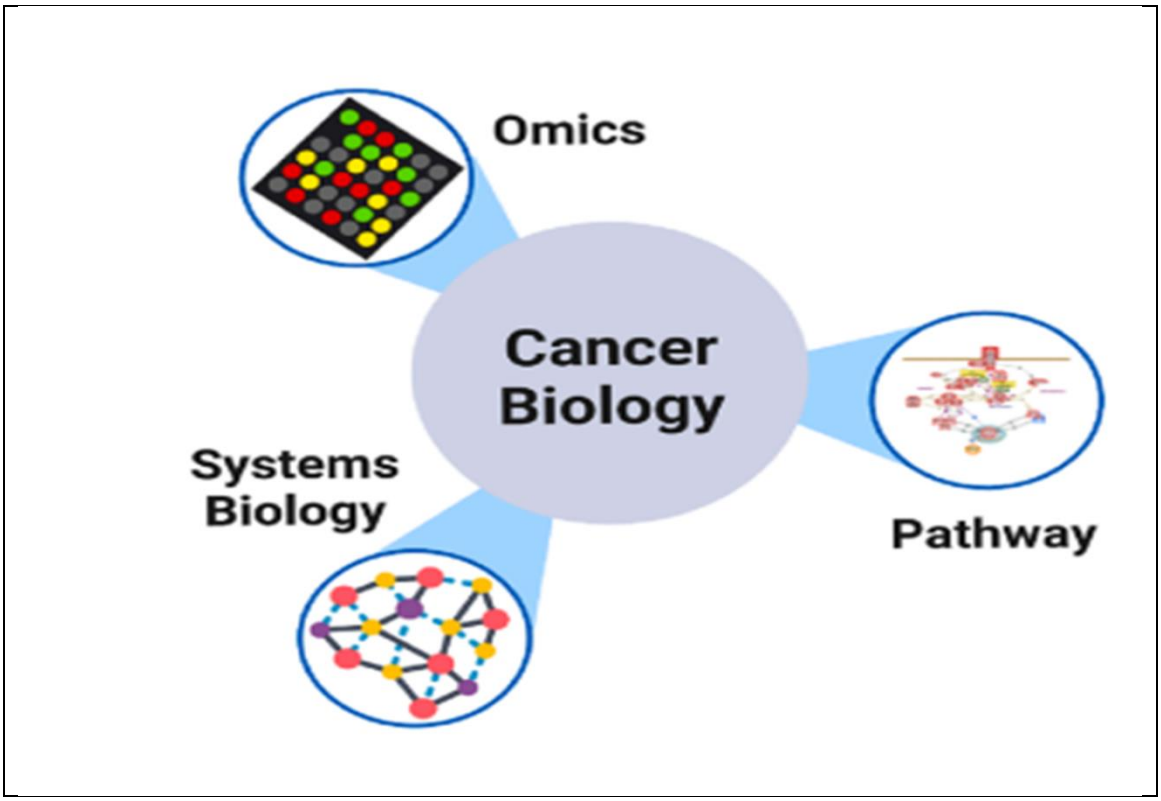

Figure 2: Different techniques for cancer analysis

Complex diseases such as cancer are the result of the combination of various factors of environmental and genetic concern. It is tough to explore pathways used by above cancerous tumors and cells to influence a phenotype so in case of diseases like cancer it becomes even harder because genetic factors affecting individuals may vary. Recently, network based, or system biology methods have been extensively studied and utilized as powerful tool for exploring complex diseases like cancer. For system biology approaches, knowledge of physical or functional interactions among drugs, targets or pathways is exploited to build the networks often referred to as interactions(Takeshima and Ushijima 2019)(Fiscon et al. 2018). A basic network is consisted of nodes and edges. Where for interactions node could be genes, proteins, drugs, and related entities and node nomenclature can be binding affinities, directions of connections between nodes, and strength of connections. Edges in the networks are used to link the nodes, and their defining feature can be functional association among nodes such proteins physical and gene regulatory interactions, disease related associations followed by capturing the activation and inhibition mechanism. Since larger networks are complex, often these are divided into measurable sub networks of functionally associated nodes to reduce the complexity(Jin et al. 2019)(Galan-Vasquez and Perez-Rueda 2021).

To further elaborate on the systems biology approaches discussed in this review, it would be beneficial to provide specific examples of node prediction, link prediction, and graph prediction. Node prediction involves predicting the behavior of individual molecules, such as proteins or

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 10, 2023

genes, within a biological network. Link prediction focuses on predicting the interactions between pairs of molecules in the network, while graph prediction seeks to predict the overall behavior of the entire network. Some examples of these approaches in action include the use of machine learning algorithms to predict drug-target interactions, the application of network-based clustering to identify disease subtypes, and the use of pathway analysis to identify key molecular pathways involved in disease(Feng, Wang, and Wang 2017)(H. Liu et al. 2019)(Lin et al. 2023).

Key concepts and areas of study in cancer biology include:

Cell Proliferation and Differentiation

Cell proliferation and differentiation show a remarkable inverse relationship. Precursor cells continue division before acquiring a fully differentiated state, while terminal differentiation usually coincides with proliferation arrest and permanent exit from the division cycle. As cells respond to external signals during the G1 phase, developmental variations in the cell division cycle may influence proliferation vs. differentiation decisions. Early studies of embryonic carcinoma cells indicated that differentiation can be rapidly induced in G1, but not in S phase. Since, developmental control over the length of G1 phase has been proposed as a differentiation-regulating mechanism(Ruijtenberg and van den Heuvel 2016)(Jiang et al. 2021). Undifferentiated cells in the early embryo of many animal systems, including flies, frogs, and zebra fish, undergo rapid cell divisions that entirely lack G1 and G2 phases. During mammalian embryogenesis, cell division cycles become very short after preimplantation embryos reach the blastocyst stage, with a subset of cells completing the division cycle in only 3 hours. Similarly, embryonic stem cells established from the inner cell mass of preimplantation embryos have unusual cell cycles with a short G1 phase of approximately 2 hours(Dayem, Lee, and Cho 2018)(Murakami and Motohashi 2015).

Probably contributing to differentiation susceptibility in G1, cyclin-dependent kinases cannot oppose differentiation-inducing mechanisms during part of G1 phase. As such, signals received in early versus late G1 can have different outcomes. In response to TGFβ-related signaling, pluripotent human embryonic stem cells in early G1 were observed to form endoderm, while late G1 cells showed neurectodermal specification. The difference was traced to activation of CDK4/6-cyclin D, which phosphorylated and blocked nuclear import of Smad2/3, thereby preventing endoderm and allowing neurectodermal differentiation. These data emphasize the intimate connection between G1 length, G1 CDK-cyclin activation and the response to developmental signals(Agathocleous and Harris 2013)(Wan et al. 2022).

Genetic and Epigenetic Changes

Cancer is associated with mutations in genes that control cell growth and division. Epigenetic changes, alterations in gene expression without changes in DNA sequence, are also important in cancer. Epigenetics is the study of heritable and stable changes in gene expression that occur through alterations in the chromosome rather than in the DNA sequence. Despite not directly

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 10, 2023

altering the DNA sequence, epigenetic mechanisms can regulate gene expression through chemical modifications of DNA bases and changes to the chromosomal superstructure in which DNA is packaged(Zabransky, Jaffee, and Weeraratna 2022)(Wen et al. 2011).

Briefly, negatively charged DNA is packaged around a positively charged histone protein octamer, which contains 2 copies of histone proteins H2A, H2B, H3, and H4. This nucleoprotein complex is a nucleosome, the basic unit of chromatin. The nucleosomes of a continuous DNA polymer are connected by linker DNA and the complex is stabilized by histone protein H1. The aggregation of chromatin results in the formation of a chromosome. The chromatin of a chromosome exists as either loose, transcriptionally active euchromatin or dense, transcriptionally inactive heterochromatin. Chemical alterations to histone proteins can induce the formation of either the open euchromatin state, which facilitates gene expression by allowing transcription factors and enzymes to interact with the DNA, or the closed heterochromatin state, which suppresses gene expression by preventing initiation of transcription(Qi et al. 2010)(D. Liu et al. 2022).

In addition to histone changes, DNA methylation is an epigenetic mechanism associated with gene silencing when the methylation occurs in CpG islands of promoter sequences. Further, non-coding RNA sequences have shown to play a key role in the regulation of gene expression. These epigenetic modifications can be induced by several factors including age, diet, smoking, stress, and disease state. Epigenetic modifications are reversible, but they rarely remain through generations in humans despite persisting through multiple cycles of cell replication(Balaton and Brown 2021)(Bobadilla Landey et al. 2015).

Metastasis

The process by which cancer cells spread to other parts of the body is called metastasis. Understanding the mechanisms of metastasis is crucial for developing effective treatments. Cancer that spreads from where it started to a distant part of the body is called metastatic cancer. For many types of cancer, it is also called stage IV cancer. The process by which cancer cells spread to other parts of the body is called metastasis(Gerstberger, Jiang, and Ganesh 2023). When observed under a microscope and tested in other ways, metastatic cancer cells have features like that of the primary cancer and not like the cells in the place where the metastatic cancer is found. This is how doctors can tell that it is cancer that has spread from another part of the body. Metastatic cancer has the same name as the primary cancer. For example, breast cancer that spreads to the lung is called metastatic breast cancer, not lung cancer. It is treated as stage IV breast cancer, not as lung cancer(Macedo et al. 2017)(Park et al. 2022).

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 10, 2023

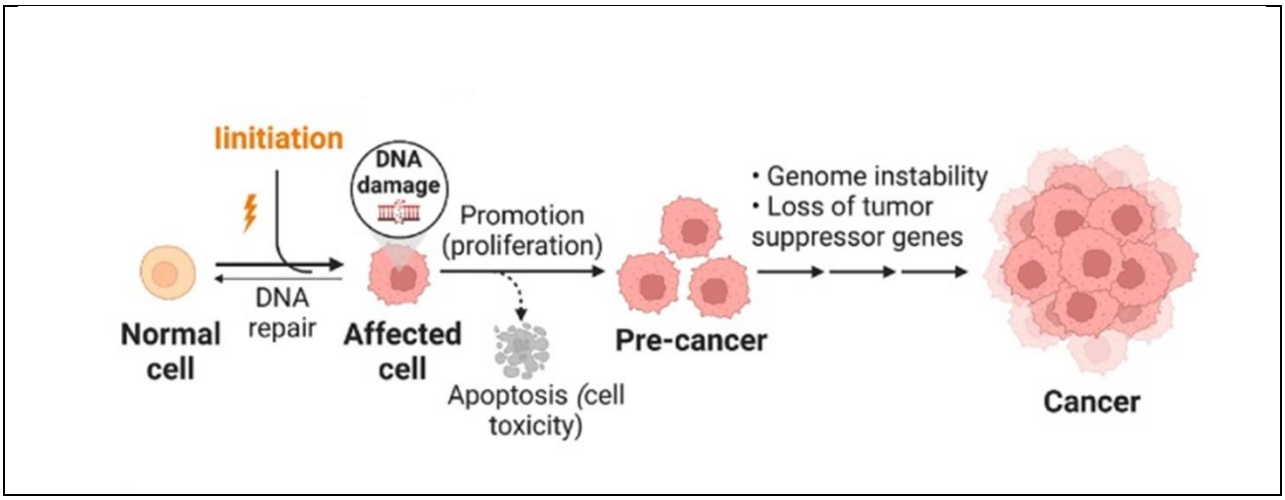

Figure 3: The process of cancer development

ORIGIN OF METASTATIC CANCER CELLS

A. Epithelial to Mesenchymal Transition (EMT)

The EMT posits that metastatic cells arise from either epithelial stem cells or differentiated epithelial cells through a step-wise accumulation of gene mutations that eventually transform the epithelial cell into a tumor cell with mesenchymal features. This idea comes from findings that many cancers arise in epithelial tissues where abnormalities in cell–cell and cell–matrix interactions occur during tumor progression(Kubik and Pawlak 2023). Eventually, neoplastic cells emerge that appear as mesenchymal cells which lack cell–cell adhesion, are dysmorphic in shape, and eventually spread to distant organs. How does this extremely complicated phenomenon actually happen? EMT might contribute to metastasis. Recent studies also suggest that misplaced (ectopic) co-expression of only two genes might be all that is necessary to facilitate EMT in some gliomas, though the process is highly complex. However, considerable controversy surrounds the EMT hypothesis of metastasis, as EMT is not often detected in tumor pathological preparations(Graziani et al. 2022)(Y. Zhang and Weinberg 2018).

B. Stem Cell Origin of Metastatic Tumor Cells

Several investigators hold that metastatic cancer cells arise from populations of tissue stem cells. Most tissues contain cells in semi-differentiated states that can replace dead or damaged cells due to natural wear and tear. These undifferentiated or semi-differentiated cells are often referred to as tissue stem cells and are considered by many to be the origin of metastatic cancers. Similarities in gene expression and biological characteristics are often seen in stem cells and cancer cells(Donizy et al. 2021). Observations that tumor cells express characteristics of undifferentiated stem cells come from the fact that embryonic stem cells and tumor cells can use anaerobic energy (fermentation) for metabolism. Telomerase activity, which is generally higher in tumor cells than in normal cells, is also linked to fermentation energy. It is therefore not surprising that numerous genetic and biochemical phenotypes are shared between tumor cells

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 10, 2023

and stem cells, as most tumor cells also use energy from fermentation for their survival and growth(Ganesh et al. 2020)(D. Cao et al. 2014).

C. Macrophage Facilitation of Metastasis

It has long been recognized that many malignant tumors contain significant numbers of macrophages and other cells of the stroma. The macrophages present in tumors are generally referred to as tumorassociated macrophages (TAM). TAM can establish the pre-metastatic niche, while enhancing tumor inflammation and angiogenesis. In other words, TAM facilitates the metastatic cascade(Seyfried and Huysentruyt 2013). While gene mutations are still thought to initiate neoplasia under this model, it is the stromal macrophages acting as cellular chaperones that facilitate tumor development, progression, and the eventual seeding of metastasis. The stromal TAM are viewed as essential participants in all phases of metastasis, but are not considered neoplastic themselves. However, we recently reviewed evidence showing that many human metastatic tumors also contain neoplastic cells with macrophage properties(Guo et al. 2016)(Mahlbacher et al. 2018).

D. Myeloid Cell Origin of Metastasis

According to our hypothesis, metastatic cancers arise from respiratory insufficiency in myeloid cells or in their lineage descendants, e.g., macrophages, dendritic cells, or lymphocytes. Chronic inflammation in the microenvironment can damage mitochondrial respiration in activated macrophage. Many metastatic cancers express aerobic glycolysis (Warburg effect), which can be detected in PET scans. Aerobic glycolysis in tumor cells arises ultimately from insufficient respiration. Fusion hybridization between macrophages and non-metastatic cancer stem cells also blurs the boundaries between the nuclear and cytoplasmic contribution to the metastatic phenotype. Before tackling these issues, it would be good to first consider the evidence that metastatic cancer cells can arise from myeloid cells(Sangaletti et al. 2021)(Yang et al. 2023).

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 10, 2023

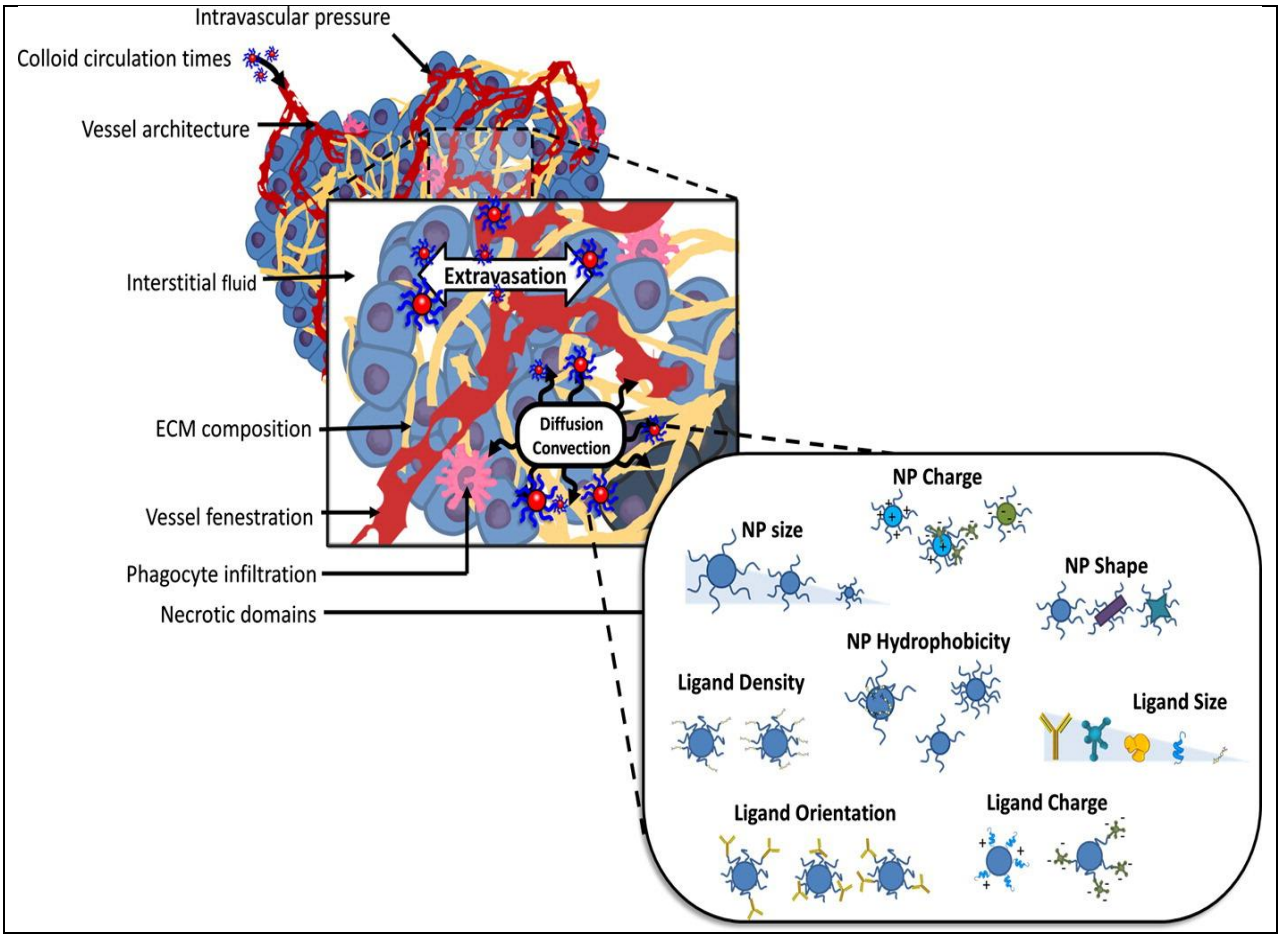

Figure 4: A deep process of cancer biology

CANCER THERAPIES:

Cancer Targeted Therapies:

Targeted treatment is defined by the US Food and Drug Administration (FDA) as a medication having an authorized label that specifically refers to a concurrently or previously approved diagnostic test that must be conducted before the patient may be considered eligible to receive the medication(Zhou and Li 2022).

Table 2: Therapeutics Using Targeted Anticancer Antibodies

Drug Name	Brand Name	Type	Target	Indication	References
Alemtuzumab	Campath	Monoclonal antibody, humanized; anticancer, immunologic; multiple sclerosis treatment; immunosuppressant	CD52	CLL	(Lee, Tan, and Oon 2018)
Rituximab	Rituxan	Monoclonal IgG1;	CD20	NHL	(Lheureux

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 10, 2023

		chimeric; anti- cancer, immunologic; antiarthritic, immunologic; immunosuppressant			et al. 2017)
Trastuzumab	Herceptin	Monoclonal IgG1 humanized; anticancer, immunologic	p185neu	Breast cancer	(Wu et al. 2020)
Gemtuzumab	Mylotarg	Monoclonal IgG4 humanized	CD33/calicheamicin	AML (patients >60 y)	(Augoff et al. 2022)
Edrecolomab	Panorex	Monoclonal IgG2A murine; anticancer	EpCAM	Colorectal cancer	(Montoya et al. 2021)

Therapy using genes and gene editing

Gene therapy has recently attracted unprecedented levels of attention from business and spinoff firms. This reflects a rising level of trust in the sector, which is supported by an increase in the number of reports of treatment success and the recent licensing of the first gene therapy products, which were authorized by the EMA in 2012. Recent developments include the FDA's August 2017 approval of Novartis' Kamiah (also known as tisagenlecleucel-T and CTL019), the first CAR T cell therapy medication. Soon after, the FDA approved axicabtagene ciloleucel, also known as Luxturna and commercialized by Spark Therapeutics and Kite Pharma, respectively, as part of another CAR T cell treatment(H. Zhang et al. 2021)(D. Zhang et al. 2022). A major paradigm shift since our 2012 analysis has been the increasing attention given to methods other than gene insertion, such as targeted recombination, RNA interference, antisense oligonucleotide-induced exon skipping, and gene editing, all of which have already reached the clinic. The significance of RNAi (e.g., to genetically down-regulate gene expression) was acknowledged in 2006 when Fire and Mello received the Noble Prize in Physiology or Medicine; these strategies will be especially crucial in the context of dominant disease processes where the simple addition of a functionally normal gene is insufficient(Hussen et al. 2023)(Karn et al. 2022).

Clinical Developments in Radiation Therapy

It is necessary for DCs to take up and cross-present tumor-derived antigens to T cells in order to activate natural anticancer T-cell responses. Type I interferon (IFN-I), which is required for DC activation and recruitment to tumors, is a critical component of this process. Preclinical research demonstrates that DNA generated from tumor cells that activates the STING pathway stimulates the production of IFN-I by DCs. It is significant to highlight that radiation increases the transport of tumor DNA to DCs, amplifying the STING-mediated pathway of IFN-I production and supporting the priming of antitumor T lymphocytes. Furthermore, it has been demonstrated that

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 10, 2023

three important chemical signals produced by radiation-induced cell death encourage DCs to take up and display tumor-derived antigens. The endoplasmic reticulum's transfer of calreticulin to the cell surface serves as a signal for DCs to pick up dying cancer cells.14 Antigen cross-presentation is promoted by the release of the nuclear protein high-mobility group box-1 (HMGB1), which binds to toll-like receptor (TLR)-4 on DCs, while adenosine triphosphate (ATP) activates the inflammasome via the P2XR7 receptor, leading to the release of interleukin (IL)-1 downstream(B. Zhang et al. 2021)(Diamond et al. 2022)(Khajeali, Khodadadi, and Pirayesh Islamian 2020).

The ineffectiveness of effector T cells UN homing to tumors is a significant impediment to tumor rejection. Chemokine control T-cell trafficking. By encouraging the development and release of chemokine like CXCL16 and CXCL10 by cancer cells and/or infiltrating immune cells, radiation can enhance the homing of effector T cells to tumors. The tumor's cancer-aberrant vasculature and defective endothelium act as a strong deterrent to T cell invasion. In a mouse pancreatic cancer model, radiation has been demonstrated to rewire tumor macrophages, improving T-cell infiltration and vascular normalization. Macrophages are crucial for inducing angiogenesis. Interestingly, this impact happened following a single low-dose radiation fraction and needed macrophages to develop inducible nitric oxide synthase(Peng et al. 2021)(L. Chang et al. 2015).

The American Cancer Society predicted that in 1993, there will be 1,170,000 new instances of aggressive cancer detected in the country. For patients first diagnosed with local and/or regional illness, new technologies have made it possible to provide a more accurate cancer evaluation and diagnosis. Numerous medicines have been researched to increase the likelihood of local control, and evidence suggests that more efficient ways to increase local and regional control would significantly increase the likelihood of long-term survival without recurring illness(Delclos and Smith 1975)(Nguyen et al. 2021). Additionally, they have been linked to higher survival rates. All of these initiatives are based on significant technological developments in terms of equipment, clinical treatment planning, physics, skilled radiation oncologists, and dosimeters. Together with a deeper comprehension of fundamental biological concepts, these advancements in radiation oncology treatment make it possible to incorporate the concepts of tumor cell healing, oxygenation, repopulation, and redistribution in novel ways throughout the radiation therapy process. Progress towards better local and regional control would not have been achievable without these significant developments in the use of radio biologic concepts in clinical radiation oncology(Brady et al. 1993).

SBRT (stereotactic body radiotherapy):

The standard course of dose-escalated external beam radiation therapy (EBRT) for males with locally advanced prostate cancer is fractionated radiation therapy with daily doses of 1.8–2.0 Gy for eight–nine weeks. Additionally, clinical evidence suggests that hypo fractionated radiation therapy may be radio biologically advantageous to smaller fraction sizes in the treatment of

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 10, 2023

prostate cancer because prostate cancer may be more sensitive to bigger daily radiation fractions(Fowler 2005). To further benefit from this proposed radiobiological advantage, stereotactic body radiation treatment (SBRT) employs increasingly greater daily percentages of radiation. Early SBRT studies were conducted using radiation delivery systems that did not provide continuous prostate location tracking with intrafractional beam aiming modification if mobility was observed(Madsen et al. 2007).

Proton treatment:

The physical characteristic of the Bragg peak, where the majority of the proton dosage is deposited within a relatively small range, with very little to no "exit dose" to normal structures in the thorax, has led to proton therapy being an alluring therapeutic option for NSCLC. Active scanning proton treatment, also known as pencil beam scanning proton therapy (PBS), and passively scattered proton therapy (PS), can be roughly categorized into the planning and administration of proton therapy(Wink et al. 2014). The dispersion of particles in a plane orthogonal to the entry of the beam and the dispersion of particles in a plane parallel to the entry of the beam are the two fundamental parts of this difficult operation(Slater et al. 1992)(H. Liu and Chang 2011).

Radiation treatment using MR guidance:

Cone-beam CT is being used in image guided radiotherapy to image the patient before radiation treatment. With integrated MRI accelerator systems, it is possible to scan the patient not only before but also during irradiation using MRI's better soft-tissue contrast. There were obstacles to be solved in order to incorporate an accelerator with an MRI: Critical accelerator components can be located near to the scanner in an area with no magnetic field thanks to enhanced active shielding of the magnet(Y. Cao et al. 2017)

Over the past few decades, radiation treatment has come a long way. Our clinical procedures have evolved as a result of the development of precise dose calculation algorithms, intensity modulated radiation treatment (IMRT), image-guided radiotherapy (IGRT), and stereotactic body radiotherapy (SBRT). For instance, at our clinic, definitive SBRT treatment for patients with early stage lung cancer is now regular practice, whereas in the past, surgery was the standard of care(J. Y. Chang et al. 2015)(Rusthoven, Kavanagh, and Karam 2015)(Shirvani et al. 2014)(Shirvani, Chang, and Roth 2013).

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 10, 2023

References

1. Agathocleous, Michalis, and William A. Harris. 2013. "Metabolism in Physiological Cell Proliferation and Differentiation." *Trends in Cell Biology*.
2. Ahmed, Faheem et al. 2023. "A Systematic Review of Computational Approaches to Understand Cancer Biology for Informed Drug Repurposing." *Journal of Biomedical Informatics*.
3. Augoff, Katarzyna, Anita Hryniewicz-Jankowska, Renata Tabola, and Kamilla Stach. 2022. "MMP9: A Tough Target for Targeted Therapy for Cancer." *Cancers*.
4. Balaton, Bradley P., and Carolyn J. Brown. 2021. "Contribution of Genetic and Epigenetic Changes to Escape from X-Chromosome Inactivation." *Epigenetics and Chromatin*.
5. Bobadilla Landey, Roberto et al. 2015. "Assessment of Genetic and Epigenetic Changes during Cell Culture Ageing and Relations with Somaclonal Variation in Coffea Arabica." *Plant Cell, Tissue and Organ Culture*.
6. Brady, Luther W. et al. 1993. "Therapeutic Advances in Radiologic Treatment of Cancer." *Cancer*.
7. Brown, Rikki A.M. et al. 2020. "Altered Iron Metabolism and Impact in Cancer Biology, Metastasis, and Immunology." *Frontiers in Oncology*.
8. Burkard, Mark E. et al. 2017. "Implementation and Clinical Utility of an Integrated Academic-Community Regional Molecular Tumor Board." *JCO Precision Oncology*.
9. Cao, Dongliang et al. 2014. "A New Tumorsphere Culture Condition Restores Potentials of Self-Renewal and Metastasis of Primary Neuroblastoma in a Mouse Neuroblastoma Model." *PLoS ONE*.
10. Cao, Yue et al. 2017. "Mr-Guided Radiation Therapy: Transformative Technology and Its Role in the Central Nervous System." *Neuro-Oncology*.
11. Cella, D. F., and E. A. Cherin. 1988. "Quality of Life during and after Cancer Treatment." *Comprehensive Therapy*.
12. Cella, D. F., and D. S. Tulsky. 1990. "Measuring Quality of Life Today: Methodological Aspects." *Oncology (Williston Park, N.Y.)*.
13. Chang, Joe Y. et al. 2015. "Stereotactic Ablative Radiotherapy versus Lobectomy for Operable Stage I Non-Small-Cell Lung Cancer: A Pooled Analysis of Two Randomised Trials." *The Lancet Oncology*.
14. Chang, Lei et al. 2015. "Targeting PI3K/Akt/MTOR Signaling Pathway in the Treatment of Prostate Cancer Radioresistance." *Critical Reviews in Oncology/Hematology*.
15. Dalton, W. Brian et al. 2017. "Personalized Medicine in the Oncology Clinic: Implementation and Outcomes of the Johns Hopkins Molecular Tumor Board." *JCO Precision Oncology*.
16. Dayem, Ahmed Abdal, Soo Bin Lee, and Ssang Goo Cho. 2018. "The Impact of Metallic Nanoparticles on Stem Cell Proliferation and Differentiation." *Nanomaterials*.
17. Delclos, L., and J. P. Smith. 1975. "Ovarian Cancer, with Special Regard to Types of Radiotherapy." *National Cancer Institute Monograph*.
18. DeSantis, Carol E. et al. 2014. "Cancer Treatment and Survivorship Statistics, 2014." *CA: A Cancer Journal for Clinicians*.
19. Diamond, Brett H., Utkarsh C. Shukla, Mark H. Sueyoshi, and Kathryn E. Huber. 2022. "Radiation Oncology." In *The History of Maxillofacial Surgery: An Evidence-Based Journey,*.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 10, 2023

20. Donizy, Piotr et al. 2021. "Merkel Cell Carcinoma of Unknown Primary: Immunohistochemical and Molecular Analyses Reveal Distinct UV-Signature/MCPyV-Negative and High Immunogenicity/MCPyV-Positive Profiles." *Cancers*.
21. Errington, Timothy M. et al. 2014. "An Open Investigation of the Reproducibility of Cancer Biology Research." *eLife*.
22. Fass, Leonard. 2008. "Imaging and Cancer: A Review." *Molecular Oncology*.
23. Fayers, P. M., and D. R. Jones. 1983. "Measuring and Analysing Quality of Life in Cancer Clinical Trials: A Review." *Statistics in Medicine*.
24. Feng, Yanghe, Qi Wang, and Tengjiao Wang. 2017. "Drug Target Protein-Protein Interaction Networks: A Systematic Perspective." *BioMed Research International*.
25. Ferlay, Jacques et al. 2015. "Cancer Incidence and Mortality Worldwide: Sources, Methods and Major Patterns in GLOBOCAN 2012." *International Journal of Cancer*.
26. Fiscon, Giulia, Federica Conte, Lorenzo Farina, and Paola Paci. 2018. "Network-Based Approaches to Explore Complex Biological Systems towards Network Medicine." *Genes*.
27. Fowler, Jack F. 2005. "The Radiobiology of Prostate Cancer Including New Aspects of Fractionated Radiotherapy." In *Acta Oncologica,*.
28. Galan-Vasquez, Edgardo, and Ernesto Perez-Rueda. 2021. "A Landscape for Drug-Target Interactions Based on Network Analysis." *PLoS ONE*.
29. Ganesh, Karuna et al. 2020. "L1CAM Defines the Regenerative Origin of Metastasis-Initiating Cells in Colorectal Cancer." *Nature Cancer*.
30. Gaudenzi, Germano et al. 2020. "Fishing for Neuroendocrine Tumors." *Endocrine-Related Cancer*.
31. Gelband, Hellen et al. 2016. "Costs, Affordability, and Feasibility of an Essential Package of Cancer Control Interventions in Low-Income and Middle-Income Countries: Key Messages from Disease Control Priorities, 3rd Edition." *The Lancet*.
32. Gerstberger, Stefanie, Qingwen Jiang, and Karuna Ganesh. 2023. "Metastasis." *Cell*.
33. Gibson, Rachel J. et al. 2013. "Systematic Review of Agents for the Management of Gastrointestinal Mucositis in Cancer Patients." *Supportive Care in Cancer*.
34. Graziani, Vittoria, Irene Rodriguez-Hernandez, Oscar Maiques, and Victoria Sanz-Moreno. 2022. "The Amoeboid State as Part of the Epithelial-to-Mesenchymal Transition Programme." *Trends in Cell Biology*.
35. Gunz, F. W. 1987. "A Look at Cancer: The Quality of Life of Cancer Patients. Monograph Series of the European Organization for Research and Treatment of Cancer." *Medical Journal of Australia*.
36. Guo, Qiujun et al. 2016. "New Mechanisms of Tumor-Associated Macrophages on Promoting Tumor Progression: Recent Research Advances and Potential Targets for Tumor Immunotherapy." *Journal of Immunology Research*.
37. Hoefflin, Rouven et al. 2018. "Personalized Clinical Decision Making Through Implementation of a Molecular Tumor Board: A German Single-Center Experience." *JCO Precision Oncology*.
38. Horak, Peter et al. 2017. "Precision Oncology Based on Omics Data: The NCT Heidelberg Experience." *International Journal of Cancer*.
39. Horneber, Markus et al. 2012. "How Many Cancer Patients Use Complementary and Alternative Medicine: A Systematic Review and Metaanalysis." *Integrative Cancer Therapies*.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 10, 2023

40. Hussen, Bashdar Mahmud et al. 2023. "Targeting MiRNA by CRISPR/Cas in Cancer: Advantages and Challenges." *Military Medical Research*.
41. Jiang, Mingzhu, Shuang Xu, Mi Bai, and Aihua Zhang. 2021. "The Emerging Role of Meis1 in Cell Proliferation and Differentiation." *American Journal of Physiology - Cell Physiology*.
42. Jin, Shuting et al. 2019. "A Network-Based Approach to Uncover MicroRNA-Mediated Disease Comorbidities and Potential Pathobiological Implications." *npj Systems Biology and Applications*.
43. Jordan, Karin, Richard Gralla, Franziska Jahn, and Alex Molassiotis. 2014. "International Antiemetic Guidelines on Chemotherapy Induced Nausea and Vomiting (CINV): Content and Implementation in Daily Routine Practice." *European Journal of Pharmacology*.
44. Karn, Vamika et al. 2022. "CRISPR/Cas9 System in Breast Cancer Therapy: Advancement, Limitations and Future Scope." *Cancer Cell International*.
45. Katti, Alyna et al. 2022. "CRISPR in Cancer Biology and Therapy." *Nature Reviews Cancer*.
46. Khajeali, Azim, Roghayeh Khodadadi, and Jalil Pirayesh Islamian. 2020. "Metal-Based Nanoparticles in Gastric Cancer Radiotherapy." *Journal of Drug Delivery Science and Technology*.
47. Kubik, Joanna, and Kamil Pawlak. 2023. "Epithelial-Mesenchymal Transition." *Current Issues in Pharmacy and Medical Sciences*.
48. Lee, Yeuan Ting, Yi Jer Tan, and Chern Ein Oon. 2018. "Molecular Targeted Therapy: Treating Cancer with Specificity." *European Journal of Pharmacology*.
49. Lheureux, S. et al. 2017. "Molecularly Targeted Therapies in Cancer: A Guide for the Nuclear Medicine Physician." *European Journal of Nuclear Medicine and Molecular Imaging*.
50. Lin, Jing et al. 2023. "Targeting Peptide-Mediated Interactions in Omics." *Proteomics*.
51. Liu, Dan et al. 2022. "Spatial Multiomics Analysis Reveals Only Minor Genetic and Epigenetic Changes in Human Liver Cancer Stem-Like Cells Compared With Other Tumor Parenchymal Cells." *Frontiers in Cell and Developmental Biology*.
52. Liu, Hui et al. 2019. "Predicting Effective Drug Combinations Using Gradient Tree Boosting Based on Features Extracted from Drug-Protein Heterogeneous Network." *BMC Bioinformatics*.
53. Liu, Hui, and Joe Y. Chang. 2011. "Proton Therapy in Clinical Practice." *Chinese Journal of Cancer*.
54. Macedo, Filipa et al. 2017. "Bone Metastases: An Overview." *Oncology Reviews*.
55. Madsen, Berit L. et al. 2007. "Stereotactic Hypofractionated Accurate Radiotherapy of the Prostate (SHARP), 33.5 Gy in Five Fractions for Localized Disease: First Clinical Trial Results." *International Journal of Radiation Oncology Biology Physics*.
56. Mahlbacher, Grace, Louis T. Curtis, John Lowengrub, and Hermann B. Frieboes. 2018. "Mathematical Modeling of Tumor-Associated Macrophage Interactions with the Cancer Microenvironment." *Journal for ImmunoTherapy of Cancer*.
57. McClellan, Kristen et al. 2022. "Therapy Resistant Gastroenteropancreatic Neuroendocrine Tumors." *Cancers*.
58. McCloskey, Deirdre. 1999. "Other Things Equal - Economical Writing: An Executive Summary." *Eastern Economic Journal*.
59. Meyskens, Frank L. et al. 2016. "Cancer Prevention: Obstacles, Challenges, and the Road

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 10, 2023

Ahead." *Journal of the National Cancer Institute*.
60. Montoya, Skye et al. 2021. "Targeted Therapies in Cancer: To Be or Not to Be, Selective." *Biomedicines*.
61. Murakami, Shohei, and Hozumi Motohashi. 2015. "Roles of Nrf2 in Cell Proliferation and Differentiation." *Free Radical Biology and Medicine*.
62. Nguyen, Julie My Van et al. 2021. "Risk of Second Malignancy in Patients with Ovarian Clear Cell Carcinoma." *International Journal of Gynecological Cancer*.
63. Ott, J. J., A. Ullrich, and A. B. Miller. 2009. "The Importance of Early Symptom Recognition in the Context of Early Detection and Cancer Survival." *European Journal of Cancer*.
64. Park, Misung et al. 2022. "Breast Cancer Metastasis: Mechanisms and Therapeutic Implications." *International Journal of Molecular Sciences*.
65. Peng, You Heng, Seidu A. Richard, Zhigang Lan, and Yuekang Zhang. 2021. "Radiation Induced Glioma in a Sexagenarian: A Case Report." *Medicine (United States)*.
66. Qi, Bao et al. 2010. "Generality and Characteristics of Genetic and Epigenetic Changes in Newly Synthesized Allotetraploid Wheat Lines." *Journal of Genetics and Genomics*.
67. Ruijtenberg, Suzan, and Sander van den Heuvel. 2016. "Coordinating Cell Proliferation and Differentiation: Antagonism between Cell Cycle Regulators and Cell Type-Specific Gene Expression." *Cell Cycle*.
68. Rusthoven, Chad G., Brian D. Kavanagh, and Sana D. Karam. 2015. "Improved Survival with Stereotactic Ablative Radiotherapy (SABR) over Lobectomy for Early Stage Non-Small Cell Lung Cancer (NSCLC): Addressing the Fallout of Disruptive Randomized Data." *Annals of Translational Medicine*.
69. Sangaletti, Sabina et al. 2021. "Myeloid Cell Heterogeneity in Lung Cancer: Implication for Immunotherapy." *Cancer Immunology, Immunotherapy*.
70. Schottenfeld, David, and Jennifer Beebe-Dimmer. 2006. "Alleviating the Burden of Cancer: A Perspective on Advances, Challenges, and Future Directions." *Cancer Epidemiology Biomarkers and Prevention*.
71. Seyfried, Thomas N., and Leanne C. Huysentruyt. 2013. "On the Origin of Cancer Metastasis." *Critical Reviews in Oncogenesis*.
72. Shirvani, Shervin M. et al. 2014. "Lobectomy, Sublobar Resection, and Stereotactic Ablative Radiotherapy for Early-Stage Non-Small Cell Lung Cancers in the Elderly." *JAMA Surgery*.
73. Shirvani, Shervin M., Joe Y. Chang, and Jack A. Roth. 2013. "Can Stereotactic Ablative Radiotherapy in Early Stage Lung Cancers Produce Comparable Success as Surgery?" *Thoracic Surgery Clinics*.
74. Siegel, Rebecca, Jiemin Ma, Zhaohui Zou, and Ahmedin Jemal. 2014. "Cancer Statistics, 2014." *CA: A Cancer Journal for Clinicians*.
75. Slater, James M. et al. 1992. "The Proton Treatment Center at Loma Linda University Medical Center: Rationale for and Description of Its Development." *International Journal of Radiation Oncology, Biology, Physics*.
76. Švajdová, Michaela, and D. Ondruš. 2020. "Assessment of Quality of Life in Patients with Head and Neck Cancer." *Klinicka Onkologie*.
77. Takeshima, Hideyuki, and Toshikazu Ushijima. 2019. "Accumulation of Genetic and Epigenetic Alterations in Normal Cells and Cancer Risk." *npj Precision Oncology*.
78. Tran, Khanh Bao et al. 2022. "The Global Burden of Cancer Attributable to Risk Factors,

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 10, 2023

2010–19: A Systematic Analysis for the Global Burden of Disease Study 2019." *The Lancet*.
79. Wan, Shuo et al. 2022. "MTORC1 Signaling Pathway Integrates Estrogen and Growth Factor to Coordinate Vaginal Epithelial Cells Proliferation and Differentiation." *Cell Death and Disease*.
80. Wen, Jing, Jianhua Fu, Wei Zhang, and Ming Guo. 2011. "Genetic and Epigenetic Changes in Lung Carcinoma and Their Clinical Implications." *Modern Pathology*.
81. Wink, Krista et al. 2014. "Particle Therapy for Non-Small Cell Lung Tumors: Where Do We Stand? A Systematic Review of the Literature." *Frontiers in Oncology*.
82. World Health Organization. 2003. "WHO Guidelines on Good Agricultural and Collection Practices (GACP) for Medicinal Plants." *World Health*.
83. ———. 2017. "World Malaria Report 2017. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO." *World Malaria Report 2017*.
84. Wu, Qinghua et al. 2020. "Selective Inhibitors for JNK Signalling: A Potential Targeted Therapy in Cancer." *Journal of Enzyme Inhibition and Medicinal Chemistry*.
85. Yang, Daowei et al. 2023. "Cross-Dataset Single-Cell Analysis Identifies Temporal Alterations in Cell Populations of Primary Pancreatic Tumor and Liver Metastasis." *Cancers*.
86. Zabransky, Daniel J., Elizabeth M. Jaffee, and Ashani T. Weeraratna. 2022. "Shared Genetic and Epigenetic Changes Link Aging and Cancer." *Trends in Cell Biology*.
87. Zehir, Ahmet et al. 2017. "Mutational Landscape of Metastatic Cancer Revealed from Prospective Clinical Sequencing of 10,000 Patients." *Nature Medicine*.
88. Zhang, Bingnan et al. 2021. "New Therapies and Biomarkers: Are We Ready for Personalized Treatment in Small Cell Lung Cancer?" *American Society of Clinical Oncology Educational Book*.
89. Zhang, Di et al. 2022. "Enhancing CRISPR/Cas Gene Editing through Modulating Cellular Mechanical Properties for Cancer Therapy." *Nature Nanotechnology*.
90. Zhang, Huimin et al. 2021. "Application of the CRISPR/Cas9-Based Gene Editing Technique in Basic Research, Diagnosis, and Therapy of Cancer." *Molecular Cancer*.
91. Zhang, Yun, and Robert A. Weinberg. 2018. "Epithelial-to-Mesenchymal Transition in Cancer: Complexity and Opportunities." *Frontiers of Medicine*.
92. Zhao, Jianhui et al. 2023. "Global Trends in Incidence, Death, Burden and Risk Factors of Early-Onset Cancer from 1990 to 2019." *BMJ Oncology*.
93. Zhou, Zhijun, and Min Li. 2022. "Targeted Therapies for Cancer." *BMC Medicine*.
94. Mandal S, Vishvakarma P. Nanoemulgel: A Smarter Topical Lipidic Emulsion-based Nanocarrier. Indian J of Pharmaceutical Education and Research. 2023;57(3s):s481-s498.
95. Mandal S, Jaiswal DV, Shiva K. A review on marketed Carica papaya leaf extract (CPLE) supplements for the treatment of dengue fever with thrombocytopenia and its drawback. International Journal of Pharmaceutical Research. 2020 Jul;12(3).
96. Pal N, Mandal S, Shiva K, Kumar B. Pharmacognostical, Phytochemical and Pharmacological Evaluation of Mallotus philippensis. Journal of Drug Delivery and Therapeutics. 2022 Sep 20;12(5):175-81.
97. Singh A, Mandal S. Ajwain (Trachyspermum ammi Linn): A review on Tremendous Herbal Plant with Various Pharmacological Activity. International Journal of Recent Advances in Multidisciplinary Topics. 2021 Jun 9;2(6):36-8.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 10, 2023

98. Mandal S, Jaiswal V, Sagar MK, Kumar S. Formulation and evaluation of carica papaya nanoemulsion for treatment of dengue and thrombocytopenia. Plant Arch. 2021;21:1345-54.
99. Mandal S, Shiva K, Kumar KP, Goel S, Patel RK, Sharma S, Chaudhary R, Bhati A, Pal N, Dixit AK. Ocular drug delivery system (ODDS): Exploration the challenges and approaches to improve ODDS. Journal of Pharmaceutical and Biological Sciences. 2021 Jul 1;9(2):88-94.
100. Shiva K, Mandal S, Kumar S. Formulation and evaluation of topical antifungal gel of fluconazole using aloe vera gel. Int J Sci Res Develop. 2021;1:187-93.
101. Mandal S, Vishvakarma P, Verma M, Alam MS, Agrawal A, Mishra A. Solanum Nigrum Linn: An Analysis Of The Medicinal Properties Of The Plant. Journal of Pharmaceutical Negative Results. 2023 Jan 1:1595-600.
102. Vishvakarma P, Mandal S, Pandey J, Bhatt AK, Banerjee VB, Gupta JK. An Analysis of The Most Recent Trends In Flavoring Herbal Medicines In Today's Market. Journal of Pharmaceutical Negative Results. 2022 Dec 31:9189-98.
103. Mandal S, Vishvakarma P, Mandal S. Future Aspects And Applications Of Nanoemulgel Formulation For Topical Lipophilic Drug Delivery. European Journal of Molecular & Clinical Medicine.;10(01):2023.
104. Chawla A, Mandal S, Vishvakarma P, Nile NP, Lokhande VN, Kakad VK, Chawla A. Ultra-Performance Liquid Chromatography (Uplc).
105. Mandal S, Raju D, Namdeo P, Patel A, Bhatt AK, Gupta JK, Haneef M, Vishvakarma P, Sharma UK. Development, characterization, and evaluation of rosa alba l extract-loaded phytosomes.
106. Mandal S, Goel S, Saxena M, Gupta P, Kumari J, Kumar P, Kumar M, Kumar R, Shiva K. Screening of catharanthus roseus stem extract for anti-ulcer potential in wistar rat.
107. Shiva K, Kaushik A, Irshad M, Sharma G, Mandal S. Evaluation and preparation: herbal gel containing thuja occidentalis and curcuma longa extracts.
108. Vishvakarma P, Kumari R, Vanmathi SM, Korni RD, Bhattacharya V, Jesudasan RE, Mandal S. Oral Delivery of Peptide and Protein Therapeutics: Challenges And Strategies. Journal of Experimental Zoology India. 2023 Jul 1;26(2).