



# CURRENT SCENARIO IN ANTICANCER DRUG THERAPY

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## Abstract:

Disease is presently the subsequent driving reason for death internationally and is relied upon to be answerable for around 9.6 million passings in 2018. With a remarkable comprehension of the atomic pathways that drive the turn of events and movement of human diseases, novel focused on treatments have become an energizing new improvement for hostile to malignancy medication. These focused on treatments, otherwise called biologic treatments, have become a significant methodology of clinical therapy, by acting to hinder the development of disease cells by explicitly focusing on atoms needed for cell development and tumorigenesis. Because of their particularity, these new treatments are required to have better adequacy and restricted unfriendly results when contrasted and other treatment choices, including hormonal and cytotoxic treatments. Various advancements are right now under assessment in clinical preliminaries or have been now brought into clinical practice. While nanomedicine is adding to the improvement of biocompatible materials both for demonstrative and remedial purposes, bioengineering of extracellular vesicles and cells got from patients has permitted planning impromptu frameworks and univocal focusing on methodologies. In this audit, we will give a top to bottom investigation of the most creative advances in essential and applied malignancy research.

**Keywords:** Cancer, tumorigenesis, vesicles, targeted therapy, immunotherapy, gene therapy, thermal ablation, radiomics, pathomics

**Introduction:-** Malignant growth is one of the primary driver of death around the world, and in the previous decade, many exploration considers have zeroed in on discovering new treatments to diminish the results brought about by customary treatments.

During malignant growth movement, tumors become exceptionally heterogeneous, making a blended populace of cells described by various atomic highlights and different responsiveness to treatments. This heterogeneity can be valued both at spatial and transient levels and is the key factor liable for the advancement of safe aggregates advanced by a specific pressing factor upon treatment organization. Generally, malignancy is treated as a worldwide and homogeneous sickness and tumors are considered overall populace of cells. In this way, a profound comprehension of these unpredictable marvels is of central significance to plan exact and productive therapies.<sup>1</sup>

Nanomedicine offers a flexible foundation of biocompatible and biodegradable frameworks that can convey traditional chemotherapeutic medications in vivo, expanding their bioavailability and focus around tumor tissues, and improving their delivery profile. Nanoparticles can be misused for various applications, going from finding to treatment.<sup>2</sup>

As of late, extracellular vesicles (EVs), answerable for disease improvement, microenvironment alteration and needed for metastatic movement, have been generally explored as effective medication conveyance vehicles. Characteristic cell reinforcements and numerous phytochemicals have been as of late presented as hostile to disease adjuvant treatments because of their enemy of proliferative and favorable to apoptotic properties.<sup>3</sup>

In this survey, we will give an overall outline of the most developed essential and applied malignant growth treatments, just as recently proposed techniques that are presently being scrutinized at the examination stage that ought to defeat the restriction of regular treatments; various ways to deal with disease determination and treatment and their momentum status in the clinical setting will be talked about, underlining their effect as inventive enemy of disease strategies.<sup>5</sup>

Directed treatment is another part of disease treatment targeting focusing on a particular site, for example, tumor vasculature or intracellular organelles, leaving the environmental factors unaffected. This colossally builds the particularity of the treatment, lessening its downsides. Another promising chance depends on quality treatment and articulation of qualities setting off apoptosis and wild sort tumor silencers, or the focused on hushing interceded by siRNAs, presently under assessment in numerous clinical preliminaries worldwide.<sup>4</sup>

Warm removal of tumors and attractive hyperthermia are opening new freedoms for accuracy medication, making the treatment limited in thin and exact regions. These techniques could be an expected substitute for more intrusive practices, like a medical procedure.

Moreover, new fields, for example, radiomics and pathomics are adding to the improvement of inventive methodologies for gathering enormous measures of information and elaborate new helpful systems and foresee precise reactions, clinical result and malignant growth repeat.

Taken all together, these techniques will actually want to give the best customized treatments to disease patients, featuring the significance of joining various controls to get the best result.

#### **Natural oxidant in drug therapy:-**

Consistently, the human body goes through a few exogenous put-downs, like bright (UV) beams, air contamination and tobacco smoke, which bring about the creation of receptive species, particularly oxidants and free revolutionaries, answerable for the beginning of numerous sicknesses, including malignancy. These atoms can likewise be delivered as a result of clinical organization of medications, however they are additionally normally made inside our phones and tissues by mitochondria and peroxisomes, and from macrophages digestion, during ordinary physiological oxygen consuming cycles. Oxidative pressure and extremist oxygen species can harm DNA (hereditary adjustments, DNA twofold strand breaks and chromosomal abnormalities and other bio-macromolecules, like lipids (film peroxidation and putrefaction and proteins (fundamentally changing the guideline of record factors and, as a result, of fundamental metabolic pathways.<sup>6</sup>

The defensive systems our body has created against these particles are at times inadequate to check the enormous harms delivered. As of late, notwithstanding investigation into the jobs of the physiological

chemicals superoxide dismutase (Turf), catalase (Feline) and glutathione peroxidase (GP), common cell reinforcements like nutrients, polyphenols and plant-inferred bioactive mixtures are being concentrated to present them as preventive specialists and expected restorative medications. These atoms have calming and against oxidant properties and are found in numerous vegetables and flavors. Nutrients, alkaloids, flavonoids, carotenoids, curcumin, berberine, quercetin and numerous different mixtures have been separated vitro and tried in vivo, showing obvious enemy of proliferative and favorable to apoptotic properties, and have been presented as corresponding treatments for cancer.<sup>7</sup>

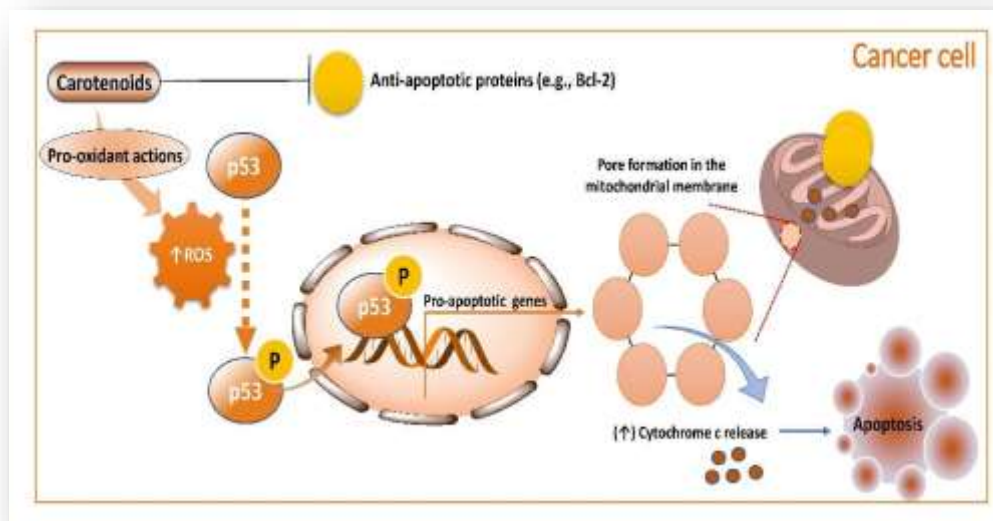


Figure No.1 Pro-oxidant Actions of Carotenoids in Triggering Apoptosis of Cancer Cells

In spite of the benefits of utilizing regular medications, their interpretation into clinical practice stays troublesome because of their restricted bioavailability and additionally harmfulness. Curcumin, a polyphenolic compound removed from turmeric (*Curcuma longa*), is a conventional Southeast Asian cure with mitigating, against oxidant and chemopreventive and helpful exercises. It has been appeared to have cytotoxic impacts in various types of tumors, like cerebrum, lung, leukemia, pancreatic and hepatocellular carcinoma, with no unfriendly impacts in typical cells at the viable helpful dosages. Curcumin can balance a plenty of cell components; be that as it may, its organic properties, and as a result, the treatment term and the proficient helpful portions, have not been totally clarified at this point. This atom is exceptionally lipophilic, ineffectively solvent in water and not entirely steady. Various procedures and explicit transporters, like liposomes and micelles, have been created to improve its bioavailability. At present, 24 clinical preliminaries including curcumin are continuous and 23 have been now completed.<sup>8</sup>

Berberine is an alkaloid compound separated from various plants, like *Berberis*. As of late, it has been shown to be viable against various tumors and to go about as a chemopreventive specialist, balancing many flagging pathways. Like curcumin, it is inadequately solvent in water; in this manner, diverse nanotechnological systems have been created to work with its conveyance across cell layers; six clinical preliminaries are open and one has been finished.

Quercetin, a polyphenolic flavonoid found in leafy foods, has been demonstrated to be compelling to treat a few tumors, like lung, prostate, liver, colon and bosom malignant growths, by restricting cell receptors and meddling with many flagging pathways. Curiously, it has been demonstrated to be viable additionally in blend with chemotherapeutic specialists. As of now, seven clinical preliminaries are open and four have been completed.<sup>9</sup> Extracellular vesicals for cancer diagnosis and therapy:- EVs are grouped in two classes dependent on their biogenesis. In particular, exosomes are little vesicles of around 30–150 nm started from endosomes in physiological and obsessive conditions and delivered by a combination of



multivesicular bodies (MVBs) to the cell film, while shed microvesicles (sMV), with a normal size of 50–1,300 nm, are available in practically any extracellular natural liquid and are liable for the trading of sub-atomic materials between cells. Exosomes are engaged with malignancy advancement and spreading, in the bidirectional correspondence between tumor cells and encompassing tissues, and in the development of the microenvironment required for pre-metastatic specialty foundation and metastatic movement. Subsequently, flowing vesicles are clinically applicable in malignant growth finding, forecast and follow up. Exosomes are really perceived as legitimate analytic devices, yet they can likewise be separated and misused as against malignancy immunizations or nanosized drug transporters in disease treatment .10

These days, one of the fundamental issues in malignant growth analysis is the early recognizable proof of biomarkers by non-obtrusive strategies. Getting a lot of data, previously and during tumor therapy, ought to permit the checking of malignant growth movement and the viability of restorative regimens. Fluid biopsies to recognize flowing tumor cells, RNAs, DNAs and exosomes have been utilized as markers for customized medication. As of late, exosomes discovery has been approved as a solid instrument for preclinical practice in various malignant growth types,, because of the distinguishing proof of their substance: twofold abandoned DNA (dsDNA), courier RNA (mRNA), miniature RNA (miRNA), long non-coding RNA (lncRNA), proteins and lipids.11

DsDNA has been recognized in exosomes disengaged from plasma and serum of various malignancy cell types, and transformed qualities engaged with tumorigenesis, for example, changed KRAS and TP53, have been distinguished as infection indicators. Likewise, exosomal AR-V7 mRNA has been utilized as a prognostic marker of protection from hormonal treatment in metastatic prostate malignancy patients. Quality articulation profiling of different RNAs from urinary exosomes has been received as a productive analytic device. LncRNAs disconnected from serum exosomes have been misused for infection visualization in colorectal malignant growth patients, and numerous miRNAs permit one to recognize diverse cellular breakdown in the lungs subtypes.12

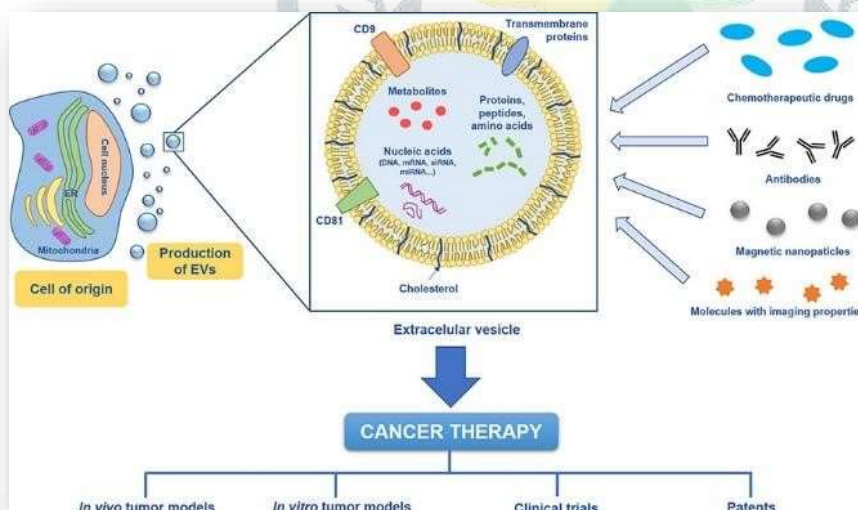


Figure No.2 Cancer therapy based on extracellular vesicles of drug delivery

As of late, new techniques to create promotion hocexosomes have been created. Cells delivering exosomes have been hereditarily designed to overexpress explicit macromolecules, or adjusted to deliver exosomes with specific focusing on atoms.

Exosomes could likewise be abused as common, biocompatible and low immunogenic nanocarriers for drug conveyance in disease treatment. They can be latently stacked by blending sanitized vesicles in with little medications , or effectively stacked through research center procedures, like electroporation and sonication. Superparamagnetic nanoparticles formed to transferrin have been tried for the seclusion of exosomes communicating transferrin receptor from mice blood. After brooding with doxorubicin, they have been utilized to target liver malignancy cells because of outer attractive fields, repressing cell development both in vitro and in vivo. Kim et al. engineered mouse macrophage-determined exosomes with aminoethyl anisamide-Stake to target sigma receptor, overexpressed in cellular breakdown in the lungs cells and inactively stacked them with paclitaxel. These frameworks went about as focusing on specialists ready to stifle metastatic development in vivo.<sup>14</sup>

Exosomes got from various disease cells have effectively been misused as malignancy antibodies. Autologous dendritic cell-inferred exosomes with improved immunostimulatory work have been tried in a stage II clinical preliminary for the actuation of CD8+ Lymphocytes in non-little cell cellular breakdown in the lungs (NSCLC) patients, noticing illness adjustment and a superior generally speaking endurance. In a stage I preliminary, ascites-determined exosomes enhanced with granulocyte-macrophage settlement invigorating element (GM-CSF) have been managed to colorectal malignancy patients, requesting a tumor-explicit insusceptible response.<sup>16</sup>

GPC1-positive exosomes have been utilized to identify pancreatic malignant growth, while coursing exosomal macrophage movement inhibitory factor (MIF) had the option to foresee liver metastasis beginning. At long last, various lipids present in urinary exosomes have been endorsed as prostate malignancy pointers. Because of the great fluctuation of patient classes and test size, and to get clinically huge outcomes for a quick and powerful conclusion, gigantic interests in exosome examination will be needed in the close future.<sup>13</sup>

Numerous issues identified with exosomes clinical interpretation stay open and are for the most part associated with the meaning of preclinical techniques for disconnection, evaluation, stockpiling and standard conventions for drug stacking. It is getting significantly more important to recognize tumor and solid platelet inferred vesicles to describe their post-separation half-life and to perform standard substance investigations. For these reasons, imaginative methodologies and advancements have been set up, for example, microarrays and explicit monoclonal antibodies and RNA markers intensification strategies.<sup>17</sup>

Three clinical preliminaries with stacked exosomes are as of now continuous for the therapy of various tumors : a stage I preliminary is assessing the capacity of exosomes to convey curcumin to typical and colon disease tissues; a stage II preliminary is examining the in vivo execution of autologous tumor cell-determined microparticles conveying methotrexate in cellular breakdown in the lungs patients and a clinical request is zeroing in on autologous erythrocyte-inferred microparticles stacked with methotrexate for gastric, colorectal and ovarian malignant growth treatment.<sup>15</sup>

### **Recent innovation in cancer therapy: radiomic and pathomic:-**

Effective malignant growth treatment at present depends on a medical procedure and, in around half of patients, on radiotherapy, that can be conveyed by utilizing an outside shaft source or by embeddings locally a radioactive source (for this situation, the methodology is named brachytherapy), consequently acquiring centered light. At present, localisation of the pillar is worked with by picture guided radiotherapy (IGRT), where pictures of the patient are obtained during the therapy permitting the best measure of radiation to be set. Because of the presentation of power balanced radiotherapy (IMRT), radiation fields of various forces can be made, assisting with lessening dosages got by sound tissues and in this manner restricting unfavorable results. At last, through stereotactic ablative radiotherapy (SABR), it has gotten achievable to pass on an ablative portion of radiation just to a little objective volume, fundamentally diminishing undesired toxicity.<sup>18</sup>

Lamentably, radioresistance can emerge during treatment, bringing down its adequacy. This has been connected to mitochondrial surrenders; consequently, focusing on explicit capacities have demonstrated to be useful in reestablishing against malignancy impacts. A new report has appeared, for instance, that radioresistance in an oesophageal adenocarcinoma model is connected to an unusual construction and size of mitochondria, and the estimation of the energy digestion in patients has permitted segregation between treatment safe and delicate patients. Focusing on mitochondria with little atoms going about as radiosensitizers is being examined for gastrointestinal malignant growth therapy.<sup>19</sup>

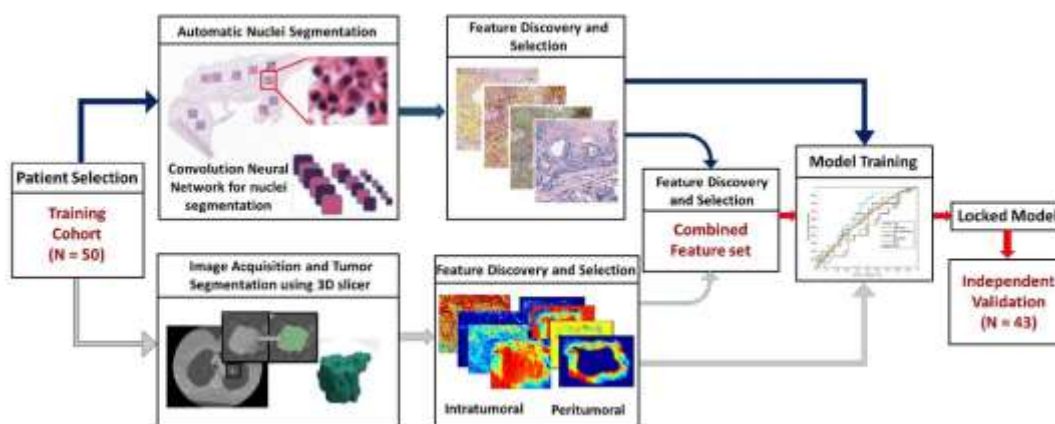


Figure No. 3 Integrating radiomic and pathomic features for predicting recurrence in early stage lung cancer

Malignancy is a mind boggling infection and its effective treatment requires colossal endeavors to blend the plenty of data procured during symptomatic and remedial strategies. The capacity to interface the information gathered from clinical pictures and atomic examinations has permitted an outline to be acquired of the entire tridimensional volume of the tumor by non-intrusive imaging techniques.<sup>20</sup> This matches with the fundamental point of accuracy medication, which is to limit treatment related results, while upgrading its adequacy to accomplish the best individualized therapy.<sup>21</sup>

Radiomics and pathomics are two promising and inventive fields dependent on gathering quantitative picture highlights from radiology and pathology screenings as remedial and prognostic markers of infection result. Numerous computerized reasoning advances, for example, AI application, have been acquainted with oversee and elaborate the enormous measure of gathered datasets and to precisely foresee the treatment adequacy, the clinical result and the illness repeat. Forecast of the treatment reaction can help in discovering a specially appointed transformation for the best anticipation and result. These days, customized medication requires a coordinated translation of the outcomes got by different indicative methodologies, and biomedical pictures are vital to give constant checking of illness movement, being rigorously corresponded to malignancy atomic characterisation.<sup>22</sup>



Radiomics is expected as the high throughput measurement of tumor properties acquired from the investigation of clinical pictures. Pathomics, on the opposite side, depends on age and characterisation of high-resolution tissue pictures. Numerous examinations are zeroing in on the advancement of new strategies for picture investigation to extrapolate data by evaluation and infection characterisation. Adaptable information bases are needed to oversee enormous volumes of information coming from quality articulation, histology, 3D tissue remaking (X-ray) and metabolic highlights (positron discharge tomography, PET) to recognize illness phenotypes.<sup>21</sup> Right now, there is a dire need to characterize univocal information obtaining rules. A few drives to set up normalized strategies and work with clinical interpretation have been now embraced, for example, quantitative imaging organization or the German Public Partner Consortium. Exact depiction of the boundaries needed for picture procurement and for the creation and utilization of computational and measurable strategies are important to set powerful conventions for the age of models in radiation treatment. As indicated by the US Public Library of Medication, around 50 clinical preliminaries including radiomics are right now enrolling patients, and a couple have effectively been completed.<sup>23</sup>

### **Targeted therapy and immunotherapy:-**

One of the principle issues of traditional disease treatment is the low particularity of chemotherapeutic medications for malignant growth cells. Truth be told, most medications act both on solid and infected tissues, creating extreme results. Specialists are investing a ton of energy into figuring out how to target just the ideal site. Nanoparticles have raised extraordinary interest for their propensity to collect more in tumor tissues because of the improved penetrability and maintenance impact (EPR). This interaction, called inactive focusing on, depends on the little size of nanoparticles and the cracked vasculature and disabled lymphatic seepage of neoplastic tissues. Inactive focusing on, notwithstanding, is hard to control and can instigate multidrug opposition. Dynamic focusing, then again, upgrades the take-up by tumor cells by focusing on explicit receptors that are overexpressed on them. Nanoparticles, for instance, can be functionalized with ligands that univocally tie specific cells or subcellular destinations. A few sorts of ligands can be utilized, like little atoms, peptides, proteins, aptamers and antibodies.<sup>24</sup>

Folic corrosive and biotin are little atoms, whose receptors are overexpressed in tumor tissues. A few nanocarriers have been functionalized with folic corrosive to target ovarian and endometrial diseases: folic corrosive formed polyethylene glycol-poly(lactic-co-glycolic corrosive) nanoparticles conveying docetaxel expanded medication cell take-up by human cervical carcinoma cells. Little ligands are modest and can be connected to nanoparticles by basic formation chemistry.<sup>25</sup>

Various types of little peptides and proteins are additionally powerful in dynamic focusing on. Angiopep-2 is a peptide that has brought incredible interest up in the therapy of mind malignancy, since it ties to low-thickness lipoprotein receptor-related protein-1 (LRP1) of endothelial cells in the BBB, and it is likewise overexpressed in glioblastoma disease cells. Bombesin peptide formed to poly(lactic-co-glycolic corrosive) (PLGA) nanoparticles stacked with docetaxel was utilized to focus on the gastrin-delivering peptide receptor, overexpressed on cell surface of prostate, bosom, ovarian, pancreatic and colorectal disease cells. Transferrin is a serum glycoprotein overexpressed on numerous strong tumors, particularly on glioblastoma multiforme cells, and on epithelial cells of the BBB. Transferrin-formed chitosan-Stake nanoparticles conveying paclitaxel showed a higher cytotoxicity towards transferrin-overexpressing human non-little cell cellular breakdown in the lungs cells (NSCLCs) (Bounce 62).<sup>26</sup> Aptamers are little engineered single-abandoned RNA or DNA oligonucleotides collapsed into explicit shapes that make them fit for restricting explicit targets. Farokhzad et al. reported that the utilization of A10 RNA aptamer formed to docetaxel-stacked nanoparticles altogether improves in vitro cytotoxicity. The equivalent aptamer has been additionally used to get ready quantum speck doxorubicin conjugates.<sup>27</sup>

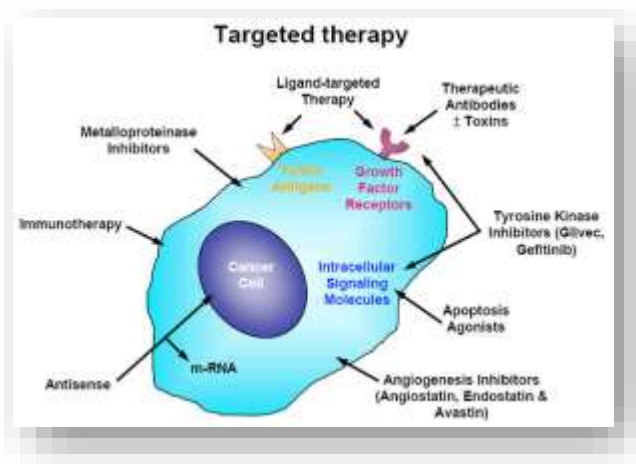


Figure No.4 Targeted therapy

Antibodies are at present the most abused ligands for dynamic focusing on. These proteins have an ordinary 'Y' shape, where the two arms are liable for the particular communication with the antigen. Antibodies can be utilized as immunoconjugates, when formed to a medication or nanoparticle, or bare. In the primary case, their capacity is for the most part to focus on a particular antigen overexpressed on disease cells. Antibodies utilized for this reason incorporate those ones that tight spot to the human epidermal development factor receptor 2 (HER2), the epidermal development factor receptor (EGFR), the transferrin receptor (TfR) and the prostate-explicit layer antigen (PSMA). Rapamycin-PLGA nanoparticle formed to EGFR counter acting agent displayed higher cell take-up by human bosom adenocarcinoma cells (MCF-7), with improved apoptotic action. Loperamide-stacked human serum egg whites nanoparticles formed to antibodies that explicitly tie transferrin receptor effectively crossed the BBB and conveyed the medication to the ideal site.<sup>28</sup>

Exposed antibodies or immunoconjugates can likewise be utilized in immunotherapy, which is a malignant growth therapy that targets animating or reestablishing the safe arrangement of the patient against disease cells. Antibodies can go about as markers for malignant growth cells to make them more powerless against the resistant framework reaction (vague insusceptible incitement), or as inhibitors for invulnerable designated spot proteins on disease cell surface, that can tweak the activity of Lymphocytes. A few antibodies have been as of now tried and acknowledged by FDA for immunotherapy, for example, rituximab, ibritumomab tiuxetan, trastuzumab emtansine, nivolumab and pembrolizumab.<sup>29</sup>

Immunotherapy can be accomplished by another procedure called receptive cell move (ACT) and it comprises of confining T-lymphocytes (White blood cells) with the most noteworthy action against disease straightforwardly from the patient's blood, extending them ex vivo, and reinfusing them again into the patient. Autologous Immune system microorganisms can be hereditarily designed in vitro to communicate a chimaeric antigen receptor (Vehicle), which makes them more explicit against malignancy cell antigens. Various Vehicles can be intended to be coordinated against a specific malignancy antigen. The hereditary alteration of White blood cells can be accomplished by various strategies like viral transduction, non-viral techniques like DNA-based transposons, CRISPR/Cas9 or other plasmid DNA and mRNA move methods (i.e., electroporation, epitome in nanoparticles). ACT conventions have been now embraced in clinical practice for cutting edge or repetitive intense lymphoblastic leukemia and for some forceful types of non-Hodgkin's lymphoma. For instance, it has been shown that the treatment of end-stage patients influenced by intense lymphocytic leukemia with Vehicle White blood cells prompted a full recuperation in up to 92% of patients. Notwithstanding these exceptionally encouraging outcomes, much examination is right now gave to understanding the long haul symptoms of Vehicle Lymphocyte treatments and their destiny inside tumors, and to improving Vehicle White blood cell extension technologies.<sup>29</sup>



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