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NANOPARTICLES TARGETING COLORECTAL CANCER: A REVIEW

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ABSTRACT

Despite great advancements in therapy, colorectal cancer (CRC) still causes major morbidity and death and is incredibly common around the world. One of the most promising approaches to treating cancer now involves the use of nanoparticles as a medication delivery mechanism. Targeted nanoparticles may take use of chemicals that are differently expressed on tumour cell surfaces to deliver cytotoxic medications to the tumour effectively. In a number of recent studies, different compounds have been used as ligands on the surfaces of nanoparticles to engage with tumour cells and facilitate the delivery of anticancer medicines. We address the prospective use of ligands and cellular targets in possible techniques for the treatment of CRCs and describe new developments in targeted nanoparticles against CRC in this article.

KEYWORDS: CRC**,** Targeted nanoparticles, Chemotherapy, ligands, stimulation.

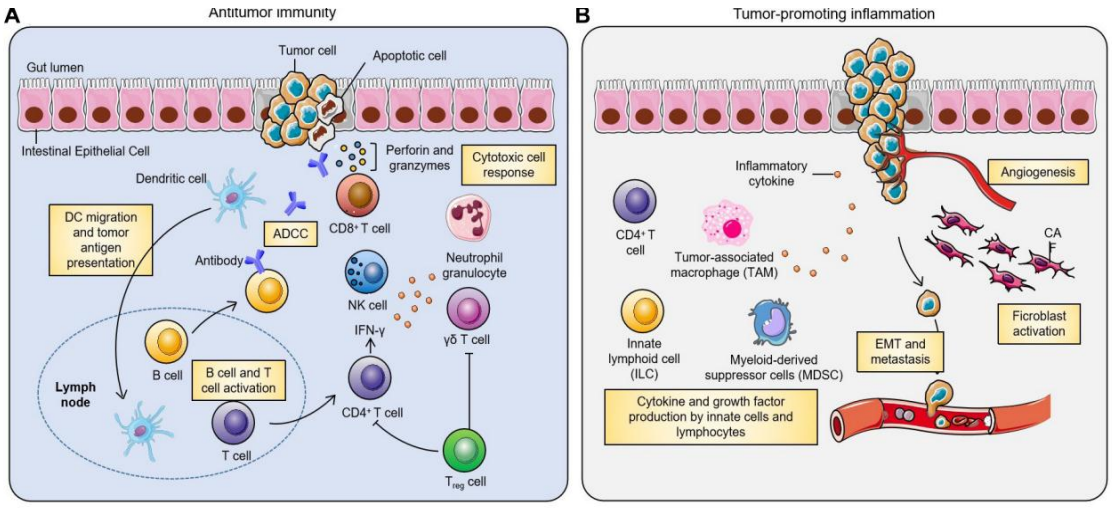
INTRODUCTION

Yearly 900,000 deaths and 1.80 million new cases of colorectal cancer (CRC) are heading the widespread of cancer and is the secondary reason of cancer-connected death rate.[1] Nearly 26% of CRC takes place in the rectum and 74% of CRC cases present in the colon.[2] By the epithelial cells, glandular cells existing in the colon, CRC is a type of malignant tumour usually developed.[3-5] Chemotherapy is one of the most obvious treatment utilised for CRC. Coming to the delivery of active chemicals in pharmaceuticals, nanoparticles specifically are successful.[6] In comparison to the free medication dose this approach has low side effects

and more intra tumoral delivery of drug.[7,8] In various treatments for cancer, treatment with nanoparticles has ranked as the effective one. Targeted nanoparticles has the advantage of expressing the molecules present on the upper layer of tumour cells, imparting efficacious release of cytotoxic drugs. Numerous works has newly claimed the applications of various moieties as ligands on upper layer of NPs to link with the tumour cells. Here, we present newly progress in targeted approaches for treatment of CRC.[9]

DETAIL OF CRC

Relating to the cancer- linked moratility CRC is obvious and it is one of the heading causes of cancer. Drastic variation the lifestyle of the people is also a cause of cancer.[10] Developed countries has made great advancements in the treatment approaches related to CRC and minimising the deaths related to CRC. By addition of population dependent evaluation programmes, deaths related to CRC can be greatly minimised.[11] Even though developed countries made advancements in the therapy of CRC, the mortality rate due to CRC continue to raise because of western country living style, intake of minimal-fibre content and diet having high fat values, excessive tobacco smoking, and also lessen physical activity among the population.[12,13] Because of high metastasis and resistant to chemo CRC is identified by poor diagnosis and treatment. Digestion and intake of water, minerals, nutrients and collection of wastes are the vital duties of rectum and colon. CRC grows in a gradual way. Cells in neoplastic cells has hand over on basic epithelial cells due to mutations in critical genes.[14] These mutations start with adenomas and then transform into carcinomas. Tumour development and histopathology are connected by these mutations which take place in step by step manner.[15] Importantly the biggest risk factor in CRC is the intestinal inflammation. The relationship between inflammation and CRC is explained in (Fig.1).[16] In the evolution of CRC, inflammation has many resisting effects. The dendritic cells which can identify and express antigen, B cells and T cells that are mediated by the various immune cells are induced by the antitumour effect in the intestine's due inflammation. Besides Innate immunity provided by natural killer cells, neutrophils, Treg cells and γδ, T cells also have anti-tumour effects of inflammation. Eventually inflammation enhances tumour development. are Enhancement of the tumour linked immune cells in tumour microenvironment leads to the production of various inflammatory factors which increases the proliferation, attack, epithelial-mesenchymal change, metastasis, angiogenesis and other procedures in tumour cells hence increase the growth of tumours. Not only tumour microenvironment but also the gut microbia play a vital part in progress of CRC.[17]



(A) In anti-tumour invulnerability, dendritic cells identifies and present tumour antigens and trigger tumour-specific B cells and T cells. CD4+ T cells, CD8+ T cells and natural killer cells (NK cells) mediates the anti-tumour immunity.	(B) Besides, inflammation can enhance tumour development. The dendritic cells which can identify and show antigen, B cells and T cells that are mediated by the various immune cells are induced by the antitumour effect in the intestines due inflammation.

Fig. 1: Role of inflammation in the development of CRC.

Poisonous and side effects takes place because of low drug availability and they are disadvantages of conventional chemotherapy.[18] Effective and safe novel treatments are required for CRC treatment. Improvement of the drug efficacy and lessen adverse effects of the unrestricted drug forms can be achieved by NP-mediated targeted systems.[19]

Various advantages of NPs as drug delivery systems

(1) NP entrapment enhances drug solubility and stability under severe Gastro intestinal environment.

(2) Drug content and half-life in blood can be improved by formulating into nanoparticles[15].

(3) Formulating into nanoparticles can increase the retention effect and permeability in tumour cells.[20]

(4) Few NP approaches have been studied to minimise the concentration of drugs needed for treatment.[21]

MOLECULAR MECHANISM OF COLORECTAL CANCER: The development of adenoma to profession of metastatic cancer contains numerous steps. Prior action starts with generation of dysplastic epithelium which is caused disabling of adenomatous polyposis coli which is a tumour suppressor gene. It is then accompanied by a alteration of the KRAS gene,

which results in the formation of adenomas, which finally concludes to the progression of carcinoma due to the sudden change in (PIK3CA) and P53 genes, etc. as presented in (Fig. 2).[22]

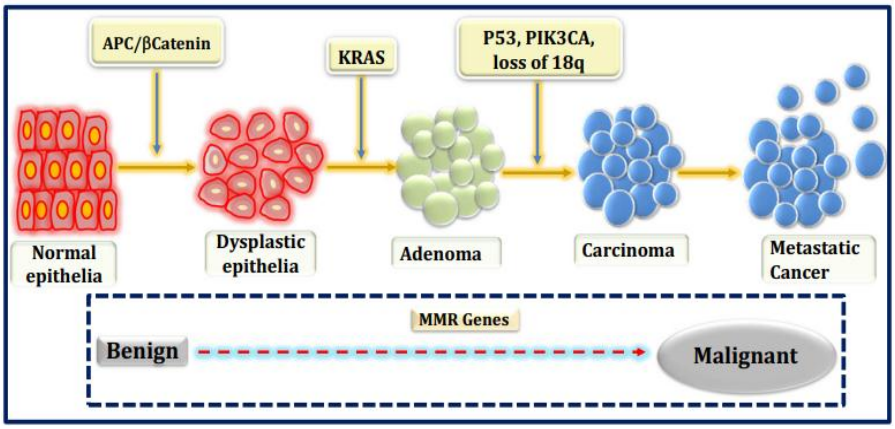


Fig. 2: Gradual transformation of adenoma-carcinoma to CRC[22]

The majority of CRCs are adenocarcinomas, which are cancerous tumours that begin to multiply and discharge mucus and other fluids. Colon cancer is divided into four stages, ranging from 0 to IV, based on histological characteristics. Numerous polyps in the mucosal surface of the colon increases in early levels. After developing, some polyps may become malignant, but in the initial process, polyps transform to tumours and infiltrate the deeper surface of the colon mucosa. In the secondary kevel metastases is spread to the outer surface and not to lymph nodes which is a characteristic of secondary level. Third level is characterised by the the spread of cancer all over the colon and adjacent lymph nodes. It entirely reaches to other organs of the body in the fourth stage, including the lungs, gut, liver, kidney, ovary, and testis, and is thus classified into metastatic colon cancer. This step is exceedingly serious, with only a 3% chance of survival.[22]

GENETICS OF COLORECTAL CANCER: Familiar adenomatous polyposis coli affects nearly 0.5 percent of CRC cases. The adenomo polyposis coli gene (a tumour suppressing gene) is undergone mutation in this case, and prevents beta-catenin breakdown. β-Catenin is a transcription factor has place in transmission of signals from E cadherin on cell lining to downstream targets like C-myc, cyclin D1, and PPAR-7 (peroxisome proliferator-activated receptor-7), among others, in the Wingless-Wnt pathway. After transcription, these target genes leads to cell augmentation and transformation. TGF- β (transforming growth factor-beta) is a cytokine superfamily polypeptide. It serves a variety of cellular tasks, including cell proliferation, differentiation, growth regulation, and apoptosis.[23] TGF- β binds to its

membrane-bound receptor and phosphorylates it, causing R-SMAD2 and 3 to phosphorylate as well. While SMAD6 and SMAD7 serve as inhibitors, this group attaches to SMAD4 and changed its location to the nucleus, where the responsive genes are duplicated. TGF-RII mutations are the most obvious modifications in TGF-expressing in CRC cells, and NSAIDs are effective in reducing CRC by 40–50% through COX-2 inhibition.[24] Galectin-3 (molecular weight 29 to 34 kDa) and other carbohydrate-binding proteins appear to play a vital role in tumour growth and development, according to mounting data. It is widely expressed in neoplasms and through contact with particular ligands, it is engaged in a variety of biological steps including cell proliferation, differentiation, inflammation. It increases chemotaxis in macrophages, reducing their mobility during the early stages of tube formation. It induces integrin overexpression after binding to its receptor, resulting in endothelial cell movement and adhesion. Galectin-3 is an attribute in pre-mRNA splitting that regulates cell cycle and prevents apoptosis, possibly through interactions with Bcl-2 group members.[25,26]

APPROACHES FOR TARGETING COLORECTAL CANCER: Researchers are experimenting with a variety of methods to improve drug penetration across the epithelial membrane of the colon. This could result in medicines being delivered both locally and systemically for the therapy of CRC. Administering chemotherapeutic drugs to the colonic region is beneficial in the therapy of diseases related to colon, because it allows for a high concentration of drugs to be obtained locally while minimising side effects caused by therapeutic release in the upper region of the GIT or systemic absorption. Several formulations were created, as well as preclinical studies, for target medications to the colon by oral delivery. It has been grouped into four main methods.

- Delivering of drugs depending on pH (activated by change in the local pH).
- Drug delivery depending on enzymes.
- Controlling of distribution of drugs in terms of timing.
- Systems basing on pressure (pressure alters through the GIT lumen activates the drug release). Prodrug-based systems, osmotic controlled drug delivery and hydrogel-based systems are some of the other options. The approaches presented have merits of their own, as well as a few drawbacks. And, in order to overcome these limitations and obtain successful drug delivery to the colon, a combination of more than two approaches are used.[27]

THERAPY OF COLORECTAL CANCER BY NANOPARTICLES: Developing of nanoparticle-based treatment approaches for cancer therapy has resulted in significant advancements in pharmacology, reducing cytotoxic drug adverse effects and enhancing effectiveness, solubility, pharmacokinetics, and biodistribution. Various nanoparticles of various forms, dimensions, and chemical moieties have demonstrated great results in entrapment different forms of anticancer drug load, involving siRNA, throughout the last 50 years.[28] These primary-generation anticancer nanoparticles enter tumour tissue easily, having advantage of the tumour's vascular and lymphatic drainage's improved penetration and retention impact; This causes nanoparticles to extravasate and accumulate within cancer cells, improving therapeutic efficacy.[29] Platforms based on liposome drug delivery are most popular, and they were the primary nanocarriers licenced for use in humans by the US FDA.[30] Inner phospholipid bilayer and exterior aqueous phase makes up the vesicles, capable of encapsulating both hydrophilic and hydrophobic medicines. Thermodox, CPX1, LE-SN38, are liposome-based nanoproducts now in clinical studies for the therapy of CRC; CPX-1 (Irinotecan HCl: Floxuridine) has finished Phase II clinical trials.[31]

Polymeric nanoparticles: Colloidal systems made up of biodegradable polymers are known as polymeric nanoparticles. These nanoparticles have a number of pros against conventional nanocarrier systems, including good biodegradability and biocompatibility, sustained release, increased half-life of drug, and greater incorporation of drug.[32] Synthetic polymers such as polycaprolactone (PCL), polylactic acid (PLA), polyethylene glycol (PEG), poly(-caprolactone)/poly(ethylene glycol) and poly(D, L-lactide-co-glycolic) acid (PLGA) are used to make polymeric nanoparticles for cancer treatment.[33] Conventional chemotherapy has a number of flaws, including a lack of specificity for cancer cells, which can cause side effects in healthy cells. As a result, TNF-related apoptosis making ligand (TRAIL) covalently linked SLN loaded with oxaliplatin were generated (CD-253) Antibody that is monoclonal. When compared to free oxaliplatin, the formulation showed a 1.5-fold increase in immuno-nanoparticle cytotoxicity (4.9μM). In relation to the free medication, the IC50 value of immuno-nanoparticles (4.6 μM) showed an 8-fold decrease in IC50 value. PLGA [poly (lactic-co-glycolic acid)] nanoparticles In mice, containing 5-FU for colon cancer targeting, the anticancer impact was improved, as were the survival rates. 5-FU-loaded PLGA nanoparticles showed anticancer efficacy and increased apoptosis in HCT-116 and HT-29 colon cancer cell lines on comparing the free 5-FU. The findings revealed that the created technology had a huge amount of potential for cancer targeting.[34] The nanoparticles showed

increased absorption in HT-29 cells, indicating that they could be used to design a CRC-targeted approach.[35] For CRC treatment, folic acid-altered nanoparticles containing 5-FU synthesised by (Zhang et al.) produced similar results.[36] The use of mucoadhesive polymers is another method for improving nanoparticle adhesion to colorectal cells. (Anitha et al.) produced nanocarriers encapsulated with 5-FU and curcumin for colon cancer treatment.[37]

Lipid-based nanoparticles: Because of their biodegradability, biocompatibility, structural flexibility, and tailorable capability, lipid nanoparticles (LNPs), particularly liposomes, are potential candidates in cancer therapy.[38] Liposomes, core-shell NPs, micelles, solid lipid nanoparticles (SLN), nanodiscs, and cubosomes are the six different types of LNPs. Liposomes surfaces are altered by integrating numerous functional subjects. LNPs are frequently employed not only because of their diversity, but also because chemotherapeutics, peptides, proteins, DNA, and RNA, can be loaded.[39] The recent advancements and uses of SNPs and liposomes were the emphasis of this section. Solid lipid NPs are made up of low-melting-point lipids and various surface active agents and/or co-surfactants.[40] The lipid and surfactant ratios used determine the drug release, magnitude, potential stability, drug loading of lipid NPs. Drugs having less water solubility are encapsulated as solid lipid nanoparticles. For example, quercetin, an antioxidant present in onions, has powerful anti-tumour properties over CRC but is poorly soluble in water. (Li et al. 2009) used emulsification and a low-temperature solidification process to create quercetin-loaded solid lipid nanoparticles (QT-SLNs).[41] The QT-SLNs(hydrophobic drugs) had a longer Tmax and MRT, as well as better relative bioavailability, showing SLNs are good oral delivery carriers. The ability of these SLNs to target tumour cells was improved, and cellular absorption was enhanced. In vivo tests revealed that SLNs efficiently suppressed primary tumour and metastatic loads while causing less systemic damage. Liposomes are divided into three categories depending on size and lamellarity. These groups include: large unilamellar vesicles (LUVs), multilamellar vesicles (MLVs), and small unilamellar vesicles (SUVs).[42,43] SUVs have particle sizes ranging from 25 to 50 nm, and LUVs have particle sizes more than 100 nm, and MLVs have particle sizes ranging from 0.05 to 10 m and are made up of multiple layer phospholipid bilayers. Hydrophilic medications are non-covalently entrapped in liposome core, whereas hydrophobic drugs are contained in the phospholipid bilayer of the liposomes. (Batist et al. 2009) created CPX-1, a new liposome-entrapped formulation of Irinotecan with floxuridine that was tuned for therapeutic synergy.[44] The co-delivery device not only successfully contained high drug levels in blood circulation next to systemic administration, it also

demonstrated higher anti-tumour action in suffering patients by CRC. A phase II trial is now underway to assess the efficacy and safety of CPX-1 for the treatment of CRC. Additionally, several natural lipid molecules have been utilised in the synthesis of lipid nanoparticles and drug derivatization. Utilising this technique (Kotelevets et al. 2017) used this approach to create squalene-dependent nanoparticles loaded with cisplatin (SQ-CDDP NP) for oral delivery, greatly increasing cisplatin efficacy.[45] Cisplatin therapy for CRC is accompanied with significant toxicity and a substantial chance of drug resistance.[46] In a nutshell, this technique connected polyunsaturated fatty acids to chemical medications (PUFAs). Such a prodrug was able to assemble itself in aqueous medium without the need for external adjuvants, resulting in potent anti-tumour actions. Finally, because of their biocompatibility, cytocompatibility, and extended functionality, LNPs are the most attractive drug delivery systems. They are suitable for cancer treatment because they enhance medication solubility, delivery effectiveness, safety.

Inorganic nanoparticles: Metal NPs and Silica NPs, can be utilised as drugs, imaging agents, gene carriers, sensors and antiseptics.[47] Because inorganic NPs can be used for a number of functions, advances in biomedicines offer a viable opportunity to formulate novel diagnostic and drug delivery systems.[48] Inorganic nanoparticles can be divided into three categories based on the materials employed and the shapes they take: round gold, mesoporous silica NPs, gold nanocage, gold nano shell, silver NPs, quantum dots, iron oxide, gold nanorod, carbon nanotubes. A basic inorganic NP is made up of three parts: an inorganic core, a tailored protective coatings, and a layer of biological molecules that have been adsorbed. The following diagram depicts the destiny of typical inorganic NPs post administration (Fig. 3).[49]

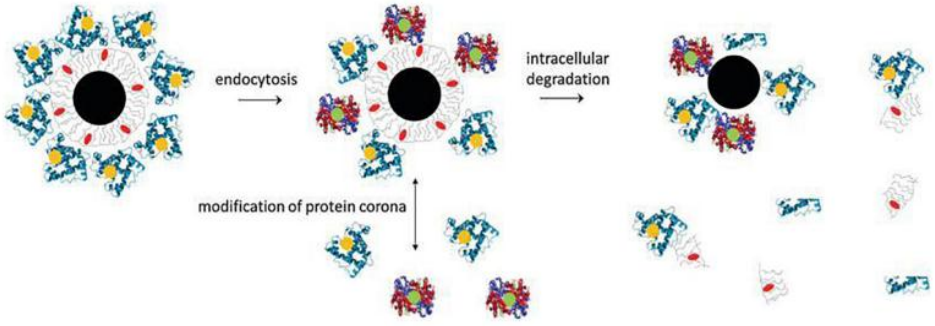


Fig. 3: Formation and in vivo degeneration of inorganic NP (Feliu et al., 2016).[49]

A general inorganic nanoparticle consists of an inorganic core, an organised surface and biological molecules that are absorbed on to the shell. In the degeneration proceeding, the NPs may crumble to separate constituents. Inorganic core would start to degenerate early, modifying its physical and surface characteristics. Intracellular degeneration partly removes the modified organic coating. In brief, pure inorganic cores, in absence of carbon-based layer, will collage in physiological settings. NPs consisting carbon-based layers shows finer biocompatibility and has better cell sticking and cellular intake properties. When incorporated, the physical and surface characteristics of NPs are modified and their inorganic core is degenerated. Organic layer shall be removed through intracellular degeneration or protein corona alteration. Metal dependent NPs are extensively utilised for treatment of CRC, as they are evaluated by great stability and chance of producing in largescale, limiting organic solvents.[50] The metal-dependent NPs can be tweaked to enhance medication delivery efficiency. -lactoglobulin (-LG) NPs were designed by (Ghalandari et al. 2014) for the delivery systems of oxali-palladium as a metal-based therapy for colon cancer.[51] -LG NPs comprising oxali-palladium crosslinked to lower methoxyl pectin (LMP) are a viable possibility for improved oral medicationtransfer for colorectal cancer treatment, according to this study.

Ligand-conjugated nanoparticles: Focusing NPs at CRC lesion areas is critical for their effective use. Various targeting ligands have been recognized and investigated to encourage effective targeting of NPs, comprising small compounds, receptors, peptides, antibodies, polysaccharides, DNA, and RNA, as illustrated in (Fig. 4).[52-54]

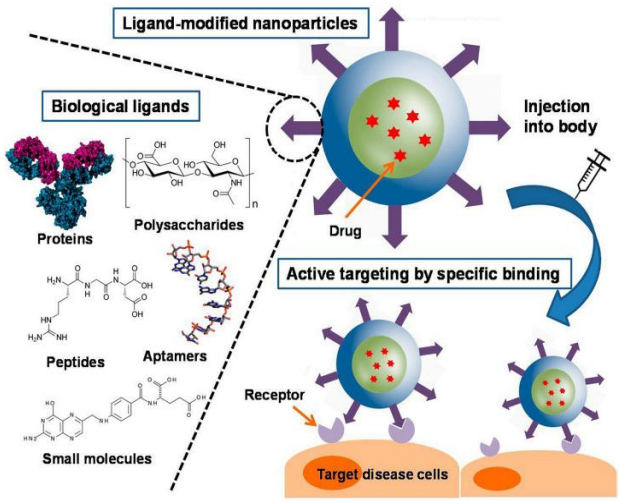


Fig. 4: Numerous forms of ligand-bounded nanoparticles containing various active compounds, as well as their targeting methods (Yoo et al., 2019).[52-54]

Higher binding and cellular ingestion are aided by improved ligand concentration. In practical nanoparticles, a diversity of ligands are utilised, aptamers, proteins, polysaccharides, peptides, and small molecules. They can be chemically or physically attached to the nanoparticles, or they would be confined to the nanoparticles' constituents before production. These ligands could attach to precise receptors on membrane of target cells, enhancing NP consumption and, as a result, therapeutic efficacy is also enhanced.[55] We categorised nanoparticles according to the sorts of changed ligands in this area. Hyaluronan (HA) is a polysaccharide made up of N-acetylglucosamine and a -glucuronic acid that is one of the external matrix's constituents.[56] Because its receptor, CD44, is upregulated in a variety of cancers, it is a prime suspect for cancer-targeting NPs. HA-NPs-PTC209, a colon melanoma method to administer the BMI-1 inhibitor PTC209, was devised by (Xu et al. 2019). PTC209 distorts the pluripotency of CRC, reducing CRC relapse and metastasis.[57] These HA-modified NPs showed a greater attraction to CRC cells with high CD44/CD168 activity and show excellent tumour location targeting. Microporous NPs (MSNs) were coupled with poly (ethylene glycol) (PEG), poly (ethylene imine) (PEI), and FA in various combinations[58] by (Desai et al. 2016). The resultant Microspheres were infused with Notch pathway-secretase antagonists for colon chemotherapy. These modified MSNs targeting the colon selectively and were easily internalised by enterocytes, preserving physical and organizational stability in the digestive region.

Stimuli-responsive nanoparticles: Extracellular matrix (ECM), cancer immune cells, neuroendocrine (NE) cells, adipose cells, blood and lymphatic vascular networks, cytokines, stroma, and other signalling moieties are all found in the tumour microenvironment.[59,60] Certain bone marrow- obtained precursor cells migrate to the TME and transform to endothelial cells, pericytes, fibroblasts, and some other stromal cells, accelerating tumour malignancy.[61,62] TME also plays an chief function in the regulation of cancer cell metabolism.[63] As a result, in tumour therapy, a deeper comprehension of the interplay amongst TME, cancer cells, and medicines is critical. Acidity, hypoxia, and thermal stability features of the tumour microenvironment are all conducive to the development of stimuli-responsive nanoparticles. Because these NPs are ineffective in bloodstream and under basal conditions, they assure tumour-targeted delivery.[64-68], once they arrive at the tumour location via active or passive targeting, they are engaged, distributing therapeutics in response to TME features, resulting in targeted medication production and less adverse effects. (Fig. 5)[69] depicts interactions across stimuli-responsive nanocarriers and TME.

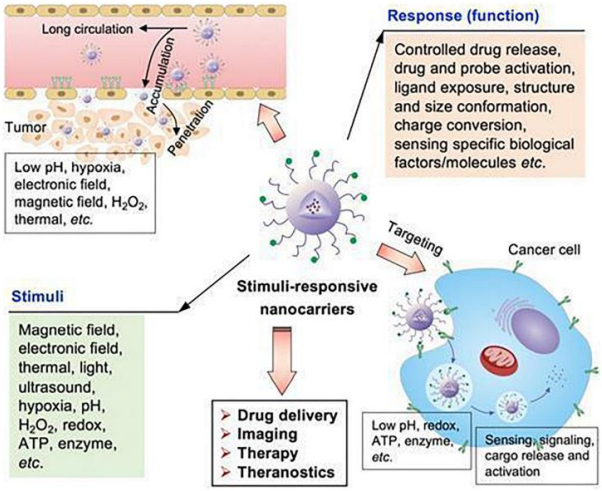


Fig. 5. Different functions of stimuli-responsive nanoparticles.[69]

Nanoparticles will clump together in tumours as a result of both internally and externally stimulation., ATP, enzyme, pH, redox and hypoxia are examples of internal stimuli, whereas external factors embrace electronic field, magnetic field, heat, ultrasound and light. The stimuli-responsive increases increased medication flow at tumour-specific locations, allowing for more exact diagnostics and tumour treatment. Drug delivery systems, and imaging, theragnostics can all benefit from stimuli-responsive nanoparticles. They have the ability to modulate release of drug, drug and device engagement, ligand availability, shape and size compliance, charge translation, and reactivity to specific biological molecules due to these features, resulting in increased site-targeted delivery.[69] Basic forms of stimuli-responsive NPs are reactive oxygen species (ROS)-responsive NPs. Self-assembly of MeO-PEGb-PMOT optimized an oral nanotherapy utilising a redox nanoparticle RNP(O) (Vong et al. 2015).[70] Nitroxide radicals, which operate as ROS scavengers, are at the heart of RNP(O). In mice, orally directed RNP(O) in conjunction with irinotecan increased therapeutic effects for CAC. Furthermore, RNP(O) given orally was successfully assimilated in cancer cells that were compared to normal cells, eliminating unwantwd adverse and cytotoxicity. For such therapy of CRC, various additional redox nanoparticles have indeed been produced. (Vong et al. 2017) created a silica-based redox nanoparticle (siRNP) capable of scavenging ROS.[71] BNS-22, a hydrophobic anticancer chemical, was also utilised as a new nanocarrier for the treatment of CRC.

Targeted naoparticles for CRC therapy: Incorporation of ligands like aptamers, antibodies, portions of antibodies, peptides, and some other mini molecules on the upper

layer of nanoparticles for cell signalling has resulted in a new type of cancer therapeutic nanoparticles with better in vivo accuracy (Fig. 6).

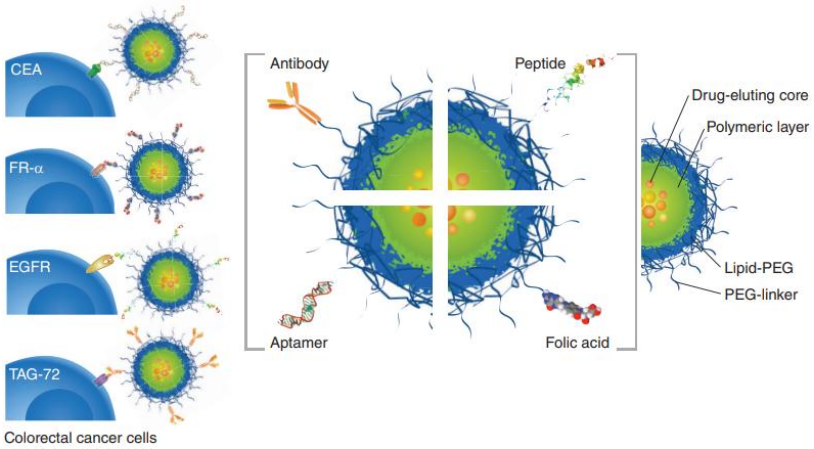


Fig. 6: The usual CRC biomarkers presented on the cellular membrane and the typical molecules/ligands utilised on the upper layer of nanoparticles in targeting approaches.[72,73]

The ingestion of these ligands is generally obtained through chemical functionalization during nanoparticle formation or chemical interaction involving ligands and polymers prior to synthesis.[72,73] Targeted nanoparticles are ones with ligands on coated surfaces and the ability to detect cells appropriately. Tumours have a small number of biomarkers that act as targets for the nanoparticles. Graf et al., for example, produced cisplatin prodrug-loaded poly (d, l-lactic-co-glycolic acid)-block-polyethylene glycol nanoparticles that adhere to the integrin receptor, which is driven largely in tumour-linked endothelial cells during angiogenesis.[74]

Nanoparticles in imaging and detection of CRC: Nanoparticles can also be utilised in the pre-diagnosis and monitoring in clinical effectiveness. Multiple different agents (e.g., radioactive, superparamagnetic), targeting groups, and biocompatible coatings[75] could be used in the synthesis of nanoparticles. Due to the constraints of low molecular-weight gadolinium and metal chelate-based dissimilarity agents, like relatively low selectivity, rapid clearance, and circulation which is not specific to the extracellular medium, nanotechnology is being used to enhance the high specificity of CRC diagnostics.[76] He et al. recently reported lectin core/shell nanoparticles made of iron oxide magnetite and gold (lectinFe2O3#Au NP), which may be used for double-modality imaging (T2-weighted MR and x-ray CT) in nude mice with CRC tumours (SW620).[77] Nanoparticles constituted with a core of superparamagnetic iron oxide nanocrystals, connected by quantum dots, and directed

with monoclonal antibody attached to CEA-linked cell-adhesion molecules[78] are yet additional approach that had excellent in-vivo potency by MRI, minimal cytotoxicity, and magnificent fluorescence constancy. A new technique that uses near-infrared fluorescence (NIRF) endoscopic detection improves the high specificity of colonoscopy in CRC patients. In research employing a mouse model of coli tis-linked cancer examined using NIRF endoscopy[79], high effectiveness was reported in the recognition of dysplastic foci with chronically swollen colons. In NIRF endoscopy for CRC cells, (Yang et al.) used folic acid-conjugated chitosan nanoparticles infused with 5-aminolaevulinic acid. In healthy cells, 5-aminolaevulinic acid is a predecessor in the formation of heme groups and quickly transformed to fluorophore protoporphyrin IX. So because breakdown metabolism in cancer cells is longer than in normal cells, protoporphyrin IX accumulates intracellularly, allowing it to be used in NIRF endoscopy and especially on CRC cells that contains the folate receptor.[80] Nanoparticles in imaging of colorectal cancer has shown promising results and aided in the early findings of CRC.

CONCLUSION

Although novel diagnostic and treatment approaches are being developed, the prevalence of CRC is rising as a result of changes in industrial society's lifestyle. Despite this, the cancer's poor survival rate may get worse as the disease becomes more common. Promising preliminary findings have come from new research that focuses on building functionalized NPs to provide more precise diagnostics and create tailored medicines. Nanoparticles are now being used in several clinical studies for CRC. But before they can be sold, the majority of these techniques still need to get through many clinical stages. It follows that more research is needed in the preclinical and clinical stages regarding toxicity, bioavailability, biocompatibility, side effects, and cost-effectiveness.

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