The significant role of biophysics in cancer prevention: An overview

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Abstract

Cancer is a dynamic, multifaceted illness caused by the abnormal growth of cells. The affected cells developed uncontrollably and destroyed various tissues. This deadly disease has become an important health issue worldwide. Current research on the biology and physics of cancer cells is a promising area with high concerns. It helps to improve the understanding of the cellular and molecular factors of cancer treatment. Studies on the biology of cancer cells have provided different types of knowledge on cancer initiation and spread of cancer cells. It also provided advanced treatment of cancer prevention. Learning the physics behind cancer cells provided comprehensive knowledge of cancer cell proliferation and the mechanical properties of tumor tissues. Understanding the biophysics of cancer cells helps to know the mutation of cell structure, dynamics, and interactions of proteins involved in signal transduction pathways. The unwanted growth of tumor cells can also be better understood by using biophysics. Integration of cancer biology and physics plays a critical role in determining the proper treatment of cancer. This review highlighted different advanced technologies and mathematical modeling used to prevent cancer cells. It also discusses about the biophysics of advanced nanotechnology and silicon nanoprobes used for cancer treatment.

Keywords: Metastatic carcinoma, Tumor biophysics, Growth factor, Biosensor, Nanomedicine.

1. Introduction

Cancer is a viral disease in current society. The uncontrolled growth of cells is detected as cancer cells. Within a very short period, cancer cells spread over the entire body. It is one of the deadliest diseases in the current generation. Numerous treatment methods have been discovered. A combination of biology and physics is known as biophysics. It plays an important role in cancer prevention methods. Different biosystems are complex, hierarchically self-organized structures with nonlinear interactions. External forces are required for biological processes. Microtubules and mitochondria help to transform energy in different biological processes in cells. Mitochondria help to distribute the proton change layer which causes a strong static electric field surrounding the cytosol. Popular scientist Warburg observed the partial inhibition of oxidative metabolism in tumors. He demonstrated the reduced activity of mitochondria [3]. This observation helps to improve cancer treatment. One can conclude that disturbances in oxidative metabolism play a significant role in the proliferation of cancer [1]. Understanding biological processes through modern communication is connected to the concept of complexity. Large complex systems with nonlinear structures are examples of biological systems. Generally, biological complex systems are open under nonequilibrium thermodynamic conditions. They can interact with their surroundings by exchanging information, mass, and energy. Different biological systems play a crucial role in controlling and steering brain activity in mammals. One of the important parts of the human body is the brain. It receives signals from the whole body and reacts to different functions [2]. However, information transmission analysis in biological systems has been done as a combination of entities. Cancer is an evolutionary process. Even though tumors spread rapidly, different fundamental functional organizing principles are found for the characterization of cancer cells. DNA instability, avoidance, and immunological reaction are examples of spreading cancer cells . Different ideas from continuous mechanics have offered comprehensive mathematical frameworks for classifying and explaining biomechanical processes and mechanisms. Over the past few years, there has been a significant increase in the study of the physics and mechanics of various biological complexes. Continuous progress in engineering, technology, and physical and informational science plays an important role in cancer prevention. There are different advanced biophysical tools are used to distinguish cancer cells from healthy cells. These tools have provided different data on the availability of cancer cells [3]. To study molecular species adhesion, they have enabled the creation of force vs displacement records of mechanical deformation for molecules and cells . The advancement of nanotechnology also helps to detect cancer cells. It may help to decrease the spread of cancer. Recent developments in computer hardware and software have facilitated the development of biomechanical models that can replicate deformation by accounting for a substantial population of relevant molecules in the cytoskeleton of particular cell types. These visualization tools and computational skills also address different problems that help to explain thoroughly and methodically the experiments [4]. Rapid increases in genetics and genomics have offered modern opportunities for updating in diagnostics and cancer therapies. Targeting particular genes has also led to new ways of understanding the cellular and molecular mechanisms which involved in the onset and progression of disease. **Fig.1** depicts the relationships between subcellular structure, cell biomechanics, motility, and disease status. According to World Health Organization (WHO) research, almost 7.6 million people died of cancer by 2005. As per these reports, the number of deaths from cancer will continue to increase globally. It reached almost 9 million by 2015 and may reach 11.4 million by 2030. Over the past few decades, significant progress has been achieved in cancer diagnosis and treatment technology. Advancements in cellular, molecular, genetic, and environmental sectors affect cancer diagnosis and treatment. Although total cancer death rates in the United States have not decreased over the previous five decades. 1.4 million Americans are diagnosed with cancer every year and 60,0000 of them passed away [5].

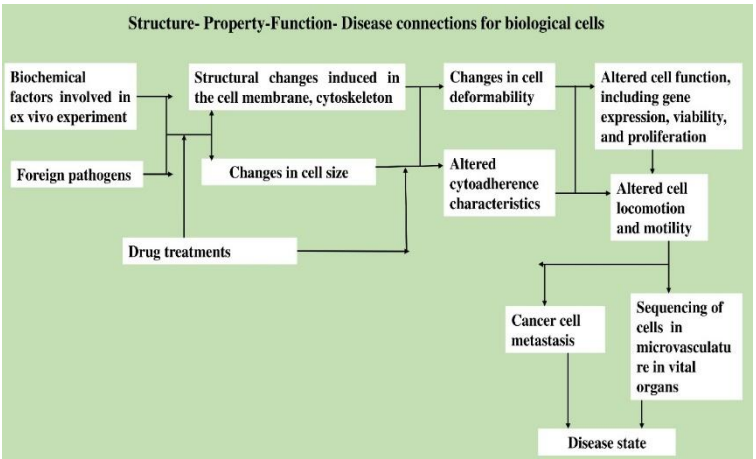

Fig.1 Schematic representation showing the relationships between subcellular structure, cell biomechanics, motility and disease status.

A rapidly growing area of scientific interest in biophysics has been found. This review article highlighted the current advancement in modern biophysics in cancer prevention methods. It helps to know modern techniques used to distinguish cancer cells from normal cells and the current research problems.

2. Objective and scope of this review

This review aims to outline the current state of biophysics in cancer treatment. Medical technology has advanced quickly, and cancer treatment has become very important with the increasing population. With advanced technology, the new generation is rapidly affected by cancer. It is very much needed to prevent this deadly disease with the help of current advanced medical science. This review is comprehensive and includes several important aspects. Firstly, this review will discuss the various advanced technologies used for cancer treatment. This provides a comprehensive explanation of the fundamental procedures used for cancer treatment, along with their drawbacks. To provide insight into the potential future direction of biophysics to help cancer treatment, Magnetic Resonance Imaging (MRI), Single Photon Emission Computed Tomography (SPECT), Positron Emission Tomography (PET) will be described properly. Secondly, this assessment will also discuss how advanced nanotechnology is used in cancer prevention. Silicon nanoparticles-based fluorescent probes and their different bioimaging methods are discussed here. How different advanced nanomedicine is helpful for cancer treatment, has been properly discussed in this paper. A clear and comprehensive knowledge of drugs (developed from nanoparticle) used for cancer therapy has been mentioned here. Finally, this review is concluded with a future aspect of the combination of biology and physics of cancer cells. Additionally, possible areas of research and required development have been proposed. It aims to be thorough and nuanced, covering both the present state of biophysics in cancer treatment and providing insights into the future.

3. Cancer disrupts biophysical processes

Scientist Warburg hypothesized that a reduction in the functional order of the cell occurs when the oxidative synthesis of ATP is partially suppressed and is replaced by fermentative (glycolytic) activities. All ensuring physical processes and biological activity that depend on mitochondria are disrupted by mitochondrial failure. In kidney and liver cells, oxidative energy generation can be 100 times higher than fermentative energy production in healthy cells. The mitochondria provide around half of the ATP that cancer cells create. One type of mitochondrial dysfunction is called glycolytic phenotype, which is caused by PDK (pyruvate dehydrogenase kinase) [6]. Numerous cancer types were shown to have mitochondrial dysfunction. We emphasize the different facts, such as a variety of information pathways and oncogenes leading to mitochondrial dysfunction, accompanied by resistance and elevated glycolysis in contrast to apoptosis. The inner membrane of the mitochondria in the majority of carcinomas is hyperpolarized and the majority of solid tumors absorb glucose more rapidly. This different characterization of mitochondria in cancer therapies could be very efficient [7]. Another crucial element in mitochondrial function is the inner membrane potential. Rhodamine 123, a fluorescent dye that is positively charged, is used to assess the potential effect. Hyperpolarization is the term used to describe large absorption and retention. The uptake and retention process may be caused by the distribution of ions like (Na^+, and K^+) within the cell, lactate generation, body water level, etc [7]. Different malignant tumor types like lung cancer, lymphomas, neuroblastomas, sarcomas, and some other cancers are caused by a lack of mitochondrial hyperpolarization. This could indicate a different glycolytic phenotype of mitochondrial defects and apoptosis blocking. An electrically neutral exchange of protons and potassium ions causes the membrane potential to increase and the pH gradient to decrease [7]. This could reduce proton transfer and cause mitochondrial dysfunction in cancer cells. On the other hand, malignant tissue reveals another divergence. The reverse Warburg effect occurs when fibroblasts connected to cancer cells with fully activated mitochondria develop mitochondrial malfunction [6]. Lactate, glutamine, and other energy-rich metabolites are transferred from the fibroblasts to cancer cells. The absence of hyperpolarization may be correlated with the state of increased mitochondrial energy production. Thus, two distinct cancer pathways can be distinguished by a fluorescent dye with their uptake and retention method.**Fig.2** depicts the mitochondrion procedure for cancer cell biology.

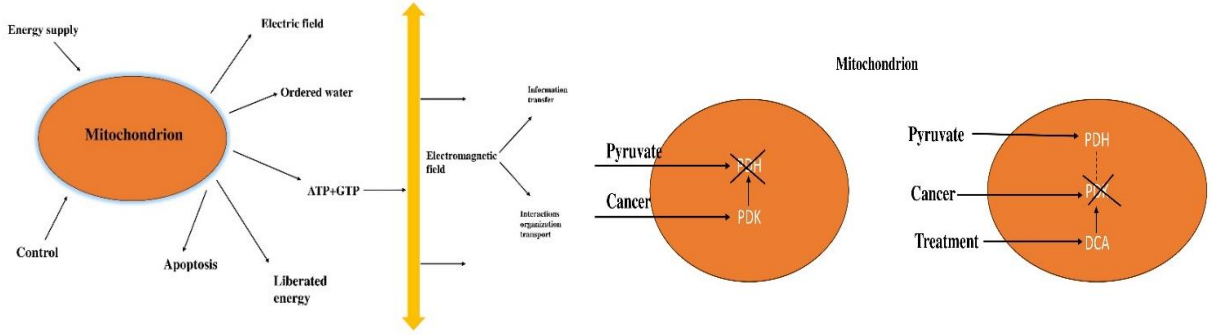

Fig.2 Mitochondrion procedure for cancer cell.

Table 1 shows a brief history of cancer cells. The essential parts of a cell's cytoskeleton are biopolymeric proteins. The extracellular matrix (ECM), which binds and clusters cells to form tissues, is made up of proteins produced in spaces between cells. Cell surface receptors known as integrins form focal adhesions, which are groups that act as binding sites between the extracellular matrix architecture and the cell surface [7,8]. By changing their mechanics of deformation, altered protein structures also affect cancer cell's capacity to stretch. Through a process known as signal transduction, those cells generate their signals for continued growth, multiplication and transfer them amongst proteins. They use a protein-based control circuit to modify their growth and division. The signals of this circuit are exchanged in two-way communication between ECM and the cell interior via the integrins and focal adhesions that bind the cell to it [8].

Table 1 enlisted a brief history of some keywords used in the biology of cancer cells.

Features	Observation
Categorization of cancers	Benign tumors are non-invasive. Malignant (invasive) tumors spread rapidly and attack the other cells.
Cell transformation	Normal cells with one layer come in contact with other cells is known as proliferation. Contact inhibition is not present in this cell.
Cell growth	A class of proteins known as Growth factors binds to particular growth factor receptors on the surface of cells, including receptor tyrosine kinase (RTK) to promote cell division and growth.
Metastasis	Metastasis is the term used to describe the spread of cancer cells from the location of abnormalities to other parts of the body. Apart from that this process includes the cancer cells' migration, penetration of tissue, colonization, and escape from the tumor mass.
Cancer cell survival	The activation of caspases causes normal cells to undergo apoptosis, which is called cell death. Cancer cells try to become immortal to form tumors. Enzymes cleave several cellular proteins during apoptosis, causing cells to break down. It increases the amounts of anti-apoptotic proteins and inactivates the p53 protein.
Signaling between ECM and the integrins	The Ras protein is the main component used in the signaling pathway which inhibits apoptosis. Cell receptors called integrins are physically attached to various components of the extracellular matrix (ECM). These receptors are focal adhesions, which are sites between the cell surface and the ECM.

4. Different imaging techniques of cancer prevention and radiation therapy

There are different bioimaging techniques are used to treat cancer cells. These imaging methods are important for cancer diagnosis and management. It may help medical experts to detect cancer cells and find the staging of cancer. With the help of these advanced techniques, oncologists can monitor the current condition of cancer patients. Magnetic resonance imaging (MRI), Positron emission tomography (PET), and Single photon emission computed tomography (SPECT) are mostly used visualizing methods.

4.1 Magnetic Resonance Imaging (MRI)

It is one of the non-invasive methods used to detect cancer cells. Nonionizing electromagnetic radiation is used in this method. With the help of radio frequency magnetic fields can get a picture of all cross-sectional areas of the body in every plane. MRI images are created by keeping the patient's body under a big magnet, generating a powerful magnetic field outside the object. During this process, many nuclei of atoms, including hydrogen, are placed in the human body [9]. When an RF signal is provided and these atoms come into contact with the magnetic field, energy is released from the body, measured, and the MR image of the organ is produced.

4.1.1 Basics Physics of MRI

The nucleus of an atom is typically made up of two particles (protons, and neutrons). Neutrons are neutral, while protons are positively charged. Electrons (negative charge) are present outer part of the nucleus. All particles have a particular motion in an atom. This motion is called spin. It comes in multiples of ½. During MRI, these spins are placed into the magnetic field with strength B, absorbing the photon with the frequency (ν). The frequency (ν) depends on the gyromagnetic ratio (ϒ) of the particle [9].

$$\nu = \Upsilon B, \quad (1)$$

$$\text{For hydrogen, } \Upsilon = 42.58 \text{ MHz / T} \quad (2)$$

For the MRI process, nuclei should have an unpaired proton or neutron, contain a net spinning charge, or have angular momentum. When the spin is connected to an electrical charge, nuclei with damaged nucleons produce a magnetic field. This causes them to function as magnets with North and South poles (magnetic dipoles) [9,10]. **Table 2** represents a brief overview of MRI history.

Table 2 An overview of MRI history

Year	Brief history of MRI
1857-1952	Larmor relationship was invented by Sir Joseph Larmor [10].
1930	The mechanical and magnetic moments of the nuclei were identified by Isidor Issac Rabi [10].
1946	MR phenomenon was founded by Bloch and Purcell [11].
1952	Bloch and Purcell were awarded with Nobel Prize [11]
1950,1960,1970	NMR was created as a tool for analysis [10]
1972	Computerized tomography [10]
1973	Back projection MRI [10]
1975	Fourier Imaging [10]
1977	Echo planer imaging [10]
1980	FT-MRI was demonstrated by Edelstein [10]
1986	Using an NMR microscope for gradient echo images [11]
1987	Angiography of MR Dumoulin [10]
1991	Ernst was awarded with Nobel Prize [11]
1992	Functional MRI [10]
1994	Imaging of Hyperpolarized 129Xe [10]
2003	Lauterbur and Mans Field were awarded the Nobel Prize [10]

MRI images offer different advantages. The radiofrequency pulses utilized in MRI do not cause ionization or the negative consequences of ionizing radiation. This method is non-invasive and can also be applied to children and pregnant women. The ability of an image process to differentiate between nearby soft tissues from one another. With the help of MRI images, oncologists can visualize direct, coronal, and oblique pictures of cancer cells. It helps to differentiate the acute and chronic transition of cancer cells [11]. However, it is difficult to purchase an MRI machine for every hospital management as it is very expensive. It requires a long scanning time. As a strong magnetic field is used in MRI images, sometimes it causes heart issues in patients. This advanced technique cannot distinguish between malignant and benign tumors. It could lead to a false positive result. **Fig.3** depicts the outline structure of magnetic resonance imaging.

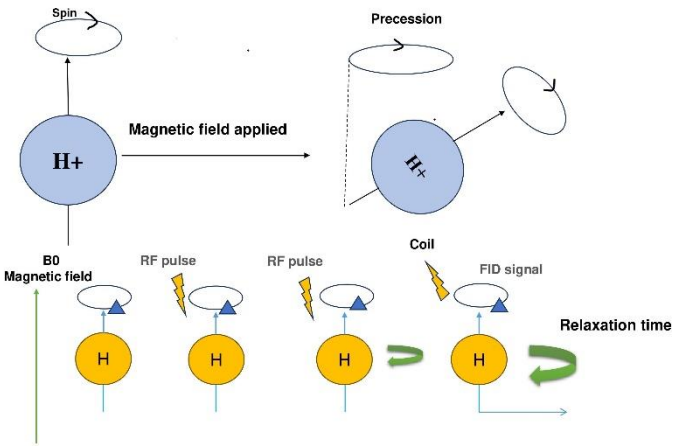

Fig.3 Basic physics behind magnetic resonance imaging.

4.2 Single Photon Emission Computed Tomography (SPECT)

Single photon emission computed tomography (SPECT) is a medical imaging method based on tomographic reconstruction techniques and standard nuclear medicine imaging. Different radiopharmaceuticals like SPECT and PET always emit ϒ ray photons. SPECT application is used for image reconstruction from numerous projections to produce the three-dimensional radioactivity distribution [12]. This method is different from the X-ray technique. The primary object of this approach is to accurately ascertain the three-dimensional radioactivity distribution, which is the outcome of different radiopharmaceutical absorption throughout the body. Instead of using PET, SPECT is used in various nuclear medicine clinics. It emits positrons of two annihilations at 511 kev, similar to PET. This method required new instrumentation and image reconstruction methods which differ from other medical imaging techniques. Increasing detection efficiency and enhancing the imaging system's spatial resolution are two main objectives of SPECT. These are achieved by placing additional detectors around the patient [12]. **Fig.4** depicts the basic components of a single photon imaging device used for SPECT imaging.

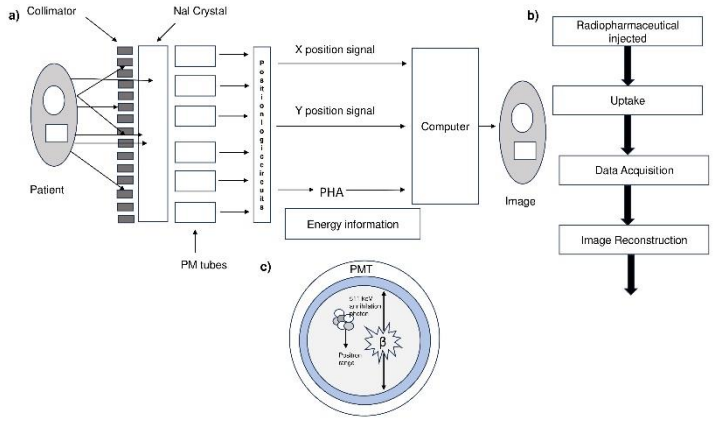

Fig.4 Basic components of SPECT.

4.3 Positron Emission Tomography (PET)

Positron emission tomography has become an essential tool in clinical oncology. The use of this instrument is increasing rapidly. It becomes very useful for working radiation oncologists to have a comprehensive study of molecular imaging about the updated condition of cancer cells. This advanced technique was developed at the end of the 20th century. With the help of the positron emission technique, different stages of cancer have been detected. PET is a rapidly growing technology that helps to find radiolabelled probes and their applications. New radiopharmaceuticals have been created that target different biological pathways including protein analysis, lipid metabolism, hypoxia, and more. Besides that, recently approved probes that target prostate-specific membrane antigens (PSMA) have been developed to target certain ligands, antigens, and receptors. These different probes helped to enhance precision medicine and treatment methods. Molecular imaging is the use of remote imaging detectors to observe, describe, and measure biological processes at the cellular and molecular level [13]. The PET/CT scan technique offers better sensitivity, specificity, and accuracy than traditional anatomic imaging. This can make it possible to image invisible lesions on CT or MRI scans. It also prevents unnecessary radiation of anatomic abnormalities that do not contain tumors [13]. PET/CT scan can reduce futile irradiation of atelectasis and edema. This method helps to find the primary tumors and lymph nodes involved in cancer. **Fig.5** depicts the basic physics of Positron Emission Tomography.

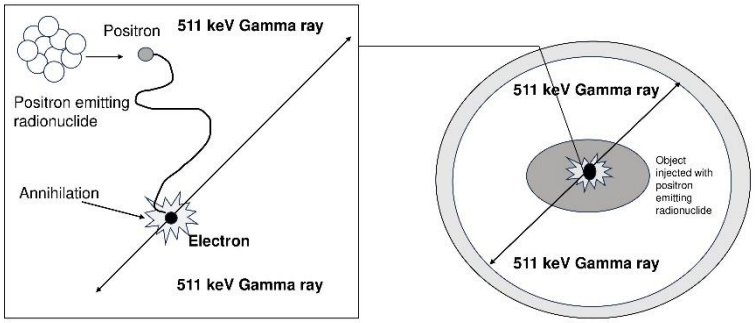

Fig.5 Basic physics of Positron Emission Tomography (PET).

5. Silicon-based Nanoparticles used as Fluorescent Probes for Bioimaging Applications (Si-NP)

One of the best non-invasive methods for a variety of biological and biomedical research is Fluorescent biological imaging. For fluorescent probes, labeling the targeted biomolecules and enhancing the fluorescence signals are important responsibilities. According to the researchers, a high-quality fluorescent probe should have outstanding fluorescence, good water dispersibility, robust photostability, and acceptable biocompatibility. Different fluorescent proteins and organic dyes are well-known as bio-probes. These have been used in various biological and biomedical studies throughout the past century. Their inadequate photobleaching properties make them inappropriate for both long-term and real-time bioimaging. Quantum dots (QDs) and fluorescent II exhibit superior photostability which has made them popular as prospective biological nanoprobes for a wide range of biological applications. However, the possible risks of QDs due to their heavy metal content are one of the causes of concern. Strong photostability, high fluorescence, and superior biocompatibility are in high demand in new biological probes [14].

The low toxicity of silicon (Si) makes fluorescent silicon nanoparticles an excellent biological probe. However, most surface ligands of silicon nanoparticles like octene, alkyl, and styrene are hydrophobic. These features of silicon nanoparticles cause poor water dispersion and also limit different bio applications [15]. Much research has been done to find different types of fluorescent water-dispersed SiNPs used as a bioimaging probe. They were also used for cellular imaging after being modified with hydrophilic molecules like acrylic acid, and allylamine [15]. **Fig.6** represents the different biological aspects of the silicon-based nanoparticle.

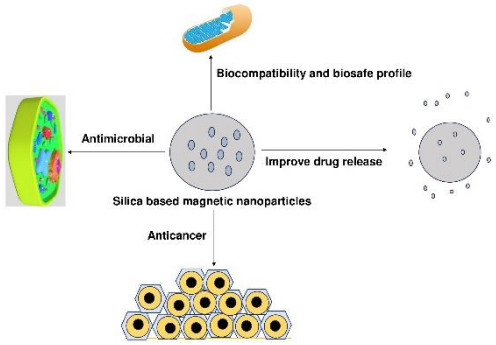

Fig.6 Different biological aspects of the silicon-based nanoparticle

Silicon nanoparticles encapsulated in phospholipid micelles with strong water dispersibility were used for in-vivo bioimaging applications. In 2009, scientists He, Lee, and associates developed a new class of water-dispersible, highly luminous, pH, and photostable SiNPs with surfaces covered with hydrophilic polymer-coated. They also demonstrated the first instance of silicon nanoparticle-based immunofluorescent cellular imaging after successfully conjugating the produced silicon nanoparticles with protein molecules [15,16]. These water-dispersible hydrophilic species are detrimental to bio applications because of their large sizes (>50 nm in hydrodynamic diameter (HD). In-vivo applications are used in Silicon nanoparticles with a hydrodynamic diameter of <10 nm [16]. In 2011, researchers created a novel microwave technique for the easy synthesis of water-dispersed silicon nanoparticles. It is used as reaction precursors in glutaric acid and silicon nanowires [16]. Silicon nanoparticles with small diameters (<5 nm) are used in ultra-high photo stabilizers. Especially, for the course of a 120-minute irradiation period, steady and brilliant fluorescence was seen for microtubes labeled with silicon nanoparticles. In contrast, the fluorescent signals of microtubes labeled with CdTe quantum dots or FITC rapidly went out after 25 minutes of observation. One can use proteins as hydrophilic ligands to create luminous, bio functional silicon nanoparticles based on the above factor [16]. These prepared silicon nanoparticles have outstanding water dispersibility and bio-specific qualities due to the abundance of hydrophilic protein molecules covering their surface [17]. Consequently, the produced silicon nanoparticles could mark cells with immunofluorescence without the need for complex protein conjugation.

To create silicon nanoparticle-based biological nanoprobes, most of the synthetic approaches frequently involved time-consuming modifications that required two separate processes. Specifically, the “top-down” approach transforms large-size silicon materials into hydrophobic silicon nanoparticles, which are subsequently surface-modified with hydrophilic ligands to create water-dispersed silicon nanoparticles [17]. A simple “bottom-up” approach is ideal for the large-scale production of water-dispersible silicon nanoparticles was recently

demonstrated. Furthermore, this process can generate a lot of fluorescent and water-dispersible silicon nanoparticles in a very short time (like 0.1 g of SiNPs/10 min) [18].

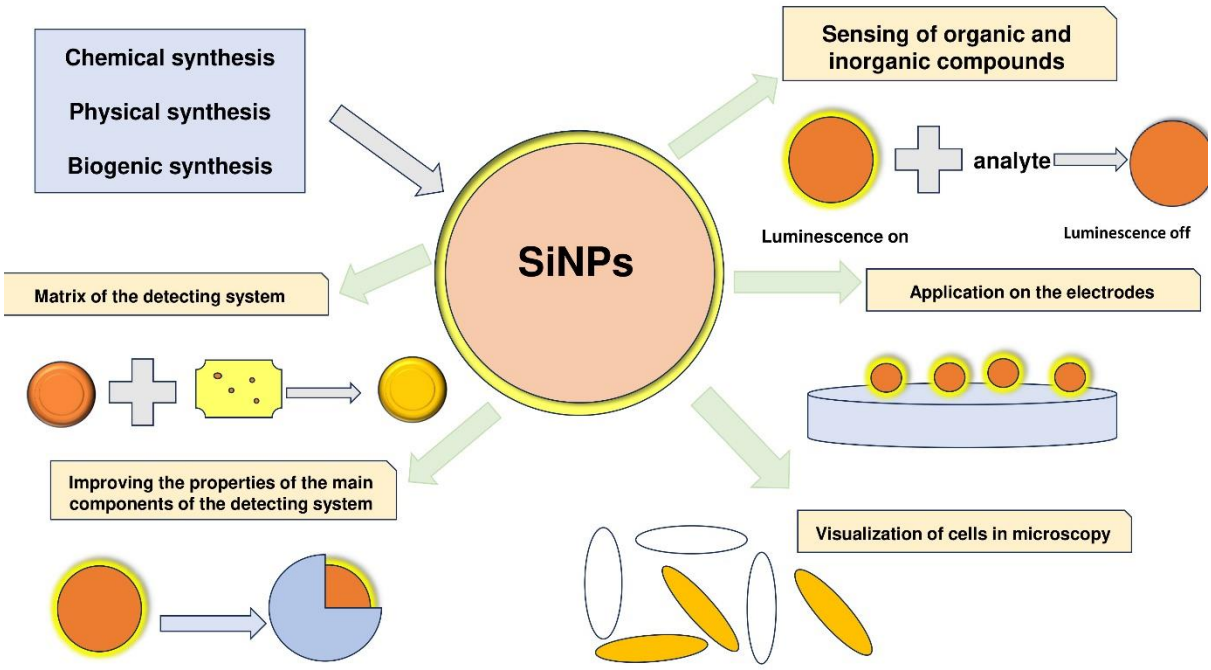

Fig.7 Different application of silicon-based nanoparticle in advanced science.

5.1 Silicon nanowires used for cancer treatment

Currently, different types of nanomaterials have been discovered to offer novel, efficient medications for the treatment of cancer. These are highly beneficial for improving the effectiveness of treatments and reducing harmful side effects. The near-infrared (NIR) spectrum is a low absorption of biological systems which makes nanomaterial-based nano agents highly promising for tumor photothermal treatment [18]. Different nanomaterials have been created as NIR hyperthermia nano agents for the treatment of cancer, including graphene, carbon nanotubes, gold nanorods, etc.

Different metal nanoparticles such as silver nano, gold nano, and quantum dot) help to decorate silicon nanowires (SiNWs). It helps to demonstrate unique electrical and optical features [17,18]. NIR light may be absorbed by SiNWs at 808 nm wavelength in the NIR range. Apart from that, gold nanoparticles had high efficiency in producing heat at the NIR region, which converted light to heat. According to a previous study, it was found that a SiNWs-based NIR hyperthermia nano agent made a gold nanoparticle complex [AuNPs@SiNWs complex]. This complex may produce high heat under the NIR region. This complex increases the temperature (Δ T) values Tisby 38.3^{O}C with 3 min [19]. This gold Nanoparticle complex treated KB cells with 3 min of NIR irradiation. A549 and Hela cells were fully destroyed by this complex within 3 min. For cancerous tumor cells, this silicon nanowire-based hyperthermia is highly effective and prevalent.

The threshold NIR laser power density of [AuNPs@SiNWs], which was used to irradiate cells was only 2W/cm^2, which is significant. According to a previous study, it was noted that employing the photo-thermal approach to treat cancer cells with gold nanoclusters (AuNC) coated with SiNWs [19]. As a result, AuNC-coated SiNWs, which are antibody-coated, can eliminate the surface of collected breast cancer cells within a short time (like 15s) under NIR irradiation at 808nm wavelength. There are interesting prospects for the simultaneous identification and treatment of circulating tumor cells with this innovative silicon nanowires-based technology [20].

In recent years, nanoparticles with high porosity and a large surface-to-volume ratio have also been used as drug nanocarriers. They have the capacity for drug nanocarriers for the treatment of cancer along with NIR hyperthermia nano agents [20]. Doxorubicin (DOX) is a conventional form of anticancer medication that has a

capacity of approximately 1200mg/g in nanocarriers based on mesoporous silica strictures. Single-walled carbon nanotubes (SWNTs) had a DOX loading capacity of 2350 or 4000mg/g [20]. Scientists demonstrated the first instance of drug nanocarriers based on silicon nanowires, which have an extremely high drug loading capacity of 20800 mg/g. It is noted that silicon nanowires (SiNWs) have remarkable tumor growth suppression effectiveness and are very useful for cancer treatment [20].

6. Nanomedicine used in cancer treatment

Advanced nanoscience plays an important role in cancer treatment. The rapid development in nanotechnology, which produces different nanomedicine products, has enormous potential to enhance cancer treatment. Different targeting techniques are used to treat cancer with the help of nanomedicine. The pharmacodynamic properties of these cutting-edge medications may increase the potency of anti-cancer medications that are currently on the market. Current advancements in nanotechnology are predicted to improve the drug delivery system. Consequently, anti-cancer medication effectiveness is increased while adverse effects are reduced. Nanocarriers are one of the widely used nanomedicines in cancer therapy. Nanoscale size, high surface volume ratio, and different advantageous physicochemical characteristics are some of the special features of nanocarriers [21]. They may change the pharmacokinetic and pharmacodynamic features of drugs and improve their therapeutic index. Nanocarriers can improve drug delivery systems by in-vivo methods. This technique prolongs the duration of blood circulation of a compound and enables controlled drug release. Nanocarriers allow different medicines to concentrate at the tumor site. They can change the drug distribution process. This process of biodistribution is called the enhanced permeability and retention effect (EPR) [21].

6.1 Therapeutic use of nanomedicine in cancer treatment

Various kinds of nanomedicine compounds like lipid-based nanocarriers, polymer-based nanocarriers, and inorganic particles have been used in the treatment of cancer. **Fig.8** depicts the types of nanomedicine used in cancer prevention.

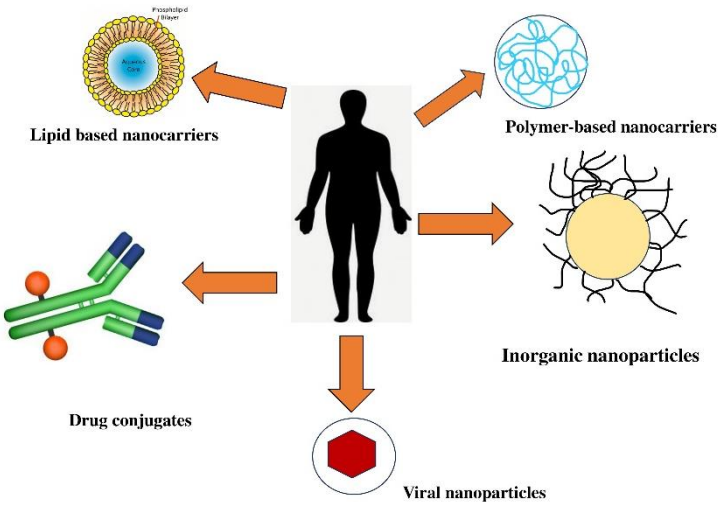

Fig.8 Different nanomedicine used in cancer therapy.

6.1.1 Applying viral nanoparticles to treat cancer

With the help of tumor-homing viruses different therapeutic proteins are designed which are used for the treatment of cancer. Certain strains of the Python viruses like myxoma or vaccinia are used to treat tumor cells. Another nanomedicine known as pox virus is also used as a cancer therapeutic. It has different features like immune evasion, dysregulation of cell reproduction, blockage of apoptotic pathways, etc. A pox virus called JX594 is made to multiply in tumor cells and kill them by turning on the EGFR-Ras-MaPK signaling pathway. Apart from that, JX594 may boost the immune system's anti-tumor response by expressing granulocyte colony-stimulating factor (G-CSF). Very few patients with metastatic liver cancer received intertumoral injections of this oncolytic virus, which led to three cases of partial remission and six cases of stable illness. The most common effects were flu-like and hyperbilirubinemia. There were twenty-three patients with advanced solid tumors received intravenous injections of JX594 [22]. The virus was able to accumulate in the tumor tissue and it was observed that JX594's dose-related anti-tumor efficacy. Noted tissue showed no signs of viral replication. The immediately neighboring epithelium took up the virus, but it did not replicate.

Patients were randomized to receive subcutaneous GM-CSF treatment and many injections of T-Vec. A GM-CSF expressing virus derived from the Herpes simplex virus (HSV) type-1, into non-visceral melanoma metastases. After doing this study, an endpoint was found. It is defined as partial or total remission for the last six months. Over 16.3% of patients who had the viral injection had a prolonged reaction [22]. It is noted that reactions were also seen in non-injected metastases. It is proved that the virus could potentially be active in tumor areas that were not injected. The most common grade ¾ toxicity, affecting 2.1% of trial participants was cellulitis. The first oncolytic virus authorized for use in cancer treatment may be T-Vec. In addition, several additional oncolytic viruses have been identified in recent years through clinical trials. However, nobody has yet attained the business value. Their main disadvantages are cytocompatibility and biosafety issues , which are found in different review papers.

6.1.2 Different organic nanocarriers for cancer therapy

There are different organic nanocarriers used for cancer treatment. Synthetic polymer-based carriers, lipid carriers, protein carriers, glycan carriers, and drug conjugates are some general categories for them. Although drug conjugates have successfully entered the cancer cells. There have been limited attempts to use lipid, protein, or polymer-based nanocarriers. **Table 3** shows the different names of the organic nanocarriers used in cancer therapy.

Table 3 Organic nanocarriers used in cancer treatment

Product	ADC	Target	Drug	Indication	Reference
Myloterg [Pfizer]	Gemtuzumb ozogamicin	CD33	Calicheamicin	Acute myeloid leukemia	[21]
Adcetris [Seattle Genetics]	Brentuximab vedotin	CD30	MMAE	Non Hodgkin lymphoma	[21]
Kadcyla [Roche]	Trastuzumab emtansine	HER2	DM1	Breast cancer	[21]

6.1.3 Glycan nanocarriers:

According to current research, there are no approved glycan nanocarrier treatments for cancer. For cancer patients with advanced solid tumors, cyclodextrin nanoparticles were used as nanomedicine. Compared to free Camptothecin, CRLX-101 showed fewer adverse effects and an almost 64% response rate. Based on cyclodextrin and PEG, another polymer nanoparticle (50-70nm) developed clinically for Si-RNA delivery is known as CALAA-01. It targets human transferrin receptors, which are overexpressed in cancer cells, to suppress the production of the M2 component of ribonucleotide reductase [23].

6.1.4 Inorganic nanoparticles for the treatment of cancer

Inorganic nanoparticles have numerous applications including medication, administration, radiation augmentation, tumor imaging, etc. Iron oxide nanoparticles are primarily used in diagnosis while some are being investigated in clinical trials for tumor magnetic resonance imaging. Nano Therm is an aqueous colloidal dispersion of iron oxide nanoparticles. When applied to the tumor, an alternating magnetic field application is used to perform thermal ablation (magnetic hyperthermia). Glioblastoma has the strongest data available [23]. Nano therm has received marketing approval in several European nations.

6.1.5 Synthetic polymer-based nanocarriers used in cancer treatment

For therapeutic applications in nanomedicine, Synthetic polymer-based nanocarriers have great potential. **Table 4** represents all synthetic polymer-based nanocarriers. PEG-PGA is one of the polymer-based nanocarriers used in cancer therapy.NC-6004 helps to treat nausea, neurotoxicity, and other cancer-related diseases. Advanced clinical trials are being conducted to examine several additional polymeric micelles, including NK-102, and NK-105 [23].

Table 4 Polymer-based nanocarriers used in cancer treatment

Product	Polymer	Drug	Indication	Reference
AB-008 [Abraxis]	Albumin nanoparticle	Docetaxel	Prostate cancer, Breast cancer	[21]
ABI-009[Celgene]	Albumin nanoparticle	Rapamycin	Bladder cancer	[22]

Lipotecan [TLC3888]	Polymeric micelle	TLC388 (Camptothecin derivate)	Liver cancer, renal cancer	[23]
Paclical[Oasmia Pharmaceutical]	Polymeric micelle	Paclitaxel	Ovarian cancer	[23]

6.1.6 Drug conjugates used in cancer treatment

In current days, the most effective and useful nanomedicine used in cancer treatments is drug conjugates. They can easily conjugate as a medicinal component and reduce nanometer-sized particles which are classified as nanotherapeutics. Targeted peptides, antibodies, and polymers are covalently bound to active ingredients. Mono or Oligomeric conjugation helps to enhance the distribution of targeted drugs without affecting the solubility, stability, and biodegradability of different used drugs [23]. In addition, drug-encapsulating nanocarriers made of synthetic polymers, lipids, proteins, and glycan form covalent bonds with the drug and the carrier. ADCs such as trastuzumab-emtansine against (HER2) overexpressing breast cancer and brentuximab-vedotin against (CD30) positive breast cancer have been approved by regulatory agencies. Anaplastic large-cell lymphoma and Hodgkin lymphoma Trastuzumab has been used as medicine for cancer treatment. They conjugate to the plant-derived microtubule inhibitor emtansine (DM1) and show their anti-tumor action[24]. Additionally, it improves the survival rate of patients with metastatic breast cancer following prior therapy. Using this medicine the rate of mortality decreases compared to the medicines lapatinib and capecitabine. **Table 5** represents different drugs used for various cancer therapies.

Table 5 Different drugs used for cancer therapy

Product	**Polymer**	**Drug**	**Indication**	**Reference**
DE-310 [Daiichi Pharmaceutical]	Carboxymethyl dextran drug conjugate	T-2513	Solid tumors	[24]
DOX-OXD (AD-70)	Dextran drug conjugate	Doxorubicin	Solid tumors	[25]
MTX-HSA	HSA drug conjugate	Methotrexate	Kidney cancer	[24]
ProLinDac (AP5346)	HPMA drug conjugate	DACH- oxaliplatin	Ovarian cancer	[24]
XMT-1001	Fleximer drug conjugate	Camptothecin	Gastric cancer	[25]
PK1(FCE28068)	HPMA drug conjugate	Doxorubicin	Breast Cancer, Lung cancer	[25]

7. Conclusion

Before studying the basic principle of cancer cells, the fight against cancer can only advance inches at a time rather than miles. As per basic science, it is said that first understand the problem and then try to solve it. Thus, it is very important first to distinguish cancer cells from normal ones and then treat them properly. We can better comprehend how biological and physical phenomena are applied to treat this deadly disease in a better way. Better treatment and preventive methods can be implemented after a better understanding of the illness. A greater comprehension of this understanding has led to a change from conventional methods to more individualized and focused methods to treat cancer. An adequate amount of cancer studies have revealed the genetic origin of cancers. It is high time that cancer cell biology and physics jointly help to treat and reduce the unwanted growth of cells in the human body. Tos combining knowledge provides proper prevention methods to reduce the rate of cancer patients. Significant developments in cancer diagnosis and therapy using biophysics concepts will result in the delivery of anticancer drugs to their proper target cells. Understanding the proper justification behind the development of cancer medicines has been demonstrated by the cellular mechanisms of cancer cells. Many

affected patients have found better results after getting knowledge about this advancement. They are effective by getting an appropriate therapeutic approach. Finally, it is very much needful to develop a connection between physical and biological cell functions in human health and cell mechanics is an innovative and significant advancement for cancer diagnostics.

8. Future Outlook

The combination of biology and physics of cancer cells helped people to get a proper diagnosis. But, the cellular mechanisms of the cancer cells have not been fully explored. Tumor-Associated Macrophage, Treg cells, and Myeloid-Derived Suppressor cells are three cells that have been identified as immune system traitors. They can aid tumor cells in escaping the immune system. These three cells could be the focus of a biophysical study in tumor immunity. The immune cells would greatly benefit if these cells could be persuaded to surrender. It would be highly beneficial for tumor immunotherapy if biophysics and molecular biology become closer and cross-checked. Some limitations in biophysics can be solved by these combining processes. One of them is the exploration of biological information in living tissues and cells with basic principles of biophysics that need to be solved. The development of instruments can solve this problem.

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10. Conflict of Interest

No conflicts of interest have been declared.

Reference

1. B.Emon, J.Bauer, Y.Jain, B.Jung, & T.Saif, Biophysics of tumor microenvironment and cancer metastasis-a mini review. Computational and structural biotechnology journal **16**, 279-287 (2018).
2. O.Warburg, On the origin of cancer cells. *Science* **123(3191)**, 309-314, (1956).
3. J.Kwapień, & S.Drożdż, Physical approach to complex systems. Physics Reports **515(3-4)**, 115-226,(2012).
4. G. Nicolis and I. Prigogine, Self-Organization in Nonequilibrium Systems, John Willey & Sons, New York, NY, USA, 1977.
5. A.Jamal , T.Murray , E.Ward , A.Samuels ,R.C. Tiwari , A.Ghafoor, Cancer statistics. CA: Cancer J Clin. **55**,10–30,(2005).
6. P.Hogeweg,The roots of bioinformatics in theoretical biology. PLoS computational biology *7***(3)**, e1002021,(2011).
7. J. S Carew, P. Huang, Mitochondrial defects in cancer. Molecular cancer, **1**, 1-12. (2002).
8. G.Bonuccelli, D.Whitaker-Menezes, R. Castello-Cros, S. Pavlides, R. G.Pestell, A.Fatatis, M. P. Lisanti, The reverse Warburg effect: glycolysis inhibitors prevent the tumor-promoting effects of caveolin-1 deficient cancer associated fibroblasts.Cell cycle, **9(10)**, 1960-1971,(2010).
9. G. D. Fullerton, Basic concepts for nuclear magnetic resonance imaging. Magnetic resonance imaging, **1(1),** 39-53(1982).
10. T.Geva,Magnetic resonance imaging: historical perspective. Journal of cardiovascular magnetic resonance, **8(4)**, 573-580,(2006).
11. C.Andrews,A.Simmons,&S.Williams,Magnetic resonance imaging and spectroscopy. Physics Education, **31(2)**, 80, (1996).
12. H. T.Edzes, D.Van Dusschoten, & H. Van As,Quantitative T2 imaging of plant tissues by means of multi-echo MRI microscopy. Magnetic Resonance Imaging, **16(2)**, 185-196,(1998).
13. D. A. Mankoff,A definition of molecular imaging. The Journal of Nuclear Medicine, **48(6)**, 18N(2007).
14. S.Song, Y. Qin, Y. He, Q.Huang,C. Fan, & H. Y. Chen,Functional nanoprobes for ultrasensitive detection of biomolecules. Chemical Society Reviews, **39(11)**, 4234-4243,(2010).
15. J. H.Park, L.Gu, G.Von Maltzahn, E. Ruoslahti, S. N.Bhatia, & M. J. Sailor, Biodegradable luminescent porous silicon nanoparticles for in vivo applications.Nature materials, **8(4)**, 331-336 ,(2009).

16. Z.Li, , & P. S. Conti, Radiopharmaceutical chemistry for positron emission tomography.Advanced drug delivery reviews, **62(11)**, 1031-1051.(2010).
17. Z. F.Li, & E. Ruckenstein, Water-soluble poly (acrylic acid) grafted luminescent silicon nanoparticles and their use as fluorescent biological staining labels.Nano Letters, **4(8)**, 1463-1467,(2004).
18. F.Erogbogbo, K. T.Yong, I.Roy, R.Hu, W. C.Law, W.Zhao, & P. N. Prasad, In vivo targeted cancer imaging, sentinel lymph node mapping and multi-channel imaging with biocompatible silicon nanocrystalsACS nano, **5(1)**, 413-423,(2011).
19. Y.He, Y.Zhong, F.Peng, X.Wei, Y. Su, Y.Lu, & S. T. Lee, One-pot microwave synthesis of water-dispersible, ultraphoto-and pH-stable, and highly fluorescent silicon quantum dots.Journal of the American Chemical Society, **133(36)**, 14192-14195 ,(2011).
20. A.Shiohara, S.Hanada, S. Prabakar, K.Fujioka, T. H.Lim, K. Yamamoto, & R. D. Tilley, Chemical reactions on surface molecules attached to silicon quantum dots.Journal of the American Chemical Society, **132(1)**, 248-253,(2010).
21. S.Su, X.Wei, Y.Zhong, Y.Guo, Y.Su, Q.Huang, & Y. He, Silicon nanowire-based molecular beacons for high-sensitivity and sequence-specific DNA multiplexed analysis .ACS nano, **6(3)**, 2582-2590,(2012).
22. Z.Liu, X.Sun, N.Nakayama-Ratchford, & H. Dai, Supramolecular chemistry on water-soluble carbon nanotubes for drug loading and delivery.ACS nano, **1(1)**, 50-56,(2007).
23. J.A. Flygare, T.H. Pillow, P. Aristoff, Antibody-drug conjugates for the treatment of cancer, Chem. Biol. Drug Des. **81,** 113–121,(2013).
24. L. W.Seymour, D. R. Ferry, D. J. Kerr, D.Rea, M.Whitlock, R.Poyner, & J. Cassidy, Phase II studies of polymer-doxorubicin (PK1, FCE28068) in the treatment of breast, lung and colorectal cancer. International journal of oncology, **34(6)**, 1629-1636 ,(2009).
25. A. Patnaik, K.P. Papadopoulos, A.W. Tolcher, M. Beeram, S. Urien, L.J. Schaaf, Phase I dose-escalation study of EZN-2208 (PEG-SN38), a novel conjugate of poly (ethylene) glycol and SN38, administered weekly in patients with advanced cancerCancer Chemother. Pharmacol. **71**, 1499–1506 ,(2013).