Advances in Science, Technology and Innovation

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Edited by

Priyanka Sharma and Sudipta K. Mishra

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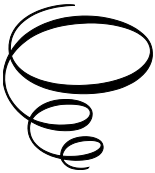

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PREFACE

In the ever-evolving landscape of human knowledge and progress, science, technology, and innovation stand at the forefront, serving as the engines driving humanity toward new frontiers. This book, "Advances in Science, Technology, and Innovation," encapsulates insights, breakthroughs, and discoveries that reflect the remarkable strides made by dedicated individuals and collaborative efforts across diverse disciplines.

As we navigate through the complexities of the 21st century, the significance of advancements in science and technology cannot be overstated. These developments shape how we perceive and interact with the world and have profound implications for the future of our society. This compilation serves as a testament to the collective ingenuity, perseverance, and curiosity that fuels the engine of progress.

The chapters in this book span a spectrum of scientific domains from cutting-edge technological innovations to profound scientific discoveries. They reflect the collaborative spirit that characterizes the global scientific community, in which researchers, scholars, and innovators are an integral part. Your broader expertise helps shed light on the frontiers of knowledge and unveils the potential for future advancement.

This book is a journey into the depths of human intellect, where curiosity and the pursuit of understanding lead to transformative breakthroughs. It commemorates the tireless endeavours of those who venture into the unknown, challenge the status quo, and expand the boundaries of what is possible, inspiring us all with the potential for profound change.

As we delve into the following pages, let us embark on a journey of discovery, marvelling at extraordinary achievements, and eagerly anticipating possibilities. Advances in Science, Technology, and Innovation call us to explore the ever-expanding horizons of human capability and remind us that the pursuit of knowledge is an eternal quest that shapes our world and propels us into a future of endless possibilities, a future that you, as part of this global scientific community, are actively shaping.

This compilation inspired, informed, and ignited the spark of curiosity within each reader, fostering a deeper appreciation of the incredible advancements that continue to define our shared human journey.

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Dr. Priyanka Sharma is an associate professor at the School of Engineering and Sciences, GD Goenka University. She has obtained a B.Sc. and M.Sc. degree in Chemistry from Mohan Lal Sukhadia University, Udaipur, a P.G. Diploma in Environmental Studies from the University of Rajasthan, Jaipur, and a Ph.D. in Synthetic Organic Chemistry from the same university. During her Ph.D., she worked on the synthesis and antimicrobial activity of bicyclic and tetracyclic benzothiazepine heterocycles, as well as their QSAR studies.

She completed a DST-SERB-sponsored research project and guided the students toward their doctoral degrees. She has published several research papers in reputed national and international journals and has presented them at prestigious national and international conferences. She also participated in several training programmes and workshops. Her research interests include Synthetic Organic Chemistry, Medicinal Chemistry, QSAR, and Environmental Chemistry.

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CHAPTER 1

UNDERSTANDING CANCER BIOLOGY FOR A BETTER DIAGNOSIS, INTERVENTION, AND PROGNOSIS

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Abstract

Cancer remains an elusive disease. Some of the earliest literature on the subject in the history of medicine dates back to 2500 BC in Egyptian medical practice.

The complex nature of disease development, which encompasses factors such as genetics, dietary habits, viruses, bacteria, mutations, and radiation, makes it challenging to diagnose at an early, benign stage. Difficulty in early diagnosis of cancer gives the disease a chance to progress and become malignant, which sets it on a path that is difficult to restore with the aid of medicine, surgery, or radiation, with little success.

Understanding cancer biology enables us to comprehend the disease in detail, thereby paving the way for determining the most effective treatment interventions. This chapter is a modest attempt to summarize the biology, progression, and management of cancer.

Introduction

Cancer is a general term for many diseases in which normal cells divide uncontrollably and invade or spread to other parts of the body. Normal cells follow the cell cycle and undergo division for growth and multiplication. If

these cells become older, damaged, and mutate, they die through a process known as apoptosis (programmed cell death), and new cells take their place (Meza-Junco, 2006). Sometimes, normal cells are damaged or mutated due to radiation, infectious agents, accumulation of genetic errors, carcinogens, environmental factors, and transformation into tumor cells. These abnormal cells multiply and form tissue lumps that can spread or invade other organs. Malignant tumors are referred to as benign tumors if they do not spread or invade other organs (Krieghoff-Henning, 2017); typically, the term "cancer" is used to describe malignant tumors.

Cancer has a multifactorial origin. Different types of cancers are observed and classified according to their location in the body. Cancer is divided into five main groups.

- **Sarcoma:** Cancer begins in the supportive or connective tissue, including blood vessels, muscles, fat, cartilage, and bone.
- **Brain and Spinal Cord Cancer:** cancer begins in the central nervous system (CNS).
- **Leukemia** cancer begins in the bone marrow, white blood cells, and the blood.
- **Carcinoma: Cancer originates in the cells that comprise the tissue lining organs; it has various** subtypes, including squamous cell carcinoma, transitional cell carcinoma, adenocarcinoma, and basal cell carcinoma.
- **Lymphoma and myeloma cancer begin** in immune system cells and affect lymphocytes and lymph nodes.

Properties of Cancer

Cancer cells exhibit characteristic features that differ from those of healthy cells. Table 1 summarizes the properties of the standard, malignant, and benign cells. Some of the properties of cancer cells are as follows:

1. **Contact inhibition:** A normal cell has a reduced rate of proliferation or division when it meets another cell. This cell growth mechanism is known as contact inhibition. Under in vitro conditions, the cells divided until they formed a monolayer, a single layer of cells. The state where the number of cells and cell death becomes constant is known as confluence. Cancer cells continue to divide even after reaching a state of confluence, forming an unorganized multilayer mass of cells (Hanahan & Weinberg, 2000).

2. **Immortalization:** A normal cell divides and grows for a specific number of generations, which is still unknown. In contrast, cancerous cells are immortal, meaning they continuously divide and grow (Hahn 1 & PMID, 2002).
3. **Density-dependent inhibition:** This is a condition in which a cell grows until it reaches a finite density, which can be observed in in vitro conditions. However, cancer cells are insensitive to density-dependent inhibition.
4. **Invasiveness:** Cancer cells invade neighboring tissues.
5. **Metastasis –** Cancer cells can invade lymphatic and blood vessels.
6. **Angiogenesis –** Cancer cells can form new blood vessels (Hahn & Weinberg, 2002).
7. **Loss of anchor–dependent growth: Normal cells attach to a surface and grow, a process** known as anchor-dependent growth. Cancer cells lack this property owing to the presence of more growth receptors.
8. **Lower growth factor:** Tumor or cancer cells can produce growth factors that bind to and stimulate receptors on the same tumor.
9. **Failure to undergo apoptosis—**Cancer cells often fail to undergo apoptosis, or programmed cell death, allowing them to live longer than normal cells. This process results in a continuous self-generated proliferative signal known as autocrine stimulation.

Table 1: Differences between normal, malignant, and benign cells

Properties	**Normal Cell**	**Malignant Cells**	**Benign Cells**
Cell type	Normal	Cancerous	Non-cancerous
Nuclei size and shape	Small and uniform	Large, variable, and abnormal	Normal but variable
Cell size and shape	Uniform	Variable size and shape	Average in size but variable in shape
Cytoplasmic volume	Large cytoplasmic volume	Small cytoplasmic volume	
Cell surface markers	Normal	Elevated	Relatively less elevated than malignant

Cell growth	Normal	Abnormal and can invade or destroy neighboring cells	Abnormal and does not invade neighboring cells
Growth rate	Normal	Relatively faster growth rate	Relatively slower growth rate than malignant

Molecular Basis of Cancer

Epigenetic and genetic changes are two types of molecular alterations that modify gene function and activation. Cancer-critical genes contribute to cancer progression after genetic and epigenetic modifications. These cancer-critical genes are categorized into two types: proto-oncogenes, which cause cancer through gain-of-function mutations, and tumor suppressor genes, which cause cancer through loss-of-function mutations. The accumulation of genetic damage, in the form of an inactivated tumor-suppressor gene and an activated proto-oncogene, is the primary driving force behind the transformation of normal cells into malignant cells.

Proto-oncogenes

Proto-oncogenes are normal genes that regulate normal cell differentiation, unlike growth. More than 40 types of proto-oncogenes have been identified in humans. Table 2 lists some proto-oncogenes, their products, functions, and associated mutations. Proto-oncogenes encode proteins involved in cell division, cell growth, transcription, and signal transduction. The proto-oncogene is converted into an oncogene through the accumulation of genetic and epigenetic mutations. Mutations in proto-oncogenes were dominant. That is, a mean gain of function in a single copy of a proto-oncogene can transform a normal cell into a cancerous cell (cells express a high number of MHC molecules on their surface as function mutations, leading to overexpression of the transcription factor, Growth factor, and a growth factor receptor that causes the uncontrolled multiplication of cells, ultimately leading to tumor formation (Torry, 1991).

Table 2: Some proto-oncogenes, their products, functions, and associated mutations.

Proto-Oncogene	Product	Function	Mutation
ABL	Tyrosine kinase	Non-receptor tyrosine kinase activity	Translocation t(9:22)
MYC	Transcription factor	Nuclear transcription	Translocation t(8:14)
RAS	GTPase	Signal transduction	Point mutation
SIS	Platelets drive growth factor	Regulates growth pathways	Overexpression
HER	Growth factor receptor	Regulate intracellular pathways	Amplification

Three main types of mutations can transform a proto-oncogene into an oncogene: point mutations, gene amplification, and chromosomal translocation.

Point mutation

Point mutations alter one or more nucleotides in a gene sequence, which can alter the protein product and its expression. Occasionally, it changes the amino acid sequence of standard proteins and interrupts gene function. This alteration may include insertion of a base, substitution of a base, or deletion of a base from a typical protein sequence. RAS is a guanosine triphosphate signal transducer, a point mutation in the RAS gene at codons 12, 13, or 61 that causes leukemia and lung, colon, and pancreatic carcinomas (Rusch, 1992).

Gene amplification

Amplification and duplication lead to protein overexpression, where more than one copy of a specific DNA sequence is formed, resulting in the overexpression of this gene. The N-MYC proto-oncogene is overexpressed owing to its amplification and ultimately causes neuroblastoma (Tuthill, 2003). Another example is the HER gene. Its normal function is receptor synthesis, but its amplification causes receptor overexpression, which is associated with breast carcinoma.

Chromosomal Translocation

Recombination occurs through the exchange of DNA segments between non-homologous chromosomes and is called translocation. Translocation triggers the overexpression of genes that lead to tumor formation. The best example of a translocation is BCR-ABL. ABL is a proto-oncogene that encodes a tyrosine kinase. The activated ABL gene stimulates cell proliferation, differentiation, survival, and death, as well as retraction and migration. The translocation is unbalanced and occurs between chromosomes 9 and 22. The ABL locus translocate from the nine chromosomes to chromosome 22 at the breakpoint cluster region (BCR) and forms a chimeric chromosome. The length of chromosome 22, also known as the Philadelphia chromosome, is shortened after a translocation (Vineet, 2020). If translocation occurs between chromosomes 9 and 22, but in a balanced manner, also known as the Philadelphia chromosome (Ph1), it causes chronic myelogenous leukemia.

Another essential translocation, Burkitt lymphoma, occurs between chromosome 8 (8q24) and chromosome 14 (14q32). MYC (c-myc) is present on chromosome 8 and encodes transcription factors. The MYC locus translocate to chromosome 14, close to the Ig heavy-chain gene. The Ig gene enhancer overexpresses the translocated MYC gene, and this continuous overexpression of transcription factors leads to uncontrolled cell proliferation and the development of cancer (Gregory, 2005). MYC gene expression is also elevated when the Avian Leukosis virus integrates its genetic material between exons 1 and 2 of the MYC gene. The avian Leukosis virus is a retrovirus with no oncogene in its genetic material. This insertion transforms normal B-cells into lymphomas.

Tumor-suppressor gene

Loss of function of tumor suppressor genes causes cancer. These genes were divided into two main categories: gatekeepers and caretakers. Table 3 lists some tumor suppressor genes and their products, functions, and mutations. Gatekeeper genes are tissue-specific; they directly suppress cell proliferation and must be inactivated before the cell becomes cancerous. The caretaker gene provides stability by preventing the accumulation of mutations.

Table 3: List of some tumor suppressor genes with their product, function, and mutation

Tumor Suppressor Gene	Product	Function	Mutation
P^{53}	Nuclear phosphoprotein	Transcription factor	Inactivation
RB1	protein	Cellecyclee check point	Inactivation
BRCA1e and BRCA2	protein	DNA repair and Transcription factor	Inactivation

p53 is the most critical tumor suppressor gene and is also known as the guardian of the genome. It is located on chromosome 17 at 17p13.1. It was composed of four identical subunits. A missense mutation in the central DNA-binding domain (DBD) of the P53 gene is involved in cancer development. DNA is involved in DNA repair systems when a cell has damaged DNA. During the cell cycle, if any DNA damage occurs, the cells are arrested in the G1 phase and undergo apoptosis. By eliminating these mutated cells, genomic stability was maintained. Under normal conditions, mdm2 inactivates P53 by forming a complex with it; if any damage occurs in the cell, mdm2 is removed, and P53 becomes active. After activation, DNA repair starts if possible; otherwise, it triggers apoptosis of damaged cells (Steele, 1998). It has also been noticed that P53 regulates cell metabolism and responses to oxidative stress.

The RB gene encodes the retinoblastoma protein, another tumor suppressor gene located on chromosome 13. In normal cells, Rb binds to E2F, a transcription factor, and inhibits transcription until the cell is ready for division. Once the cell is ready to grow, Rb is phosphorylated and E2F is accessible for transcription. In cancerous conditions, the Rb gene fails to bind to E2F, resulting in continuous transcription that leads to uncontrolled cell growth and, ultimately, cancer.

BRCA1 and BRCA2 are genes associated with an increased risk of breast cancer. BRCA1 is located on chromosome 17, and BRCA2 is located on chromosome 13. These genes are involved in transcriptional regulation, DNA repair, and the regulation of the cell cycle. Mutations in this gene are associated with hereditary ovarian and breast cancers (Mansoureh, 2016). Point mutations are involved in BRCA mutations. Under normal conditions,

the BRCA gene encodes ATM and CHK2 proteins, which are involved in DNA repair. However, in cancerous conditions, ATM and CHK2 do not repair DNA; instead, they continuously transcribe mutated proteins, leading to uncontrolled expression and growth, and ultimately, cancer.

Carcinogens

Carcinogens are agents that promote cancer development. These agents can be physical, chemical, or biological.

Physical carcinogens: Physical carcinogens are solid particles that are insoluble in water. These include UV exposure, ionizing radiation, and metal particles such as nickel and copper.

Chemical carcinogens are chemicals that have toxic effects and can cause immediate death or become carcinogenic, such as aflatoxin (Smela ME, 2002), asbestos, pesticides, ethylene dibromide, and dioxin.

Biological carcinogens—biological agents that cause cancer — are known as such, including viruses (such as EBV), bacteria (like Helicobacter pylori), fungi (like Aspergillus flavus), and parasites (like *Schistosoma*).

Tumor Markers

Biomarkers are measurable substances that indicate biological conditions such as infections and diseases. Some biomarkers are synthesized in excess concentrations in various types of cancer or neoplastic cells. Table 4 lists tumor markers and their associated cancer types. Biomarkers specific to cancerous cells are known to be tumor markers. Based on their chemical nature, tumor markers can include carbohydrates, conjugated proteins, and peptides. Tumor markers used for:

- Diagnosis of specific types of tumors
- Monitoring of cancer survivors after treatment
- Screening of common cancers on a population basis
- Determine the stage of the tumor
- Verification of the effect of treatment

Some markers are tumor-specific, whereas others are present in more than one type of tumor.

Table 4: Tumor markers and their associated cancer

Tumor marker	Tumor type
CA15-3, CA27.29, CA-125, NSE	Associated with breast cancer (Luftner, 2000)
Alpha-fetoprotein (AFP), hCG	Associated with Germ cell tumor and hepatocellular carcinoma
CA19-9, CA-125, CEA	Associated with gastrointestinal tumors
CA-125, CEA, GCDFP-15, hPG80, tumor M2-PK	Associated with ovarian cancer
Vimentin, tumor M2-PK, TTf-1, thymidine kinase, neurofilament	Associated with lung cancer (Schneider, 2003)
Chromosome 3,7,17 and 9p21	Associated with bladder cancer

Tumor Immunology

Cancerous cells attempt to evade immune cells, while immune cells strive to eliminate cancerous cells. Immune cells detect molecules that are considered non-self. When normal cells transform into cancerous cells, they acquire antigenicity, which is considered non-self by the body's immune cells (Mocellin, 2007). Both adaptive and innate immunity play a role in combating cancer cells. Normal cells express many MHC molecules on their surface, unlike cancerous cells, and the lipid composition differs between normal and cancerous cells. Based on these differences, immune cells detect cancer cells as non-self-cells.

The immune system comprises antibodies, natural killer cells, and phagocytic cells, including macrophages and monocytes, which act against cancer (Naftzger, 1991). Macrophages form clusters around tumor cells and eliminate them by engulfing and digesting them, a process known as phagocytosis. Natural killer cells are the first to detect cancer cells and distinguish them from normal cells by measuring the inputs of inhibitory and activating signals received from target cells through their surface receptors. NK cells secrete interferon-gamma, perforins, and granzymes that kill cancer cells.

Cancer cells can escape T-cell responses by decreasing MHC-I molecules on their surfaces. Due to the low expression of MHC-I, immune cells are unable to detect cancer cells. Cancer cells also minimize costimulatory signals. The interaction between B7, which is present on B cells, and CD28, which is present on T cells, is known as a costimulatory signal, enhancing

the activation and proliferation of the immune response. A weak immune response is generated when this signal is not adequately regulated. The immune system produces anticancer antibodies. Anti-cancer antibodies have a lower toxic effect on target tumor cells and bind to cancer antigens on the cell surface (Ross et al., 2003). Immune cells do not recognize cancer antigens because anticancer antibodies mask them.

Anti-Cancer Drugs

Anticancer drugs, also known as antineoplastic agents, are effective in treating various types of cancer, as listed in Table 5. Many major classes of anticancer drugs include alkylating agents, antimetabolites, natural products, and hormones (Lammers, 2012).

Table 5: Anti-cancer drugs and their targets

S.No.	Drugs	Targets
1	Abarelix	Gonadotropin-releasing hormone receptor
2	Docetaxel	Tubulin beta-1 chain
3	Methotrexate	Thymidylate synthase
4	Irinotecan	DNA topoisomerase 1
5	Ciprofloxacin	DNA topoisomerase four subunit A DNA gyrase subunit A
6	Anastrozole	Cytochrome P450 19A1 or non-steroidal aromatase inhibitor (AI)
7	Alemtuzumab	CAMPATH-1 antigen
8	Cemiplimab	Programmed cell death protein 1
9	Everolimus	Serine/threonine-protein kinase mTOR
10	Metyrosine	Tyrosine 3-monooxygenase
11	Rilonacept	Interleukin-1 beta Interleukin-1 alpha
12	Tisotumabvedotin	Tissue factor

Treatments

There are various types of cancer treatments, including surgery, chemotherapy, radiotherapy, immunotherapy, hormonal therapy, nanoparticle therapy, and CAR T-cell therapy. The type of treatment given to a person depends entirely on the advancement of cancer.

Chemotherapy

Chemotherapy is a treatment process in which drugs reduce the number of cancer cells in the tumor and their ability to metastasize (https://www.cancer.gov/about-cancer/treatment/types/chemotherapy, 2022). These drugs target fast-growing and reproducing cells, a property common to cancer cells. These drugs travel through the bloodstream and damage the metastatic cancer cells in other organs. Chemotherapeutic drugs cannot distinguish between cancer cells and rapidly growing normal cells, such as those found in the bone marrow and hair follicles. As a result, they produce side effects, such as a weakened immune system, hair loss, anaemia, and fatigue.

Radiotherapy

Radiations can be used to kill cancer cells and control their growth by damaging the DNA of cancer cells (https://www.cancer.gov/about-cancer/treatment/types/radiation-therapy, 2022). Intensity-modulated radiation therapy (IMRT) can be used to provide a higher dose of radiation to cancer cells and to spare normal tissue around the cancer cells. CT scans help specify the details and create a 3-dimensional image of the tumor, which aids in radiotherapy. Side effects may include localized hair loss, skin irritation, and inflammation at the tumor site.

Hormonal therapy

Hormonal therapy blocks or alters hormones to prevent or slow the growth of cancer (https://www.cancer.gov/about-cancer/treatment/types/hormone-therapy, 2022). This therapy is used to treat cancers that depend on hormones for growth, such as breast, adrenal, and prostate cancers. Hormonal therapy can be administered as a pill, liquid, or injection.

Immunotherapy

Immunotherapy strengthens the immune system, which helps fight cancerous cells (https://www.cancer.gov/about-cancer/treatment/types/chemotherapy, 2022). White blood cells (WBCs) recognize the antigens present on the cell surface. The antigens of normal and cancerous cells differ, which enables WBCs to identify damaged cells. Immune cells produce antibodies and mark damaged cells for destruction.

Nanotechnology therapy

Cancer treatment therapy nanoparticles have cancer-specific ligands that attach only to cancerous cells. These are administered as nanomedicines. These nanomedicines attach to cancer cells and are taken up by them. The particles release toxic drugs inside the cells, thereby destroying cancer cells. Nanoparticles act as drug delivery agents that do not affect normal cells.

CAR T-cell therapy

Chimeric Antigen Receptor T-cell therapy is a treatment in which a patient's T-cells are modified to express tumor-specific receptors through Chimeric Antigen Receptors (CARs). T-cells isolated from patients are genetically modified using viruses, such as lentivirus, which has genetic material that codes for CARs. These modified T cells, equipped with CARs, were expanded and subsequently infused back into the patient. Chimeric antigen receptors recognize cancerous cells, and the release of cytokines destroys cancer cells.

Discussion

Cancer is a multifactorial disease, making it difficult to predict its course. Nevertheless, significant progress has been made in recent times to understand disease biology, disease manifestation, and prognosis.

With advancements in instrumentation and cell surface studies, we can now gain a deeper understanding of cancer cells. However, the development of a cancer management regime has always been challenging. Most treatment modalities are not specific to cancer cells only; therefore, drugs or radiation, whichever is applied, also affect healthy cells, which is a significant disadvantage.

With the advancement of nanotechnology, immunology, and site-specific gene editing technologies, progress is being made in personalized medicine, and the hope of curing cancer is gaining momentum. Future cancer therapies rely primarily on the development of immunological interventions, site-specific gene editing technologies, and targeted drug delivery. However, early diagnosis of cancer still poses a fundamental question. Until we can develop an early diagnosis of the disease, we cannot expect much progress in the prognosis of cancer. With the advancement of genomics, stem cell biology, and developmental biology, the early diagnosis and prediction of predisposition to specific types of cancer are rapidly evolving. With

advancements in diagnosis, predisposition studies, and treatment modalities, we are moving closer to effective cancer management.

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CHAPTER 2

MANAGEMENT AND TREATMENT OF DIABETES MELLITUS

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Abstract

Diabetes mellitus is a metabolic condition characterized by an individual as blood sugar level increasing due to a defect in insulin production or insulin action. As of 2014, 387 million people are expected to have diabetes mellitus globally. Diabetes is expected to affect 537 million individuals (20-79 years old) by 2030; this figure is expected to reach 643 million, and by 2045, it will reach 783 million. As illness increases, blood vessel and tissue damage occur, which causes severe side effects such as nephropathy, ulceration, retinopathy, neuropathy, and cardiovascular issues. Chemical medications are mainly used to treat these symptoms. The primary goal is to prolong life by reducing or eliminating several risk factors that can prevent the long-term consequences of diabetes. Food and lifestyle decisions are regarded as essential components for the treatment and maintenance of type 2 diabetes, whereas insulin treatment is the primary focus for patients with type 1 diabetes. Insulin becomes crucial when diet, exercise, weight loss, and oral medicines fail to regulate blood glucose levels in people with type 2 diabetes. This review focuses on diabetes-related complications, advanced treatment, and the management of diabetes mellitus.

Introduction

Diabetes mellitus (DM) is prevalent worldwide in both developing and developed countries. According to the International Diabetes Federation, 537 million adults aged 20-79 years live with diabetes, and this number is expected to increase to 783 million by 2045. In 2021, diabetes will cause 6.7 million deaths. India has the largest diabetic population in the world (IDF et al., 2021). Patients with diabetes are required to receive multiple daily insulin injections. Repeated injections are neither patient-compliant nor provide adequate metabolic control. Diabetes mellitus is a metabolic condition characterized by persistent hyperglycemia and alterations in the metabolism of carbohydrates, fats, and proteins, resulting in inadequate insulin secretion and subsequent complications. Additional signs include hunger, polyuria, increased thirst, and glucose levels in the urine (Deshpande et al., 2008).

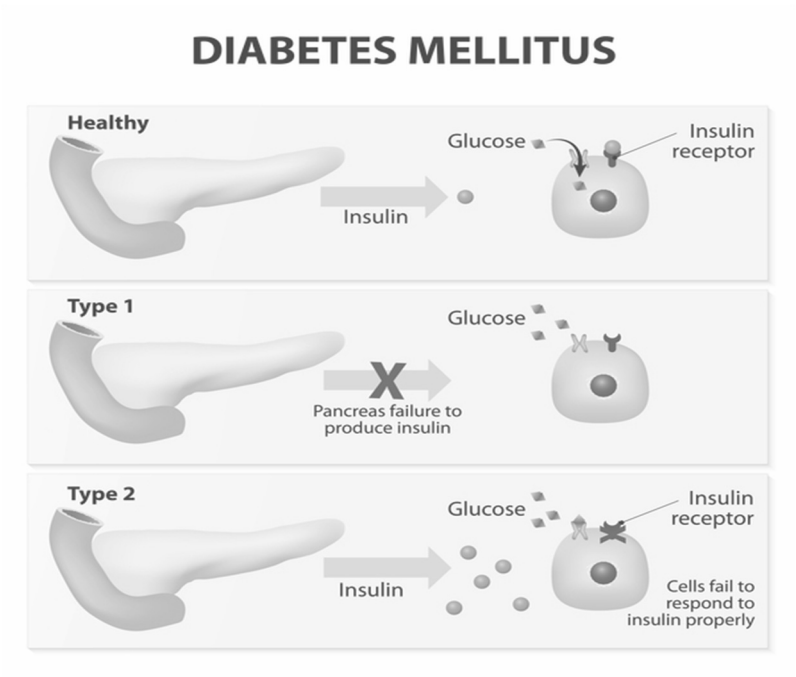

Figure 1: Response of the pancreas in a) a healthy individual, b) a type 1 diabetic patient, and c) a type 2 diabetic patient. (Source: MedlinePlus Genetics)

The test criteria, which clinically establish an individual suffering from diabetes mellitus, include:

Test criteria	Pre-Diabetes	Over Diabetes Mellitus
Fasting plasma glucose test	100-125 mg/dL	≥126
Plasma glucose test, during an oral glucose tolerance test	140 to 200 mg/dL	Two hrs.: ≥ 200
Random glucose test with symptoms of hyperglycemia	Not applicable	≥ 200
Glycosylated hemoglobin (HbA1c) test	5.7% - 6.4%	≥ 6.5%
American Diabetes Association. (n.d.). Retrieved January 6, 2023, from https://diabetes.org/diabetes/a1c/diagnosis		

1. Type-1/ Insulin-dependent diabetes mellitus (IDDM)

Type 1 diabetes results from the autoimmune destruction of the β-cells in the islets of Langerhans, leading to an absolute insulin deficiency. It is more prevalent in children and young adults and is therefore called "Juvenile Diabetes" (Bujang, 2019). The symptoms of type 1 diabetes include frequent urination, excessive thirst, extreme hunger, irritability, and increased fatigue.

2. Type-2 / non-insulin dependent diabetes mellitus (NIDDM)

Type-2 diabetes is much more prevalent, accounting for 90–95% of diabetes cases (Kadiki et al., 1996). This is caused by a decrease in insulin production and progressive loss of β-cells in many patients, but to a much lower extent than in IDDM, as depicted in Figure 1. The onset of NIDDM occurs after 40 years of age and generally in overweight teenagers (Roep et al., 2021).

In both forms of diabetes, glucose levels increase, a condition known as hyperglycemia. And this hyperglycemia may lead to the following complications:

- Retinal damage due to diabetes (diabetic retinopathy) can lead to blindness (Forga et al., 2016).
- Kidney damage in diabetes (diabetic nephropathy) can lead to kidney failure (*Sagoo et al*., 2020).
- Nerve damage is caused by diabetes (diabetic neuropathy), which causes foot wounds and ulcers (Feldman et al., 2019).
- Diabetes accelerates atherosclerosis, the formation of fatty plaques within the arteries, which can lead to blockages or clots (thrombi) that may result in heart attacks, strokes, and impaired circulation in the arms and legs (Jenny et al., 2008).

Treatment of Diabetes

Insulin has extended the lives of patients with IIDM, and the effectiveness of islet/pancreas transplantation as an IIDM treatment has directly demonstrated the viability of re-establishing cells in vivo. Stem cell therapy plays a vital role in diabetes by collecting adherent cord blood-derived multipotent stem cells and administering educated lymphocytes into the patient's circulation (Singh et al., 2016).

Diabetes Mellitus and Insulin

The human pancreas contains 1-2 million islets of Langerhans, and each islet is composed of three distinct types of cells: alpha, beta, and gamma cells, which secrete various hormones essential for the human body, as illustrated in Figure 4. The beta cells in Langerhans constitute approximately 60 percent of all the cells and secrete insulin. Insulin carries information from one part of the body to another (Kulkarni, 2004). Specifically, insulin informs the body's cells that glucose can be used in the bloodstream. Glucose cannot enter the cell until the insulin "unlocks" it, allowing it to receive the glucose and burn it for energy. Diabetes mellitus results from a deficiency in insulin secretion by beta cells. Heredity typically plays a significant role in determining who develops diabetes and who does not (Bryant, 2022). Banting and Best discovered insulin in 1921 and established its relationship with diabetes mellitus (DM). In 1928, insulin was first identified as a protein. However, the sequence of 51 amino acids was first determined in the pioneering work of Ryle et al. Insulin is a small protein with a molecular weight of 5808 Da. The A and B chains are peptide chains that make up insulin. Two disulfide bonds bind the A and B chains, along with a disulfide bond (Figure 5). In some species, the A chain consists of 21

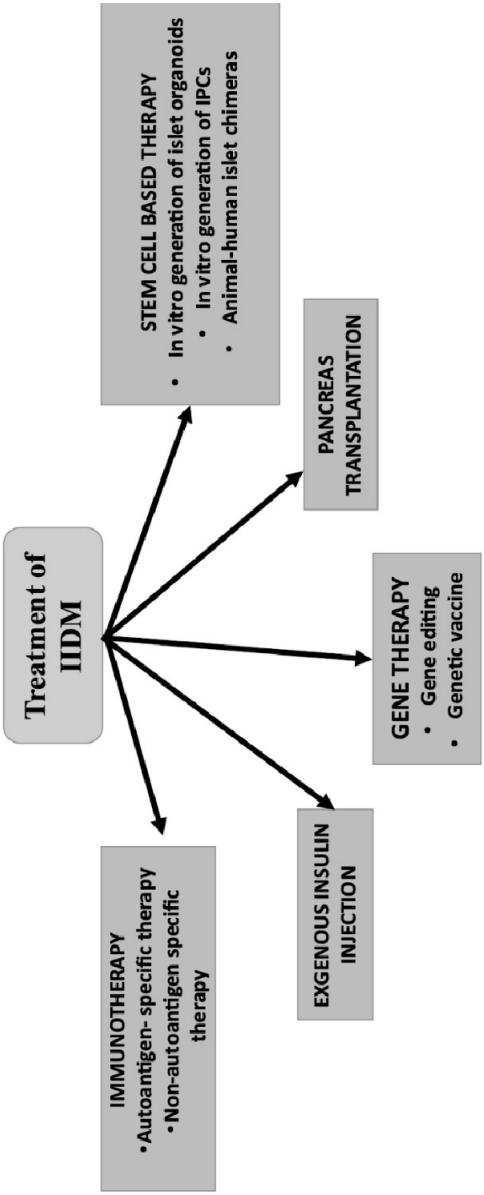

Figure 2: Possible treatments of insulin-dependent diabetes mellitus