CHAPTER NO.2
CANCER- AN INTRODUCTION

Cancer is a class of diseases or disorders characterized by uncontrolled division of cells and the ability of these cells to invade other tissues, either by direct growth into adjacent tissue through invasion or by implantation into distant sites by Metastasis. Metastasis is defined as the stage in which cancer cells are transported through the bloodstream or lymphatic system. Cancer may affect people at all ages, but risk tends to increase with age, due to the DNA damage becomes more apparent in aging DNA damage becomes more apparent in aging DNA.

2.1 HISTORY

Today, carcinoma is the medical term for a malignant tumor derived from epithelial cells. It is Celsus who translated carcinos into the Latin Cancer, also meaning crab. Galen used “oncos” to describe all tumors, the root for the modern word oncology. Hippocrates described several kinds of cancers. He called benign tumors oncos, Greek for swelling and malignant tumors carcinos, Greek for crab or crayfish. This name probably comes from the appearance of the cut surface of solid malignant tumors, with a round dish hard center surrounded by pointy projection, vaguely resembling the shape of a crab. He later added the suffix “oma”, Greek for swelling, giving the name carcinoma. Since it was against Greek tradition to open the body, Hippocrates only described and made drawings of outwardly visible tumors on the skin, nose, and breasts. Treatment was based on the humor theory of
four body fluids (Black and Yellow bile, blood, and phlegm). According to the patient’s humor, treatment consisted of diet, bloodletting, and laxatives. Through the centuries it was discovered that cancer could occur anywhere in the body, but humor theory based treatment remained popular until the 19th century with the discovery of cells\textsuperscript{13}.

Through treatment remained the same, in the 16th and 17th centuries it became more acceptable for doctors to dissect bodies to discover the cause of death. The German professor Wilhelm Fabry believed that breast cancer was caused by a milk clot in a mammary duct. The Dutch Professor Francois de la Boe Sylvius, a follower of Descartes, believed that all disease was the outcome of chemical processes, and that acidic lymph fluid was the cause of cancer. His contemporary Nicolaes Tulp believed that cancer was a poison that slowly spreads and concluded that it was contagious.

With the widespread use of the microscope in the 18th century, it was discovered that the ‘cancer poison’ spread from the primary tumor through the lymph nodes to other sites (metastasis). The use of surgery to treat cancer had poor results due to problems with hygiene. The renowned Scottish surgeon Alexander Monro (1697 – 1767) saw only 2 breast tumor patients out of 60 surviving surgery for two years. In the 19th century, asepsis improved surgical hygiene and as the survival statistics went up, surgical removal of the tumor became the primary treatment for cancer. With the exception of William Coley who in the late 1800s felt that the rate of cure after surgery had been higher before asepsis (and who injected bacteria into tumors with mixed results), cancer treatment became dependent on the individual art of the surgeon at removing a tumor. During the same period, the idea that the body was made of various tissues, that in turn were made up of millions of cells, laid rest the humor-theories about chemical imbalances in the body. The age of cellular pathology was born.

When Madam Curie and Pierre Curie discovered radiation at the end of the 19th century, they stumbled upon the first effective non-
surgical cancer treatment with radiation came also the first sign of multi-disciplinary approaches to cancer treatment. Cancer patient treatment and studies were restricted to individual physicians’ practices until World War II, when medical research centers discovered that there were large international differences in disease incidence. This insight drove national public health bodies to make it possible to compile health data across practices and hospitals, a process that many countries do today\textsuperscript{14}.

2.2 EPIDEMIOLOGY

Cancer epidemiology is the study of the incidence of cancer as a way to infer possible trends and causes. The first such cause of cancer was identified by British surgeon Percivall Pott, who discovered in 1775 that cancer of the scrotum was a common disease among chimney sweeps. In some western countries, such as the USA and the UK, cancer is overtaking cardiovascular disease as the leading cause of death. In many Third World countries cancer incidence (in so far as this can be measured) appears much lower, most likely because of the higher death rates due to infectious disease or injury with the increased control over malaria and tuberculosis in some Third World countries, incidence of cancer is expected to rise; this is termed the epidemiologic transition in epidemiological terminology. Cancer epidemiology closely mirrors risk factor spread in various countries. Hepatocellular carcinoma (liver cancer) is rare in the West but is the main cancer in China and neighboring countries, most likely due to the endemic presence of hepatitis B and aflatoxin in that population. Similarly, with tobacco smoking becoming more common in various Third World countries, lungs cancer incidences have increased in a parallel fashion\textsuperscript{15}.  


2.3 CLASSIFICATION\textsuperscript{16-18}

Cancers are classified by the type of cells that resembles the tumor and therefore, the tissue presumed to be the origin of the tumor. The following general categories are usually accepted.

1) **Carcinoma** - Malignant tumors derived from epithelial cells. This group represents the most common cancers, including the common forms of breast, prostate, lung and colon cancer.

2) **Lymphoma and Leukemia** - Malignant tumors derived from blood and bone marrow cells.

3) **Sarcoma** – Malignant tumors derived from connective tissue or mesenchymal cells.

4) **Mesothelioma** - Tumors derived from the mesothelial cells lining the peritoneum and the pleura.

5) **Glioma** – Tumors derived from glia, the most common type of brain cell.

6) **Germinoma** – Tumors derived from germ cells, normally found in the testicle and ovary

7) **Choriocarcinoma** – Malignant tumors derived from the placenta.

Carcinogenesis, which means the initiation or generation of cancer, is the process of dearrangement of the rate of cell division due to damage to DNA. Proto-oncogenes are genes which promote cells growth and mitosis, a process of cell division, and tumor suppressor genes discourage cells growth, or temporarily halt cell division in order to carry out DNA repair mutations to these genes are required before a normal cells transforms into a cancer cells.

Proto-oncogenes promote cell growth through a variety of ways. Many can produce hormones, a “chemical messenger” between cells which encourage mitosis, the effect of which depends on the signal transduction of the signal transduction of the receiving tissue or cells. Some are
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responsible for the signal transduction system and signal receptors in cells and tissues themselves, thus controlling the sensitivity to such hormones. They often produce mitogens, or they are involved in transcription of DNA in protein synthesis, which creates the proteins and enzymes responsible for producing the products ad biochemical cells use and interact with.

Mutations in proto-oncogenes can modify their expressions and function, increasing the amount or activity of the product protein. When this happen, they become oncogenes, and thus cells have a higher chance to divide excessively and uncontrollably. The chance of cancer cannot be reduced by removing proto-oncogenes from the genome as they are critical for growth repair and homeostasis of the body.

Tumor suppressor genes code for anti proliferation singles and proteins that suppress mitosis and cell growth. Generally tumor suppressors are transcription factors that are activated by cellular stress or DNA damage. Often DNA damage will cause the presence of free-floating genetic material as well as other sings, and will trigger enzymes and pathways which lead to the activation of tumor suppressor genes. The functions of such genes are to arrest the progression of cell cycle in order to carry out DNA repair, preventing mutations from being passed on to daughter cells. Canonical tumor suppressors include the p53 protein, which is a transcription factor activated by many cellular stressors including hypoxia and ultraviolet radiation damage.

The Warburg effect is the preferential use of glycolysis for energy to sustain cancer growth. p53 has been shown to regulate the shift from the respiratory to the glycolytic pathway. Synthesis of Cytochrome c Oxidase 2 (SCO2) has been recognized as the downstream mediator of this effect. SCO2 is critical for regulating the cytochrome c Oxidase complex within the mitochondria, and p53 can disrupt the SCO2 gene p53 regulation of SCO2 and mitochondrial respiration may provide a possible explanation for the Warburg effect.
However, a mutation can damage the tumor suppressor gene itself, or the signal pathway which activates it, “switching it off”. The invariable consequence of this is that DNA repair is hindered or inhibited: DNA damage accumulates without repair, inevitably leading to cancer.

In general, mutation in both types of genes is required for cancer to occur. Usually, oncogenes are dominant, as they contain gain of function mutations, while mutated tumor suppressors are recessive, as they contain loss of function mutations. Each cell has two copies of the same gene, one from each parent, and under most cases gain of function mutation in one copy of a particular proto-oncogene is enough to make that gene a true oncogenes, while usually loss of function mutation needs to happen in both copies of a tumor suppressor gene to render that gene completely non functional. However, cases exist in which one loss of function copy of a tumor suppressor gene can render the other copy non functional. This phenomenon is called the dominant negative effect and is observed in many p53 mutations.

Mutations of tumor suppressor genes that are passed on to the next generation of not merely cells, but their offspring can cause increased likelihoods for cancers to be inherited. Members within these families have increased incidence and decreased latency of multiple tumors. The mode of inheritance of mutant tumors suppressors is that affected member inherits a defective copy from one parent, and a normal copy from another. Because mutations in tumor suppressor act in a recessive manner, the loss of the normal copy creates the cancer phenotype.

Cancer pathology is ultimately due to accumulation of DNA mutations that negatively affect expression of tumor suppressor proteins or positively effect the expression of protein that drive the cell cycle. Substances that cause these mutations are known as mutagens, and mutagens that cause cancers are known as carcinogens. Particular substances have been linked to specific types of cancer. Tobacco smoking is associated with lung cancer. Prolonged exposure to
radiation, particularly ultraviolet radiation from the sun, leads to melanoma and other skin malignancies. Breathing asbestos fibers is associated with Mesothelioma. Other types of mutations can be caused by chronic inflammation, as neutrophils granulocytes secrete free radicals that damage DNA. Chromosomal translocations, such as the Philadelphia chromosomes translocations, such as the Philadelphia chromosomes, are a special type of mutation that involves exchange between different chromosomes.

2.4 ETIOLOGY

Viruses are responsible for 15% of human cancer worldwide. The main viruses associated with human cancers are human papilloma virus, hepatitis B virus, Epstein-Barr virus, and human T-lymphotropic virus. Experimental and epidemiologic data imply a causative role for viruses and they appear to be the second most important risk factor for cancer development in humans, exceeded only by tobacco usage. The mode of virally induced tumors can be divided into two, actually transforming or slowly transforming. In actually transforming viruses, the viral particles carry a gene that encodes for an overactive oncogenes called viral-oncogenes and the infected cell is transformed as soon as v-one is expressed in contrast slowly transforming. In actually transforming viruses, the viral particles carry a gene that encodes for an overactive oncogenes called viral-oncogenes, and the infected cell is transformed as soon as v-one is expressed.

In contrast, in slowly transforming viruses, the virus genome is inserted, especially as viral genome insertion is an obligatory part of retroviruses, near a proto-oncogene in the host genome. The viral promoter or other transcription regulation elements in turn cause over expression of that proto oncogenes which in turn induces uncontrolled cellular proliferation. Because viral genome insertion is not specific to proto-oncogenes and the chance of insertion near that proto-oncogene is low, slowly-transforming viruses have very long tumor latency compared to acutely- transforming viruses, which already carry the viral-oncogenes.
2.4.1 Chemical substances

Chemical substances of certain types have a propensity for causing mutations. For instance, various aniline dye derivatives are likely to cause cancer. The greatest number of death in our society is due to the carcinogens present in the cigarette smoke. Laboratory studies in animals, research in to excessive alcohol use, and observations of people who take certain drugs have also contributed to knowledge of the role of chemicals in cancer. For example, studies of a number of cases of vaginal cancer among young woman determined the cause in this instance to be diethylstilbestrol, a synthetic hormone that had been given to their mother to prevent miscarriage during pregnancy. Divalent metal ion like Ni\(^{2+}\), Pb\(^{2+}\), Cd\(^{2+}\) are electrophillic and therefore, react with macromolecules, the metal ions react with guanine and phosphate groups of DNA. Some metals can bind to purine and pyrimidine base through covalent bonds or electrons of the base metal ions such as Ni\(^{2+}\), Pb\(^{2+}\), Cd\(^{2+}\) and can depolymerise polynucleotides. These reactions can lead to DNA adduct formation, and this may be critical step in tumor initiation\(^\text{20}\).

2.4.2 Radiation

Ionizing radiation such as x-rays, gamma rays and particle radiation from radioactive substances and even ultraviolet rays in sunlight can predispose to cancer. Ions formed in tissue cells under the influence of such radiation are highly reactive and can rupture DNA strands, thus causing many mutations.

2.4.3 Physical factors

Physical irritants can also lead to cancer, such as continued abrasion of the linings of the intestinal tract by some type of food. The damage to the tissue leads to rapid mitotic replacement of the cells. The more rapid the mitosis the greater is the chances for mutations.

2.4.4 Hereditary factor
In many families there is a strong hereditary tendency to cancer. This probably results from the fact that most cancers require not one mutation but two or more mutations. In those families that are particularly predisposed to cancer, it is presumed that one or more of the genes had already mutated in the inherited genome. Their fore, fewer additional mutations are required in such a person to develop a cancer. Hereditary cancer syndromes are indicated by a strong family history e.g. familial retinoblastoma, familial adenomatous polyp sis etc.

2.4.5 Role of Diet and Lifestyle

Foodstuffs may cause cancer in some of the following ways, by being direct carcinogens. Carcinogens may be produced by cooking, microorganism may produce carcinogens in stored foods, Foodstuffs may act as substrates for the formations of carcinogens in the body, and Food stuffs may alter the bacterial flora of bowel, thereby producing carcinogens. Methyl nitrosoamines found in non-vegetarian foods, particularly red meat are also carcinogenic. The bitter taste in peanuts is caused by aflatoxins. When this aflatoxin reach the liver they are broken down in to epoxide remains in the body before being flushed out it damages the DNA.

2.5 SIGNS AND SYMPTOM

Roughly, cancer symptoms can be divided in to three groups

1. Local Symptoms - unusual lumps or swelling (tumor), hemorrhage (bleeding), pain and/or ulceration. Compression of surrounding tissues may cause symptoms such as jaundice.

2. Symptoms of metastasis (spreading) - enlarged lymph nodes, cough and hemoptysis, hepatomegaly (enlarged liver), bone pain, fracture of affected bones and the first symptom.

3. Systemic symptoms - weight los s poor appetite and cachexia (wasting), excessive sweating (night sweats) anemia and specific paraneoplastic phenomena,
i.e. specific conditions that are due to an active cancer, such as thrombosis or hormonal changes\textsuperscript{22-23}.

2.6 TREATMENT OF CANCER\textsuperscript{24-25}

Cancer can be treated by surgery, chemotherapy, radiation therapy, immunotherapy, monoclonal antibody therapy or other methods. The choice of therapy depends upon the location and grade of the tumor and the stage of the disease, as well as the general state of the patient (performance status). A number of experimental cancer treatments are also under development.

Complete removal of the cancer without damage to the rest of the body is the goal of treatment. Sometimes this can be accomplished by surgery, but the propensity of cancers to invade adjacent tissue or to spread to distant sites by microscopic metastasis often limits its effectiveness. The effectiveness of chemotherapy is often limited by toxicity to other tissues in the body. Radiation can also cause damage to normal tissue.

2.6.1 Surgery

In theory cancers can be cured if entirely removed by surgery, but this is not always possible. When the cancer has metastasized to other sites in the body prior to surgery, complete surgical excision is usually impossible. Examples of surgical procedures for cancer include mastectomy for breast cancer and prostatectomy for prostate cancer. The goal of the surgery can be either the removal of only the tumor, or the entire organ. A single cancer cell is invisible to the naked eye but can regrow in to a new tumor, a process called recurrence. For this reason, the pathologist will examine the surgical specimen to determine if a margin of healthy tissue is present, thus decreasing the chance that microscopic cancer cells are left in the patient. In addition to removal of the primary tumor, surgery is often necessary for staging, e.g. determining the extent of the disease and whether it has metastasized to regional lymph nodes. Standing is a major determinant of prognosis and of the need for adjuvant therapy. Occasionally,
surgery is necessary to control symptoms, such as spinal cord compression or bowel obstruction. This is referred to as palliative treatment.

2.6.2 Chemotherapy

Chemotherapy is the treatment of cancer with drugs that can destroy cancer cells. It interferes with cell division and various possible ways, e.g. with the duplication of DNA or the separation of newly formed chromosomes. Most forms of chemotherapy target all rapidly dividing cells and are not specific for cancer cells. Hence, chemotherapy has the potential to harm healthy tissue, especially those tissues that have a high replacement rate intestinal lining. These cells usually repair themselves after chemotherapy. Because some drugs work better together than alone, two or more drugs are often given at the same time. This is called combination chemotherapy. Most chemotherapy regimens are given in a combination. Anticancer drugs can be classified in the following categories on the basis of their varying mechanisms of action.

2.6.3 Monoclonal Antibody Therapy

Immunotherapy is the use of immune mechanisms against tumors. These are used in various forms of cancer, such as breast cancer and leukemia. The agents are monoclonal antibodies directed against proteins that are characteristic to the cells of the cancer in question or cytokines that modulate the immune system’s response.

2.6.4 Immunotherapy

Other more contemporary methods for generating non-specific immune response against tumors include intravesical BCG immunotherapy for superficial bladder cancer, and use of interferon and interleukin. Vaccines to generate non-specific immune responses are the subject of intensive research for a number of tumors, notably malignant melanoma and renal cell carcinoma.

2.6.5 Radiation therapy
Radiation therapy is the use of ionizing radiation to kill cancer cells and shrink tumors. Radiation therapy can be administered externally via external beam radiotherapy or internally via branchy therapy the effects of radiation therapy are localized and confined to the region being treated. Radiation therapy destroys cells in the area being treated by damaging their genetic material making it impossible for these cells to continue to grow and divide. Although radiation damages both cancer cells and normal cells, most normal cells can recover from the effects of radiation and function properly. The goal of radiation therapy is to damage as many cancer cells as possible, while limiting harm to nearby healthy tissue. Hence, it is given in many fractions allowing healthy tissue to recover between fractions.

Radiation therapy may be used to treat almost every type of solid tumor, including cancers of the brain, breast, cervix, larynx, lung, pancreas, prostate, skin stomach uterus, or soft tissue, or soft tissue sarcomas. Radiation is also used to treat leukemia and lymphoma. Radiation dose to each site depends on a number of factors, including the radio sensitivity of each cancer type and whether there are tissues and organs nearby that may be damaged by radiation. Thus, as with every form of treatment, radiation therapy is not without its side effects.

**2.6.6 Hormonal suppression**

The growth of some cancers can be inhibited by providing or blocking certain hormones. Comma examples of hormone-sensitive tumors include certain types of breast and prostate cancers removing or blocking estrogen or testosterone is often an important additional treatment.

**2.6.7 Symptom control**

Although the control of the symptoms of cancer is not typically thought of as a treatment directed at the cancer. It is an important determinant of the quality of life of cancer patients, and plays an important role in the decision whether the patient is able to undergo other treatments. Although all practicing doctors have the therapeutic skills to control pain, nausea, vomiting,
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diarrhea, hemorrhage and other common problems in cancer patients, the multidisciplinary specialty of palliative care has arisen specifically in response to the symptom control needs of this group of patients. Pain medication, such as morphine and oxymoron and antiemetic, drugs to suppress nausea and vomiting, are very commonly used in patients with cancer-related symptoms.

2.6.8 Cancer vaccines

Considerable research effort is now devoted to the development of vaccines to prevent infection by oncogene infections agents, as well as to mount an immune response against cancer specific epitopes and to potential venues for gene therapy for individuals with genetic mutations or polymorphisms that put them at high risk of cancer. Treatment of cancer patients with antilogous tumor cell preparation is considered as the first use of tumor vaccine in human beings.

As of October 2005, researchers found that an experimental vaccine for HPV types 16 and 18 was 100% successful at preventing infection with these types of HPV and thus are able to prevent the majority of cervical cancer cases. Process of tumor genesis is associated with the alteration in gene sequences and expression level of various protein antigens. These changes lead to the expression of several tumor associated antigens, e.g.; CEA, MAGE

2.6.9 Complementary And alternative medicine

Complementary and alternative medicine (CAM) treatments are the diverse group of medical and health care system, practices and products that are not presently considered to be effective by the standards of conventional medicine. Conventional medicine practitioners may describe non conventional medicine. Conventional medical practitioners may describe non conventional treatment methods as a “complements” to conventional treatment, to provide comfort or lift the spirits of the patients, while others are offered as alternatives to be used instead of conventional treatments in hope of curing the cancer.
Some complementary measures include prayer or psychological approaches such as “imaging” or meditation to aid in pain relief, or improve mood. The benefits of these approaches have not been scientifically proven and therefore face skepticism. Other complementary approaches include traditional medicine like traditional Chinese medicine.

A wide range of alternative treatments have been offered for cancer over the last century. The appeal of alternative cures arises from the daunting risks, costs, or potential side effect of many conventional treatments, or in the limited prospect for cure. Proponents of these therapies are unable or unwilling to demonstrate effectiveness by conventional criteria. Alternative treatments have included special diets or dietary supplements eg. grape diet, cabbage diet, electromagnetic therapy with electrical devices (eg. “Rhumart”, “Zapperes”), especially formulated compounds e.g. laetrile and homeopathic remedies, unconventional use of conventional drugs (e.g. Insulin), purges of enemas, Physical manipulation of the body, various herbs or herbal preparations such as essiac. Some of these alternative treatments may be ineffective or dangerous. Using these modalities as sole treatment for potentially fatal conditions such as cancer are generally not recommended by the majority of medical professionals. The Ralph Moss Reports are a source of information on CAM and conventional cancer treatments from a biologically based, alternative medicine point of view with detailed reports on a variety of cancer types.

Once referred to as the c-word, cancer has a reputation for being a deadly disease. While this certainly applies to certain particular types, the truths behind the historical connotation of cancer are increasingly being overturned by advances in medical care. Some types of cancer have a prognosis that is substantially better than nonmalignant diseases such as heart failure and stroke.

Progressive and disseminated malignant disease has a substantial impact on a cancer patient’s quality of life, and cancer (such as
chemotherapy) may have severe side effects. In the advanced stages of cancer, many patients need extensive care, affecting family members and friends. Palliative care solutions may include permanent or respite hospice nursing.

2.7 Cyclin Dependent Kinase Inhibitors; Upcoming Novel Class of Anti-cancer Drugs

Cyclin Dependent Kinase (CDK) are serine threonine kinase enzymes which only become functional when bound to their cyclin partner. There are 11 members of the CDK family known till now. Among these CDK 1,2,3,4, and 6 are known to play important roles in the cell cycle this critical importance of CDK in cell cycle has driven interest in the development of selective and potent inhibitors for overall blockade of cell cycle to achieve growth arrest. Different CDK control the different phase of cell cycle as follows.

1) The complex of Cyclin C and CDK3 helps the cell to efficiently exit the go phase and enter the G₁ phase this is accomplished by the stimulation of retinoblastoma protein (pRb) Phosphorylation of Go/G₁ transition.

2) CDK4-6 on binding to Cyclin D begins the Phosphorylation of pRb complexes to E2F/DP (transcription factors). Following this Cyclin E activates CDK2 to effect further Phosphorylation of pRb, thereby enabling the cells to cross the G₁ phase and enter S phase.

3) Cyclin A and CDK2 complex known to phosphorylate various substrates for DNA replication and ultimately inactivates G₁ transcription factor. Transition from S to G₂ phase occurs via complexation of Cyclin A with CDK2

4) On completion of the S phase CDK1/ Cyclin B is activated. Progression from G₂ to M phase requires sustained activity of CDK1/Cyclin B complex within the nucleus.

5) Complexes of CDK2 with Cyclin E and complexes of CDK2 with Cyclin A are inhibited by the binding with members of CDK inhibitors protein
family these endogenous inhibitors not only regulate the G\textsubscript{1} to S phase transition but G\textsubscript{2} to M as well.

6) Subsequent entry into the anaphase relies critically on the sudden destruction of CDK1/ Cyclin B activity, which guarantees the global inhibition of protein biosynthesis, DNA replication and DNA transcription.

7) Cyclin h complexes with CDK activating kinase (CAK) when Cyclin from the CDK holoenzyme, CAK phosphorylate these complexes at specific residues, resulting in their activation.

8) Inappropriate cell cycle progression is the root of human tumors. Cyclin D1 and Cyclin E are often over expressed in human breast and colon cancer as well as several other types of human cancer. Amplification and over expression of CDK4 are also seen in human cancer. Phosphates that activate Cyclin CDK complexes are frequently over expressed in human breast cancers non small cell cancers and head and neck cancers. Arrest of the cell cycle at the G\textsubscript{1} or S phase is a necessary part of cancer treatment.

CDK inhibitors have potential anti-mitotic activity. They possess the three lucrative properties which encourage them as anti-cancers drugs.

1) As potent anti-proliferative agents arresting cells in G\textsubscript{1} or G\textsubscript{2} /M transition

2) Induction of apoptosis, alone or in combination with other treatments

3) Cell differentiation.

CDK are appearing to be the critical targets to develop the new inhibitors to treat variety of diseases.

2.8 CANCER RESEARCH\textsuperscript{31}

Cancer research is the intense scientific effort to understand disease processes and discover possible therapies. Targeted therapy which first became available in the late 1990s has had a significant impact in the treatment of some types of cancer, and is currently a very active research area. This constitutes
the use of agent’s specific deregulated proteins of cancer cells. Small molecules and monoclonal antibodies have proven to be a major step in oncological treatment. Targeted therapy can also involve small peptide structures as homing device which can will to cell surface receptors or affected extra cellular matrix surrounding the tumor. Radionuclides which are attached to the peptides eventually kill the cancer cell if the include decay’s in the vicinity the cell. Especially oligo or and multimeris of the binding motifs are of great interest, since this can lead to enhanced tumor specificity and avidity.