Introduction

Breast cancer is the most common cancer affecting women globally. It is the leading cause of death from cancer in women and has age–standardized annual incidence and mortality rates of 37.4 and 13.2 per 100 000 women. The outcome of breast cancer is predicted by the extent of spread of the tumor to locoregional lymph nodes, which, in turn, predicts distant spread. Patients with advanced metastatic disease have a very poor prognosis, hence the importance of effective early diagnosis and treatment to prevent later recurrences and improve survival ***(Lonning et al., 2007).***

Multimodality approach is required for early stage breast cancer. These include surgery, radiotherapy, chemotherapy, and endocrine therapies which aim both to eradicate residual cancer and prevent recurrent disease hence increased survival. Recent improvement in outcome in patients with breast cancer appears to result largely from the use of adjuvant therapies, including chemotherapy and endocrine manipulations ***(Mauriac et al., 2006).***

The approach to increase survival in cancer breast is targeting therapy, they act by targeting the pathways that promote, sustain growth and invasion of carcinoma cells and is critical to effective treatment of breast cancer ***(Lin et al., 2005)***

Targeted therapy is a type of medication that blocks the growth of cancer cells by interfering with specific targeted molecules needed for carcinogenesis and tumor growth, rather than by simply interfering with rapidly dividing cells (e.g. with traditional chemotherapy). Targeted cancer therapies may be more effective than current treatments and less harmful to normal cells ***(Zhukov et al., 2008).***

The definitive experiments that showed that targeted therapy would reverse the malignant phenotype of tumor cells involved treating Her2/neu transformed cells with monoclonal antibodies in vitro and in vivo ***(Gupta et al., 2009).***

Molecular target approaches in breast cancer is the targeting of the estrogen receptor with tamoxifen which is responsible for improvement in outcome, reduced the risk of new primary breast cancer and improves survival. Targeted therapies are now a component of treatment for many including colorectal, lung, and pancreatic cancers, as well as lymphoma, leukemia, and multiple myeloma. Recent identification of specific molecular target in cancer cells, leads to development of new targeted therapeutic approach, signal transduction, angiogenesis, and more approaches are induction of apoptosis or inhibition of antiapoptosis which offer the possibility of improving outcome for patient with early as well as metastatic breast cancer ***(Schlotter et al., 2008)***

The targeted therapy refers to a new generation of anticancer drugs that are designed to interfere with a specific molecular target, usually a protein. This approach differs from the more empirical approach used in conventional cytotoxic chemotherapy. In contrast to conventional chemotherapy, it interferes with molecular targets that have a critical role in tumor growth or progression. Since it is directed against cancer specific molecules and signaling pathways, it has limited non-specific toxicities ***(Modi et al., 2005).*** The molecular targets are usually located in tumor cells, some like anti-angiogenic agents may target other cells such as endothelial cells. Targeted therapies have a high specificity toward tumor cells, providing a broader therapeutic window with less toxicity. They are also often useful in combination with cytotoxic chemotherapy or radiation to produce additive of synergistic anticancer activity because their toxicity profiles often do not overlap with traditional cytotoxic chemotherapy ***(Noguchi et al., 2008).***

Rationale of targeting therapy

The normal cell growth and division are largely under the control of a network of chemical and molecular signals that gives instructions to cells. Genetic alterations can disrupt the signaling process so that cells no longer grow and divide normally, or no longer die when they should. Alternations in two types of genes can contribute to the cancer process. Proto-oncogenes are normal genes that are involved in cell growth and division. Changes in these genes lead to the development of oncogenes, which can promote or allow excessive and continuous cell growth and division. Tumor suppressor genes are normal genes that slow down cell growth and division. When a tumor suppressor gene does not work properly, cells may be unable to stop growing and dividing, which leads to tumor growth ***(Perez et al., 2007).***

Aim of the Work

To spot light on targeted therapy, as an effective method for treatment of breast cancer.

Cell biology and Function

The word *cell* comes from the Latin *cellula*, meaning, a small room. It was discovered by Robert Hooke and is the functional unit of all known living organisms. It is the smallest unit of life that is classified as a living thing, and is often called the building block of life ***(Maton et al., 1997).***

Some organisms, such as most bacteria, are unicellular . Other organisms, such as humans, are multicellular. Humans have about 100 trillion or 10^{14} cells; a typical cell size is 10 µm and a typical cell mass is 1 nanogram ***(Campbell et al., 2006).***

Anatomy

There are two types of cells: eukaryotic and prokaryotic. Prokaryotic cells are usually independent, while eukaryotic cells are often found in multicellular organisms.

Proka

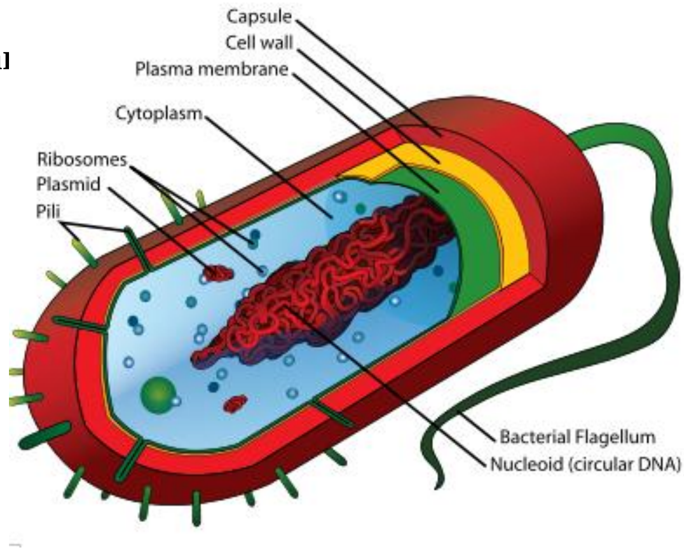

Figure (1): Typical prokaryotic cell ***(Mitiz, 2010).***

The prokaryote cell is simpler, and therefore smaller, than a eukaryote cell, lacking a nucleus and most of the other organelles of eukaryotes. There are two kinds of prokaryotes: bacteria and archaea; these share a similar structure. Nuclear material of prokaryotic cell consist of a single chromosome that is in direct contact with cytoplasm. Here, the undefined nuclear region in the cytoplasm is called nucleoid ***(Mitiz, 2010).***

A prokaryotic cell has three architectural regions:

- On the outside, flagella and pili project from the cell's surface. These are structures (not present in all prokaryotes) made of proteins that facilitate movement and communication between cells;

- Enclosing the cell is the cell envelope – generally consisting of a cell wall covering a plasma membrane though some bacteria also have a further covering layer called a capsule. The envelope gives rigidity to the cell and separates the interior of the cell from its environment, serving as a protective filter. Though most prokaryotes have a cell wall, there are exceptions such as *Mycoplasma* (bacteria) and *Thermoplasma* (archaea). The cell wall consists of *peptidoglycan* in bacteria, and acts as an additional barrier against exterior forces. It also prevents the cell from expanding and finally bursting (cytolysis) from osmotic pressure against a hypotonic environment. Some eukaryote cells (plant cells and fungi cells) also have a cell wall.

- Inside the cell is the cytoplasmic region that contains the cell genome (DNA) and ribosomes and various sorts of inclusions. A prokaryotic chromosome is usually a circular molecule (an exception is that of the bacterium *Borrelia burgdorferi*, which causes Lyme disease). Though not forming a *nucleus*, the DNA is condensed in a *nucleoid*. Prokaryotes can carry extrachromosomal DNA elements called *plasmids*, which are usually circular. Plasmids enable additional functions, such as antibiotic resistance ***(Mitiz, 2010).***

Eukaryotic cells

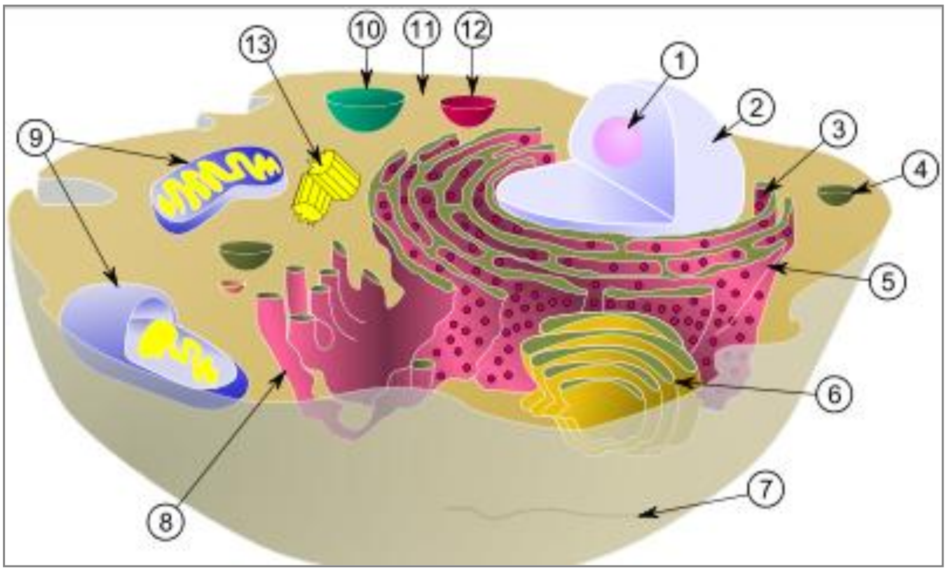

Figure (2): Diagram of a typical animal (eukaryotic) cell, showing subcellularf components. Organelles: **(1)** Nucleolus, **(2)** Nucleus, **(3)** Ribosome, (4) Vesicle, **(5)** Rough endoplasmic reticulum (ER), **(6)** Gilgi apparatus, **(7)** Cytoskeleton, **(8)** Smooth endoplasmic reticulum, **(9)** Mitochondria, **(10)** Vacuole, **(11)** Cytoplasm, **(12)** Lysosome, **(13)** Centrioles within centrosome.

Eukaryotic cells are about 15 times wider than a typical prokaryote and can be as much as 1000 times greater in volume. The major difference between prokaryotes and eukaryotes is that eukaryotic cells contain membrane-bound compartments in which specific metabolic activities take place. Most important among these is a cell nucleus, a membrane-delineated compartment that houses the eukaryotic cell's DNA. This nucleus gives the eukaryote its name, which means "true nucleus." Other differences include:

- The plasma membrane resembles that of prokaryotes in function, with minor differences in the setup. Cell walls may or may not be present.
- The eukaryotic DNA is organized in one or more linear molecules, called chromosomes, which are associated with histone proteins. All chromosomal DNA is stored in the cell nucleus, separated from the cytoplasm by a membrane. Some eukaryotic organelles such as mitochondria also contain some DNA.
- Many eukaryotic cells are ciliated with primary cilia. Primary cilia play important roles in chemosensation, mechanosensation, and thermosensation. Cilia may thus be "viewed as sensory cellular antennae that coordinate a large number of cellular signaling pathways, sometimes coupling the signaling to ciliary motility or alternatively to cell division and differentiation ***(Satir et al., 2008).***

- Eukaryotes can move using *motile cilia* or *flagella*. The flagella are more complex than those of prokaryotes.

Subcellular components

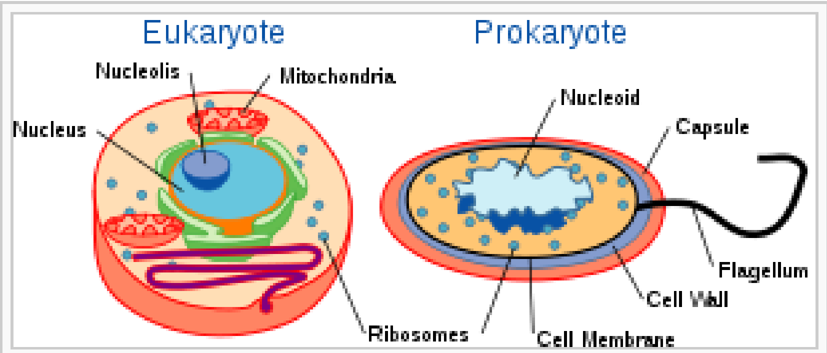

Figure (3): The cells of eukaryotes (left) and prokaryotes (right) ***(Michie et al., 2006).***

All cells, whether prokaryotic or eukaryotic, have a membrane that envelops the cell, separates its interior from its environment, regulates what moves in and out (selectively permeable), and maintains the electric potential of the cell. Inside the membrane, a salty cytoplasm takes up most of the cell volume. All cells possess DNA, the hereditary material of genes, and RNA, containing the information necessary to build various proteins such as enzymes, the cell's primary machinery. There are also other kinds of biomolecules in cells. This article lists these primary components of the cell ***(Michie et al., 2006).***

Membrane

The cytoplasm of a cell is surrounded by a cell membrane or *plasma membrane*. The plasma membrane in plants and prokaryotes is usually covered by a cell wall. This membrane serves to separate and protect a cell from its surrounding environment and is made mostly from a double layer of lipids (hydrophobic fat-like molecules) and hydrophilic phosphorus molecules. Hence, the layer is called a phospholipid bilayer. It may also be called a fluid mosaic membrane. Embedded within this membrane is a variety of protein molecules that act as channels and pumps that move different molecules into and out of the cell. The membrane is said to be 'semi-permeable', in that it can either let a substance (molecule or ion) pass through freely, pass through to a limited extent or not pass through at all. Cell surface membranes also contain receptor proteins that allow cells to detect external signaling molecules such as hormones ***(Revathi et al., 2009).***

- **Cytoskeleton**

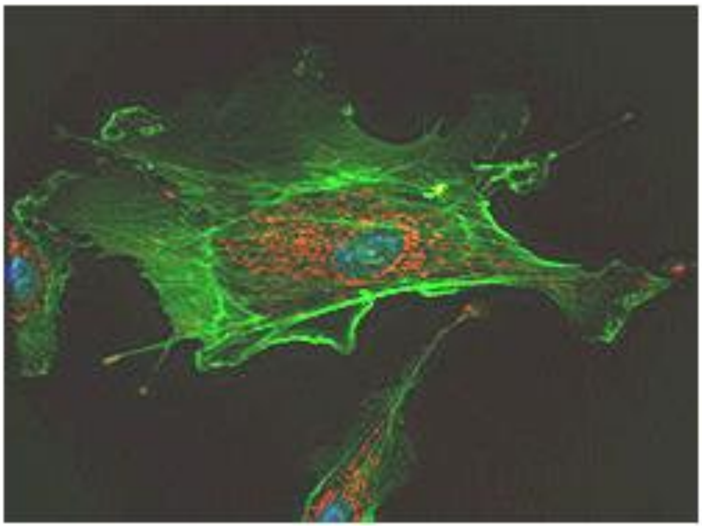

Figure (4): Bovine pulmonary artery endothelial cell: nuclei stained blue, mitochondria stained red, and F-action, an important component in microfilaments, stained green. Cell imaged on a fluorescent microscope ***(Schaletzky et al., 2007).***

The cytoskeleton acts to organize and maintain the cell's shape; anchors organelles in place; helps during endocytosis, the uptake of external materials by a cell, and cytokinesis, the separation of daughter cells after cell division; and moves parts of the cell in processes of growth and mobility. The eukaryotic cytoskeleton is composed of microfilaments, intermediate filaments and microtubules. There is a great number of proteins associated with them, each controlling a cell's structure by directing, bundling, and aligning filaments. The prokaryotic cytoskeleton is less well-studied but is involved in the maintenance of cell shape, polarity and cytokinesis ***(Schaletzky et al., 2007)***

Genetic Material

Two different kinds of genetic material exist: deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). Most organisms use DNA for their long-term information storage, but some viruses (e.g., retroviruses) have RNA as their genetic material. The biological information contained in an organism is encoded in its DNA or RNA sequence. RNA is also used for information transport (e.g., mRNA) and enzymatic functions (e.g., ribosomal RNA) in organisms that use DNA for the genetic code itself. Transfer RNA (tRNA) molecules are used to add amino acids during protein translation.

Prokaryotic genetic material is organized in a simple circular DNA molecule (the bacterial chromosome) in the nucleoid region of the cytoplasm. Eukaryotic genetic material is divided into different, linear molecules called chromosomes inside a discrete nucleus, usually with additional genetic material in some organelles like mitochondria and chloroplasts ***(Alberts et al., 2002).***

A human cell has genetic material contained in the cell nucleus (the nuclear genome) and in the mitochondria (the mitochondrial genome). In humans the nuclear genome is divided into 23 pairs of linear DNA molecules called chromosomes. The mitochondrial genome is a circular DNA molecule distinct from the nuclear DNA. Although the mitochondrial DNA is very small compared to nuclear chromosomes, it codes for 13 proteins involved in mitochondrial energy production and specific tRNAs.

Foreign genetic material (most commonly DNA) can also be artificially introduced into the cell by a process called transfection. This can be transient, if the DNA is not inserted into the cell's genome, or stable, if it is. Certain viruses also insert their genetic material into the genome ***(Alberts et al., 2002).***

Organelles

The human body contains many different organs, such as the heart, lung, and kidney, with each organ performing a different function. Cells also have a set of "little organs," called organelles, that are adapted and/or specialized for carrying out one or more vital functions. Both eukaryotic and prokaryotic cells have organelles but organelles in eukaryotes are generally more complex and may be membrane bound.

There are several types of organelles in a cell. Some (such as the nucleus and golgi apparatus) are typically solitary, while others (such as mitochondria, peroxisomes and lysosomes) can be numerous (hundreds to thousands). The cytosol is the gelatinous fluid that fills the cell and surrounds the organelles ***(Campbell et al., 2006).***

Cell nucleus – eukaryotes only - a cell's information center

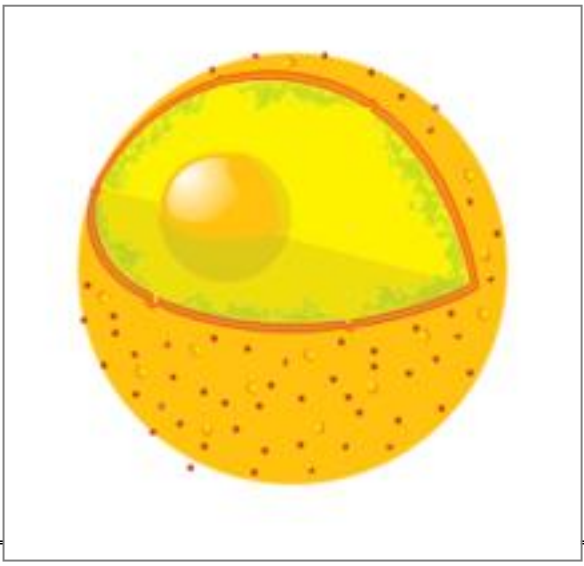

Figure (5): Diagram of a cell nucleus ***(Michie et al., 2006).***