A Review on Regulation of autophagy by microRNA in human breast cancer

By

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Declaration

It is hereby declared that

1. The thesis submitted is my/our own original work while completing degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

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Approval

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This study does not involve any human and animal trial.

Abstract/ Executive Summary

A conserved catabolic process called autophagy involves the recycling of cytosolic organelles or components via a lysosome-dependent pathway. A number of disorders, such as Alzheimer's disease, Parkinson's disease, and cancer, are linked to abnormalities in autophagy. According to the current theory, autophagy appears to act as a tumor suppressor during the early stages of the development of cancer, but as the disease progresses, autophagy may promote and/or assist the growth and spread of the tumor as well as make it more resistant to treatment. Autophagy is therefore regarded as a stagedependent dual player in cancer. Endogenous non-coding short RNAs called microRNAs (miRNAs) control posttranscriptional gene expression in a negative manner.Additionally, mounting evidence from the literature suggests that dysregulation of miRNA expression affects how cancer forms, invades, metastasizes, and responds to chemotherapy or radiotherapy. As a result, research on autophagy-regulating miRNA in cancer will aid in the creation of new disease indicators and therapeutic approaches as well as a better understanding of malignancies given the significance of autophagy for cancer biology. Several of these cancer-related miRNAs may be studied since they have a role in controlling autophagy. We will concentrate on autophagy, miRNA, risk factors, cancer diagnosis, and cancer treatment in this review.

Keywords : tumor suppressor, endogenous, microRNA,transcriptional gene expression,dysregulation,radiotherapy,chemotherapy,malignacy,cytosolic organelles.

Dedication

Dedicated to all young women

Acknowledgement

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List of Acronyms

ASIR: Age-standardized incidence rates

LCIS : lobular carcinoma in situ

DCIS : .Ductal carcinoma in situ

ILC : Infltrating lobular carcinoma

CCND1 : Cyclin D1

DALYs : Disability-Adjusted Life Years

NIBC : Non-invasive breast cancer

IBC : Invasive breast cancer

MRI : Magnetic resonance imaging

ROQ :Reactive oxygen species

HCQ: Hydrochloroquine

CQ : Chloroquine

Baf,A1: bafilomycin A1 3-MA : Three methyladenine mTOR: The mammalian target of rapamycin

AMDK : Activated protein kinase

AKT : Protein kinase B

RAS : Rat sarcoma

UVRAG:UVradiation resistance-associated gene

PET: Polyethylene terephthalateOT

EMT : Emergency Medical Technican

Chapter 1

1.1.Introduction

The most common form of cancer in women globally, breast cancer is treatable in between 70 and 80 percent of early-stage patients. The cancer spreads to other parts of the body if untreated. Different treatment approaches are used in people who have been diagnosed with breast cancer.Various methods of management, such as targeted therapy, hormone chemotherapy, surgery, radiation therapy, and nal therapy.Managements are used in people with distant metastases when typically intended to improve survival rates and quality of life.

MicroRNAs (miRNAs) are 18–25 nucleotide long, single-stranded, endogenous non-coding RNAs (ncRNAs). Moreover, autophagy is a conserved, common, and significant cellular catabolic and degradative activity that strives to preserve cellular homeostasis.Non-communicable diseases associated with autophagy, such as cardiovascular disease, neurological disease, and skin disease, can be further classified as malignant or non-cancerous. Colorectal cancer, gastric cancer, breast cancer, lung cancer, leukemia and lymphoma, ovarian cancer, and a few other cancers are among the malignancies linked to autophagy dysregulation. Autophagy is crucial for giving cancer cells the nutrition they need to develop while also getting rid of useless cellular macromolecules that can endanger the cancer cells. In other words, a number of miRNAs have been demonstrated to have the ability to either

up- or down-regulate cellular autophagy, which would ultimately increase or repress the evolution of breast cancer. (Gozuacik,2017)

1.2.Breast Cancer Epidemiology

Malignant neoplasms cause 106.9million Disability- Adjusted Life Years (DALYs) in worldwide.Each year, 2.26 million new cases of breast cancer are recognized in women worldwide. According to the 2018 GLOBOCAN statistics (HDI),ASIR of breast cancer are highly and favorably linked with the index of Human Development. Breast cancer kills more young aged women than other cancers, in addition to being the most common. (Akram et al.2017) Breast cancer claimed the lives of 684,996 people globally.Despite having the highest incidence rates, Asia and Africa accounted for 65% of all deaths worldwide in 2021.Breast cancer survival rates are greater for women in developed countries than under developed countries.

1.3.Aim of the project

The main goals of treatment for breast cancer are typically palliative because it is commonly thought to be incurable. Yet, the goal in the metastatic context has changed with the development of newer agents: extending survival. Even though long-term survival rates are modest, many patients are now living longer with few

disease-related symptoms because to the primary goals of treatment, such as advancements in time to progression and duration of response. Researchers are constantly working to develop novel medications or therapeutic approaches. One of these is autophagy, a conserved catabolic process that involves the recycling of cytosolic organelles or components via a lysosome-dependent pathway. The project's goal is to comprehend drug resistance mechanisms, which are valuable and have clinical relevance.The project's objective is to comprehend medication resistance mechanisms, which are crucial and clinically significant for enhancing the prognosis of breast cancer. and to ascertain when to boost or inhibit autophagy, as well as when to regulate the particular autophagic process, in order to make breast cancer cells more responsive to treatment.

1.4.Objectives of this study :

1)To understand the prevalence of breast cancer.
2)To identity risk factors that should prompt.
3)To create awareness among young women

Chapter 2

2.1.Etiology

In general health screening for women, determining characteristics linked to a higher risk of breast cancer development is crucial. Several major categories can be used to classify breast cancer risk factors:

2.1.1.Age: As the female population becomes older, the age-adjusted incidence of breast cancer keeps rising.

2.1.2.Gender: Women are the main victims of breast cancer. Personal breast cancer history A second primary malignancy in the contralateral breast is more likely if one breast has a history of cancer.

2.1.3.Histologic risk factors: One significant group of breast cancer risk factors is histologic abnormalities identified by breast biopsy. These abnormalities include proliferative alterations with atypia and lobular carcinoma in situ (LCIS). (Yisheng ,2017)

2.1.4.Genetic risk factors with breast cancer in the family history: First-degree relatives of breast cancer patients have a 2- to 3-fold increased risk of getting the illness.Genetic factors may be the cause of 5% to 10% of all breast cancer occurrences, but they may also be the cause of 25% of instances in women under the age of 30. The two most significant genes linked to an elevated risk of breast cancer are BRCA1 and BRCA2. (Elizabeth ,2020)

2.1.5.Reproductive risk factors: A woman's lifetime estrogen intake is thought to be increased by reproductive milestones, which may raise her risk of developing breast cancer. These include menarche beginning before the age of 12, the first live birth occurring after the age of 30, nulliparity, and menopause occurring after the age of 55.

2.1.6.Exogenous hormone use: Progesterone and estrogen are used therapeutically or in supplemental amounts to treat a variety of conditions. The two most frequent uses are contraception in premenopausal women and hormone replacement therapy in postmenopausal women.

2.1.7.Cancer and genetic factors :

Breast cancer is a very diverse illness that arises from the interaction of environmental and genetic risk factors. It causes breast cancer cells to gradually accumulate genetic and epigenetic alterations. (Cathcart-Rake et al,2020) The best epidemiological evidence for breast cancer is familial history, notwithstanding the existence of other risk factors (such as age, obesity, alcohol consumption, and lifetime estrogen exposure). Nearly 20% of all breast cancers are familial in origin and etiologically linked to a particular predisposing gene. (Ruddy ,2018)

2.1.8.Nutritional factors and breast cancer: Weight gain and high calorie intake are two nutritional factors that contribute to the development of breast cancer. According to Kopans and Greenwald, post-menopausal women with high BMIs and obesity have an increased risk of breast cancer, whereas premenopausal women do

not. Research findings originally demonstrated in 1940 that an increase in fat consumption causes breast tumors in animals. In general, it's unclear how breast cancer risk relates to other factors. On the one hand, calorie intake causes weight growth and obesity; on the other, it causes preterm menopause and increased height in youth. Both of these elements can set the stage for cancer growth in the future.

2.1.9.BRCA1 and breast cancer : Hormonal variables are the main non-genetic risk factors for breast cancer. For instance, gender, menopause and menarche ages, reproductive history.It is possible to bring up breastfeeding and the use of exogenous estrogen. Most frequently, menopausal women with high estrogen receptor expression develop non-genetic breast cancer. In the development of breast cancer, estrogen plays at least two key roles:

(1) Estrogen metabolites can alter DNA or produce DNA-damaging free radicals, and (2) estrogen's hormonal activity can promote cell proliferation in precancerous and cancerous tumors. In addition, additional processes are also implicated in the development of breast cancer because a substantial component of breast carcinoma is estrogen-receptor negative.By the ages of 50 and 70, respectively, a BRCA1 mutation increases the risk of breast cancer to 51% and 85%; it also increases the risk of ovarian cancer to 23% and 63%, respectively. (Akram et al,2017)

2.1.10.Lifestyle and environmental factor :

Lack of physical activity: Living a sedentary lifestyle with minimal exercise can raise your risk of developing breast cancer.

Poor Diet: A diet low in fruits and vegetables and heavy in saturated fat can raise your risk of breast cancer.

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Table 1: Additional genes associated with breast cancer

Gene	Function	Abnormality in breast cancer	Reference

P53	Tumor supressor gene	Mutation in 30% of breast cancer	(Varna et al.2011)
PTEN	Tumor supressor gene	Loss of PTEN protein expression in up to 33% of breast cancers	(Loibt et al.2016)
CDH1	Tumor supressor gene	Inactivation of CDH1 in 85% of lobular breast carcinomas	(Desmedt et al.2016)
Maspin	Tumor supressor gene	Expression of Maspin in 20-80% invasive breast cancer	(Berardi et al.2013)
CCND1	Oncogene	Overexpression in 50% of breast tumors	(Inoue et al.2015)
RB1	Tumor supressor gene	Rb1 inactivation in 20-35% of breast cancer	(Cheng et al.2010)

2.2. Types of Breast Cancer

There are two types of breast cancer: invasive and non-invasive.

2.2.1.Non-invasive breast cancer (NIBC) :

It is a malignancy that has not spread beyond the ducts or lobules in which it is located. Ductal carcinoma in situ is a type of non-invasive breast cancer. When abnormal cells form inside milk ducts but do not spread outside the milk ducts or to nearby tissue, the condition is known as ductal carcinoma in situ. (Akram et al,2017)

2.2.2.Lobular carcinoma in situ (LCIS):

The most common classification for lobular carcinoma in situ is non-invasive breast cancer. Breast lobules form as a result of this type of breast cancer. (Inoue ,2017)

2.2.3.Ductal carcinoma in situ (DCIS):

It is the type of non-invasive breast cancer that affects the breast duct only and is the most prevalent. Ductal comedocarcinoma is an illustration of ductal carcinoma in situ. (Nakhlis ,2003)

2.2.4.Invasive breast cancer (IBC) :

Cancer that has spread to nearby healthy tissue from the breast, where it first started. Invasive ductal carcinoma, the most prevalent form of invasive breast cancer, starts in the lining of the milk ducts.(Harris,et al.2016)

2.2.5.Infltrating lobular carcinoma (ILC):

A related term for invasive lobular cancer is invasive lobular carcinoma. ILC begins in the breast milk glands but frequently spreads to other parts of the body (Arpino,et.al.2004)

2.3.Stages of breast cancer :

There are four stages of breast cancer such as:

2.3.1. Stage 0 :

In the ductal cell carcinoma in situ tumor stage, which is a type of a non-invasive tumor stage, are accommodate within the confines of the breast region where the tumor first manifests and there is no indication of their invasion of the tissues nearby. (Bednarek,1997)

2.3.2. Stage 1 :

This is referred to as invasive breast cancer, and microscopic invasion is still possible.It is divided into two stages: stage 1A and stage 1B. A tumor up to 2.0 cm in size with no lymph nodes involved is classified as category 1A, but a small cluster of cancer cells which is greater than 0.2 mm is classified as stage 1B. (Segal,2001)

2.3.3. Stage 2 :

Two categories: 2A and 2B. Stage 2A which represents a malignancy seen in the sentinel or axillary lymph nodes .The tumor's size might range from less than 2 to 5cm. Stage 2B, on the other hand, states that the tumor maybe greater than 5.0 cm but cannot reach the axillary lymph nodes (Moran,2014)

2.3.4. Stage 3:

Three subcategories: 3A, 3B, and 3C. Stage 3B is defined as a tumor of any size that has caused irritations or an ulcer on the skin and has spread to up to 8 axillary lymph nodes , whereas stage 3A is defined as a tumor that is not found in the breast but may be found in 4 to 8 axillary lymph nodes . Infammatory breast cancer, also known as stage 3B breast cancer, is distinguished by red, hot, and swollen breast skin. Stage 3C, on the other hand, denotes tumor development to 10 or more axillary lymph nodes. (Jacquillat,1990)

2.3.5. Stage 4:

This stage is metastatic, and it demonstrates how the disease has spreadout to body organs such as the liver, lungs, bones, , brain, and others. (Neuman,2015)

Chapter 3

3.1.Breast cancer in young women

Before the age of 40, 5 to 7% of patients in the industrialized world are diagnosed with breast cancer, making it mostly an old people's illness. A larger percentage of individuals are diagnosed breast cancer before the age of 40, up to 20%, in less developed places like Africa and the Middle East where population based screening is not common and people are generally considerably younger. There is continuing research to establish whether there are genetic abnormalities or environmental factors that may make African and Middle Eastern women more likely to contract the disease at a young age. (Ferlay et al. 2008) Nonetheless, even when more aggressive therapies are used, young age at breast cancer diagnosis has become recognized globally.

In younger patients, there seems to be a difference in the expression of important biomarkers, such as endocrine receptors, HER2, and proliferative markers. Younger women are more develop more aggressive tumor subtypes, recent studies have made an effort to account for these subtypes. According to two studies, young patients with liminal B malignancies may have particularly poor outcomes when compared to older women. Two investigations indicated that young patients with luminal-B cancers often had worse outcomes than older women. (Sidoni et al. 2003). It was

expected that until ten years ago younger patients were not administered standard hormonal therapy and that young patients have lower compliancy with hormone therapy. Although young luminal-B patients had worse outcomes, a study of women who did not get systemic adjuvant therapy also found this to be the case. These findings suggest that biological differences may contribute to the more aggressive nature of malignancies in younger patients.We go through theain characteristics of breast cancer which is developed in younger women, the newly discovered link to reproductive activities including pregnancy and breastfeeding, as well as any potential clinical repercussions.(Howard et al. 2012)

Table 2 : Unique features of young age breast cancer compared to breast cancer in older women :

Consideration	Unique features	Reference

Biological characteristics	Higher proliferation rates,more gradws ¾ & higher ER negativity,more BRCA1/2	(Walker et al.1996)
Diagnostic delay	More advanced stage at presentation	(Barber et al. 2004)
Progmosis	Worse in ER-Positive breast cancer 5% increased risk of death/1-year reduction in age	(Ahn et al.2007)
Local therapy	More IBTR Higher importance of sufficiant resection margina	(Fourquet et al.1989)
Adjuvant chemotherapy	Less chemotherapy-induced amenorrhea Greater benefits from chemotherapy	(Goldhirsch et al.2001)

3.2. Effects of pregnancy on breast cancer biology :

Studies done decades ago have shown that pregnancy increases breast cancer risk temporarily but has a long-term beneficial effect. Numerous large studies have recently looked at the relationship between different reproductive behaviors and

both the risk and phenotype of acquiring breast cancer. According to recent studies, parity may protect against the development of ER-positive malignancies at the expense of a disproportionately higher incidence of individuals with triple-negative cancer, especially in the absence of nursing care(Azim et al. 2012).

Contrarily, breastfeeding appears to provide protection against triple-negative breast cancer. This holds true for BRCA1 carriers as well, who have been shown to have a 32% or 49% decreased risk of breast cancer, respectively, after breastfeeding for a year or two. It is unknown from a biological standpoint how breast cancer risk is impacted by pregnancy and nursing. Russo and colleagues discovered significant differences between the gene expression profiles of microdissected epithelial cells from normal breast tissue from 41 parous and 8 nulliparous post-menopausal breast cancer patients and those of 18 parous and 7 nulliparous post-menopausal women without breast cancer (Schedin et al.2006).They found that people with parous non-cancer had unique gene expression patterns, including differential expression of genes related to apoptosis and others involved in cell cycle and cell signaling.

It was implied that being pregnant might set off a protective signature against breast cancer. It was unable to guarantee that none of the women in the parous non-cancer group went on to develop breast cancer because of the study's limited sample size and lack of long-term follow-up. The expression of ER and genes associated with inflammation was higher in the parous groups, although ER, PgR, and HER2

expression was lower. The groups of women who were recently and distantly pregnant had no discernible changes.(Obrein et al 2010)

Chapter 4

4.1. Mechanism of action of autophagy

The five major stages of the autophagic route are initiation, elongation, maturation, fusion, and degradation.

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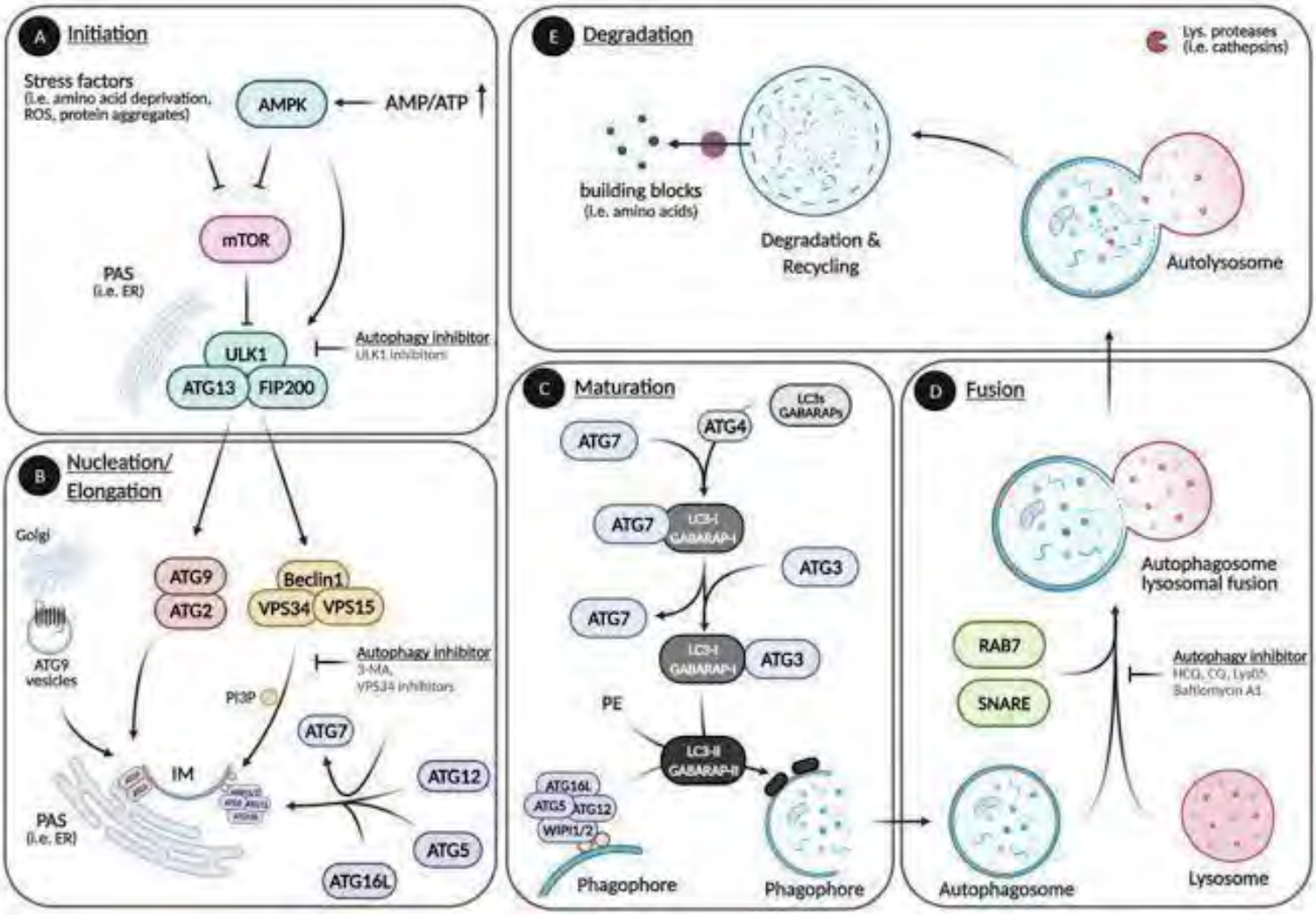
nes.

Figure1:Molecular mechanism of autophagy



Chapter 5

5.1. The role of autophagy in cancer

Autophagy's principal responsibilities include the degradation of worn-out organelles and obsolete proteins, as well as the maintenance of cellular homeostasis. Autophagy promotes and controls tumor growth while simultaneously boosting

cancer cell proliferation and division in cancer biology. (White,2015)Autophagy can be controlled by a few anticancer drugs. As a result, autophagyregulated chemotherapy can influence cancer cell survival or death. Autophagy regulation also influences the expression of oncogenes and tumor suppressor proteins. Because of the negative regulation of tumor suppressor factors by mTOR and AMPK, autophagy is triggered and cancer progression is prevented.mTOR, class I PI3K, and AKT, on the other hand, may activate oncogenes, reducing autophagy and increasing cancer growth. (Choi,2013)

Reduced and abnormal autophagy in oxidatively challenged cells hinders the breakdown of damaged proteins or components, promoting cancer growth. Furthermore, basal autophagy is thought to be a cancer-fighting mechanism. (Wang,2018).Autophagy proteins that are important for tumor suppression can alter. A variety of cancer types, including colorectal and gastric cancer, have been linked to abnormal or absent BIF1 proteins that are linked to BECN1. UVRAG proteins, in addition to BECN1, act as autophagy regulators. The UVRAG mutation reduces autophagy in colorectal cancer cells, boosting cancer cell proliferation.Certain RAS-activated cancer forms, such as pancreatic cancers, have high baseline levels of autophagy. As a result, autophagy plays a role in tumor formation and control.(Yang,2014)

5.2Regulations of autophagy by MIRNAS in breast cancer

Autophagy both inhibits and stimulates tumor growth in a variety of cancers. Furthermore, autophagy affects stem cell of cancer characteristics by assisting stem cell preservation, managing tumor recurrence, and enhancing treatment resistance. Autophagy is another function that it balance miRNAs in breast cancer cells. MiR-20a is one of the miRNAs that is increased in breast cancer, namely in triplenegative breast cancer cells. The activity of the autophagy/lysosome pathway has been demonstrated to be negatively associated with miR-20a expression. MiR-20a inhibits lysosomal-associated proteolysis action .Furthermore, this miRNA alters a variety of key autophagy regulators, such as BECN1, ATG16L1, and SQSTM1. BECN1, ATG16L1, and SQSTM1 genes, in particular, have been found to be downregulated in triple-negative cancers. Furthermore, miR-20a upregulation has been linked to a greater incidence of a number of differences and changes in genetic conditions in breast cancer samples. The imapct of miR20a on the enhancement of cancer and proliferation is established in a breast cancer model which is called xenograft. Several miRNAs were increased, which decreases basal induced autophagy. As a result, by influencing the expression of RB1CC1/FIP200, miR-20a and miR-20b can modulate autophagy.According to study, miR-25 is the main target of ISL for activating flux of autophagy . Furthermore, mechanistic studies show that reducing miR-25 induces autophagy via raising the ULK1.ISL autophagy

can be cured by rising the expression of miR-25 .ISL create cancer cells more sensitive to chemotherapeutic treatments by upregulating miR-25, decreasing LC3-II, and activating ULK1.

Chapter 6

6.1.Diagnosis

6.1.1.History and Physical Examination : Family history and personal history should be identified.Personal history means age,if she has previously diagnosed breast biosies or not or if she has used other treatment options for the prevention of breast cancer.Family history means if any member of her family has ovarian cancers or not,or if any members of relatives has first stage of breast cancer or not. (Barclay et al. 1993)

Patients should checkup their weight,if she has pain in bone or not,if she tired or not or if she has breast pain or not,it should be examined carefully. (Rosso et al.2014) Other examinations should be done such as neck surrounding area,armpits,collarbone.Breast are evaluate for any malformation for example :lymphs or lymp nodes should checkup as it can be enlarged during breast cancer (Lichi et al.2014)

6.1.2.Nuclear Medicine : It is a therapy which uses a radioactive material that bind to cancer tissues and these radiotracers destroy the cancer cell.Combining CT with gamma cameras and CT with PET is a significant advancement in improving disease detection and localization (Husarik et al. 2007)

6.1.3.Breast Biopsy : Among all the process, breast biopsy is the best for the diagnosis of breast cancer and it is a technique to remove a breast tissue .There are

several types of breast biospies.It is the best way to evaluate if the lump in your breast cancerous or not. (Kanter et al,2003)

6.1.4.Surgical Biopsy : It is a technique that involves the surgical removal of a abnormal tissue for checkup under a microscope.In order to minimize the quantity of tissue taken, nonsurgical core needle biopsies are frequently advised for the diagnosis of breast cancer. (Karg et al.1993).Using a needle biopsy for diagnosis lowers the number of people who undergo unnecessary surgery because many people who are advised to get a breast biopsy do not have cancer. (Lyman et al. 2014)

6.1.5.Diagnostic Mammography : It is comparable to screening mammography, with the exception that additional breast images are taken. When a person exhibits symptoms, such as a new lump or
nipple discharge, it is frequently used. If a screening mammogram reveals anything worrisome, diagnostic mammography also
be used. (Abdulkareem et al. 2014)

6.1.6.Estrogen and progesterone receptors: This tests give information about the aggressiveness of cancer and also shows the response of drugs which are used for the identification of breast cancer.

6.1.7.Magnetic Resonance Imaging (MRI) : It is used to detect breast cancer and to determine or measure the condition of the cancer or abnomalities of the breast tissues.It shows a clear image of breast tissues and also shows more accurate results.

6.1.8.Ultrasound Breast Imaging : It shows the location and size of the tumor either is filled up with liquid or solid or it should be biopsed (Kelly et al. 2010)

Chapter 7

7.1. Treatment

It mainly depends on the types of the breast cancer or stage of the tumor or size of the tumor. (Ellis et al. 2017) There are several treatment options :

7.1.1.Surgery : Depending on the situation or nature of the tumor ,there are several types of surgery are involved. Surgery has been done to remove the tumor of the breast tissues and it determine if the cancer has spreadout to the lymph nodes and it is also used for breast reconstitution that means to get back the shape of the breast after the tumor is removed. (Ellis et al. 2017). Most familiar surgery includes :

7.1.2.Lumpectomy : It is a surgery that removes abnormal tissues and a small piece of normal healthy tissues around it.It helps to prevent the regrowth of tumor and it is best for early stage of breast cancer.

To restore the chances of regrowth of cancer,lumpectomy is followed to remove cancer by radiation therapy.After the surgery, you may feel pain and get tired. Around the incision, your skin may feel bruised, tender and swollen and Tenderness will go away within three or four days and the bruishing will go away within three weeks and swelling may last for a long time.(Fisher et al. 1995)

7.1.3.Mastectomy : It is a surgery which is used to prevent a breast cancer by removing all breast tissues and it is best for early stage of breast cancer.

During mastectomy surgery, breast reconstitution has done to get back the normal shape.However, most women experience despair as a result of losing their breasts since it causes them to feel asexual and lose their sense (Tuttle et al.2007)

Chapter 8

8.1.Discussion :Large number of miRNAs are involved in the progression of breast cancer and by regulating Autophagy techniques, it influence treatment response. Four miRNAs are involved in breast cancer cells to supress autophagy. One miRNA is involved to encourage chemoresistant and others are involved in chemosensitivity.miRNA and the modulation of autophagy plays an important role in cellular modulation and tumorigenesis.It also helps to suppress tumorigenesis and promote sensitize the cells of breast cancer. By regulating both apoptosis and autophagy,it enhance the PAD2 protein expression and sensitize the cells of cancer towards tamoxifen.The level of miR-125b-5p should be observed in cancer patients because by doing that it helps to monitor the progression of disease and influence the treatment response by others therapy.

However, miRNA plays a major role as a therapeutic agents by inhibiting the progression of breast cancer cells and only miR23b-3p helps to promote resistance and autophagy in breast cancer and others promote autophagy and tamoxifen resistance. And an autophagy has an ability to expend tumor promoting and suppressing effects.The dysregulation of autophagy can able to promote a specific tumor therapy. Autophagy play a duel role in promoting cancer suppression and progression.It also helps to provide nutrients for the cells of cancer to grow and

eliminate macromolecules but there is excessive autophagy it may lead to apoptosis or cell death.

Chapter 9

9.1. Conclusion

One of the most common and rapidly spreading cancers was and is breast cancer. Breast cancer is an illness that consumes a lot of material and spiritual resources while involving the patient, family, and community. This cancer develops in the ducts and lobules of the breast. Although it rarely occurs in men, breast cancer is not a gender-specific disease. Specific risk factors have been found, despite the fact that the cause of breast cancer is unknown. There are various risk factors for various cancers. A few of these risk factors, like smoking cigarettes, drinking alcohol, and food, are modifiable and influenced by a person's lifestyle. Other elements, such as age, color, gender, and family history, are set and unavoidable, though. Even if you have one or more of these risk factors, you may not really be afflicted.(Hadden,1992)

Although several of these risk factors raise the likelihood that breast cancer will develop and advance, the precise process by which this happens is unclear. Although the development and progression processes of some forms of breast cancer remain unclear, it appears that hormones play a significant role in these diseases. Overall, it can be stated that aging, family history of breast cancer, specific breast abnormalities, genetic changes, menopause history, a lack of physical exercise, alcohol use, food and nutrition, race, and chest radiation therapy are all risk factors for breast cancer.Different physical, mental, and social facets of a woman's life are affected by this disease. (wright et al. 2012)

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