CHAPTER 2

REVIEW OF LITERATURE

Greenlee, R.T. et al. (2001) mentioned that, as per American Cancer Society, more than one million cancer patients have been reported in 2001 and approximately fifty percent of the population was died. The total occurrence of malignancies against rates of mortality have been decreasing year by year in males and females in early 1990s and the decline in total death but cancer was enhance in latest tenure. The existence of patients of cancer shows the poor detection of disease of cancer at advanced condition of disease and inferior existence within each stage of finding.

Cancer Research UK (2012) says that more than ten lacs female are detected with cancer on breast tissue every annum. The data has been generated by collective study of samples from different European countries including 41523 cases from England, 2569 from Wales, 4578 from Scotland, 1266 from Northern Ireland and 49936 cases from other places.

Rodney, C. et al. (2003) mentioned that over 90 percent of cancer in breast tissue are are generated by epithelial elements of breast and cancer in breast has been categorized into two main subtype, i.e. non-invasive carcinomas (in-situ) and infiltrating carcinomas (invasive). The non-invasive carcinomas (in situ) may be arises in lobular or epithelium of ducts, but stay limited without invasion to other tissue hence negligible possibility of metastases. Extension of the ductal or lobular malignancy outside the basement membrane can constitute the malignancy and it is considered invasive.

Beiki, O. et al. (2012) studied on breast cancer of women of Sweden and collected the data between 1961 and 2007 for threat ratio with nintyfive percent sureness tenure and incidence rate ratio (IRR). They found that the incidence of cancer in breast cells is inferior in between immigrants but not in immigrants daughter or native Swedes. They mentioned that the incidence and case fatality is significantly depends on age at immigration and duration of residence.

Duffy, M.J. (2001) demonstrated that approximately one in eleven developing the malignancy and one in therty dies from the breast carcinoma. He mentioned that the ER and PR are the greatest valuable biomarkers in cancer of breast that used to predict the response to hormonal therapy. Cancer antigen CA15-3 along with CA 27.29 is furthermore encouraging markers for the diagnosis of cancer of breast.
Daniele, A. et al. (2013) analyzed the preoperatively and postoperatively serum samples of 726 breast carcinoma patients for CA 15-3 by chemoluminescent immunometric assay (CLIA). They found that mean of the serum concentration of cancer antigen 15-3 in pre-surgical patients were significantly higher compared with those of post-surgical patients which is interrelated with the incidence of disease with metastatic characteristic and concluded that increased concentrations of cancer antigen 15-3 before operation may be a convenient prognostic biomarker for progression of cancer in postoperative patients.

Laessig, D. et al. (2007) examined 119 patients sample of cancer of breast and evaluated the presence of cancer antigen 15-3 along with CEA at first reappearance and at every advance progression of disease. They found that elevated levels of cancer antigen 15-3 and CEA were establish in correlation to disease progression. They concluded the correlation of elevated level of cancer antigen 15-3 and CEA with disease progression of metastatic breast carcinoma.

Duffy, M.J. et al. (2004) measured the concentration of cancer antigen 15-3 in six hundred prospectively clinical samples having histologically confirmed cancer in breast. They found that after follow-up of more than six years, patients had short survival pattern with high concentrations (preoperative) of cancer antigen 15-3 (greater than thirty units per liter) than patients with short amount of CA15-3. The level of cancer antigen 15-3 was self-governing of status of node (axillary), tumor size along with stage of patients.

Gion, M. et al. (1999) have studied to measures the cancer of breast linked glycoprotein cancer antigen 27.29 and compared the cancer antigen 27.29 concentration with cancer antigen 15.3 in primary breast cancer. They concluded that measure of cancer antigen 27.29 differentiates primary cancer of breast from normal individual superior than cancer antigen 15-3.

Begum, M. et al. (2012) have done the immunohistochemistry for the measure of Her 2 receptors, ER, PR expression and found positive in 50% and 65% in premenopausal and postmenopausal women respectively. CA15-3 was measured by ELISA kit. They have concluded that, numerous physiological factors involved in breast cancer includes high level of CA15-3, ER, PR and Her2/neu hormonal imbalance in the body.
Sliwowska, I. et al. (2006) demonstrated the diagnostic importance of measuring cancer antigen 15-3 (CA15-3) along with TPS and TPA in breast carcinoma patients. They found that TPA has good diagnostic sensitivity for cancer present in breast tissue and they reported the sturdy relationship between level of all 3 diagnostic markers and the advancement of breast cancer.

Klee, G.G. and Schreiber, W.E. (2004) mentioned that cancer antigen 15-3 is a merged outcome of mucin 1 gene which is mucinous carbohydrate antigen originally identified by two mAb which is 115D8 mAb raised against membrane of milk fat globule and DF3 mAb developed against a membrane portion of metastatic liver.

Kufe, D.W. (2013) demonstrated that several circulating mucinous markers including cancer antigen 15-3 is a secreted antigen of the polymorphic mucin 1 and utilized as biomarkers for diagnostic purpose of cancer of breast tissue. He demonstrated that transmembrane MUC1-C-terminal is a pharmacological target to designing agents which blocked function of MUC1-C. He also mentioned that, inhibition of the MUC1-C subunit inhibited its carcinogenic function and induced apoptosis of breast carcinoma cells in xenograft model and in vitro model.

Parry, S. et al. (2001) have demonstrated that mucin1 is a large glycoprotein of 1255 amino acid with theoretical protein molecular weight 122 kDa without any glycosylation or without any post translational modification. MUC1 have three domains including extracellular topological domain containing 1-1161 amino acid residues, transmembrane region containing 1162 to 1179 amino acids and a cytoplasmic topological domain containing 1180 to 1255 amino acids.

Baldus, S.E. et al. (2004) mentioned that mucins are the family of glycoproteins having tandem repeats and have dense O-glycosylation. They have also mentioned that MUC1 is involved in interaction with the immune system and in cell adhesion and mucin 1 is regulated by several hormones and cytokines.

Steeg, P.S. (2006) mentioned that mucin 1 (MUC1) is extensive studied mucin for cancer of breast tissue diagnostics. It is a transmembrane member glycoprotein, associated with metastatic progression. Numbers of steps are involved in tumor progression to become metastatic, includes intra-vasation and extra-vasation, invasive capacity, colonies formation and localized to other parts.

Kaur, S. et al. (2014) demonstrated that expression of mucin 1 along with mucin 4 in urothelial carcinoma (UC) and found the increase concentration of mucin 1 and
decrease expression of mucin 4 in UC. The results suggest differential expression of mucin 1 and mucin 4 genes during the expansion and advancement of cancer in bladder.

**Gendler, S.J. (2001)** mentioned that mucin 1 (MUC1) is one of the large, glycosylated mucin present on the surface of gastrointestinal, urinary, respiratory, mammary gland and reproductive tracts. Its expression with heavily glycosylation is also reported in hematopoietic cells and reported for protection and provides lubrication of epithelial surfaces. MUC1 is also reported for its capability of interaction with different proteins and participate in cell adhesion and signal transduction.

**Lavrsen, K. et al. (2012)** has mentioned that in cancer condition, changes in glycosylation pattern of protein are very common phenomena which forms cancer related carbohydrate antigens. They reported that MUC1 humanized mice and human have not shown immuno- tolerance against Tn-mucin 1 in immuno-dominant cancer specific epitope. Mouse antibody mAb 5E5 antibody against Tn MUC1 revel the presence of Tn MUC1 epitope in cancer of breast tissue. 5E5 mAb also induced antigen dependent cell toxicity in T47D and MCF7 cell lines.

**McGuckin, M.A. et al. (1995)** mentioned for the conflict about the connection between survival in breast cancer patients and mucin 1 translation. They used monoclonal antibody BC 2 and performed immunohistological analysis of mucin 1 expression. They found that the existence of metastases in axillary node and estrogen receptors is closely related to the high translation of mucin1.

**Greenberg, R. et al. (2003)** worked on the mucin 1 and methylated hepatocytes growth factor prognostic value in axillary drainage in cancer of breast. They have collected the output of drains from mammary cancer patients and checked for the Met-HGF/SF and MUC1 by mRNA analysis. They have established that axillary fluids of individual with mammary cancer shows Met-HGF/SF and MUC1. The availability of both tumor biomarkers in axillary drainage of mammary cancer is closely related to progression of disease.

**Schroeder, J.A. et al. (2003)** have mentioned that mucin 1 interacts with receptors of erbB, GSK-3 beta, protein kinase C delta, beta-catenin and its complex which might be involved in the cells invasion in cancer. They reported that, if expression of MUC1 was deleted from transgenic mice(MMTV-Wnt-1), development tumor in mammary glands has taken more time. They also reported the interaction of MUC1 / beta-
catenin in primary human adenocarcinomas but found drastically increase in metastatic lesions.

**Park, S. et al. (2012)** studied on CA15-3 levels in different subtype of cancer and concluded that concentration of CA15-3 and MUC1 was found high in Her 2 positive patients of cancer of mammary and the data suggest for the therapeutic potential of CA15-3 in breast cancer with clinical trial studies.

**Budiu, R.A. et al. (2011)** have mentioned that the concentration of CA15-3 (a production of MUC1) and CA125 (a product of MUC16) tumor antigens are up-regulated in the blood of cancer of ovary. The increased concentration of both induced increased antibody response in platinum-resistant cancer of ovary which could be used for the therapeutic use of these antibodies. These antibodies can be IgM or IgG subtype.

**Wang, L. et al. (2007)** mentioned that MUC1 is tumor-associated antigen (TAA) responsible for tumorigenicity and cellular transformation and can be a good target for the for cancer therapy. They have evaluated the presence of mucin 1 in epithelial tissue of ovarian cancers (EOCs) and found that high expression of mucin 1 was reported in more than 90% of EOC late stage as well as in metastatic lesions. This data suggested using MUC1 antigen as therapeutic target for treatment and recurrence of EOC.

**Dong, Y. et al. (1997)** have first time described the correlation of MUC1 and MUC2 with ovarian cancer prognosis. They analyzed the tissues of epithelial ovarian tumours for the expression of mucin 1 and mucin 2 core proteins by immunohistochemical method and found high expression of mucin 1 in most of the primary low malignant potential tumours. So that low mucin 1 translation in cytosolic fraction could be a good tool for prognosis.

**Cozzi, P.J. et al. (2005)** have mentioned that researchers have great interest on mucins as theranostics target for human cancers. They examined different mucins include mucin 1, 2, 4, 6 and mucin 5AC from CaP tissues. They found that in 58% samples, the MUC1 concentration is high but the concentration of mucin 2, 4, 5AC and mucin 6 was found low.

**Retterspitz, M.F. et al. (2010)** have examined 94 diffuse and mixed type of subcardial carcinomas in gastric track and done the immunohistochemical study for the detection of presence of different antigens include mucin 1, β-catenin and c-Met. They found that c-Met has not shown any correlation while MUC1 has shown
correlation with metastasis of lymph node and stage. The data shown that they are independent predictor of a worse prognosis.

**Yonezawa, S. et al. (2012)** mentioned that MUC1 cytoplasmic domain have several function in the development of cancer and cell adhesion so that they have targeted to developed monoclonal antibody against MUC1 cytoplasmic domain and used synthetic 10 amino acid peptide having RYVPPSSTDRPYEKVSAG: N-1217-1235-C residues. They developed MUC1-014E mAb and found that this mAb is highly reactive to specimens of gastrectomy (90-95 %). They have shown that this mAb very useful for detection for scirrhous gastric cancers cells.

**Zhang, K. et al. (2009)** have been worked on mucin (KL-6) localization in the tissues of carcinoma of colorectal and cancer of liver tissues. KL-6 mucin having sialylated epitopes which was recognized by KL-6 Ab. They found all the samples with liver metastasis of hepatocellular carcinoma and colorectal carcinoma of were positive for KL-6. So that they concluded that KL-6 mucin might be utilized as diagnostic marker for liver metastasis and colorectal carcinoma and it can differentiate metastatic liver cancer from hepatocellular carcinoma.

**Mizumoto, M. et al. (2011)** mentioned that IPMNs i.e. Invasive type of ductal neoplasms of pancreatic tissue, have bad prognosis. They analyzed the presence of MUC1, MUC2, MUC5AC antigens along with p53 and Ki67 in IPMNs. They have segregated the samples in 4 groups including mucin 1 positive with p53 positive, mucin 1 positive with p53 negative, mucin 2 positive and mucin 1 negative with mucin 2 negative. They have reported that mucin 1, mucin 2 and p53 expression might be good indicators of malignancy, recurrence and tumor invasion.

**Xu, H. et al. (2011)** mentioned that KL 6 mucin 1 expression with aberrant glycosylation has been associated with inferior behavior of tumor in different carcinomas. They have established the expression and participation of KL 6 mucin 1 in carcinoma of pancreatic tissue. They also found that KL 6 mucin 1 over translation in the tissue of pancreas might have correlation with pancreatic cancer metastasis by regulation of E cadherin with bete catenin complex.

**Hamada, T. et al. (2012)** have worked on OSCC for the prognostic significance of DF3/MUC1 expression. By the help of immunohistochemistry they found that DF3/MUC1 expression with aberrant glycosylation is not dependent prognostic factor, representing inferior prognosis in OSCC patients. They concluded that the
translation of mucin 1 is a critical element for successive metastasis in lymph node in OSCC.

**Liu, X.Y. et al. (2007)** have tested different samples of esophageal squamous cell cancer (ESCC) patients with different disease conditions and determined the MUC1 mRNA concentration by RT-PCR and found that genetic diagnosis specificity was 30/30 (100.0%) for micrometastasis in occult lymph node and 27/30 (90.0%) for micrometastasis in lymph node.

**Leroy, X. et al. (2002)** studied on MUC1 and epithelial membrane antigen expression in immunohistochemical analysis, in renal cell carcinomas (RCCs). The stained cells percentage was calculated for each tumor and found that patients with significantly lower metastasis-free survival rate shown more than 70 % staining so that they concluded that Mucin 1 (MUC1 expression is directly proportional to metastasis in renal cell carcinomas (RCCs).

**Hasegawa, H. et al. (2011)** have reported that mucin 1 (MUC1) has been highly expressed in cells of adult T cell leukemia and T cells lymphoma. It was reported that high concentration of mucin 1 is accompanying with inferior prognosis which suggested that mucin 1 can be used as prognostic marker for ATL. On the bases of other studies and this result they have concluded that mucin 1 performed an crucial function in progression of T cell leukemia or lymphoma in adults.

**Kaira, K. et al. (2011)** studied on 55 patients of thymic epithelial tumors for the expression of mucin 1 (MUC1). Tissue section of thymic epithelial tumors were analyzed by staining using different immunology method for the presence of VEGF, MUC1 and microvessel density (MVD) which was determined by p53 and CD34. They found that high concentration of mucin 1 is directly associated with advancement of thymic epithelial tumors metastasis and the concentration of MUC1 is having direct correlation with p53, VEGF and MVD.

**Sanislo, L. et al. (2011)** have studied on migrating cells of tumor in the patients of carcinoma of breast tissue. They did immunomagnetic separation to get more malignant cells in blood because in normal blood the number of circulating cancerous cells is very low. By laser scanning cytometry (LSC), they analyzed the cells and found that 50 % sample was found positive for circulating tumor cells (CTCs) but they are not able to distinguish between normal cells of tumor cells because they have not gone through CD45 staining. They found that Her-2 positive shown CTCs.
Deng, G. *et al.* (2008) mentioned that circulating cells of tumor are detected in almost every type of cancer and there is a need to establish the system to monitor these cells in cancer. Because of less in number, enrichment of CTCs is required for detection. Anti-EpCAM antibody based technology is generally used for enrichment of CTCs with some limitations. They reported that malignancy specific intracellular CK marker would be more efficient for the enhancement of CTCs.

**de Albuquerque, A. *et al.* (2012)** done the study on circulating cells of tumors isolated from blood of cancer patients and analyzed by using panel of multi-marker. They used RT-PCR for isolation of mRNA as a tool for markers EPCAM, MUC1, KRT19, ERBB2, SCGB2A2 and BIRC5. They found good result with RT PCR technique and concluded that this approach using CTCs with multi-marker panel will provide the actual picture of disease stage and progression.

**Aktas, B. *et al.* (2011)** have reported that most of the CTCs are devoid of ER and PR. They worked on four hundreds primary breast cancer patients for expression profile of ER, PR, HER2 in CTCs and the primary tumor differs. It was found that in metastatic characteristic of CTCs reflects the characteristic feature of metastatic conditions.

**Thie, H. *et al.* (2011)** mentioned that specific and high affinity antibodies against MUC1 will be a promising target for therapy in case of breast cancers and ovarian carcinomas, but making this kind of antibody is difficult task. They isolated human scFv antibody against mucin 1 and after mutagenesis the affinity and stability of antibody was boost. This antibody also bound with MCF-7 and T47D cell line.

**Kruit, A. *et al.* (2010)** have mentioned that KL-6 is a mucin which is an epitope of MUC 12 detected by IL 6 antibody present in increased amount in lung diseases and in various other cancers. Cancer antigen 15-3 having same function as KL06 but having different epitope and hence antibody. They found that KL 6 and cancer antigen 15-3 are equally specific and sensitive for ILDs but because of low cost, availability make CA15-3 most possible marker for pulmonary fibrosis.

**Duffy, M.J. *et al.* (2000)** mentioned that cancer antigen 15-3 is promising diagnostic serum marker for cancer of breast tissue. Mucin 1 is likely to do a crucial function in adhesion of cells and its high expression with aberrant glycosylation may because of its involvement in cancer. They mentioned that prognostic potential of cancer antigen 15-3 is crucial tools other than tumor size and they concluded that cancer antigen 15-3 could be the first well established prognostic blood marker for tumor of mammary tissue.
Gonzalez-Sistal, A. et al. (2012) have studied on 340 women with breast cancer ductal carcinoma. Serum concentrations of CA15-3 were determined by an immuno-radiometric method. ER/PR receptors, androgen receptor, bcl-2, Ki67, p53 were determined by relative immuno-histochemical methods. They have concluded that serum level of CA15-3 is directly correlated with tumor progression.

Kaira, K. et al. (2012) reported that the concentration of depolarized mucin 1 was considerably accompanying with bad consequence and was strictly linked with hypoxia (HIF-1α), carbohydrate metabolism, amino acid metabolism (LAT1), angiogenesis (vascular endothelial growth factor and micro-vessel density) and EGFR expression.

Rakha, E.A. et al. (2005) have examined tumor that 1400 cases of invasive type of breast cancer for the presence of different mucins i.e. mucin 1, 2, 3, 4, 6 and mucin 5AC and its prognostic potential. They found that MUC1, MUC3, MUC4 was expressed in more than 90 % tumors. Other mucins like mucin 2, mucin 5Ac and mucin 6 were present in 8.3 %, 37 % and 20 % respectively. So most breast cancer expressed MUC1, MUC3 and MUC4 but MUC1 and MUC3 having strongest association with patient outcome.

Ghosh, M. et al. (2005) have reported that mucin 1 core protein would be a good antigen marker for gallbladder cancer. They used surgical specimens of gall bladder cancer and stain MUC1 with DF3 and CA15-3 monoclonal antibody. They found significant higher concentration of MUC1 in gallbladder cancer as compared to non malignant cells and the translation of mucin 1 was found much lower in case of non invasive conditions, so that mucin 1 would be a good diagnostic antigen marker for gall bladder malignancies.

Spicer, A.P. et al. (1995) have developed mucin 1 deficient mice by homologous recombination procedure in stem cells of embryo and check the development of mice. They found that mice grow normally in terms of health, fertility. They induce polyoma middle T antigen for the development of primary breast tumor into it and found that the growth of primary breast tumor was very slow. These results indicated that mucin 1 was involved in the tumor enhancement of breast tissue.

Schroeder, J.A. et al. (2004) have mentioned that mucin 1 having association with several other protein includes erbB receptors, beta-catenin and c-Src. They reported that multiparous transgenic mice (MMTV-MUC1) have developed carcinoma in mammary gland late in life. It was found that there was a co-immunoprecipitation of
MUC1 and beta-catenin in these tumors. So these finding suggested that overexpression of MUC1 promotes the in-vivo carcinogenesis of mammary gland.

**Pochampalli, M.R. et al. (2007a)** mentioned that transforming growth factor alpha (TGFalpha) is an effective cellular transformation inducer which functions through binding followed by triggering of EGFR. They also mentioned that mucin 1 prevents the ligand stimulated degradation of EGFR in epithelial cell lines of breast. They reported that MUC1 is one of the important modulator of tumor progression which is transforming growth factor alpha.

**Besmer, D.M. et al. (2011)** reported that over concentration aberrantly glycosylated MUC1 was observed in 60% of ductal adeno-carcinomas in pancreas. They have developed mouse model which developed pancreatic ductal adeno-carcinoma (KC) spontaneously, one was expressed MUC1 (KCM) and second was MUC1-null (KCKO). KCKO shown slower rate of tumor progression and secondary metastasis as compare to KCM. That shows the involvement of MUC1 in pancreatic ductal adeno-carcinomas disease progression.

**Finn, O.J. et al. (2011)** have mentioned that mice are generally used for the experimentation related to cell biology of cancer its initiation, progression, and metastasis. Several studies have been done to by implanting tumor in the mice and effect of drugs, survival and disease progression. They review mouse and genetic model for the humen adenocarcinomas based on a mutation of Kras type (MUC1 with aberrant glycosylation) which promotes metastasis and cancer progression.

**Rye, P.D. et al. (1996)** have mentioned that human cell line of mammary carcinoma MA11 was developed from cells which were isolated from a bone marrow sample by using BM 2 and anti mucin 1 antibody conjugated immunomagnetic beads. This cell line have shown selective favorite in athymic nude mice for metastasis. Injections of these cells in different organs have developed tumors.

**Gao, J. et al. (2009)** have mentioned that, in human lung cancer and in other cancer, there was aberrantly activator of transcription 3 and activation of signal transducer and this is linked in carcinogenesis and metastasis. They reported that activated STAT3 regulates MUC1 expression followed by progression of lung cancer progression and metastasis. So mucin 1 seems to be conjoining oncoprotein and would be a good target for the treatment of lung carcinoma.

**Tsutsumida, H. et al. (2006)** have down regulated the translation of mucin 1 by RNA interference in S2-013 cell line (human pancreatic cancer). Mucin 1 suppressed the
clones S2-013.MTII.C1/C2 and analyzed the effects on malignant and metastatic potential. MUC1 suppressed clones S2-013.MTII.C1/ C2 have shown reduced proliferation in in vitro and in vivo conditions significantly. They have concluded that mucin 1 is significantly contributed in the disease progression and metastasis in pancreatic adenocarcinoma.

**Mikami, Y. et al. (2009)** have demonstrated that malignant tumor have featured with hypoxia which enhanced the mucin 1 mRNA and protein concentration in cell line of adenocarcinoma of lung and it was mediated by of MUC1 promoter transcriptional activity. Even in the presence of CoCl which is an promoter element of hypoxia inducible factor (HIF)-1 alpha, mucin 1 mRNA expression was increased. They concluded that hypoxia enhances the MUC1 expression.

**Gaemers, I.C. et al. (2001)** have reported that presence of mRNA of episialin mucin 1 is increase upto ten times in carcinoma cells of breast tissue. They have found that five hundred bp upstream of site of transcription start of episialin MUC1 promoter that have binding site for STAT transcription factors responsible for overexpression of MUC1 in tumor cells.

**Aubert, S. et al. (2009)** demonstrated that mucin 1 is over translated in kidney cancer and signaling pathway of factor induced hypoxia is common as the important pathway of renal carcinogenesis. They have reported that knockdown of mucin 1 gene induces the diminishing of penetration and migration features of kidney cancer cells under the influence of critical hypoxia. Thus mucin 1 could be used for the potential therapeutic target in renal cell carcinomas (RCC).

**Khodarev, N. et al. (2010)** mentioned that STAT1 is seems to be activated in inflammatory response to interferons. They reported that mucin 1 cytoplasmic domain (MUC1 C) directly interact to the STAT1 binding domain of DNA and developed an auto inductive loop. STAT1 and mucin 1 pathway activation have poor prognosis values in the patients of breast carcinoma.

**Pochampalli, M.R. et al. (2007b)** demonstrated that ErbB receptors are one of the key regulators in normal and transformed tissues for cell survival and growth. They reported that expression of mucin 1 is a powerful regulator of triggering of erbB1 receptor, binding partner , substrate of erbB1 and able to enhanced the transformation process through erbB1 degradation inhibition.

**Li, Y. et al. (2001)** have demonstrated that MUC1-C domain is reported to interact with GSK3 beta and hence suppress the mucin 1 binding with beta-catenin. They have
found that domain of cSrc SH 2 directly interact to YEKV motif and prevent the collaboration of mucin 1 and GSK3 beta interaction. They have reported that phosphorylation of mucin 1 enhanced the interaction of mucin 1 with beta catenin.

Rajabi, H. et al. (2011) studied on signals for translation of mucin 1 in the cells of malignancies of prostate. They have used androgen dependent and androgen independent cancer cell lines of prostate to analysed the concentration of mucin 1 by quantitative RT PCR. They have observed the activation of mucin 1 promoter by immunoblotting. They found that signaling of androgen receptor regulates the MUC1 expression by different process includes posttranscriptional and transcriptional mechanisms in the cells of tumor of prostate.

Mitchell, S. et al. (2002) reported the regulation of mucin 1 (androgen-dependent). Previously it was reported that MUC1 was regulated at transcription stage by progesterone, glucocorticoids, estrogen. They have done the study on breast and prostatic cell lines and groped as expression of androgen and MUC1. Out of which, only cell line which is AR+MUC1+ shown a significant increase of expression of MUC1 expression with androgen activation.

Lacunza, E. et al. (2010) have studied on the role of MUC1 expression at transcription and translational stage in development of breast cancer in human. They have analyzed 83 tissue samples of breast cancer by immunohistochemical methods and real time PCR (RT-PCR) for MUC1 expression at transcription (gene expression) and translational stage (protein expression). They have found that the copy number of MUC1 was increased in primary invasive type of mammary carcinomas as compared to negative control tissue and having correlation with translation of mucin 1 protein.

Rajabi, H. et al. (2010) have mentioned that mucin 1 protein is highly present in human breast but micro RNA, miR-125b, is down regulated in the cells of cancer of breast tissue. They found that miR-125b induces the decrease concentration of mucin 1 levels and it promote the program cell death response of ZR 75 1 cells to chemotherapy cisplatin treatment. So that miR 125b has diminished the amount of mucin 1 and that miR-125b have functions as deactivator of tumor of breast.

Regimbald, L.H. et al. (1996) have reported that mucin 1 is a ligand for ICAM-1 molecule. It was found that antibodies against ICAM-1 and mucin 1 inhibited the adhesion of human and transfected mouse. Pretreatment with purified mucin 1 or with recombinant human ICAM-1 was found an equal effective inhibitor for adhesion
process of cells. The collaboration between mucin 1 and ICAM-1 could be very critical to the process of blood borne cancer of mammary.

**O’Day, E. and Lal, A. (2010)** have mentioned that miRNAs are the major kind of little endogenous RNA that oppose the expression of gene at post-transcription stage. They reported that several miRNA are over expressed includes miR-10b, 21, 155, 373 & miR 520 c and several miRNA are decreased let-7, 31 and 34, 17-5p, 125a, 125b, 200 and miR-206 in breast cancer.

**Sachdeva, M. et al. (2010)** have mentioned that microRNAs are a generally negatively regulate the gene and it is work through a mechanism of post transcriptional repressor. Different experimentation data have shown that micro RNAs play a critical basic function including apoptosis, differentiation and cellular proliferation. MicroRNAs can be function as oncogenes or antioncogen in metastatic cancer. They have reported that in tumor tissue, miR-145 expressed in low amount and also inhibiting the growth of tumor cells.

**Ciborowski, P. and Finn, O.J. (2002)** have developed the synthetic MUC1 tandem repeats without any glycosylation having 100 amino acid residues (5tandem repeats) but in natural conditions MUC1 is expressed with heavily O glycosylated tandem repeat domain. They reported that synthetic mucin 1 (5TR) is act as inhibitor for breast tumor cells as compared to human lung tissue sections. So the result indicated that non-glycosylated form of mucin 1 facilitated the carcinoma cells to attached to tissue with distant site.

**Chaika, N.V. et al. (2012)** have reported that MUC1 with aberrant glycosylation is over translated in cancer of pancreas and enhanced the tumor progression. MUC1 aberrant high expression promotes the glycolytic activity in the cells of pancreatic cancer and it also increase the glucose uptake and enhances the gene expression involved in glucose uptake in pancreatic cancer. So that mucin 1 serve as a key regulator of the metabolic activity which facilitate metabolic alteration and provide the best environment for survival of tumor cells.

**Geng, Y. et al. (2012)** have used flow cytometer to determine the concentration of mucin 1 in MCF 7 and ZR 75 1 cell lines. While altered form of mucin 1 and mucin 1: ICAM-1 association was confirmed by immunofluorescence microscopy. They have found that mucin 1 having capability of synergistic adhesion in cascade where the analyzed differential adhesion is constant with the potential of relative metastasis is higher in ZR75 1 and weakly in MCF 7 cell lines.
Shen, Q. et al. (2008) have shown that mucin 1 binds to ICAM-1 of accessory cells on surroundings and enables the migration of MUC1 bearing cells. They have shown that mucin 1 activates the Rac1- and Cdc42 dependent actin cytoskeletal action by ligating ICAM-1 at the heterotypic cell to cell contact sites using assay of actin cytoskeletal reorganization.

Rahn, J.J. et al. (2005) have demonstrated that migration of cells which are expressing MUC1 endogenously or by transfection could be influenced by ICAM 1. Consecutive addition of ICAM-1 translating cells and ICAM 1 inducing inflammatory cytokines (TNF α and IL 1 β) has enhanced the migration of MUC1 expressing cells in stepwise manner. Specific antibody against ICAM-1 or MUC1 (DF3 etc.) could repeal the increase in migration.

Horn, G. et al. (2009) have mentioned that different splicing aberrantly products of human mucin1 (MUC1) is products in carcinomas. They have transfected the of human mucin 1 truncated genomic fragment in DA3 mouse mammary tumor cells which undergo EMT. In EMT, these cells have shown the altered signaling pathways along with altered morphology, and altered expression of mesenchymal and epithelial markers.

Yao, M. et al. (2011) studied on MUC1 over expression and its biological significance in lung cancer angiogenesis. They have expressed MUC1 forcefully in 3 NSCLC cell lines i.e. NCL-H460 and A549 which is having low endogenous MUC1. They concluded that high translation of aberrant mucin 1 promotes the tumor angiogenesis in NSCLC by ERK pathways along with Akt pathways activation and elevation of VEGF concentration. So that mucin 1 could be a good anti angiogenic target in NSCLC.

Woo, J.K. et al. (2012) have reported that concentration of mucin 1 enhanced VEGF synthesis and secretion through AKT signaling pathway. Mucin 1 expression promotes VEGF in cancer of breast tissue and activates the insulin like GF1 receptor which is associated with VEGF translation. They have concluded that expression of MUC1 promotes angiogenesis in cancer of breast tissue in both in vivo and in vitro conditions.

Horm, T.M.B.B. et al. (2012) have characterized the low rate of metastasis in PMIP treatment by conducting motility assay and found that PMIP deactivates the cell motility in cancer of mammary. They found that effect of EGF along with mucin 1 on
cancerous phenotypes was dependent upon c-Met action. These results indicated that PMIP are able to block the translation of a key metastatic mediator i.e. mucin 1.

Li, Y.Q. et al. (2003) have reported that in the cells of cancer of breast tissue, mucin 1 (MUC1) is correlated with ErbB2 and MUC1-ErbB2 complex is formation increased while treatment with HRG. So that mucin 1 functions as shuttle vector for HRG-induced nucleolus targeting of gamma-catenin and cross linked between Wnt pathways and ErbB2.

Ahmad, R. et al. (2012) have been demonstrated that mucin 1 C domain associated with Bax protein (responsible for apoptosis process) in human breast cancer. In oxidative stress and by genotoxin induction, MUC1-BAx complex are detected in mitochondria and cytoplasm. So it was found that MUC1 is binds to Bax protein by several way and block the apoptosis function of it and promotes metastasis progression.

Raina, D. et al. (2006) mentioned that non receptor c-Abl tyrosine kinase interacts to 14-3-3 proteins in cytosole followed by apoptotic response for DNA damage. This function has direct correlation with MUC1 dependent mechanism. They reported that c-Abl does phosphorylates the mucin 1 on position Tyr-60 and develop a complex with mucin 1 by c-Abl SH2 domain. They concluded that MUC1 complex with cAbl in cytoplasm inhibits the apoptosis process in response to DNA damage done by anticancer agents.

Ren, J. et al. (2002) have demonstrated the phosphorylation of MUC1 by protein kinase C delta (PKCdelta) increased the MUC1 binding with beta-catenin in vitro and in vivo. It was found that mutation in binding site of MUC1-PKCdelta decreased the MUC1 mediated binding to beta-catenin to E-cadherin. So that this study shown the important role of PKC delta in regulation of mucin 1 and the beta-catenin signal pathway.

Rajabi, H. et al. (2012) have demonstrated that mucin 1 C subunit have association with TCF7L2 transcription factor. The cytoplasmic domain of mucin 1 (mucin 1-C) directly binds to TCF7L2 C-terminal region. They concluded that the oncoprotein mucin 1-C contributed to the activation of TCF7L2 and promoted cyclin D 1 expression in cells of breast carcinoma.

Pandey, P. et al. (1995) have been studied on MCF-7 cell and reported the interaction of tyrosine phosphorylated DF3 with Grb2 adaptor protein, SH2 domain and found that pYTNP site in DF3 is responsible for this interaction. They further reported the
association of DF3/Grb2 complex with guanine nucleotide exchange protein Sos and it binds to domain SH3 of Grb2.

Yuan, Z. et al. (2007) have taken breast (MCF-7) and pancreatic (PANC1) cancer cells which were 'knockdown' of MUC1 gene. It was found that translation of beta catenin and E cadherin proteins were up regulated in both PANC 1 and MCF-7 cells also reported that the low concentration of mucin 1 also induce the relocation of beta-catenin to cytoplasm from nucleus. They suggested that mucin 1 may regulate the migration of cancer cell and increasing the complex formation of E-cadherin/beta-catenin.

Bernier, A.J. et al. (2011) have first time reported the MUC1 interacts to ICAM-1 which is expressed in cancer of breast tissue throughout migratory tract of metastasis. They found binding of MUC1 with ICAM-1 cause cytoskeletal reorganization, oscillations of calcium and simulated trans-endothelial migration. They also reported the mechanism of MUC1/ICAM-1 signaling, in which non-cysteine linked MUC1 dimerization is required for migration of cancer cells.

Agrawal, B. et al. (1998) have mentioned that cancer-associated MUC1 in secreted form is immunosuppressive and reported for inhibition of T-cell proliferation in human. They have reported the expression of freshly synthesized mucin 1 (MUC1) on human T cells (which was mitogen-activated) surface and also reported in cultures supernatants of mitogen-activated human T cells as soluble form. MUC1 expression was diminished when removed the mitogenic stimulus from the culture of T-cell. This indicates the important immune modulator function of mucin 1 for human T cells.

Gendler, S.J. et al. (1995) have mentioned that analyses of mucin genes at molecular level have assured the diagnostic tools for cancer including breast cancer. Studies on its protein structure, composition provide the tools to access its expression, secretion, involvement in cancer progression and metastasis. These data also helps to understand the machinery of cell to cell adhesion, modulation of immune response and association with MUC1.

Hilkens, J. et al. (1995) have mentioned that episialin is recognized for breast cancer serum marker. Its expression was present in high amount in the patient serum of cancer of breast in comparision with normal negative control. In vitro episialin high expression was reported on cell surface which reduces the cell to extracellular matrix adhesion and same result was reported in in-vivo conditions.
Kamoshida, S. et al. (1998) have been investigated the presence of mucin 1 in follicular dendritic cells (FDC), in normal plasma cells, malignant plasma cells, perineurial cells (PNC) and myofibroblasts (MFB) cells. By using different mAb of E29, 115D8, DF3 alone or different combinations of three by immunohistochemical and immunoelectron microscopy. They found MUC-1 in PC cells in different disease conditions includes allergic rhinitis, chronic synovitis, chronic cervicitis, tuberculous lymphadenitis, Hodgkin's disease etc. Levitin, F. et al. (2005) have mentioned that some of the MUC proteins may involve in barriers and have protective function for body. They have derived the MUC1 small protein (MUC1/ZD) by alternate splicing. They take N terminal sequence of MUC1 contained signal peptide, and followed 30 amino acids. They reported that novel MUC1 protein isoform MUC1/ZD which deletes the array of tandem-repeat but leads to the development of C-terminal common reading frame. Hudson, M.J. et al. (2001) have mentioned that mucin 1 is a high translated in mainstream of glandular epithelia. While embryonic development the glandular differentiation and change pattern of mucin 1 (MUC1) translation coincides. They have transfected full length of cDNA of mucin 1 in MDCK cells and murine mammary adenocarcinoma and found that MUC1 might have induced the changes in tissue architecture. Zaretsky, J.Z. et al. (1999) have mentioned that to know about the mechanism of overexpression of MUC1 will help to understand the molecular approaches for the treatment of breast carcinoma. They have analyzed the functional activities MUC1 promoter with several deletion mutants. They found that transcriptional cis-factor fragment present in between SacI and XmnI sites are sufficient for translation of mucin 1 protein isoform with tandem repeats. Fedorova, L. et al. (2003) have mentioned that introns are a portion of eukaryotic genomes which are involved in several functions and actively involved in gene evolution. These functions includes carriers of transcription regulatory elements, crossing over enhancers by meiotosis within coding sequences, an actors in trans-splicing and alternative splicing, sources of non-coding RNA, signaling for mRNA export and substrates for exon shuffling. Meseguer, M. et al. (2001) have been investigated the hormoral immunity regulation of mucin 1 in blastocyst and in cycle of hormonal substitution therapy. They also examined the mucin 1 embryonic regulation in epithelial cells of endo metrial
location. Blastocysts express MUC1 was confirmed by immunocytochemistry and RT-PCR which was localized at the trophectoderm. Endometrial mRNA of mucin 1 and immuno-reactive protein increased in respective endometrium as compared to non-receptive endometrium.

M.Guckin, M.A. et al. (1998) have inspected the effects of progesterone and estrogen on mucin 1 translation in mammary cells of cancer i.e. ZR75 1 and MCF 7 grown in steroid-free medium. It was found that progesterone synergistically with estrogen increase the expression of secreted MUC1 while alone estrogen triggered the high concentration of mucin 1 in both cellular and secreted form. They also reported that progesterone could control the mucin 1 concentration in cancer cells of breast.

Zhou, X. et al. (1998) have reported that in mucin 1 (MUC1), a promoter (5.4 kb) was isolated from a mouse genomic library and at -748 to -735 location bp it have one potential full ERE (GCTCGCGGTGACC). It was found that ER alpha nor ER beta were not able to bind efficiently to this sequence. They concluded that ER usually required other factors to regulate the mucin 1 gene promoter in murine.

Botti, C. et al. (1997) have demonstrated that progesterone (Pg), 17 beta-estradiol (E2), steroid-free fetal calf serum (FCS) regulate the expression of MUC1 in the hormone-sensitive MCF7 cell line. They mentioned that MUC1 modulation by steroids may be because of low FCS concentration preventing the permissive action of regulation of possible gene regulation.

Shiraga, T. et al. (2005) have identified the hypersensitive sites of DNase I at 750 bp upstream position and 250 bp upstream position in mucin1 (MUC1) gene promoter. Foot printing of DNase I using nuclear extracts from breast tumor cells (MCF7) and human pancreatic tumor cells (HPAF) recognized the three binding elements in these regions which are -750 FP, FP2 and -250 FP1.

Morris, J.R. et al. (2001) have mentioned that mucin 1 is highly translated in several cancer conditions and also demonstrated that upstream sequences in between 62 to 119 locations are able to adjust transcription of mucin 1 expression. They found that the positioning of the GC box was critical for directing translation of mucin 1.

Hurd, C. et al. (1997) have used ER positive cell line of mammary carcinoma T47D and determined the regulation of high expression of different malignancies deactivator protein include p53 and retinoblastoma by using estrogen molecule and anti estrogens molecules. They have reported the translation of p53 and hyper phosphorylation of pRB in reported cells is ER mediated mechanism.
Hanson, J.M. et al. (2001) have reported that mucin 1 glycoprotein which is translated in cancer conditions with aberrant glycosylation. Primary tumours treated neo-adjunctively with 3 weeks of tamoxifen have lower expression of MUC1 as compared to the group which was not treated with tamoxifen.

Paszkiewicz-Gadek, A. et al. (2003) have reported that high concentration of mucin 1 in human endometrial adenocarcinoma is controlled by tamoxifen and estradiol hormone. They have reported that estradiol up regulated the translation of mucin 1 while tamoxifen down regulated the translation of mucin 1 in human endometrial adenocarcinoma.

Haspel, R.L. et al. (1999) have reported that the presence of phosphatase inhibitor sodium vanadate was phosphorylated the STAT 1 collected in the nucleus and the total amount of STAT 1 was decreased in cytosole of cells. They have found that nucleus of cells is the site for STAT1 inactivation and de-phosphorylation of STAT 1 is required fast export of STAT 1 in nucleus of cells.

Bakhos, A. et al. (2009) have reported the secretion of gluc protein in cultured cells, in blood and urine in vivo. The feature of gluc protein would be utilized for the secretory expression of protein in mammalian cells. Several reports suggested that this protein at amino terminal has guide the whole recombinant protein to be secreted into the media.

Wille, T. et al. (2012) have mentioned that gluc protein sequence is reported as a reporter sequence in eukaryotic heterogeneous expression system. The 17 amino acid sequence of gluc protein are responsible of its secretion. This feature can be utilized to expressed recombinant protein in mammalian cells.

Sahraei, M. et al. (2012) have mentioned that pancreatic ductal adenocarcinoma (PDA) is reported with worst prognoses. They reported a unique association of PDGFA with mucin 1. PDGFA is reported as driving factor of growth of tumors, angiogenesis and carcinogenesis in pancreatic ductal adenocarcinoma. They found that MUC1 regulated the PDGFA signaling so that it can be used for therapeutics of PDA.

Singh, P.K. et al. (2007) have mentioned that MUC1 cytoplasmic domain (MUC1C) is linked with actions of signaling that stimulus the uncontrolled cell generation and spreading of cancer cells. They have reported that PDGFR beta is responsible for MUC1 phosphorylation is some case which increased the invasive properties of pancreatic adenocarcinoma cells.
Julian, J. et al. (2009) have described that processing pathway which is TACE/ADAM17 initiated the MUC1 cleavage. They reported that mucin 1 full length undergoes proteolysis mediated by PDGS factor. They have not detected this proteolytic phenomenon (availability of mucin 1 cleavage products) in the presence of different proteosomal inhibitor and this revealed that proteolysis is either extremely efficient or non proteosomal.

Leng, Y. et al. (2007) have mentioned that the mucin 1 cytoplasmic domain (MUC1 C) is not reported with any signal mechanism for nuclear localization. They have reported the association of mucin 1 C fragment with importin β but not with importin α. As same as importin beta mucin 1 C domain interacts to nucleoporin p 62 (Nup 62) central domains and indirectly interacts to the nucleoporin p 62 C terminal α helical coiled domain. These findings suggested that Nup 62 is involved in the nucleus localization of MUC1-C oncoprotein.

Wei, X. et al. (2007) have mentioned that MUC1 C subunit present in nucleus where it was linked with TP 53 and it regulates TP 53 governed transcription. Intact form of p53 is prerequest for the integrity of healthy cells. This study has shown that mucin 1-C fragment repressed the p53 gene activation. So these finding indicated that mucin 1 over expression is crucial for the diminishing of p53 in cancer of breast.

Bitler, B.G. et al. (2010) have mentioned that a receptor of tyrosine kinase i.e. EGFR with aberrant nuclear localization in several epithelial carcinomas is a poor prognostic indicator. They observed that loss of expression of MUC1 cause decrease in the interaction between the CCND1 promoter and EGFR, which caused less cyclin D1 protein expression. So this study provides a novel mechanism for the regulation of EGFR nuclear function.

Lau, S.K. et al. (2012) have mentioned that in different carcinoma conditions tumor cell penetration and tumorigenesis of cells is essential role of integrins and receptor tyrosine kinases. They have shown that EGFR mediate by integrin αvβ5 induces the invasion of human carcinomas and metastasis. They reported that Src activity and EGFR activity involved in invasion of carcinoma cells and metastasis which is mediated by integrin αvβ5 by MUC1 proteolytic cleavage.

Baldus, S.E. et al. (2004) have performed the immunohistochemical double staining to study the MUC1 and beta-catenin subcellular distribution in case of colorectal cancer. They have suggested that both beta-catenin and MUC1 are expressed together
at the time of invasion in colorectal carcinomas and this phenomenon is directly correlated with diseases progression and worse prognosis.

Roy, L.D. et al. (2011) have mentioned that tumor cells of pancreas increased the motility and invasion properties which is association with epithelial of mesenchymal transition and they reported that mucin 1 high concentration triggers the molecular mechanism of EMT in pancreatic cancer which is responsible for the increased invasiveness and metastasis. This study may help to design the MUC1 based therapy for pancreatic cancer.

Behrens, M.E. et al. (2010) mentioned that phosphorylated forms of the mucin 1 CT conducts signals from growth factors and cytokines stimulation for reprogramming of transcriptional profile of cell by specific association with transcription factors. They performed the analysis of gene expression by microarray and found that when mucin 1 is highly expressed, induction of CTGF synthesis and secretion is happened.

Bitler, B.G. et al. (2009) have mentioned that MUC1 generally binds to beta-catenin and inhibiting the EGFR degradation and hence increased the metastasis process. They designed the peptide (MUC1 inhibitory peptide) based therapy which interfere with protein-protein interaction intracellular and act as breast cancer treatment. They conclude that intracellular MUC1 peptides have important antitumor activity which can be exploiting for cancer treatment.

Zhang, L. et al. (2012) have mentioned that cigarette smoking revokes cell to cell adhesion in between epithelial cells by E-caddisrupting. They have prepared the culture of primary HBE cells and exposed with smoke containing medium to evaluate the importance of p120 ctn interaction with the MUC1 CT in same condition. They concluded that mucin 1 CT with p120 ctn is an important regulator of epithelial polarity in smoke induced process.

Klinge, C.M. et al. (2011) have found that interaction of intracellular MUC1-C domain with ER α increases the gene transcription in the cells of breast carcinoma. They mentioned that MUC-C blockage with PMIP (an inhibitory peptide) oppose the tumor growth in breast cancer. They found that in H1793 cells, PMIP inhibits the transcription of endogenous cyclin D1, estradiol-activated reporter gene, and the transcription of nuclear respiratory factor-1.

Raina, D. et al. (2011) have mentioned that mucin 1 with aberrantly glycosylation is over translated in NSCLC cells. MUC1 cytoplasmic domain is often associated with PI3K p85 in NSCLC cells and it was reported that the blockage of mucin 1 CD has
blocks its association with PI3K p85 and diminished the Akt phosphorylation and mTOR. These findings suggested that NSCLC cells are depend on mucin 1-C for initiation of the PI3K to akt pathway.

**Yin, L. and Kufe, D. (2011)** have reported that mucin 1 C domain is overexpressed in chronic myelogenous leukemia blasts but not in cells of chronic phase. They have demonstrated that inhibition of mucin 1 C induced the ROS mediated deactivation of translation of beta catenin. They also reported that GO 203 action is directly correlated with decreases in energy in the form of ATP (ROS induced) and loss there survival by apoptotic function and necrosis at late stage.

**Hisatsune, A. et al. (2011)** have reported that, MUC1 is internalized through macro-pinocytosis pathway after binding with mucin 1 antibody present on the surface of cell at intracellular region. In cancer cells MUC1 are closely associated with EGF receptor (EGFR). They analyzed the effect of mucin 1 antibody on pathways of EGFR. They found that mucin 1 antibody GP 1.4 induced the EGFR internalization in malignant cells of pancreas and cause ERK phosphorylation inhibition by EGF stimulation.

**Schettini, J. et al. (2012)** have reported that intra tumor delivery anti mucin 1 antibody which is of CpG-conjugate enhances the anti tumor activity of cells of natural killing. Using of monoclonal body for the activation of ADCC is always the main interest for clinician. They also reported that HMFG 2A band CpG oligo deoxynucleotide (CpG ODN) could be identified by natural killer cells on the mAbm containg tumor cells and it triggers the ADCC.

**Wang, L. et al. (2011)** have used mucin 1 mAb C595 (MAb C595) with docetaxel (DTX) and got higher effectiveness of DTX in cultured human EOC cells and finally it undergone for apoptosis process. They have used combination therapy and suggested that combination strectgy would be effectively reduce the tumor load and reduce the formation of ascites in patients. This approach increases the life span of animals through apoptosis and necrosis process.

**Oei, A.L. et al. (2008)** have examined the patients of epithelial ovarian cancer by insertion of yttrium-90-labeled in murine HMFG1 which developed IgG antibody to mucin 1 and had an impact on progression of disease. They used the samples from 407 patients for analysis of IgG antibody against MUC1 and concluded that therapy by immunological method to mucin 1 would be an effective tool for management of ovarian carcinoma.
Apostolopoulos, V. et al. (2006) have injected the mannan mucin 1 in oxidized or placebo form in early stage of mammary carcinoma patients and they found that the patients received immunotherapy have no recurrence of mammary cancer as compared to negative control. The patients who have received oxidized mannan mucin 1 shown measurable antibodies to MUC1 in 69 % and remaining patient’s shows mucin 1 specific response of T cell but none of the placebo treated patients had humoral or cell mediated response to mucin 1.

Kamata, M. et al. (2002) have used C57BL/6 mice and intradermal immunized with different doses of purified plasmid DNA pCEP4 containing full-length MUC1 cDNA (22 tandem repeats). Immunization was done thrice in a week and observed serum antibodies to synthetic peptide of TR of mucin 1 and the specific antibody titer was correlated to the dose of plasmid DNA in lung cancer patients which shows the potential of cDNA of MUC1 as vaccine.

Kovjazin, R. et al. (2011) have mentioned that any vaccine for cancer should be able to induce specific immunological response. They have developed mucin 1-SP-L which is 21 amino acid peptide having entire signal sequence of mucin 1 and this peptide is generally expressed by each solid or non-solid tumors in different cancer include breast cancer. They found very satisfactory result which indicates the potential use of this peptide as well defined vaccine.

Lloyd, K.O. et al. (1996) mentioned that in different study, MUC1 is hypoglycosylated in different carcinoma conditions. This hypo-glycosylation allows recognition by the specific monoclonal antibody. Hence mucin 1 has been considered as TAA which could be a good targeted for therapeutic approach using mAb.

Singh, P.K. and Hollingsworth, M.A. (2006) mentioned that transmembrane domain of MUC’s are associated in signal transduction through its extracellular cytosolic domain which are generally binds to ligands or receptor. They mentioned that MUC1CT, a cytoplasmic tail of Mucin 1 is best characterized mucin of transmembrane mucin family. MUC1CT is involved in different signaling pathways include beta-catenin, p53, p120 catenin, estrogen receptor alpha and Ras.

Bafna, S. et al. (2010) have reported that all mucins are expressed as large and O linked glycoproteins and their main functions are to provide defensive layer to human body system tracks and function to protect the cells from infection, hydrate conditions and provide lubrication for epithelial luminal surfaces of the ducts present in different
tracks. They also mentioned that mucin 1 is become carcinogenesis by alteration in the growth of cells.

**Rahn, J.J. et al. (2001)** worked on 71 breast cancer patients and examined for staining pattern of MUC1 along with beta-catenin and E-cadherin. They found that all invasive cancer showed MUC1 staining. By staining, MUC1 was observed in 15 % in apical membrane, and 93 % in cytoplasm respectively in invasive ductal carcinomas. They found poor prognosis with high cytoplasmic staining hence MUC1 expression is associated with the better prognosis.

**Mukherjee, P. et al. (2005)** determine the possible function of mucin 1 in signal transduction while development of cells of lymphoma (Jurkat). They have mentioned that mucin 1 is phosphorylated in Jurkat T cells and in normal T cells. It is linked with lck tyrosine kinase in co-immunoprecipitation experiments. They concluded that the management role of mucin 1 in modulating the proximal signal transduction process through its linkage with activation complex proteins.

**Oosterkamp, H.M. et al. (1997)** have done the comparative study of translation of mucin 1 in tumor cell lines (epithelial and non epithelial) and demonstrated MUC1/Z as new short variant form of MUC1. Using RT-PCR, immunocyтомeter, radio-immunoprecipitation and northern blot analysis they found a new short form i.e. mucin 1 / Z which is lacking tandem repeats and different from MUC1/Y. They also reported the different amount of MUC1 mRNA in non-epithelial tumor cell lines in lower amount.

**Shindo, Y. et al. (2014)** have demonstrated the clinically proof efficiency of generating immunotherapy with DC’s pulsed with mucin 1 protein and CTLs. It enhanced the anti-tumor immunity by gemcitabine (GEM) by opposing regulatory thymus generating cells. They have found that adoptive immuno therapy with mucin 1 DCs and mucin 1 CTLs along with GEM would be a potential and efficient therapy for cancer in pancreas.

**Lu, H. et al. (2008)** have mentioned that different tumor antigens have been reported in several cancers and these antigens also able to elicit humoral response in human body. Generation of auto antibodies against TAA can be used as a biomarker for treatment and diagnosis of cancer. It was found that some antigens which are present in minimal concentration are also able to produce autoantibody in detectable amount.

**Tainsky, M.A. et al. (2009)** different molecules which are indicators of biological state of body called biomarkers and these molecules are generally present in urine,
blood, tissue and in other body fluid. Generally only disease related biomarkers is expressed and presence of these biomarkers could be a symptom for diagnostics and monitoring of effect of treatment on disease progression. Different technology has been developed to monitor these marker to reduce mortality rate.

**Mintz, P.J. et al. (2003)** mentioned that there is molecular diversity found in different disease is required for targeted therapies. They have developed a procedure of screening of molecular diversity which was established on phage display library to predicts specific amino acid streach and that identified by tumor linked antibodies circulated in blood stream. They have identified peptide which bound by circulation antibody in prostate cancer patients.

**Snijdwint, F.G. et al. (1999)** have demonstrated the cytotoxic immune response against mucin 1 and its VNTR containg peptide in the patient blood and in single nuclear cells (PBMC) in cancer of ovary. They have reported that mucin 1 and free migrating Ig G ab against MUC1 in blood was considerably higher in patient of ovarian cancer as compared to control.

**Tarp, M.A. et al. (2008)** have mentioned MUC1 having O glycans and also found in other glycoprotein’s. O-glycosylation involved the attachment of first carbohydrate residue GalNAc by GalNAc-transferases to select threonine and serine residue in proteins. Site directed O glycosylation can be used for the therapeutic potential.

**Hollingsworth, M.A. and Swanson, B.J. (2004)** have mentioned that mucin’s are heavily glycosylated extracellular proteins are function as discriminating molecular barrier on the surface of epithelial cell and participated in signaling pathways. Alteration in the glycosylation pattern of mucin 1 was observed in different cancer. So that mucin 1 could be used for the diagnosis of cancer and its therapeutic potential is under investigation.

**Hattrup, C. L., Gendler, S. J. et al. (2008)** have mentioned that mucins of cell surface are large transmembrane protein with heavily glycosylation, participated in different function includes making a coat on airway epithelium to protect the track against pathogenic infection and serve as first line of defense. It also regulate the transcription and cellular signaling in the track. They mentioned that different mucins including MUC1, MUC4, and MUC16 are highly expressed in respiratory track.

**Taylor-Papadimitriou, J. et al. (1999)** have mentioned that MUC1 have protective function in natural condition and having tandem repeats. Each tandem repeat is composed of twenty amino acids and having five glycosylation sites (Thr & Ser)
preferably serine and threonine residue. O glycosylation occurred in these site only and in cancer conditions, aberrant glycosylation was reported which is responsible for the tumor progression and metastasis.

Horm, T.M. and Schroeder, J.A. (2013) have mentioned the function of mucin 1 in metastatic progression and reporting the expression of MUC1 in different disease stage. They reported that the translation of mucin 1 was maximized in several malignancies including carcinoma of mammary tissue and it enhances the tumor progression and metastasis. They also reported the interactions between MUC1 with surrounding environment.

Singh, R. and Bandyopadhyay, D. (2007) have mentioned that mucin 1 is generally over translated in most of the cancer conditions of breast with aberrant glucosylation (underglycosylated form) and exposing the extracellular core peptides which can be a potential target for the therapeutics. It was also reported that aberrant glycosylation enhance the internalization of MUC1 in cytoplasm making potential target for drug delivery and therapeutics.

Wandall, H.H. et al. (2010) have reported aberrant truncated glycoforms of MUC1 was absent or present in non-detectable amount in serum of cancer patients using an antibody based immunoassay. They have developed O linked glycopeptide microarray and detected the presence of IgG ab against aberrantly O-glycopeptide epitopes in clinical sample which was previously immunized with truncated mucin 1 peptide conjugated with hemocyanin.

Furr, A.E. et al. (2010) have reported high concentration of mucin 1 in cancer of colon and in other tumors epithelial cells. This mucin 1 is over expressed with hypoglycosylation. This is the tumor form of MUC1 and antibodies specific for it was reported in cancer patients. They reported that MUC1 is over expressed with hypoglycosylation in inflammatory bowel disease (IBD) and may be responsible for the pathogenesis of IBD.

Kurtenkov, O. et al. (2007) have investigated the antibody immune responses (humoral response) against mucin 1 sequence and mucin 1 related Thomsen-Friedenreich (TF) glycotyple in gastric cancer patients along with chronic gastroduodenal diseases. They reported that IgG against MUC1 was enhanced in gastric cancer patients. These antibodies may be very useful for the prognostic marker in gastric cancer.
Hamanaka, Y. et al. (2003) have reported that MUC1 antigen was over expressed in different cancer including pancreatic cancer and induced humoral immune response. They found the high titer of migrating mucin 1 antibodies in cancer of pancreatic tissue with disease progression so that this IgG anti-MUC1 antibody can be serving as prognostic marker of pancreatic cancer.

Hirasawa, Y. et al. (2000) have reported that mucin 1 antigen was over translated in different cancer including NSCLC and induced in vivo humoral immune response. They found the high titer of migrating mucin 1 antibodies in NSCLC with disease progression so that this IgG mucin 1 antibody can be serving as prognostic marker for NSCLC.

Pinheiro, S.P. et al. (2010) have analyzed the correlation of anti mucin 1 antibodies with risk of ovarian cancer by ELISA as method. They collected the plasma sample of more than 100 clinical samples of cancer of ovary and analysed the concentration the plasma mucin 1 antibodies. They found that detection anti mucin 1 antibodies before several years of diagnosis of disease could be correlated with minimum risk of cancer of ovary at higher age.

Blixt, O. et al. (2010) have developed microarray platform (a synthetic screening) of O- O-PTMs for superficial display of mucin 1. After screening they have confirmed that mucin 1 glyco oncopeptides could be assembled and this feature could be utilized for the detection of autoantibodies in the serum of vaccinated patients and in the serum of patients with confirmed disease.

Brockhausen, I. (1999) has mentioned that glycoproteins which have carbohydrate chains of complex structures linked O glycosidically are found in secretory form and on the tumor cells surface. They have suggested that presence of glycosylated epitopes may be the best tools for the diagnosis of cancer at different stage. The presence of these glycans may also be used for the potential used of therapeutic target.

Kessler, J.H. and Melief, C. J. M. (2007) have mentioned that efficiency of T cell mediated immunotherapy for the treatment of various carcinoma is depend upon the optimal immune-stimulatory and specific tumor-associated antigens (TAA) with high quality and optimal quantity and also T cell epitope should be present on these tumor-associated antigens (TAA).

Kufe, D. (2010) has mentioned that mucin 1 oncogene is aberrantly highly translated in most of the malignancies including hematological carcinomas. It was reported that approximately 65 % of cancer patients have high expression of MUC1. They have
mentioned that MUC1 would be a highly attractive target for diagnostic and therapeutic target for cancer.

Ioannides, C.G. et al. (1993) have reported that CTL are able to mediate the lysis of tumor targets after in vitro culture which was fishout from tumor infiltrating lymphocytes or tumor linked lymphocytes (TAL) of ovarian tumors. They have reported that ovarian CTL TAL can recognize mucin 1 core peptide. These data suggested that specific antigen recognized by ovarian CTL-TAL would be the great target for ovarian cancer immunotherapy.

Takahashi, T. et al. (1994) have reported that mucin 1 was found in myeloma cells and in the clinical samples of patients of multiple myeloma. In cancer of breast tissue and pancreatic cancer patients, HLA-unrestricted cytotoxic T cell lymphocytes recognize tumor linked epitopes on mucin 1. They have concluded that CTL (anti-MUC1 reactive) and precursors of HLA-unrestricted could exist in the serum of patients of multiple myeloma and that myeloma cells can express epitopes on MUC1, which will recognized by CTL.

Noto, H. et al. (1997) have found that CTL cytotoxicity against the transfectant and immune reactivity of anti mucin 1 core protein mAb was increased several times by cell treatment with inhibitor of O type glycosylation. HLA unrestricted the CTL that distinguish the mucin 1 (under glycosylated) using their T cell receptor in multiple myeloma patients.

Tempero, R.M. et al. (1998) have reported that mucin 1 Tg mice (transgenic C57BL/6 mouse having human mucin 1) which are exercised with syngeneic tumors expressing mucin 1 have developed growing mucin 1 containing tumors progressively whereas native type C57BL/6 mice have developed mucin 1 deficient tumors with very minimum rate. They have developed a transgenic mucin Tg mouse and evaluated the development of mucin 1 specific tumor immunity in an animal.

Deguchi, T. et al. (2010) have reported that mucin 1 is highly translated with aberrantly glycosylation in greater than eighty percent of human carcinoma in the ducts of pancreas. They reported that vaccination with mucin 1 peptides was fails TAA including mucin 1 are week to induced immune response in cancer patients. They have also reported that the immunization using cells planned to express alpha galactose epitope would be a noval approch for handling of cancer of pancreatic tissue.
Chen, J. et al. (2011) have investigated that DCs transfected with amplified mucin 1 mRNA developed cell based T lymphocytes (CTLs) immunity in cancer of pancreatic tissue. They have transfected the mRNA of mucin 1 by electroporation method and the translation of mucin 1 was analyzed by immuno blot and quantitative PCR (RT-PCR). In this case the CTL responses only identified and lyse HLA-A2+ / mucin 1 + PC suggested using mucin 1 as a target for immuno therapeutic strategies for cancer in pancreatic tissues.

Ramlau, R. et al. (2008) have mentioned that TG4010 is a virus based vector expressing recombinant IL 2 and TAA type mucin 1. This vector TG4010 has been used for the development of cellular immune response generated against mucin 1 expressing tumors and cells. In advanced NSCLC the TG4010 along with standard chemo therapy has been shown good results, as fas as patient disease condition is concerned.

Dreicer, R. et al. (2003) have analyzed the impact of couple of schedules of TG4010 on PSA in malignancy of prostate. They have conducted the phase second trial in forty patients with increased profile of PSA. They have reported that TG4010 have biologic activity in cancer of prostate with PSA elevation.

Lepisto, A.J. et al. (2008) have mentioned that biliary and pancreatic cancer are comparatively resistant to chemotherapy and radiation so there is a need to develop immunotherapy for the treatment of biliary cancer and pancreatic tissue carcinoma. They have performed a phase one and phase tow clinical trial of mucin 1 peptide which loaded the dendritic cell vaccine. They found that 4 out of 12 patients have survived after four years and there was no evidence of re occurrence of disease.

Kondo, H. et al. (2008) have evaluated the immunotherapy clinical effectiveness using DC containing mucin 1 peptide (MUC1-DC) and CTL exposed with cancer of pancreatic tissue (YPK-1). They have found that both were able to express mucin 1 (mucin 1-CTL). They concluded that with mucin 1-DC and mucin 1-CTL adoptive immunotherapy would be possible and it could be an efficient immunotherapy for cancer of pancreas.

Pegram, M.D. et al. (2009) have mentioned that AS1402 is a humanized IgG1k mAb which binds to VNTR region at PDTR amino acids of TR of mucin 1 that are generally not present for immunogenicity in the control cells. AS1402 was found to be a powerful promoter of humoral antibody response ADCC particularly against
tumor cells which are mucin 1-expressing but the toleration was observed by repeated immunization of AS402 humanized ab.

**Sharma, S. et al. (2011)** have mentioned that cancer in lung tissue is most life threatening type of cancer and in present scenario; the survival rate of patient is very low with existing therapeutic efforts. Immunotherapy approaches for lung cancer would be a potential option with surgery, radiotherapy and chemotherapy or combination of these treatment methods. Immunotherapy would have better response because of low side effects as compared to existing methods.

**Sangha, R. and North, S. (2007)** have mentioned that cancer vaccine have great interest along with identification of tumor associated antigen for vaccine development and what factors are regulating the pathways of immunity. BLP 25 has been reported as artificial liposomal vaccine for the treatment of cancer that targets VNTR sequences (20 amino acids) of the mucin 1. They reported that this cancer vaccine is proficient to generate the cytotoxic T cell mediated immune response which encourages using L-BLP 25 for the cancer cell regulation.

**Palmer, M. et al. (2001)** have mentioned that immunotherapy with specific liposomal vaccines targeted MUC1 have shown promising outcome in mouse models. They have conducted the phase one study and assessed the immunogenic response of double quantity of mucin 1 liposomal vaccine preparation i.e. BLP 25. They have found that BLP 25 liposomal vaccine was efficiently tolerated and were able to induced immunity in these tumor atients.

**Roulois, D. et al. (2012)** have mentioned that specific treatments against carcinogenic MPM having great potential because resistance of this disease against conventional treatment approach. They have assessed the effects of different drugs including 5 azaCtR, a DNA hypomethylating drug, a inhibitor of histone deacetylase and valproate on translation and recognition of mucin 1 by Tc cells. Mucin 1 was considered as TAA which is present in excess in malignant pleural mesothelioma.

**Jeschke, U. et al. (2012)** determined the expression of MUC1 gene with CA15-3, CA27.29 and mucin 1 antibody in serum of clinical sample of cancer of ovary and in the clinical samples originated from benign tumor of ovary. They found substantial differences of mucin 1 concentration in non malignant tumor and malignant ovarian diseases condition. Average values of mucin 1 have been elevated in ovarian cancer patient’s serum in comparision with benign cysts.
Blixt, O. et al. (2011) have used 60 mer MUC1 glycopeptides in microarray platform to confirm the availability of autoantibodies to altered glycosylated mucin 1 in primary stage of malignancy in breast tissue. They have found that concentration of autoantibodies was meaningfully elevated in the serum of malignancy of breast tissue against negative controls which suggested that autoantibodies against aberrantly glycosylated MUC1 can alter disease progression.

Pedersen, J.W. et al. (2014) have suggested the diagnostic importance of autoantibodies against aberrantly glycosylated MUC1 in colorectal cancer. They generated O type glycosylated artificial mucin 1 along with mucin 4 peptides to mimic tumor linked glycosylated forms and demonstrated on microarray screening of serum samples of malignancy of colorectal track diagnosis along with negative controls. They found that combination of antibody (MUC1 and p53) hallmark may have participated as a part of biomarker panel for the detection at first stage of malignancy in colorectal track.

Akewanlop, C. et al. (2001) demonstrated that Mucin1 (MUC1) and erbB-2 is usually expressed in adenocarcinoma including eighty percent and thirty percent of cancer in breast respectively. Expressions of mucin 1 and erbB 2 have partial overlying but there is no coordination between them. In vitro model demonstrated that MAb DF3 (specific for MUC1 tandem repeats) and bi specific antibody Bs Ab DF3 x H22 can successfully arbitrate phagocytosis of mucin 1 expressing breast cancer tissue by monocyte-derived macrophage (MDM) cultured in GM-CSF.

Croce, M.V. et al. (2003) demonstrated the expression pattern of mucin 1 cytoplasmic tail i.e. mucin 1 CT in carcinoma of breast tissue by immuno histochemical (IHC) analysis using anti mucin 1 CT antibody (CT2 mAb) and C595 monoclonal antibody against an extracellular mucin 1 core protein and suggested that because MUC1 CT is not depending on glycosylation, its expression may constitute as mucin 1 production indicator.

Wang, S. (2014) has found that pancreatic ductal adenocarcinoma (PDCA) has worst prognosis in any gastro intestinal cancer with high mortality rate. He has done the meta-analysis of MUC1 diagnostic role in pancreatic ductal adenocarcinoma (PDCA) and found that mucin 1 assay performed an important characteristic in the detection of PDAC.

Suzuki, Y. et al. (2012) have demonstrated that core 2 type of various glycans of mucin 1 functions as molecular protection against the killer cell (NK) and enhance the
metastasis in case of bladder cancer. They have also mentioned that galectin-3 (a potential cancer marker) binds to mucin 1 through poly N acetyl lactosamine in core 2 type glycans at surface of cells.

**Joseph, Z. et al. (2006)** demonstrated the structure of mucin 1 promoter and transcriptional activity of the promoter of human mucin 1. They have used two different software platforms for analysis of binding sites of transcription factor of the mucin 1 promoter. They use MCF 7 and T47D cancerous cell line to analyse the role of estrogen on expression of MUC1 isoform and they show that the translation of mucin 1/SEC is dependent on estrogen whereas mucin 1/ TM translation having independency.

**Lakshminarayanan, V. et al. (2012)** have identified the minimum requirements (as a vaccine for immunity) to consistently induce CTC and humoral antibody cytotoxicity immune response in mammary cancer of mouse model specific for tumor form of mucin 1. The vaccine was prepared by combination of immuno adjuvant Pam 3 Cys SK4, a peptide T helper epitope and an altered glycosylated form of mucin 1 peptide.

**Obermair, A. et al. (2002)** have done the expression study of the different isoforms of mucin 1 includes mucin 1 / TM, mucin 1 / X, mucin 1 / Y and mucin 1 / Z and found that these isoforms are also present in malignant tumors, whereas MUC1/SEC expression is observed mostly in nonmalignant tissues or cells.

**Baruch, A. et al. (2011)** have demonstrated that MUC1 gene generates different forms of mucin 1 proteins out of which some contain a muc like domain and others are devoid of this domain in human breast cancer by alternative splicing. They have identified equivalent binding proteins that precisely linked with an extra cellular fragment of mucin 1 / Y isoform in breast cancer tissue by co-immunoprecipitation analyses.

**Hartman, M. et al. (1999)** have identified MUC1/Y, a protein merchandise of the mucin 1 gene which is transmembrane protein devoid of the TR array. They have mentioned that anti MUC1/Y antibody would be usefull for targeting of MUC1/Y translating on the surface of mammary carcinoma cells and it can act as important reagents for diagnosis of epithelial tumor and immunotherapy.

**Baruch, A. et al. (1997)** have demonstrated that MUC1/Y isoform have a cytokine receptor similar fragment which was suggested to perform a crucial step in signal transduction. The participation of human mucin 1/Y in oncogenic phenomena was
recognized by representing its probability to augment tumor activation and tumor expansion.

**Akagi, J. et al. (2001)** have demonstrated the correlation for presence of cancer antigen 19-9 and mucin 1/Y in malignancies. They have confirmed that cancer antigen 19-9 epitope is produced only on mucin 1/Y core protein which suggests that cancer antigen 19-9 epitope would be a specific biomarker for mucin 1/Y protein translation.

**Rachagani, S. et al. (2009)** have mentioned that on the bases physiological destiny and biological characteristics, different mucins are grouped into three main category i.e. (a) membrane bound mucins (mucin 1, 3A, 3B, 4, 11, 12, 13, 15, 16, 17, 20 and mucin 21), (b) secreted gel forming (mucin 2, 5AC, 5B, 6 and 19) and (c) soluble mucins (mucin 7, mucin 8 and mucin 9).

**Desmetz, C. et al. (2009)** have studied on section of auto antibodies to multiple tumor linked proteins as a method for detection of tumor at early stage of mammary carcinoma. They have evaluated the mRNA and protein expression and immuno reactivity of five auto antigens i.e. PIA, PRDX2, FKBP52, HSP60 and MUC1 with the use of definite immuno assays. Three out of five autoantibodies i.e. PIA, FKBP 52 and PRDX 2 showed meaningfully elevated reaction in primary cancer of breast tissue.

**Hermsen, B.B. et al. (2007)** have evaluated the humoral immune response to mucin 1 in genetically high risk patient of breast cancer and reported that the concentration of natural antibody against mucin 1 in serum are inferior in BRCA1 and 2 mutation carrier than in healthy people. Moreover no increased mucin 1 IgG antibodies were detected in patient with hereditary high risk and developed carcinoma in mammary tissue. They have concluded that immuno therapy with mucin 1 substrates may reduce the hazard of cancer in mammary in BRCA1 and 2 mutation carrier patients.

**Chapman, C. et al. (2007)** have examined for the occurrence of autoantibodies against TP 53, HER 2, BRCA 1, BRCA 2 and mucin 1 antigens by ELISA in serum of healthy controls, primary cancer in breast and patients with DCIS. They have found that autoantibodies are present in breast cancer at early stage for single or multiple tumor associated antigens as mentioned.

**Lumachi, F. et al. (2004)** have studied to analyze the correlation between serum tumor markers CEA and cancer antigen 15-3 before operation, at different stage of the patients, TNM phases, ER, PR status in patients who have gone through operation for
primary malignancy of mammary. They have found that in cancer patients of breast, serum CEA and cancer antigen 15-3 have correlation in terms of mass of tumor but both markers have low reactivity with no substantial connection.

von Mensdorff-Pouilly, S. et al. (2000) have studied to measure the monomeric IgG and pentameric IgM ab to mucin 1 in cancer patients of breast tissue and found that in cancer patients of breast tissue at early stage with a native antibody response to mucin 1 have better disease explicit existence. Both types of antibodies to mucin 1 might control the tumor distribution in blood stream and over growth by demolition of mucin 1 expressing malignant cells.

Wandall, H.H. et al. (2010) confirmed that IgG auto antibodies to aberrant O type glycopeptide epitopes of mucin 1 were identified but not against peptide epitope. That represents a productive foundation of reactive biomarkers for early identification of cancer in breast tissue. This study therefore noticeably supports the strategy of discovery of autoantibody biomarker against aberrant posttranslational modifications in breast cancer.

Burchell, J.M. et al. (2001) have mentioned that glycosylation is a very important post translational phenomenon and a structure change in glycans added to glycolipid and glycoprotein is a frequently observed in several cancers. Mucin type O linked glycosylation is most extensively studied glycosylation profile. Truncated mucin O-glycans (core 1 type) is generally found in breast cancer Patient against core 2 type O-glycans in healthy people.

Sorensen, A.L. et al. (2006) have mentioned that mucin 1 altered glycoforms signifying possible objectives for theranostics purpose and they have shown that mucin 1 with Tn and sialyl Tn O glycosylation is a specifically cancer glycoforms.

Backstrom, M. et al. (2003) have expressed 16 tandem repeats (TR) of mucin 1 in CHO-K1 cells. They expressed this protein as tagged protein with murine Ig G Fc fraction containing an enterokinase tag removal site for Fc fragment from fusion protein. They found the protein is secreted into the media. They have concluded that recombinant mucin 1 (16 TR) with a carcinoma of mammary type O glycosylation would be used for the immunotherapy of carcinoma of mammary tissue.

Tarp, M.A. et al. (2007) developed monoclonal antibody against MUC1 and reported that GSTA region of 20 tandem repeats (HGVTSAPDTRPAPGSTAPPA) of MUC1 is highly immuno foremost epitope when expressed with truncated O glycans. Most of the other mucin 1 antibodies are specific for PDTR amino acid of 20 tandem repeats.
von Mensdorff Pouilly, S. et al. (2000) have mentioned that antibodies (Abs) against mucin 1 is naturally present in both cancer patients and healthy individuals and production of antibodies to mucin 1 which can be induced by mucin 1 peptide immunization. They have immunized the cancer patients of breast tissue with mucin 1 peptides coupled with KLH and mixed with QS-21 and concluded that MUC1 glycopeptide would give better immune response than a nonglycosylated peptide.

Storr, S.J. et al. (2008) have investigated that aberrant O linked glycosylation of mucin 1 which was purified from serum of cancer patients of breast tissue, has been truly associated with progression of disease. After analysis of O-Glycans they concluded that core 1 type glycans dominantly present with high levels of sialylation. They also mentioned that breast cancer cell line T47D expressed the MUC1 protein which mimics the glycosylation pattern of breast cancer patients.

Brockhausen, I. (2006) mentioned that mucin type O glycans have various tumor related structures including the T, Tn and some lewis element. The changes in these antigens structure could be responsible for the altered cell function including its antigenic activity, adhesion, invasion and tumorogenic properties. This study is focused on glycosyl transferases activity and pathways of O glycosylation in mammary and colon carcinoma cells.

Ohyabu, N. et al. (2009) mentioned that KL-6 glycoprotein which is classified as a polymorphic epithelial mucin (PEM) is a biomarker for breast cancer and other cancer condition like lung carcinoma, colorectal adenocarcinoma, and liver carcinoma. They mentioned that mAb of KL-6 could be a potential theranostics reagent.

Muller, S. et al. (1999) have purified mucin 1 by affinity chromatography followed by enzymatic partially deglycosylated with alpha-sialidase/beta-galactosidase and fragmented by proteolytic cleavage. By reversed phase HPLC they isolated the PAP20 glyco-peptides and analyzed the structure by electrospray ionization mass spectrometry and sequencing. They have found that all positions of T and S of TR region have the O glycosylation targets in the malignant cells including the T residue.

Kufe, D.W. (2009a) has mentioned that most of the previous study has been conducted on mucin 1 N terminal sequence but MUC 1 C ter has good potential as its interacted with various effectors includes receptor tyrosine kinases, c-Src, β-catenin, c-Abl, TP 53, heat shock proteins and human galectin-3. MUC1-C ter has involvement in induction process of transformation of cells. They have also
demonstrated that direct targeting of mucin 1-C function stops the carcinogenicity of breast carcinoma cells in human.

**Takeuchi, H. et al. (2002)** have generated the monoclonal antibody (mAb) MY.1E12 against human milk fat globule (HMFG) in mice. They enzymatically glycosylated the peptides corresponding mucin 1 TR with N-acetylgalactosamine, d-galactose and sialic acid. They found that the affinity of MY.1E12 Ab was higher with peptide having sialylation at Thr residue than un-sialylated Thr containing peptide.

**Hinodaet, Y. et al. (1998)** mentioned that mucin 1 core protein having an important tumor associated antigen peptide which induces the T cell immune response but the immunogenic sites is generally masked by glycosylation. To confirm this result they have done immuno staining of periodic acid treated tissue blocks of in cancerous tissue and normal gastric tissue with an anti mucin 1 core protein MUSE11 mAb and suggests that deglycosylation of mucin 1 core protein might be a critical approch to elicit anti cancerous immunity in gastric cancer.

**Apostolopoulos, V. et al. (1997)** have immunized transgenic mice HLA-A*0201/Kb with MUC1 fusion antigen containing five TR sequence of VNTR region and got highly active CD8+ CTLs against MUC1 peptides. They have reported that different peptide with different adjuvant having different immunogenic activity and these finding will help to make the strategy for tumor immunotherapy in breast cancer.

**Brossart, P. et al. (1999)** have demonstrated that mucin 1 is highly translated in several hematological and epithelial tumors so that it is a suitable entity for vaccine therapies. They have explained that MHC restricted cytotoxic T cells identified the epitopes of mucin 1 tandem repeats. It was also reported that MHC restricted T cells immunity has been activated by dose with mucin 1 fragment containing tandem repeats.

**Brossart, P. et al. (2001)** demonstrated that mucin 1 is highly translated on various B cell lymphomas (BCL) and myelomas (multiple) and on cell surface of many epithelial malignancies. By studies, two human leukocytes Ag-A2 restricted T-cell epitopes was identified of mucin 1 oncoprotein and demonstrated that these peptides are antigens of tumors in acute myelogenous leukemia and in various cancers that might be a potential tool of immunotherapeutic.

**Ninkovic, T. et al. (2009)** mentioned that glycoprotein MUC1 can be presented by antigen presentation cells on MHC type II molecules to activate specific T helper cells. They have shown that octa to decameric glycopeptides from the MUC1 repeats
generated by human immuno proteasomes and cathepsin-L and they identified that the glycan on SAP10 (decameric glycopeptides) is predicted by molecular modeling to presented out into the MHC1 groove. Peptide (SAPDTRPAPG) and the respective glycoprotein stimulated cytotoxic T-cells in vitro which can be used for development of vaccine.

Hiltbold, E.M. et al. (1998) mentioned that in human, under glycosylated (or altered) form mucin 1 is expressed on adenocarcinomas which act as antigen in several cancer including mammary, ovarian, pancreatic etc. They have presented that mucin 1 specific CD4+ T cells response will be generated if immunized with suitable MUC1 peptide or protein will used. They also reported that when amino acid sequence PGSTAPPAHGVT presented by HLA-DR3, it produces the immune response.

Hiltbold, E.M. et al. (1999) have reported that in serum, soluble form glycosylated mucin 1 antigen is not administered by DC and does’nt able to produce any response of MHC class two restricted T helper cell. But synthetic protein from the mucin 1 TR region is usually exposed by MHC type II molecule and hence elicits T helper cell responses. They also reported that 100 amino acid long peptide gives good cytotoxic cell response than glycosylated protein.

Vlad, A.M. et al. (2002) have studied on management of glycosylated proteins by DCs for antigen presentation to desired cells and they have originated the mouse T cell hybridoma to understand the antigen presentation process of mucin 1 glycoprotein. They have reported that dendritic cells endocytose mucin 1 molecule and transported to acidic compartments. It was further converted into smaller peptides and presented to MHC class two molecules with carbohydrates moiety.

Napoletano, C. et al. (2007) demonstrated that type of immunity generated is usually depend upon the interaction between tumor antigens and dendritic cells (a type of antigen presenting cells). They have selected the glycopeptides (contains 3 tandem repeats of mucin 1) and mucin 1 containing tumor specific glycan Tn. They have mentioned that macrophage galactose type c lectin translated on primary dendritic cells is a receptor which optionally internalized the short GalNAcs carrying immunogen.

Hiltbold, E.M. et al. (2000) demonstrated a mechanism by which MUC1 glycoprotein (potentially immunogenic) fail to develop strong immune response. They have reported that soluble form of MUC1 in serum and ascites internalized by
dendritic cells (DR) is not transported to endoplasmic reticulum for further processing and remain there for long term and stop the processing of other molecule by DR.

Ninkovic, T. et al. (2007) demonstrated that O-glycosylated MUC1 peptide are effective substrates of immuno-proteasomes, but the cleavage pattern is affect by O-glycosylation. The nonglycosylated MUC1 tandem repeat peptide (clusters of oligorepeats AHGVTSAPDTRPAPGSTAPP or AHGVTSAPESRPAPGSTAPA) is cleaved preferably.

Soares, M.M. et al. (2001) found that antibody response and T cell mediated mucin 1 specific immun response increased in homo sapience mucin 1 transgenic (Tg) mice in comparision to control mice. They mentioned that low titer of IgM and Low-frequency of cytotoxic T lymphocytes immune response present against MUC1 tumor antigen but not able to check tumor growth.

Kohlgraf, K.G. et al. (2004) have examined the tumor cells rejection by involvement of the TR and CT fragment of human mucin 1. Complimentary DNA constructs of mucin 1 (either TR or CT domain was removed from DNA construct) were transfected in two different B16 and Panc 02 murine cell lines. They have found that TR region and a mucin 1 CT domain was involved for the rejection of T helper cell of mucin 1 expressing B16 malignant cells but not in mucin 1 expressing Panc 02 malignant cells.

Rowse, G.J. et al. (1998) mentioned that in human MUC1 could be a potential target for immunotherapy because of presence of immune response against MUC1 expressing cells and this characterstic was found in the clinical samples of mammary and ovarian cancer. These reported that mucin 1 endogenous expression by MUC1-transgenic mice induces T-cell. These finding provide the useful model to understand mechanism which is regulating immunological tolerance.

Tempero, R.M. et al. (1999) have developed the transgenic mice C57BL6 for human MUC1 tumor antigen (mucin 1 Tg) and examine the autoimmune response. They found that migrating mucin 1 reactive antibodies were detected in mucin 1 transgenic mice but substantial quantities of these antibodies were not absorbed by MUC1 expressing organs. These finding suggested that high translated of mucin 1 primarily by secretory epithelium cells which is organ specific and not detected by migrating antibodies.

Budiu, R.A. et al. (2009) have mentioned that mucin 1 is usually available on endometrial glands and increased translation was reported in endometrioid clear cell
of ovarian tumors along with ectopic lesions of ovary endometriosis. Additionally variations in mucin 1 translation in endometriosis may endorse anti mucin 1 immunity that potentially plays a process in progression of tumor.

**Ryan, S.O. et al. (2009)** have demonstrated that when experimental mice was immunized with hundred amino acid long peptide of mucin 1, it produces weaker immune responses may be because of self-tolerance. But when immunized with glycosylated Tn antigen it induces the specific T cell immune response and antibody responses in mice. These actions help to elicit the responses in mucin 1 transgenic mice.

**Tang, C.K. et al. (2008)** have emphasized on DNA vaccine could be a better option. They investigated carriers for MUC1 DNA vaccination i.e. OMPLL and RMPLL for cancer immunotherapy. Data shown that OMPLL mucin 1 DNA and RMPLL mucin 1 DNA immunized mice (C57BL/6) shows better immune response as compared with MUC1 DNA immunized mice.

**Choi, D.H. et al. (2011)** have demonstrated that the strength of anti cancer molecular vaccine using MUC1 fusion vaccine. For better presentation of antigen and tumor suppressive effect, mucin 1 gene was fused with HSP70 gene and after expression fusion protein was found in media. When this chimeric fusion vaccine was introduced to mice, CTL immune response was observed. This result indicated that HSP70 enhanced the anti malignant efficiency of DNA vaccine.

**Wright, S.E. et al. (2010)** worked on, whether Mucin1 (MUC1) with altered glycosylation will act as immunogen for adenocarcinomas (ADCs) or not. In this work they substituted the MUC1 tandem repeat at O-linked glycosylation sites on tyrosine and serine with asparagine and found that there is no effect on development of mucin specific CTLs with this substitution. This data demonstrated that mucin 1 TR altered sequences can be useful as DNA vaccine which generally prevents O-linked glycosylation.

**Kobukai, S. et al. (2011)** have determined the function of elicit presentation of antigen in DC based immunotherapy. They immunized the animals group with 2 antigens of MUC1-MPA11P pulsed dendritic cells (DC), they found that tumor shows regression as compared to the mouse which exposed with DCs alone or DCs with mucin 1 peptide. They have demonstrated that the increased antigen intake using an MPA11P delivery entity upgraded the potential of cell immuno therapy.
Choi, Y. et al. (2011) have a method of immuno therapy method using immuno competent mice as an experiment model. They have increased the intencity of mucin 1 DNA vaccine by combinantion with m ANT 2 shRNA and found that it increased the apoptosis process in B16F1 cell line of murine which cotranslating the mucin 1 and fluc gene and that BMF condensed cell are highly suseptable to lysis by mucin 1 linked Tc cells.

Pinkhasov, J. et al. (2011) have successfully highly expressed the MUC1 TR peptide as a fusing protein with mucosal targeting E. coli LTB mucin 1 in a plant cells using viral replicon system. They also confirmed that only glycosylated LTB-MUC1 is detected by specific monoclonal antibody. They have concluded that plant derived MUC1 antigen mimicking the natural MUC1 antigen.

Jeon, Y.H. et al. (2007) used cDNA of hMUC1 and cloned in pcDNA3.1 vector and used as DNA vaccine and after injecting with subcutaneously of CT26 / h mucin 1 - fluc into mice which was previously immunized with construct pcDNA3-hMUC1, they observed the inhibition of tumor growth by an optical imaging method against control i.e. pcDNA3.1 backbone vector.

Mohebtash, M. et al. (2011) have developed a PANVAC recombinant vaccine that is composed of transgenes for mucin 1, CEA and T cell stimulatory molecules. They have given this vaccine monthly to 26 patients and they got mixed response. They have concluded that the patient with low burden of tumor and got minimal prior chemotherapy have shown good response to this vaccine.

Ibrahim, N.K. et al. (2011) have reported that AS1402 antibody is a humanized IgG1 that targets the mucin 1 having aberrantly glycosylation. The aberrantly glycosylated mucin 1 is reported in several studies in almost 90% of breast cancer patients. They have compared the result of cancer patients of mammary tissue which was exposed with letrozole with AS1402 or without AS1402 and found that there is no significant difference in outcome.

Wright, S.E. et al. (2009) reported that breast cancer patient have invers effect of cytotoxic T lymphocytes (CTL) response with tumor burden. They have studied on four previously treated patients of metastatic cancer of breast. Out of which two were with macroscopic disease and two were with no disease. They have reported that CTL elicit from person having high tumor burden had less generation of cytokines as compared to control.
Raina, D. et al. (2012) mentioned that MUC1-C transmembrane domain having a CQC motif which generally forms dimer and its tumorogenic function in cancer of breast tissue and cancer of lung. The dimerization of mucin 1 C is found in cytoplasm and independent of presence of mucin 1 N subunits that are present outside the cells. They have found that some reducing agents are able to reduce the dimerization process of mucin 1 C in both natural and in vitro conditions.

Brayman, M.J. et al. (2007) have mentioned that mucin 1 translation is initiated by several factors includes progesterone (P), TNF α, and IFN gamma. They have demonstrate that translation of mucin 1 is down regulated by higher expression of inhibitor of protein, PIAS1, PIAS3, PIASx-alpha, PIASx-beta and PIASy in human cancer cell line of breast, T47D.

Nath, S. et al. (2014) have mentioned that MUC1 expressed in normal condition differs from tumor-associated MUC1 in terms of its cellular distribution, function and biochemical features. Tumor associated mucin 1 are involved in the pathway of intra cellular signal transfer and involved in regulation of targeted gene and hence protein.

Tholey, R.M. et al. (2015) have described that mucin 1 is highly translated in PDA and it is linked with malignancy aggressiveness, signifying mucin 1 as a therapeutic target for PDA. They also mentioned that translation of mucin 1 in initial and metastatic lesions provides a rational for the developmental approach of therapy.

Acres, B. et al. (2000) have conducted the immunization of mice with several MUC1 vaccine and analyses for cytotoxic T cell responses. They have immunized the mice with MUC1-GST, MUC1-GST+mamman (MFR) and recombinant MUC1 (from vaccinia virus) with IL-2. They observed that immune response was different with different mice strains.

Apostolopoulos, V. et al. (2003) have reported that in in-vivo and in-vitro conditions, mucin 1 (MUC1) binds to H-2Kb and showing complete cross-reactivity with nonglycosylated variant. They have reported that glycopeptides associated with major histocompatibility complex-1 (MHC-I) associated glycopeptides anchored the peptide allow if for binding with high affinity.

Jia, Y. et al. (2010) have reported that different mucins includes mucin 1, mucin 5AC and mucin 6 constitute the first line of defense or barrio in stomach and this barrio protect the epithelium wall from different pathogens, acid, base etc. They reported that mutations in these gene caused genetic alteration hece responsible for the development of cancer.
Kufe, D.W. (2009b) has mentioned that epithelia in different location are generally protected by mucous barrier from adverse conditions. These mucous barriers are constituted by transmembrane mucins and secreted mucins. Aberrant translation in the structure of these mucins was reported in various cancers. In some malignancies, body produced large amount of transmembrane mucins to neutralize the inflammation and cancer.

Bowen, J.A. et al. (1996) have done the analysis of mucin 1 in freeze tissue of pregnant tissue graft, uterine epithelium and tissue graft from ovary with immunological florescence technology. They found the down regulation of mucin 1 with altered form of glycosylation after treatment.

Yin, L. et al. (2010) have demonstrated that C terminal domain of mucin 1 is triggered the NF-kappaB pathway. This domain with altered glycosylation pattern was found in high amount in MM cells. They have reported that mucin 1 C terminal domain inhibitors diminished the expansion of myeloma tumor cells in human. They have concluded that expansion of tumor of MM cells is depending upon the unaltered form of C domain of mucin 1.

Yin, L. et al. (2012) have demonstrated that C terminal domain of mucin 1 is present in cell of multiple myeloma with altered form of glycosylation. They have studied on MM cells and elucidated that inhibitor of C terminal domain of mucin 1 treatment on MM cells is directly linked with higher amount of ROS etc. This phenomena is diminished the protective function of p53 called TIGAR. They have concluded that MM cells are depend on function of p53 i.e. TIGAR and C terminal domain of mucin 1.

Yin, L. et al. (2014) have demonstrated that BTZ inhibitor triggered the oxidative stress in MM cells. Targeting of C terminal domain of mucin 1 with its inhibitor GO-203 is efficiently triggered the ROS mediated MM cell death. They have reported that BTZ along with GO-203 diminished the function of p53 protective mechanism TIGAR. They have also reported that GO-203 is an efficient tool for treatment of MM cells which is BTZ resistant.

Linden, S.K. et al. (2009) have reported that MUC1 in protective barrier protect the epithelia from Helicobacter pylori infection. They concluded that mucin 1 protects the epithelial cells of body from different non mucin 1 binding bacterium by opposing the adhesion by steric hindrance to the surface of cells.
Ng, W. *et al.* (2008) have mentioned that MUC1 is highly expressed with aberrant glycosylation in stomach cancer and act as ligand for *Helicobacter pylori* which is responsible for the development of gastric carcinogenesis. They have reported that 9 amino acid of splicing variant insert into the signal peptide and associated with carcinogenesis.

Liu, X. *et al.* (2014) have reported that tumor associated mucin 1 which interacts with p120 and β-catenin that regulates the cyclin D1. Mucin 1 promotes the activities of both beta catenin and p 120 catenin hence modulating WNT signaling.

Mori, Y. *et al.* (2014) have mentioned that tumor associated mucin 1 (MUC1) is involved in signal transfer by linkage with different receptors and participate in growth and several factors, which promote the development of tumor. They have reported that MUC1 induced the uPA, which enhanced the MMP 2 and MMP 9 activities, followed by cell invasion.

Kannan, K. *et al.* (2015) have mentioned that ovarian cancer is most notarious deaths causing cancer in women. They analyzed the chimeric mRNA which was generated by splicing between MUC1, KRTCAP2 and TRIM46 molecules. They found 6 different combinations of these molecules by using RT-PCR analysis but not found in non-cancerous cells. They concluded that chimeric from of MUC1-TRIM46-KRTCAP2 isoforms can be used for the clinical diagnostic and therapeutic.

Beatson, R. *et al.* (2015) have mentioned that O-glycosylation is the hallmark of MUC1 in breast cancer and this glycoform was interacted through lactins to cells involved in immune system. They found in breast cancers carry, most of cell carry Tn antigen and it is closely associate with T glycan (Galβ1,3GalNAc). These two glycol antigen are reported in most of the cancer.

Zelasko-Leon, D.C. *et al.* (2015) have mentioned that mucin 1 is over translated in several cancers and this could be a unique target for cancer treatment using nano particles. They have immobilized the MUC1 antibody along with albumin on gold nanorods surface. They found that in the absence of photothermal treatment, these agents are not showing cytotoxicity. The technology can provide a better tool for the analysis and treatment of cancer of breast.

Tagde, A. *et al.* (2016) have mentioned that mucin 1 C oncoprotein is translated in multiple myeloma. Silencing of MUC1-C oncoprotein by the GO-203 inhibitor with CRISPR/Cas9 editing is correlated with MYC mRNA and protein down regulation.
They have concluded that MUC1 expression directly associated with MYC expression in progression of multiple myeloma.

Raina, D. et al. (2015) have established that mucin 1 cytosolic subunit is involved in cancer progression. They demonstrated that amino acid sequence CQCRKK (highly conserved sequence) presented the two cysteine residues by making a small pocket and form disulfide bonds. This motif is directly interacts to the CQC motif. They mentioned that mucin 1 cytoplasmic domain CQC motif can be a potential target for several cancerous cell types.

Koning, N. et al. (2015) have reported human milk having beneficial effects which protects from infections and autoimmune disorders. A glycan present in milk is C-type lectin which is intercellular adhesion molecule specific to dendritic cell (DC-SIGN), interacts with fucose at terminal. They reported that MUC1is the major milk glycoprotein that serve as first line of defense.

Wang, X. et al. (2015) have mentioned that there is no such effective treatment for melanoma at late metastatic phase although at early stage, removal of that part is the only treatment approach. They have mentioned that mucin 1 promotes the migration of melanoma through protein kinase B signaling pathway. They have suggested that this is a unique mechanism essential for the metastasis of melanoma cells and this would be a potential target for treatment.

Wang, H.S. and Wang, L.H. (2015) have worked on the expression and significance of MUC1 along with Galectin-3 in tissue of colorectal cancer. They have done the study by immunohistochemistry streptavidin-peroxidase method on colorectal cancer tissues and normal tissue and found that MUC1 and Galectin 3 were found in high concentration as compared to non-cancerous tissue which was adjacent to carcinoma.

Hasegawa, M. et al. (2015) have mentioned that MUC1-C protein is an intracellular druggable target with some potential inhibitor. They have taken GO-203 which is potential inhibitor of MUC1-C and encapsulated with unique polymeric nanoparticles. They have found that GO-203 from these nanoparticles was release and shown more effective treatment of mucin 1 C positive lung and mammary carcinoma cells in vitro as compared to control.

Ren, J. et al. (2004) have mentioned that mucin 1 have resistance against anti-tumor drugs after development of its altered form. They have mentioned that mucin 1 C terminal fragment gone to mitochondria in cells of colon carcinoma. It triggered the release of death factors by programmed way. It also triggered the caspase-3 and
induced cell death. These phenomena reflected that mucin 1 diminished the apoptotic activity against damage of genetic material and resist the cells from anti-tumor drugs. **Pimental, R.A. et al. (1996)** have mentioned that various mucins are protective in function in natural condition and protect the apical surface from various microbes and adverse conditions. They have demonstrated the mechanism and kinetics of mucin 1 cassette, its translation, expansion, localization and final deactivation in mice. **DeSouza, M.M. et al. (1999)** have studied on activity of mucin 1 in reproductive system. They have mentioned that reproduction track of females have protective covering which provide suitable conditions for embryo development and protect from external environment including microbial infection. They have reported that higher concentration of various mucins including mucin1 is present in this track and involved in lubrication and protective mechanism. **Siragusa, M. et al. (2007)** have mentioned that role of mucin in development of tumor of thyroid is not so clear. They have mentioned that mucin 1 is present in various cancers and protect the tumor cell from antitumor drugs. They have mentioned that IL-10 and IL-4 regulates the tumor cell of thyroid and its survival even in the presence of antitumor drugs. The concentration of both cytokine is diminished in malignant condition and it is directly proportional to the concentration of mucin 1. **Brayman, M. et al. (2004)** have mentioned the presence of mucin 1 in reproductive track. It provides the lubrication, makes wet conditions for cell surface and shows protective function again endogenous, external microbes and several toxins. It also prevents the attraction of malignant cell to normal cells. It was also reported that its native forms is reduced in cancer condition which is directly proportional to the concentration apoptotic agents. **BarrattBoyes, S. M. (1996)** has demonstrated that the various immunological and biochemical function of mucin 1 and emphasized on its potential in diagnostic field of mammary cancer and several other cancer. He also mentioned that its different form and variant are present in various cancers and pay crucial role for development of cancer. Several studies was conducted on mucin 1 using transgenic animals and found positive correlation with disease progression. **Kontani, K. et al. (2003)** have mentioned that DC cells could be a potential vaccine for the diminishing of tumor progression. They have analyzed the property of DC to trigger the cell based immunity since it is involved in antigen presentation. They used 14 patients with 9 mucin 1 positive sample. They have concluded that mucin 1 is able
to trigger the B and T cell immunity when immunized with DC vaccine which targeting mucin 1.

**Peterson, J. A. et al. (1997)** have reported that radio immunotherapy for the treatment of malignancies of mammary tissue. They have used iodine 131 labeled antibodies in several experimentation and found effective suppression of tumor burden in mammary tissue. Same type of result was reported in different mammary carcinoma tissue.

**Li, Y. and Cozzi, P. J. (2007)** have reported that mucin 1 can be used for the therapeutic potential of malignancy of Prostate tissue. They have mentioned that mucin 1 having different and unique glycosylation pattern which enable it as good prognostic and therapeutic factor.

**Pietersz, G.A. et al. (1997)** have done the comparative study on 2 different antibodies hCTMO1 and BC2 characterized as anti mucin1 antibody for its therapeutic approach. They have reported that both antibodies having same affinity to cancer tissue. Because of high rate of internalization and retention hCTMO1 is more efficient and suitable antibody.

**Burton, J. et al. (1999)** have worked on mucin 1 and its specific antibody for the treatment of multiple myeloma (MM). They have mentioned that this malignancy is the second lethal cancer type. They used radioactive iodine labeled with antibody and got god response in terms of tumor burden.

**Li, Y. et al. (2003)** have mentioned that mucin 1 known antigen which was studied for its diagnostic and therapeutic potential in several malignancies. Its altered form expression was reported in various cancers and involved in disease progression and activation. They have reported that mucin1 is involved in cell transformation. These all feature of MUC1 and its different isoform shows the diagnostic importance in the diagnosis and prognosis for different cancers, especially breast cancer.