
Diagnostic

diseases; AFP cannot be used for screening in patients suffering with hepatitis C or cirrhosis [80,81].

Cancer antigen 125 (CA125)

CA-125 antigen is known to be the primary serum tumour marker used in ovarian cancer for prognosis, response to chemotherapy and disease progression. The CA 125 antigen is found out to be a membrane glycoprotein delivered by tissues derived from coelomic epithelium expressed by most epithelial ovarian cancers. The Major drawback in using the CA125 test as a screening tool is its lack of sensitivity and its inability to detect early stage cancers. It may also be elevated in other malignant cancers, including those originating in the lungs, fallopian tubes, breast, endometrium, and gastrointestinal tract [82-87].

Thyroglobulin (Tg)

Thyroglobulin (Tg) is an organ-specific tumour marker; associated with patients possessing differentiated thyroid cancer that emerge from the follicle cells which increases the levels of thyroglobulin in the blood. It is considered to be a large glycoprotein stored in the follicular colloid of thyroid gland which acts as pro-hormone in the intra-thyroid synthesis of thyroxine (T4) and triiodothyronine (T3) [88-90].

Heat shock protein (Hsp)

Hsp has gained importance due to its implication in tumour progression and response to therapy which has led to the development of targeted therapy by the usage of Hsps as immunological adjuvant in anticancer vaccines. Heat shock proteins (Hsps) are overexpressed in various human cancers and are involved in cell cycle related processes. It might be due to the stimulation of the Hsp induction by physio-pathological features of the tumour microenvironment [91-95].

Human chorionic gonadotrophin (hCG)

Human Chorionic Gonadotrophin (hCG) is a hormone normally produced by placenta, which are found to be high in the blood of patients with certain types of ovarian cancers, testicular and choriocarcinoma. The elevation of serum levels of hCG and its metabolites cannot be considered for prognosis as it is estimated that hCG might directly modify the growth of the cancer, leading to a worse outcome. Pregnant women are tested with the presence of hCG levels and may not be useful as a marker under this condition [96-100].

Therapeutic biomarkers

Cytotoxic chemotherapy and radiotherapy are considered to be the best medications available for malignancy; however, these may cause serious side effects causing damage to normal cells along with the tumor cells. Recent advancements in understanding the underlying mechanism Cancer has led to the development of targeted therapies which may inhibit the growth of the tumor cells interfering in their molecular pathways leading to apoptosis. For example, Imatinib and Erlotinib drugs can inhibit the activity of Protein tyrosine kinases targeting the Epidermal Growth Factor Receptor (EGFR). Other targeted therapies like antibody bevacizumab will act upon a growth factor that stimulates tumor blood vessel growth [101-105].

Glycolysis

Most of the malignant tumours depend on glucose for their development. When human tumour cell lines were studied with varying degrees of glycolysis, it has been observed that there is an inverse relationship between the rate of glycolysis and damage induced by chemotherapeutic drugs and radiation. Studies have shown that 2-DG selectively sensitizes tumour cells to ionizing radiation, without causing damage to normal cells. Thus, Clinical trials in brain tumour patients using a hypofractionted radiotherapy protocol combined with 2-DG proved to be successful. Combination therapy has resulted in minimal acute toxicity and late radiation effects and there is significant increase in survival rate and improvement in quality of life has been reported [106-110].

Mammalian target of rapamycin (mTOR)

Mammalian target of rapamycin (mTOR) is a serine-threonine protein kinase which fits in with the PIKK [phosphoinositide 3-kinase (PI3K)-related kinase] family, assumes a noteworthy part in regulating cell development and proliferation. When mTOR is activated, the phosphorylation levels of its downstream targets p70S6K and 4EBP1 are promoted, which leads to increased levels of ribosome biogenesis, translation, inhibition of autophagy and reorganization of the actin cytoskeleton. Studies have shown that the (PI(3)K–PTEN–mTOR signaling pathway is aberrantly activated in many tumours, resulting in dysregulation of cell growth and proliferation. Loss of PTEN mRNA or protein production in tumour tissue can be considered as Biomarkers to evaluate the activation of the pathway. Proliferative marker Ki-67 is used to evaluate the Inhibition of mTOR by rapamycin, which can measure the presence of phosphorylated form of the ribosomal protein S6, and its therapeutic effects on tumour cells [110-114].

Telomerase

Telomerase is an enzyme known as reverse transcriptases, which uses RNA as a template for producing DNA and it contains both RNA and protein components. The enzyme is sole responsible for protecting the cell from degradation and death by the maintenance of telomere. Thus it can be treated as one of the best diagnostic markers for human cancer, related to malignant tumours, thus making it an ideal target for chemotherapy [115-119].

p53

The p53 gene is known to be a tumour suppressor gene which prevents the uncontrolled multiplication of abnormal cells. Radiation and many other anticancer drugs cause damage to the DNA of cancer cells, which activates the p53 gene leading to apoptosis. During treatment, an intact wild type p53 gene is essentially required to stimulate programmed cell death of a cancer cell. Thus p53 gene is a well-studied potential biomarker for predicting prognosis and patient's response to therapy [120,121].

Tyrosine kinase

Tyrosine kinases belong to group of enzymes that regulate various cellular processes like cell growth, differentiation, migration, and apoptosis that aids in tumour development and progression. Thus targeting protein Tyrosine kinases as a therapeutic biomarker is an attractive approach to inhibit the tumour growth. For example,

tyrosine kinase inhibitor GeŽtinib and Trastuzumab have proved to be anti-cancer agents [122-124].

Cells as Biomarker

Circulating tumour cells (CTCs)

Circulating tumour cells can be considered as a powerful biomarker to predict the disease progression and response to therapy. Increase in CTCs at any time during therapy is an indication of progression, whereas decreased number of CTCs shows the effectiveness of the therapy. Studies have shown that they can be considered as standard tumour markers (e.g., Ca27-29) in predicting prognosis [124].

T-regulatory cells (CD4+, CD25+ and Foxp3+)

T regulatory cells (T-regs) are considered to be important in inducing and maintaining peripheral self-tolerance, consequently preventing immune pathologies. They are assumed to control both natural and acquired immune responses. T-regs is well known as a surrogate immune marker of cancer progression; also acts as a predictor of response to targeted therapies. The presence of FoxP3+ cells within tumours has proven to predict the prognosis, metastatic ability and invasiveness of some tumours by modulating the ability of the immune system to target tumour cells [125-127].

Cancer stem cells (CSCs)

Cancer stem cells are subpopulation of cells that have the capacity to self-renew and to generate the more differentiated progeny which make up the bulk of a tumour. Studies have shown cancer stem cells (CSCs), tumourigenic cancer cells, or tumour-initiating cells, can give rise to new tumours when transplanted into immuno-deŽcient animals. Therefore, it is utmost importance to identify CSCs for every possible tumour which may lead to new therapeutic avenues [128-131].

Epigenetic biomarkers

It is well known that, in cancer cells, genes are either altered by mutations, or through epigenetic modiŽcations to chromosomes that change gene-expression patterns. Epigenetic modiŽcations are supposed to occur either through DNA methylation of genes or by acetylation, methylation, or phosphorylation of histones and other proteins around which DNA is wound to form chromatin [132-134]. Recent advancement in the Želd has led to the awareness of the epigenetic changes driving neoplasia to be used as signiŽcant cancer biomarkers. Studies have shown that the activity of DNA methyltransferases (DNMTs), are altered in tumour cells and are

20.

69. Mathivanan S (2012) Quest for Cancer Biomarkers: Assaying Mutant Proteins and RNA that Provides the Much Needed SpeciẐcity. J Proteomics Bioinform 5: 13-17.

70.

112. Tyagi AK, Prasad S (2015) Targeting P53 Pathway by Curcumin for Cancer Prevention and Treatment. Cell Dev Biol 4: e131.

113. Leitch C, Andresen V, Gjertsen BT (2013) Impaired Ribosome Biogenesis and P53 Activation in Haematological Disease: Novel T erapeutic Strategies. J Bone Marrow Res 1: 121.

114. Naga Deepthi CH, VVL Pavan Kumar A, Rameshbabu, Indirapriyadarshini U (2011) Role of Tumor Suppressor Protein p53 in Apoptosis and Cancer T erapy. J Cancer Sci T er S17-001.

115. Kuroda J, Taniwaki M (2013) Principles and Current Topics Concerning Management of Tyrosine Kinase Inhibitor T erapy for Chronic Myelogenous Leukemia. Transl Med S2-001.

116. Chen MS, Liu CY, Wang WT, Hsu CT, Cheng CM (2011) Probing Real-Time Response to Multitargeted Tyrosine Kinase Inhibitor 4-N-(3′-Bromo-Phenyl) Amino-6, 7-Dimethoxyquinazoline in Single Living Cells Using Biofuntionalized Quantum Dots. J Nanomed Nanotechnol 2: 117.

117. Ahn JM, Cho JY (2013) Current Serum Lung Cancer Biomarkers. J Mol Biomark Diagn S4-001.

118. Falasca M (2012) Cancer Biomarkers: T e Future Challenge of Cancer. J Mol Biomark Diagn S2-e001.

119. Trugenberger CA, Peregrim D (2013) Discovery of Novel Biomarkers by Text Mining: A New Avenue for Drug Research? J Mol Biomark Diagn S3-004.

120. Sharma M, Mohanty S (2013) Molecular Biomarkers in Cytogenetically Normal í Acute Myeloid Leukemia: harnessing the targets. J Mol Biomark Diagn S8-009.

121. ElDeeb WM (2013) A Novel Biomarkers for Pneumonia in Calves. J Veterinar Sci Technol 4: e111.

122. Szajnik M, Derbis M, Lach M, Patalas P, Michalak M, et al. (2013) Exosomes in Plasma of Patients with Ovarian Carcinoma: Potential Biomarkers of Tumor Progression and Response to T erapy. Gynecol Obstetric S4-003.

123. Valiyaveedan