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A significant role of biomarkers in breast cancer, cervical cancer and colorectal cancer - A review

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ABSTRACT

The early discovery of malignancy can altogether reduce disease mortality and spares lives. In this way, a lot of exertion has been dedicated to the investigation of new advancements to distinguish early indications of the ailment. Biomarkers have various potential applications in oncology, including peril examination, screening, differential end, an affirmation of figure, desire for response to treatment, and checking of development of illness. Malignant growth biomarkers spread an expansive scope of biochemical substances, for example, nucleic acids, proteins, sugars, little metabolites, and cytogenetic and cytokinetic parameters, just as whole tumor cells found in the body liquid. They can be utilized for hazard appraisal, finding, anticipation, and for the expectation of treatment adequacy and danger and repeat. A thorough comprehension of the pertinence of cach biomarker will be imperative for diagnosing the malady dependably yet in addition help in the decision of various restorative choices at present accessible that is probably going to profit the patients. In this review, we provide a information about late advances in disease biomarker discovery, different signalling pathways for specific tumors like breast malignancy, cervical malignancy, colorectal malignancy and finding, forecast and restorative purposes, which incorporate markers as of now in clinical practice just as different upcoming biomarkers.

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INTRODUCTION

Malignancy, an intricate gathering of maladies portrayed by the uncontrolled development and spread of strange cells, has for quite some time been the main source of death in numerous nations. In view of GLOB-CAN 2012 estimates (Ferlay, 2010) there are a million peoples are affected by cancer in the world

Malignant growth markers or biomarkers are characterized as particles which show the nearness of disease or gives data about the probable future conduct of a disease (Duffy, 2013). As of late, biomarkers have started to assume a undeniably imperative job in malignancy recognition, treatment and patient consideration Biomarker examination in disease not just gives extra data about traditional clinical variables, yet in addition empowers patients with a progressively good benefit- hazard parity to get certain medicines (Polley *et al.*, 2013). The character of huge numbers of the qualities inclining to genetic disease disorders has been set up (Munafò *et al.*, 2005). This advising must incorporate the exchange of conceivable dangers and advantages of malignancy early identification and avoidance

modalities (Robson *et al.*, 2010). The main aim is to discuss about the advancement of biomarker and care in cancer, use of biomarkers in cancer detection and various signalling pathways with different diagnosed cancers

MATERIALS AND METHODS

Biomarkers

The term biomarker can be applied to any measurable biological unit that is characteristic of a biological state (Atkinson *et al.*, 2001). These are classed in various way,

1. Investigative
2. Prognostic -

Predictive – allowing insight into likely response or resistance to a targeted therapy. Kang *et al.* (2015); Buyse *et al.* (2010)

Biomarkers are measurable either in tumour tissue at the point of biopsy, or biomarkers are circulating in the blood, urine and other fluids, which are not considered in tissue biomarkers and time to detection and analysis can be long. Though, while circulating markers will be easier to observe throughout illness progression, their origin and accuracy is commonly placed into question, shown in Figure 1.

Advance in biomarker discovery

Nowaday biomarker are developed including 2-dimensional electrophoresis(2-DE) and mass spectroscopy(MS) using gene arrays in addition to proteomic machineries, have use for few newer biomarker discovery (Konety and Getzenberg, 2001). Newly, the new urine biomarkers are approved y FDA a d including bladder tumor antigen (BTA) and the diagnostic agent for bladder cancer is nuclear matrix protein-22 (Mungan *et al.*, 2000). Recent investigation in genetic science and genetics technologies as well as mass chemical analysis have given any desire for finding examples of different biomarkers as well as 'signature' protein/quality profiles explicit to each express malignancy (Ramaswamy *et al.*, 2001). For this situation, the clinical 'marker' might be all the more precisely be an example of qualities or proteins that give a sign of the nearness of malignant growth in a person. (Vijver *et al.*, 2002) the cancer is detected by any normal tissue and out into a plasma stream, and it increases a background level.

RESULTS AND DISCUSSION

Biomarkers In Cancer Care

A biomarker is an equitably estimated trademark that portrays an ordinary or unusual natural state in a life form by breaking down biomolecules, for example, DNA, RNA, protein, peptide, and biomolecules synthetic adjustments (Micheel and Nass, 2012). "A biomarker is any substance, structure or procedure that can be estimated in the body or its items and impact or foresee the rate of result or ailment." (Lassere, 2008). More explicitly as far as clinical utility, a malignancy biomarker may gauge the danger of creating disease in a particular tissue or, on the other hand, may quantify danger of malignant growth movement or potential reaction to treatment. The calculated structure of malignant growth biomarker advancement has likewise been developing with the fast extension of our omics investigation capacity of clinical biospecimens dependent on the customary way of biomarker arrangement (World Health Organization, 2001), are shown in Figure 2.

Prescient biomarkers

Expectation reaction to explicit restorative mediations, for example, inspiration/initiation of HER2 that predicts reaction to trastuzumab in breast malignant growth (Piccart-Gebhart *et al.*, 2005). Additionally, KRAS-actuating changes anticipate protection from EGFR inhibitors, for example, cetuximab in colorectal malignancy (Cutsem *et al.*, 2009).

Prognostic biomarker

It may not be specifically connected to or trigger explicit restorative choices, yet plan to advise doctors with respect to the danger of clinical results, for example, malignant growth repeat or illness movement later on. A case of a prognostic disease biomarker is the 21 quality repeat score which was prescient of bosom malignant growth repeat and by and large survival in hub negative, tamoxifen-treated breast malignancy (Paik *et al.*, 2004).

Diagnostic biomarker

It is utilized to recognize whether a patient has a particular sickness condition. Indicative biomarkers have as of late been executed for colorectal malignant growth observation by testing for stool disease DNA.

Biomarker In Var ious Cancer

Breast Cancer Biomarkers

In breast malignancy, biomarker investigation is normal way. It initially started with testing for hormone receptor articulation to control tamoxifen therapy (Palacios *et al.*, 2009).

The positive prognostic receptor is estrogen receptor (ER)- alpha and intensely prognostic of a reac-

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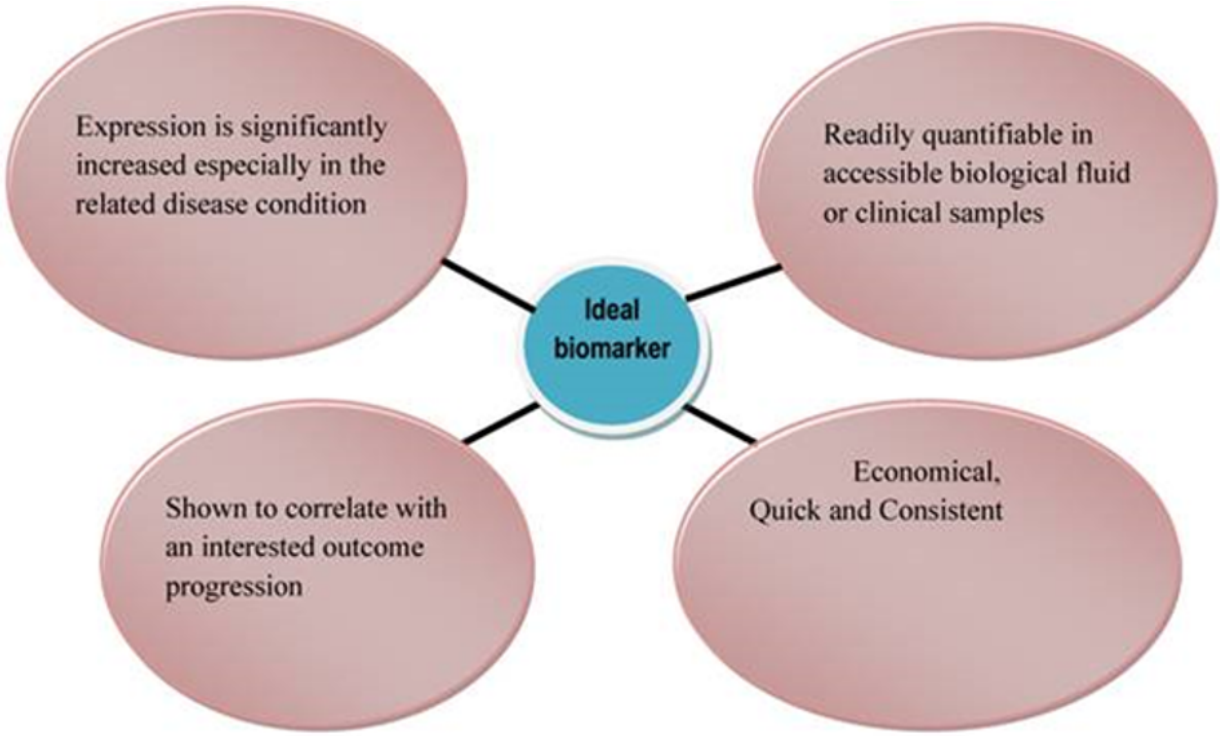

Figure 1: Significant role of ideal biomarkers

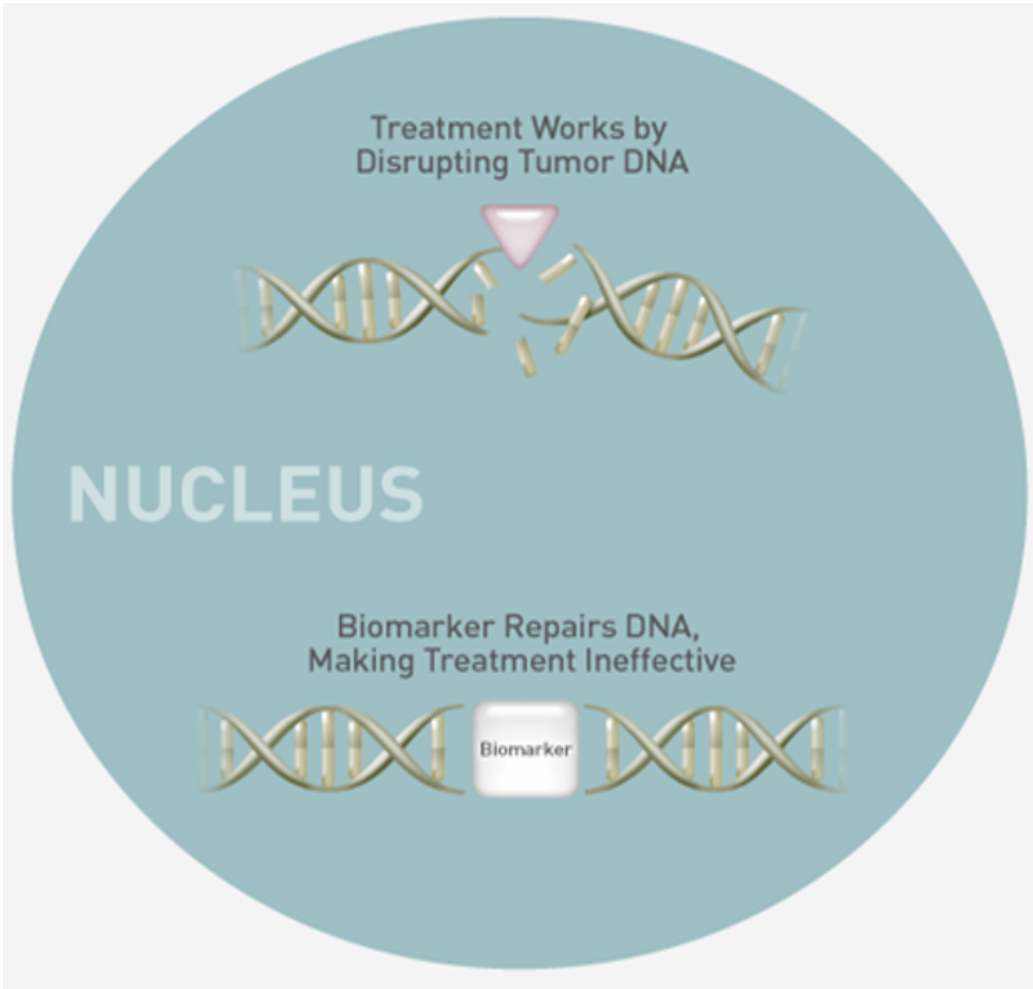

Figure 2: Biomarkers in cancer care

tion to hormone treatment (Manni *et al.*, 1980). Roughly 30– 40% of patients with estrogen receptor (ER) communicating propelled breast disease will have a target reaction to hormone treatment, and a further 20% of patients will accomplish ailment adjustment. Besides, the hormone treatment reaction in patients with early ER-communicating breast malignancy, regarding generally and illness free survival, is notable (Goss *et al.*, 2005; Dowsett *et al.*, 2015), shown in Figure 3.

Ki-67

Immunohistochemical appraisal of Ki-67 is the technique most generally utilized in clinical practice to decide the proliferative action of breast disease. Ki-67 is especially critical for recognizing hazard bunches in carcinomas positive for estrogen receptor(ER-alpha) and progesterone receptor(PR). The accessible rules on Ki-67 appraisal in breast malignant growth address methodological issues in the different stages (Dowsett *et al.*, 2011).

HER2

The most imperative prognostic and prescient marker in breast cancer. The breast malignant growths that overexpress HER2 speak to an exceedingly forceful organic subtype (Slamon *et al.*, 1987). Any intrusive breast carcinoma ought to be tried for HER2 overexpression, alongside estrogens, progestrone and Ki-67. A CNB test is adequate, and as a rule, the test shouldn't be rehashed on material from the careful example. Fixation time is significantly more institutionalized for CNBS (regularly 6-24 h) than for careful examples, and concordance between the two tests is high (98-99%) (Lebeau *et al.*, 2010; Chen *et al.*, 2012).

Cervical Cancer

Some encouraging biomarkers have as of late been de-lineated by concentrate the major atomic occasions associated with cervical carcinogenesis. To encourage the understanding of the fundamental atomic concepts that lead to the identification of these markers, we briefly condense the most important steps in cervical change with regards to biomarker revelation. The underlying occasion in cervical change is contamination with high hazard human papilloma infections high-risk human papillomavirus (HR-HPV). Most of the high-risk human papillomavirus [HR-HPV] contaminations relapse precipitously, just a little extent endures and induces cervical intraepithelial neoplasias (CIN). The risk of movement to obtrusive diseases ascends with the injuries, shown in Figure 4.

p16INK4a

The overexpression of the cyclin subordinate kinase inhibitor p16INK4a is a direct sequence of deregulated human papillomavirus(HPV] oncogene articulation (Khleif *et al.*, 1996). Generally, an official of PRB to E2F squares E2F driven cell cycle enactment. In imitating cells, E2F is directed by phosphorylation of RB. Rb phosphorylation is ordinarily intervened by cyclin subordinate kinases (CDK4, CDKO) that are controlled by a few kinase inhibitors (INKS). Distorted articulation of E7 in basal cells upsets authoritative of pRB to E2F that is neutralized by the monstrous articulation of p16INK4a, a critical CDK inhibitor Since E7-subordinate E2F discharge isn't intervened by phosphorylation of pRb, the counter administrative p16INK4a expression has no effect on the activated cell cycle (Sana *et al.*, 1998).

ki67

The extended increase of cervical epithelial cells induced by deregulated human papilloma infection (HPV) oncogene explanation is reflected by the activation of multiplication markers, for instance, ki67 (MIB-1). This protein is insistently ex-crushed in CIN injuries, anyway can in like manner be discovered communicated in run of the mill basal cells that hold duplication limit. By exploring the connection between sore assessment and the epithelial region of ki67 positive cell clusters, Kruse et al. have shown that ki67 cell bunches are a respectable standard to isolate low-quality CIN wounds from common and responsive epithelia (Pirog *et al.*, 2002).

Colorectal Cancer

As of late, a significant consideration is given to tumor endothelial cells (TEC). Variations from the norm among tumor and typical endothelial cells open a chance to distinguish explicit markers (tumor endothelial markers (TEMs)) connected to tumorigenesis (Toiyama *et al.*, 2014). Markers that could recognize physiological and obsessive angiogenesis are a critical issue for malignant growth discovery (Fearon and Vogelstein, 1990). It is generally acknowledged that biomarkers offer opportunities to set up a prognostic marker in CRC and for their point of view used in clinical applications. Restraining angiogenesis is a critical procedure for current treatments of disease patients (Barrow and Michels, 2014).

K- RAS G13 Dgene mutation

Ras characteristics are among the practice once in a while, sanctioned oncogenes. K-ras is found in adenocarcinomas that transduces extracellular signs from the EGFR deeply. K-ras is the primary perceptive biomarker set up for unfriendly to EGFR monoclonal insusceptible reaction in colorectal dangerous development. Around 40% of colon dan-

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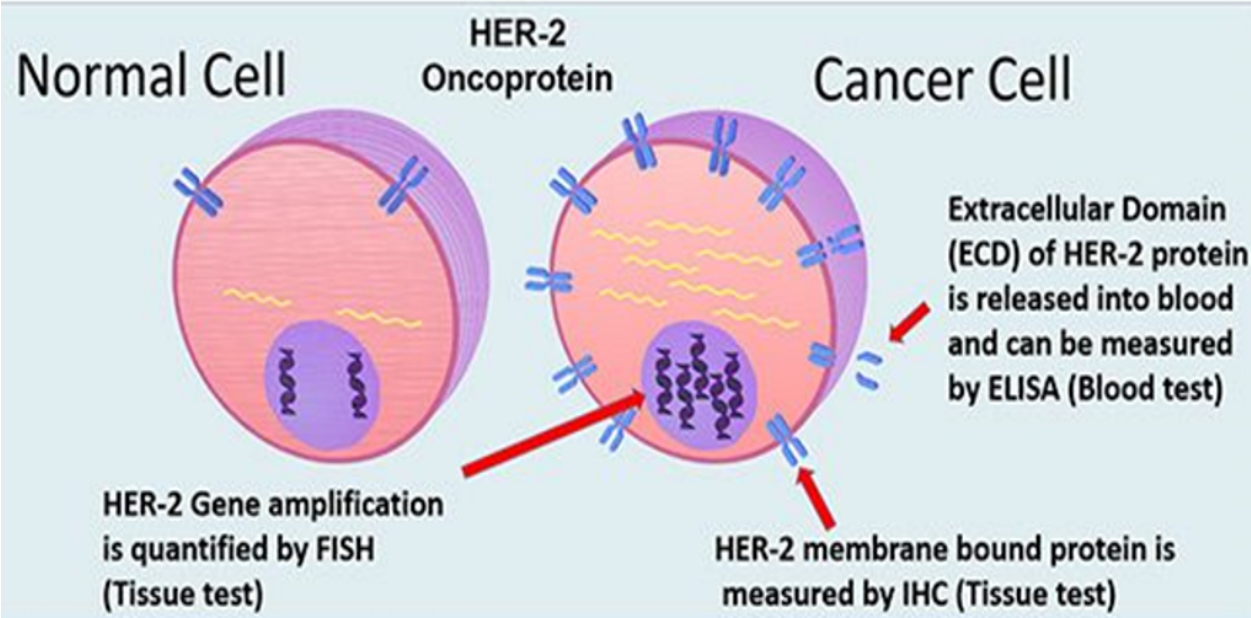

Figure 3: Signaling pathway of breast cancer

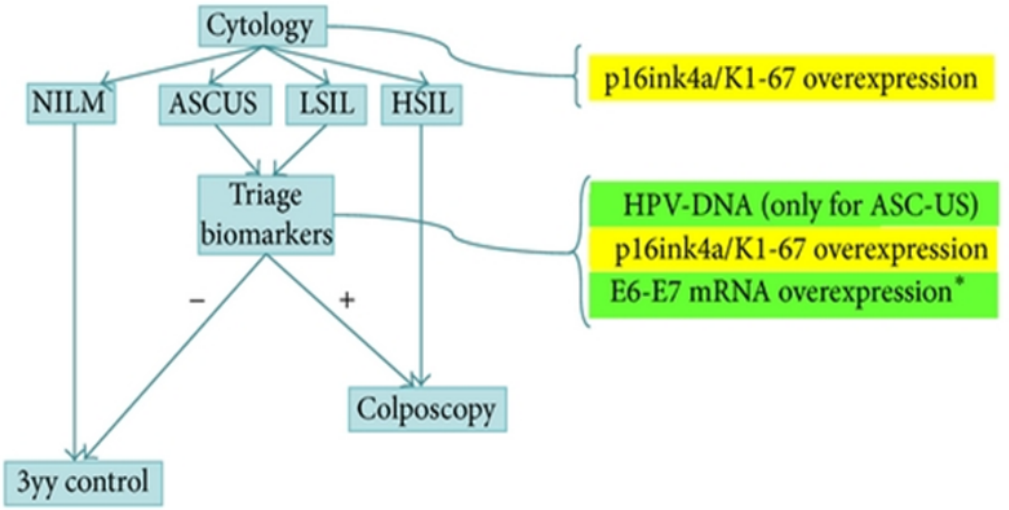

Figure 4: Signaling pathway of cervical cancer

gerous developments are certain for changes in K-ras in codons 12,13,61 of colorectal ailment and are impenetrable to unfriendly to EGFR monoclonal antibodie.

Angiogenesis assumes a critical job in the movement of colorectal carcinoma (CRC). Proof from premedical and medical investigations demonstrates that vascular endothelial development factor (VEGF) is the transcendent angiogenic factor in colorectal carcinoma (CRC). Evaluation of VEGF-1 articulation appears to give profitable prognostic data in colorectal carcinoma (CRC), especially in choosing those patients at high hazard for sickness movement who are probably going to profit by adjuvant treatment. Rising biomarkers for CRC are bevacizumab and aflibercept concentrating on VEGF; regorafenib concentrating on multikinase (VEGFRI, VEGFR2, VEGFR3, PDGFRbeta. Tie-2.FGFR1, RET and BRAF) (Sideris and Papagrigoriadis, 2014).

Limit ations of biomarker development

A large portion of the biomarkers as of now known are of restricted clinical use. Early examinations needed epidemiological legitimacy or factual power and in this way needed the widespread application to populaces. Absence of pre-expository examinations and institutionalized conventions crosswise over labs adds to lessened reproducibility. These issues render numerous markers inadequately del-

icate or sufficientexplicit for clinical use. The utilization of uniform gauge as recommended by Pepe ought to encourage the interpretation of newfound biomarkers to the center (Pepe *et al.*, 2001).

Therapy Predictive Markers in Cancer

Treatment prescient biomarkers tentatively distinguish patients who are probably going to react or be impervious to explicit medications. Prescient biomarkers are important as patients with malignancies of a similar organ type react very distinctively to a particular medication.

Hence, reaction rates for unselected patients with various kinds of cutting edge malignant growth to at present accessible foundational medicines change from < 10% to > 90% (Duffy and Crown, 2014). New prescient biomarkers are particularly required for the recognizable proof of patients liable to profit by explicit cytotoxic medications (taxanes, anthracyclines, platinums), hostile to angiogenic treatment (bevacizumab, aflivercept) and immunotherapies (ipilumumab, against PD-1 antibodies). Generally speaking, treatment prescient biomarkers are essential in patient administration and customizing treatment. Their estimation can expand sedate adequacy and result in diminished lethality. This thusly, ought to diminish by and large medicinal services expenses and lead to an upgraded personal satisfaction for patients (Duffy, 2013).

CONCLUSION

Discovery and clinical utilization of new biomarkers is expected to assume a huge job in reshaping life science research and life science industry, in this manner significantly affecting the recognition and treatment of numerous maladies and malignant growth specifically. Contemporary as well as upcoming genomic and proteomic advances are very encouraging in distinguishing new biomarkers, which can fundamentally upgrade the adequacy of malignancy the executives by facilitating the individualization of treatment focusing on the patient explicit sub-atomic injuries and furthermore by giving devices to predicting/checking of remedial reaction. In spite of the fact that the present comprehension of signalling pathways has recognized explicit focuses for creating more up to date medications and helpful systems, a far-reaching comprehension of how the unpredictable signalling systems work in an unblemished cell is as yet required, to develop procedures dependent on the hereditary modifications in individual malignant growths. This review provides on-going endeavours to develop different chemical tools for the sensitive detection of cancer biomarkers. As for the present and future innovations for disease diagnostics all in all, and malignant growth biomarker identification specifically, thorough work still should be completed. However, the investigation of new advances and new biomarkers for fundamental and advanced cancer diagnostics is always picking up momentum

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