American Journal of
Biomedical Science & Research

www.biomedgrid.com
ISSN: 2642-1747

Mini Review

Gal-GalNAc: A Proven Qualitative Screening tool for Cancer

Maliha M Ahmed[1]* and Md Sohrab Alam[2]

[1]*Founder and Executive Director Organikare and a Columnist, Bangladesh*

[2]*Oncos Molbiol Lab, Bangladesh*

***Corresponding author:** Maliha M Ahmed, Founder and Executive Director Organikare and a Columnist at Daily Dhaka Tribune, Bangladesh.

To Cite This Article: *Maliha M Ahmed, Md Sohrab Alam. Gal-GalNAc: A Proven Qualitative Screening tool for Cancer. Am J Biomed Sci & Res. 2022 - 15(5). AJBSR.MS.ID.002155.* DOI: 10.34297/AJBSR.2022.15.002155

Received: March 08, 2022; **Published:** March 14, 2022

Abstract

Cancer is a leading cause of death worldwide, and according to World Health Organization, 2020 saw 10 million deaths from cancer. Even though breast, lung, gastrointestinal tract, and prostate cancers are quite common, the underlying pathology takes a while to propagate and requires a series of alterations of the normal cells to transform into malignant cells. But once that happens, the rapid growth of abnormal cells spreads beyond the originating tissues and invades other organs. This process is called metastasis- it happens silently but, in some cases, virulently. By the time cancer is detected, it becomes difficult to eradicate. Therefore, an early detection of cancer cells or its products will immensely help in diagnosis and treatment. Cancer detection is expensive and usually by the time people seek medical help, it is already quite late. Individuals who are at risk of getting cancer need to be identified early with the help of rapid, simple, accurate, and inexpensive tests that are minimally invasive or non-invasive to generate acceptability by all. If screening test becomes positive, it will need further diagnostic procedures to confirm the presence of the disease.

Introduction

A general cancer screening test that can detect cancerous changes in multiple organs, even before symptom onset will reduce the chance of death and the expensive cancer treatment protocol. The routine tests like mammograms of breast, pap test for cervix, CT scan for lungs, colonoscopy, sigmoidoscopy, CA-125 test for ovaries are invasive and sometimes uncomfortable [1]. Also, A tumor must attain a minimum size before it can be 'visible' by the imaging technologies like mammogram, chest X-ray, low dose CT etc [2]. Biochemical tests, e.g., fecal occult blood test (FOBT), PSA, Carbohydrate antigens etc. are unsuitable for early detection or screening purposes. They are mainly used to monitor the recurrence and treatment efficacy of the tumor.

Multicancer early detection tests that use body fluids to measure biological signals that are shed by cancer and precancerous cells are given a lot of focus. These signals, known as biomarkers, can help diagnose different types of cancer [1]. Which is why, this study, done over three decades to detect precancerous and cancerous tissue by using the Galactose-Oxidase-Schiff technique to assess the usefulness of D-galactose-β (1→3) N'-acetyl-D-galactosamine (Gal-GalNAc) as a common marker of carcinomas can be a cheaper alternative to the expensive and difficult diagnostic tools of cancer detection [2].

The Galactose Oxidase – Schiff Test

The marker Gal-GalNAc and the Galactose Oxidase – Schiff Test (GOS, also known as rectal mucus test, Shams' test, and EARLY Test) is a screening test that satisfies all the criteria of an ideal screening test as per the US National Cancer Institute [3]. The high accuracy has been consistently demonstrated independently by numerous investigators in three continents.

The test is based on operation of

i. Field-effect of carcinogens,

ii. A marker differentially and specifically expressed during carcinogenesis, which is shared by both cancer and precancer, but not by normal or regenerating tissue [2].

The Field-Effect Theory

The field effect in carcinogenesis is characterized by the occurrence of genetic and epigenetic alterations in normal-appearing tissues, leading to increased risk for synchronous or metachronous primary tumors. According to this theory, the tumor is encircled by precancerous cells which, even after resection of the malignancy can potentially form second primary tumors. The concept of "field cancerization" (or field effect) was first proposed by Slaughter *et al* in 1953 [4]. In the genetically altered carcinogenesis model, the stem cell escapes normal growth control, gains growth advantage, and develops into an expanding clone of tumor initiating stem cells or tumor propagating cells. Initially a patch is formed with genetically altered clonal daughter cells, the lesion gradually becomes a field, which displaces the normal epithelium and eventually results in cancer. The epigenetic changes alter gene expression but does not involve change in primary DNA sequence.

DNA methylation is one of the well-known epigenetic mechanisms where methylation turns genes "off" and demethylation turns genes "on". Hypermethylation is known to turn tumor suppressor genes "off". Environment and behavior result in epigenetic changes. It happens in higher frequency than gene mutation and is reversible upon treatment with pharmacological agents and removal of triggers [5]. Field-Effect phenomenon indicates that the carcinogenic agents affect form one or more foci in the target tissue along with precancerous changes in the surrounding areas.

The modern molecular technologies help trace the abnormalities in affected tissues that appear normal by field effect biomarkers. Such biomarkers have been reported in common cancer sites- head and neck, colon, rectum, prostate, breast, lung, esophagus, stomach, and skin. The potential utilization of field effect biomarkers will help in cancer prevention, surgical considerations, and clinical prognosis [6]. Adenocarcinoma is one of the most common types of cancer and an important biological feature of this disease is the qualitative and/or quantitative alteration in the composition of secreted mucus that persists through precancerous and cancerous tissues. The main component that changes within this mucin is the carbohydrate chains. The carbohydrate moiety Gal-GalNAc is a disaccharide tumor marker of cancer tissues as well as precancer tissues like dysplasia, which is a precancerous condition that progresses to cancer.

The expression of Gal-GalNAc may be one of the earliest phenotypic abnormalities that precedes morphological changes of neoplasia, the presence of which is strong and distributed in secreted mucin, cytoplasmic mucin droplets, serous adenocarcinomas, and also in the structural glycoconjugates [2]. Even the morphologically normal-appearing epithelium and their secretions in the surrounding areas (field) of carcinoma in breast, bronchus, endometrium, and pancreatic ducts expressed Gal-GalNAc in contrast to normal tissues obtained from noncancerous individuals, which were totally nonreactive [2]. The findings from these studies prove that the tumor marker Gal-GalNAc detected/visualized by a simple enzymatic galactose oxidase-Schiff reaction is highly expressed by a variety of adenocarcinomas and also by the apparently normal-appearing epithelia and their secretions in the vicinity of carcinomas, strongly supporting the field effect theory of carcinogenic agent(s). This can be the basis for mass screening for cancer and precancerous conditions [7].

Biomarker Criteria

Gal-GalNAc and the EARLY Test fulfill the six criteria outlined by the Division of Cancer Control and Prevention (DCCP) at the US National Cancer Institute for intermediate endpoint biomarkers of use in chemoprevention [3].

1. The expression of biomarker Gal-GalNAc can only be detected in cancerous/precancerous specimen and not in specimens from healthy individuals. It was tested in tissue samples from breast (19/19 adenocarcinomas), lung (12/ 12 pulmonary adenocarcinomas), ovary (15/15), pancreas (6/6), stomach (16/17), prostate (62/65) and uterine (11/12) along with respective normal controls [2]. The expression of Gal-GalNAc was determined in a total of 133 tissue samples from 81 cases of the carcinomas of the breast, ovary, pancreas, stomach, and endometrium and 52 cases of respective normal controls [8].

The "field-effect" phenomenon was proved by the detection of cancers in the various segments of the colon remote from the rectum where the mucus was sampled from. Same was observed in breast, lung, prostate, other cancers [8].

2. Gal-GalNAc is expressed very early during carcinogenesis. For instance, in 28 cases of patients whose sputum cytology showed various degrees of dysplasia, 21 were found Gal-GalNAc positive of which 15 patients were identified to have lung cancer on further investigation. Thus, concept of false

positive as generally used does not apply to Gal-GalNAc and the EARLY Test since they take the precancerous lesions and early cancers into consideration [8].

3. The marker and its assay provide 70-100% sensitivity, specificity, and accuracy. Gal-GalNAc is carcinogenesis specific [8].

4. The marker is easily detected by EARLY test which is non-invasive, done on secretion or discharge mucus sample obtained during routine digital rectal examination, coughed-up sputum, nipple aspirate, prostatic massage, endocervical mucus, etc. This can be used as point-of-care test for breast, lung, colon, prostate, and uterus [8].

5. The marker can be modulated by chemopreventive agents. Antineoplastic actions by the chemopreventive agent Inositol hexaphosphate (InsP6) was demonstrated to suppress Gal-GalNAc expression in both colon and breast cancer [8,9].

6. The modulation of the intermediate biomarker correlate with a decrease in cancer rate- this will require years of research [8]. To prove this, the simple, cost-effective test must be made widely available, especially in regions where cancer is becoming a burden in the healthcare cost.

Conclusion

Early cancer screening and detection will save and improve quality of life. The current precision medicines designed to target the specific cancers can be most effective. If performed routinely on lymph node sections and secretions will help detect and arrest metastasis early [2]. Surveillance of colorectal, breast, and prostate cancers is generally an excellent method to reduce mortality from new lesions in individuals previously diagnosed with adenoma or curable cancer. This screening test can be an ideal common tumor marker. It will immensely help countries that are suffering from double burden of communicable and noncommunicable diseases, where resources are limited [6].

References

1. https://www.cancer.gov/about-cancer/screening/screening-tests
2. Shamsuddin AK, Tyner G, Yang GY (1995) Common Expression of the Tumor Marker d-Galactose-β- [1→3]-N-Acetyl-d-Galactosamine by Different Adenocarcinomas: Evidence of Field Effect Phenomenon. Cancer Res 55(1): 149-152.
3. Kelloff GJ, Malone WF, Boone CW, Steele VE, Doody LA (1992) Intermediate biomarkers of precancer and their application in chemoprevention. J Cell Biochem Suppl 16G: 15-21.
4. https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/field-cancerization
5. https://www.cdc.gov/genomics/disease/epigenetics.htm
6. Chai H, Brown RE (2009) Field Effect in Cancer-An Update. Ann Clin Lab Sci 39(4): 331-337.
7. Yang GY, Shamsuddin AK (1996) Gal-GalNAc: A biomarker of colon carcinogenesis. Histol Histopathol 11(3): 801-806.
8. Shamsuddin AK (2021) A Simple Screening Test for Cancer. Advances in Cancer Research & Clinical Imaging 3(2).
9. Sakamoto K, Venkatraman G, Shamsuddin AM (1993) Growth inhibition and differentiation of HT-29 cells in vitro by inositol hexaphosphate (phytic acid). Carcinogenesis 14(9): 1815-1819.