International Scientific Journal
Medical and Biological Sciences
http://bioscience.scientific-journal.com

Skin cancer biomarkers

Soheila S. Kordestani
Biomaterial Group, Medical Engineering Department
AmirKabir University of Technology
Tehran, Iran
sskordestani@aut.ac.ir

Farzaneh NayebHabib
Biomaterial Group, Medical Engineering Department
AmirKabir University of Technology
Tehran, Iran
fnayebh@aut.ac.ir

Abstract— **Skin cancer is the most common type of cancer and there are two forms: melanomas and melanoma (basal cell carcinoma and squamous cell carcinoma). The main risk factor in both types of skin cancer is exposure to sunlight and other sources of ultraviolet radiation. In comparison with basal or squamous cell carcinoma melanoma skin cancer is less common but more serious if not treated early, and can lead to death. Non melanoma skin cancer, the most common human cancers in which incidence of basal cell cancer (BCC) are 80-75 % and up to 25% is squamous cell (SCC). Due to the rise in skin cancer in recent decade's diagnosis and treatment has become more important. Non melanoma skin cancer is the most common cancer in Iran which current method of diagnosis is invasive biopsy, a procedure in which detection take place after entire formation of cancer. Bleeding, infection, scar formation and scar are disadvantages of this method that motivate the researchers to investigate noninvasive method during the last decade, in addition early detection of cancer, leading to more effective treatment. Positron Emission Tomography (PET), nuclear resonance imaging (MRI) and Raman spectroscopy are noninvasive skin cancer instrumental detection methods. In this research plan, based on scientific data obtained from biochemical changes in cancer cells, we consider to investigate and invent a non-instrumental method for early detection with universal application.**

Keywords— ***Skin cancer, non-melanoma skin cancer, non-invasive detection, early detection***

I. Introduction

Squamous cell carcinoma is one type of skin cancer which present within the skin and oral cavity. In some cases SCCs become metastatic that would leads to metastasis-associated death. The rate of metastasis in skin SCCs is between 0.1% and 10%, with low differentiated tumors. Differentiated tumors with greater vertical tumor thickness have more risk of metastasis.

The way of genetic changes and intrinsic tumor cell properties which control SCC metastasis are unknown in much aspect. Genetically engineered mice provide a new and useful tool for analyzing driver mutations that take part to SCC initiation and metastasis. In recent date, low genetic mutations that cause formation of spontaneous SCC and metastasis have been found, especially metastasis to the lung. Metastasis to the lung is the leading cause of SCC-associated death. Mice with a *Smad4* deletion in stratified epithelia develop spontaneous SCCs in the fore stomach, skin, and oral cavity. Along with these types, oral SCCs metastasize to lymph nodes, whereas skin and fore stomach SCCs do not metastasize (1).

Usually most SCCs, are easily treated by normal ways but some of them would progress to regional or distant metastasis and cause death (2).

As invasive cSCC displays a potential for recurrence and metastasis, SCC of the skin is responsible for the majority of non-melanoma skin cancer deaths. Today, cSCC is primarily a disease of the old people, but the incidence is also increasing in younger people individuals due to excessive recreational exposure to sunlight. The growing rate incidence of cSCC is also a reason for increased demand for drug and treatment related to skin cancer. Demand for treatment is estimated to grow 5% in the Central Europe per year (3).

Many studies for early detection of cancer have been done and most of them are focused on active detection behaviors, such as performing breast, testicular and skin self-examination, or on detection by medical health care providers, such as taking part in screening programs and having check-ups by a physician yearly (4–10).

Since active detection contributes to early detection of cancer, a significant contribution can also be made by passive detection and by searching health help promptly when potential cancer symptoms are discovered (11). Scientists for making clear what kind of cancers can be self-detected classify cancers in three types: 1. cancers of the organs which can be observed such as skin, breast and testis can be detected by looking for lumps, ulcerations or moles or by palpation; (2) cancers of the hollow organs, such as urinary bladder, lungs, etc. which can be detected by examining and being alert on, for instance, bleeding; (3) cancer of deep organs, that does not give any signals in the early development of the cancer and which cannot be detected by examining with hands.

An easy, noninvasive technique that provides opportunity for characterization of skin lesions prior to biopsy would be useful. Instrumental techniques such as infrared (IR) spectroscopy would be useful .The IR spectrum is divided into three regions: near-IR (700±2500 nm), mid-IR (2500±50,000 nm), and far-IR (beyond 50,000 nm). Since light in the far-IR region is completely absorbed by tissues, usage of this region for tissue analysis is little. Mid-IR light is absorbed by a variety of materials in skin, thus providing an insight into skin biochemistry. Scientists have shown that biopsies from basal

cell carcinoma (BCC), squamous cell carcinoma (SCC), and melanocytic tumors have distinct mid-IR spectrum when compared with normal skin; however, as complete absorption of mid- IR light results with samples greater than 10±15 mm in thickness the diagnostic potential of mid-IR spectroscopy in vivo is limited. In contrast, near-IR light allows the examination of much larger volumes of tissue and the potential for in vivo studies because this light scattered to a much greater extent than it is absorbed, making tissues relatively transparent to near-IR light (12).

II. Experimental Methods

Tests for many tumor markers are available through commercial testing labs, but these are seldom used. Some of these tests may even be advertised as being better than the more common markers, but this hasn't yet been shown in scientific studies. In some of these cases, the tests have been taken off the market at the request of the Food and Drug Administration (FDA). Still, there are tests available for many types of cancer, but they have not yet been proven to work.
Due to the fact that the access to tumor tissue is difficult, up to now predictive and pharmacodynamics biomarkers are increasingly being used in clinical trials of cancer drugs.
Promising new sensors which have the potential to analyze the tumor on the molecular level 'non-invasively' are the focus of our researches.

- Analyzing circulating tumor cells.
- Mutation-specific PCR on the circulating DNA.
- Proteomic approaches to study serum or plasma.
- Assessing autoantibody specific for tumor cells

Melanoma is the major cause of skin cancer-related which leads to death, resulting in about 48,000 deaths around the world each year with striking differences in stage-specific survival. Localized disease is often curable, making it imperative to detect the disease early. Histological analysis of skin biopsies – the current especial treatment and standard for melanoma diagnosis, however, remains subjective, invasive and poorly standardized. Several biomarkers including BRAF V600E mutation of cutaneous melanoma and KIT gene of mucosal melanoma can be useful in the diagnosis of melanoma and impact the choice of treatment. Success in proteomic and genomic tools has led the way to the discovery of several promising melanoma-specific biomarkers; however these markers are not validated completely and have not led to complete replacement of histological evaluation. The major challenge exists in predicting the behavior of clinically and histologically ambiguous lesions. Several recent reports describe the use of chromosomal copy number variations which have been successfully linked to malignant lesions; however this is only done in conjunction with histology. In the future, the behavior of these types of lesions may be more easily and accurately predicted through the use of reliable biomarkers. Such biomarkers may also help in creating targeted therapies (13).

Previous studies illustrated the capability of chemical sensors to capture different (Volatile organic compound) VOCs in the urine of cancerous mice with tumor. These results motivates scientists to use a sensors array to characterize the pattern of fingerprint of VOCs evaporated from well-characterized human tumorigenic melanoma cell lines, pertained to different cancer types. This approach allows reducing the sources of disturbances and then to better investigating the potential uniqueness of the VOCs released by tumor type during the proliferation phase. Tumors characterized by the description and the analysis of the results of two experiments. A preliminary in vitro experiment, recently described was aimed at discriminating the melanoma cell lines from other tumorigenic cell lines. The contribution of each sensor in the melanoma cells identification is investigated. On the basis of the first experiment results, a second in vivo experiment is also performed where two melanoma cell lines are xenografted in nude mice and monitored during the tumors growth (14).

III. Results and Disscusion

There are some sensors for early detections. Defects (mutations) in the BRAF gene can be found in melanoma, thyroid cancer, and colorectal cancer. About half of melanomas have a BRAF mutation, most often the one called BRAF V600. This mutation causes the gene to make an altered BRAF protein that signals melanoma cells to grow and divide. This mutation can be tested for in tumor tissue. If it's found, the patient can be treated with a drug that targets the altered BRAF protein, such as vemurafenib (Zelboraf®).
S-100 is a protein found in most melanoma cells. Tissue samples of suspected melanomas may be tested for this marker to help in diagnosis.
Some studies have shown that blood levels of S-100 are elevated in most patients with metastatic melanoma (melanoma that has spread to other parts of the body). So, this test is sometimes used to look for melanoma spread before, during, or after treatment.

IV. Conclusion

Cancer biosensors are the most promising technology for early detection. These biosensors enable human to detect and treat cancers efficiently.

References

[1] Ruth A. White, Jill M. Neiman, Anand Reddi, Gangwen Han, Stanca Birlea, Doyel Mitra, Laikuan Dionne, Pam Fernandez, Kazutoshi Murao, Li Bian, Stephen B. Keysar, Nathaniel B. Goldstein, Ningjing Song, Sophia Bornstein, Zheyi Han, Xian Lu, Joshua Wisell, Fulun Li, John Song, Shi-Long Lu, Antonio Jimeno, Dennis R. Roop, and Xiao-Jing Wang, "Epithelial stem cell mutations that promote squamous cell carcinoma metastasis," The Journal of Clinical Investigation, vol. 123, pp. 4390-4404, October 2013.
[2] Anne Kricker, Bruce Armstrong, Vibeke Hansen, Alan Watson, Gurpreet Singh-Khaira, Christophe Lecathelinais, DESS de Math_ematiques Appliqu_ees, Chris Goumas, and Afaf Girgis, "Basal cell carcinoma and squamous cell carcinoma growth rates and determinants of size in

community patients," J AM ACAD DERMATOL, vol. 70, 2014, pp. 456-464.
[3] Atte Kivisaari and Veli-Matti Kähäri, "Squamous cell carcinoma of the skin: Emerging need for novel biomarkers," World J Clin Oncol, vol 4, 2013, pp. 85-90.
[4] Bostick RM, Sprafka JM, Virnig BA, Potter JD. "Knowledge, attitudes, and personal practices regarding prevention and early detection of cancer", Prev Med, vol 22, 1993, pp.65–85.
[5] Budden L. "Young women's breast self-examination knowledge and Practice", J Commun Health Nurs, vol 12, 1995, pp.23–32.
[6] Friedman LC, Webb JA, Bruce S, Weinberg AD, Cooper HP. "Skin cancer prevention and early detection intentions and behavior", Am J Prev Med, vol 11, 1995, pp.59–65.
[7] Lechner L, De Vries H, Offermans N. "Participation in a breast cancer screening program: influence of past behavior and determinants on future screening participation", Prev Med, vol 26, 1997, pp.473–82.
[8] Lechner L, Oenema A, De Nooijer J. "Testicular self-examination (TSE) among Dutch young men aged 15–19: determinants of the intention to practice TSE.", Health Educ Res , vol 17, 2002, pp.73–84.
[9] Wardle J, Steptoe A, Burckhardt R, Vogele C, Vila J, Zarczynski Z. 'Testicular self-examination: attitudes and practices among young men in Europe.' Eur J Cancer Prev, vol 4,1994, pp.61–8.
[10] Wardle J, Steptoe A, Smith H, "Breast self-examination: attitudes and practices among young women in Europe.", Eur J Cancer Prev, vol 4, 1995, pp. 61–8.
[11] Qin DX, Wang GQ, Zhang XH, Zuo JH, Yuan FL. "New concept for cancer screening." Eur J Cancer Prev, vol 5, 1996, pp.121–4.
[12] Laura M. McIntosh, Randy Summers, Michael Jackson, Henry H. Mantsch, James R. Manseld, Marilyn Howlett, A. Neil Crowson,* and John W. P. Toole, "Towards Non-Invasive Screening of Skin Lesions by Near-Infrared Spectroscopy", THE JOURNAL OF INVESTIGATIVE DERMATOLOGY, vol 116, 2000, pp. 175-181.
[13] Sumit Paliwal, Byeong Hee Hwang, Kenneth Y. Tsai , Samir Mitragotri, "Diagnostic opportunities based on skin biomarkers", European Journal of Pharmaceutical Sciences, 2012, pp. 1-11.

[14] G. Pennazza, M. Santonico, E. Martinelli, R. Paolesse, V. Tamburrelli, S. Cristin , A. D'Amico, C. Di Natale, A. Bartolazzi, "Monitoring of melanoma released volatile compounds by a gas sensors array:From in vitro to in vivo experiments", Sensors and Actuators B: Chemical, vol 154, 2011, pp.288-294.