

## Genetically predisposed, life style and occurrence of metastatic cancer

Nitya G. Chakraborty

Department of Medicine, University of Connecticut Health Center, CT 06030-1628, USA

The incidence of spontaneous cancers and immunosurveillance or host defense mechanisms are under the direct control of multiple gene products. Number of genes are identified those are directly associated with cancer. Natural killer T (NKT) cells and natural killer (NK) cells the two most important components of innate immunity directly involved in immunosurveillance for cancer. Certain genes are identified as mutated within a family and members of such family are considered to be at risk of getting the particular cancer in their lifetime. Expression of the mutated genes and thus their products are capable of changing the activities of innate immune system followed by inappropriate adoptive immune response. Adequate nutrition along with good life style could stop the expression of those bad genes and eventually offer a cancer free life.

It has been well documented that immunity against cancer exists<sup>[1-4]</sup> but there is no such antigen that has been identified as exclusively tumor specific. Number of tumor associated antigens (TAA) are being identified, those are largely self-antigens and, therefore, TAA-specific immune responses, whether cellular or humoral, are weak and difficult to measure. As such standard tests for measuring immune competence to tumor-associated antigens (TAA), similar to those available for the assessment of responses to foreign antigens such as bacterial, viral or fungal antigens, have not been available. According to the immune surveillance theory NKT cells and NK cells are responsible for early recognition and elimination of malignant cells.<sup>[5,6]</sup> The NK activity might not be effective enough in patients who develop malignancy. There are convincing evidences that individuals who are older, who have been on immunosuppressive medications over prolonged period of time or

have underlying immune abnormalities, such as a chronic infection are particularly at high risk of cancer.<sup>[3,4]</sup> Apart from genetic predisposition to cancer<sup>[5]</sup> most common risk factors for cancer are age, poor nutrition, stress, smoking and excessive drinking.<sup>[6,7]</sup> Poor nutrition, stress, smoking, drinking are also associated with more or less pronounced abnormalities in the immune system.

Although testing for immune competence in populations at high risk for malignancy has not been routinely performed, a low NK activity has been reported in familial breast cancer patients as well as their clinically asymptomatic first degree relatives.<sup>[6]</sup> Other studies have shown that members of cancer families have lower levels of natural cytotoxic activity than age-matched individuals without cancer in first degree relatives.<sup>[6,7]</sup> These studies suggest that among the unaffected family members, persons with lower NK cell activity may be at higher risk of cancer.<sup>[8]</sup> Further detailed studies with unaffected family members of the high risk group revealed that the members who maintain a reasonably good life style, do have NK activity equivalent to those members of no risk group with good life style (unpublished data). All these studies implicate significantly lower levels of NK cell activity for patients with advanced malignant disease and a persistently low NK cell activity as a risk for developing malignancy. Also, inappropriate innate or NK activity leads to inadequate adoptive immune responses by T cells (helper or cytotoxic) in individuals who later developed a malignancy.<sup>[9]</sup> Although these reports have not been uniformly accepted as evidence for a lack of immune surveillance in individuals at high risk of cancer, number of evidence suggest that good life style could prevent or delay the expression of cancer associated familial genes. Table 1 gives the evidence that

**Address for Correspondence:** Nitya G Chakraborty, Department of Medicine, University of Connecticut Health Center, CT 06030-1628, USA. E-mail: chakraborty@uchc.edu

**Table 1: Mutated genes and occurrence of malignant diseases**

Members of family with Mutated gene	Food habit	Life style	Cancer type	Natural killer activity
BRCA-I and II	High calorie	Stressed life,	Metatatic breast cancer	--
	Burgers, Hot Dog,	Smoking	Average age 35.	
	Pizza, Red meat	Drinking		
	Soft drink, Cola	Drug abuse		
	Moderate Calorie	Moderate	Metastatic breast cancer	+
	High carbohydrate,	stress level	Average age 55	
	Fish, white meat	No smoking		
Adenomatous polyposis coli (APC)	Avoid soft drink	No drinking		
		No substance abuse		
	High calorie	Stressed life,	Metatatic colon cancer	--
	Burgers, Hot Dog,	Smoking	Average age 30.	
	Pizza, Red meat	Drinking		
	Soft drink, Cola	Drug abuse		
	Moderate Calorie	Moderate	Metastatic colon cancer	+
High carbohydrate,	stress level	Average age 55		
Fish, white meat	No smoking			
Avoid soft drink	No drinking			
	No substance abuse			

how cancer associated gene expression could affect NK activity and occurrence of cancer.

All the available reports together indicate that the host immune competence in respect to innate as well as adaptive immunity is important and perhaps necessary for cancer prevention.

Table 1 is an example of food habit and life style and subsequent loss of natural killer cell activity in members of the families having mutated genes, breast cancer associated gene I and II (BRCA-I and II) and adenomatous polyposis coli which is associated colorectal carcinoma.

It appears that good life style is an important factor so as the appropriate nutrition. In the advanced countries and in the developing countries, where good nutrition is not a big factor, only a good life style would help to prevent or significantly delay the onset of the expression of the bad gene. In poor or under developed countries both nutrition as well as good life style should be under consideration. Another very important point is that the first degree relatives without being too much worried about getting the disease should take appropriate measure regarding the life style and nutrition and routine medical check-ups.

## References

- Whiteside T. Immune suppression in cancer: Effects on immune cells, mechanisms and future therapeutic intervention. *Semin Cancer Biol* 2006;16:3-15.
- Burnet F. Cancer: A biologic approach. *Br Med J* 1957;1:841-7.
- Fearon ER. Human cancer syndromes: Clues to the origin and nature of cancer. *Science* 1997;278:1043-50.
- Perera FP. Environment and cancer: Who are susceptible? *Science* 1997;278:1068-73.
- Pawelec G, Quyang Q, Colonna-Romano G, Candore G, Lio D, Caruso C. Is human immunosenescence clinically relevant? Looking for immunological risk phenotypes. *Trends Immunol* 2002;23:330-2.
- Strayer DR, Carter WA, Brodsky I. Familial occurrence of breast cancer is associated with reduced natural killer cytotoxicity. *Breast Cancer Res Treat* 1986;7:187-92.
- Bovbjerg DH, Valdimarsdottir H, Familial cancer, emotional distress and low natural cytotoxic activity in healthy women. *Ann Oncol* 1993;4:745-52.
- Shevde LA, Joshi NN, Shinde SR, Nadkarni JJ. Studies on functional status of circulating lymphocytes in unaffected members from cancer families. *Hum Immunol* 1998;59:373-81.
- Reuben JM, Hersh EM. Delayed hypersensitivity responses of cancer patients to recall antigens using a new "multi test" applicator. *Ann Allergy* 1984;53:390-4.

**Source of Support:** Nil, **Conflict of Interest:** None declared.