Humoral immune response for early diagnosis of breast carcinoma

Mortality from cancer, in particular breast carcinomas, has decreased in the last decade, due principally to early diagnosis of the disease. A major effort to improve diagnosis further by identifying serological markers indicative of early-stage disease has met with little success, except for a few oncotypes not including breast carcinoma. Indeed, the release of tumor markers into the serum is a late event associated with a large tumor mass and thus not useful for early diagnosis [1].

In non-oncological diseases such as infectious diseases, early diagnostic tests are mainly based on the humoral immune response elicited by the infectious agent rather than on detection of the agent per se. We speculated that the presence of specific antibodies against cancer cells might precede the detection of specific markers released by the tumor. However, studies have clearly indicated that the genetic alterations responsible for the disease are potentially numerous and not all gene products are immunogenic. Recently, SEREX analysis has been used to dissect the patient’s immune response and to select numerous tumor-associated antigens [2]. As expected, none of these tumor-related molecules alone were recognized at a sufficiently high frequency or showed sufficiently restricted immunological recognition by breast cancer patient sera to be used as a diagnostic tool. Our SEREX screening of a cDNA library from a breast carcinoma cell line with a selected patient’s serum identified 14 different gene products recognized by antibodies (unpublished). Considering the frequency of antibodies in patients and age-matched healthy donors directed against five antigens with the highest tumor restriction, i.e. lactate dehydrogenase-A (LDH-A), lactate dehydrogenase-B (LDH-B), fibulin-1, thyroid hormone-binding protein (THBP) and one novel antigen, none of these immunogenic molecules can be used alone for early detection of cancer. However, when reactivity against three of these five molecules was considered positive, 15 out of 20 patients with early breast carcinoma scored positive compared with only one out of 20 healthy donors (Table 1). In these pathological sera, detection of routine breast tumor markers such as c-erbB-2, Ca15.3 and CEA was low and therefore not diagnostic. Our findings point to the promise of early disease diagnosis based on the presence of specific antibodies directed against transformation-related molecules by selecting the appropriate set of SEREX-defined antigens with the highest tumor specificity and the highest frequency of patient recognition among those in the broad array of the cancer immunome repertoire.

S. M. Pupa, S. Forti, A. Balsari & S. Ménard
Molecular targeting Unit, Department of Experimental Oncology, Istituto Nazionale Tumori, Via Venezian 1, 20133 Milan; Institute of Pathology, University of Milan, Italy
(E-mail: menard@istitutotumori.mi.it)

References

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