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Lewis C is the Most Perspective Glycan in Breast Cancer Immunological Approaches to Diagnosis and Possible Immune Corrections

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Clinical tumor immunologists are increasingly focusing on natural humoral immunity. It was forgotten for long time and in scientific papers natural IgM antibodies were called as parias, orphaned molecules in immune surveillance, and the ignored weapons in tumor immunity and at last nature's best weapons to fight cancer [1-4].

Exact evidences proving the role of natural IgM antibodies in anti-tumor immune surveillance were obtained with trioma technology of human monoclonal antibody against cancer antigens production. Now there are already hundreds of such antibodies, which are synthesized by CD5+ B1−lymphocytes, react with tumor-specific glycan's and do not react with normal tissues. Binding of those antibodies to tumor cells leads in many cases to malignant cell death via apoptosis [5,6].

Recently, we have published new data on Lewis C in cancer [7]. This glycan is very interesting and seem perspective in cancer diagnosis and possibly immunotherapy. In 1994, P.D. Rye & R.A. Walker produced monoclonal IgM antibody LU-BCRU-G7 against breast cancer-associated glycoprotein [8]. In early breast cancer, expression of this marker was seen in a group of patients with poor prognosis. Antibody recognized disaccharide Galβ1-3GlcNAc or Lewis^C (Le^C), blood group H1-antigen precursor [9]. The antibodies to Le^C isolated from human sera recognize the disaccharide but do not bind to glycan's terminated with Le^C [7].

We have studied glycan expression on tumor cells and anti-glycan antibodies in more than 240 breast cancer patients. Immunohistochemical study in 89 cases of early breast cancer ($pT_{1-2}N_0M_0$) revealed antigen expression in 57% of cases. Expression of Le^C was significantly more frequent in tumors of larger sizes (> 3 cm): 85,0% vs 48,5% (p=0,004). Expression of Le^C was much more frequent in breast cancers in which lung metastases were noticed in patient's follow up (more than 1 year) after operation (p=0,047). In Le^C positive cases shorter (p < 0,1) DFS-diseases-free survival was noted, differences in DFS being near significant (p = 0,05) in malignancy grade 3, and in moderate and prominent lymphoid infiltration (p=0,02), as well as long (> 4 years) patient's follow up [10]. That data confirmed the note of Rye and Walker on poor prognosis of early Le^C-positive breast cancer [8].

In 67% of breast cancer patients small proportion of peripheral blood B-lymphocytes (up to 0,9% of B-cells) specifically bound Le^C, i.e. expressed B-cell receptor for Le^C. Up to 50% of these B-cells expressed CD5, so belonged to B1-natural immunity branch [10].

Serum levels of antibodies to Le^C were significantly higher in healthy woman then in breast cancer patients [11,12]. Opposite relations between anti- Le^C and serum, levels of CA 15.3 were noticed [11]. Membrane expression of Le^C on breast cancer cells was confirmed by flow cytometry [10]. There were no relations between Le^C expression on tumor cells and levels of serum antibodies to Le^C in breast cancer patients, in 36% of patient's tumor cells were Le^C -positive with low concentrations or absence of anti- Le^C in sera [10,11]. The last group of patients seem to be perspective in study of anti- Le^C adoptive therapy approach.

In conclusion. Lewis C blood group antigen expression takes place in 57% of early breast cancer, associated with poorer prognosis. Levels of anti- Le^C in breast cancer patients are lower than in healthy woman, in 36% of Le^C-positive cases being almost no detectable. Taking in mind important role of natural IgM anti-glycan's in cancer surveillance, it seems perspective to study in this well characterized group of breast cancer patients some anti-

Le^C adoptive therapy to see if compensation of anti- Le^C immune deficiency can be beneficial for patients.

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