

PANCREAS NEWS

Lymphocytes and Pancreatic Cancer: The Effects of These Cells on Diagnosis and Patient Survival

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Cancer of the pancreas is a very aggressive disease and is the fourth leading cause of death from cancer. Surgery is currently the most effective treatment, but only 20% of patients are candidates for this approach; the survival rate is variable and there are few predictors of prognosis.

A number of studies have been published concerning the role of inflammation in pancreatic cancer. In fact, the development and spread of pancreatic cancer may be influenced by the inflammatory process [1, 2, 3, 4]. Chronic inflammation produces a cycle of repeated cellular damage and subsequent healing; cellular injury determines DNA damage with mutations of proto-oncogenes and/or tumor suppressor genes [1] and the healing process, guided by the release of growth factors may lead to the proliferation of transformed cells. In addition, many factors produced by tumor cells promote tumor angiogenesis and the generation of extracellular matrix [5].

Furthermore, the development of more effective therapies is based on a better understanding of the factors causing cancer aggressivity; in addition, we need to identify the prognostic factors in order to guide the therapy in a more efficacious manner. We are presently aware of a series of factors isolated in tissue or in plasma produced by pancreatic tumors which may explain, at least in part, their progression [6, 7, 8]. However, most of them seem not to be useful for in diagnosis or as prognostic factors [7]. In animal studies, it has been shown that the induction of Th17 in the tumor microenvironment produces an antitumor effect [9]. The importance of lymphocytes in

pancreatic cancer has recently been pointed out by two groups of researchers in humans [10, 11].

In the first paper [10], the authors studied the peripheral blood mononuclear cells from pancreatic cancer patients and matched healthy controls, analyzing them by means of whole genome cDNA microarray. They found that 383 genes were significantly different between pancreatic cancer patients and healthy controls, and 65 had at least a 1.5 fold change in expression. Pathway analysis revealed that many of these genes fell into the pathways responsible for hematopoietic differentiation, cytokine signaling, and natural killer cell and CD8+ T-cell cytotoxic response. Unsupervised hierarchical clustering analysis identified an eight-gene predictor set, consisting of *SSBP2*, *Ube2b-rs1*, *CA5B*, *F5*, *TBC1D8*, *ANXA3*, *ARG1* and *ADAMTS20* capable of distinguishing pancreatic cancer patients from healthy controls with an accuracy of 79% (sensitivity 83% and specificity 75%). Thus, in the future, these data may help in diagnosing pancreatic cancer earlier.

The second group of researchers [11] has identified the complex interaction involving cells (such as stromal cells and immune cells) and tumor cells in the tumor microenvironment. The result of this dialogue is an alteration of the T-cells which, instead of producing cytokines effective in fighting cancer, produce cytokines capable of promoting further progression of the disease; this lymphocyte derangement has been called "deviant lymphocytes" by the authors. The authors also identified molecules involved in this mechanism which will allow the development of therapies to curb this activity. Antibodies are already available for some of these molecules and they are capable of blocking their activity. Most important, in a series of patients undergoing surgery, the authors also showed the existence of a correlation between the quantity of "deviant cells" present in the tumor and patient survival in order to stratify pancreatic cancer patients into two categories having a better or a worse prognosis. Research in the war against pancreatic cancer continues; these are buds which about to bloom.

Key words Lymphocytes; Pancreatic Neoplasms; Prognosis; Survival

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