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Blood monocytes and tumor-associated macrophages in human cancer: differences in activation levels

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This study was performed to investigate functional properties of mononuclear phagocytes isolated from ascitic fluid in patients with peritoneal carcinomatosis (PC), and potential immunomodulatory effects of soluble factors produced or induced by human metastatic malignant cells. Phagocytic activity and nitric oxide production of peripheral blood monocytes (PBMo) and tumor-associated macrophages (TAM) or peritoneal macrophages (PEM) were synchronously examined in cancer patients and control individuals. Our results showed that contrary to peripheral blood monocytes, where phagocytic activity was not altered, TAM had impaired phagocytic activity. Moreover, dilutions of crude supernatant from short-term cultures of the peritoneal cells obtained from ascitic fluid of patient with PC, cause a significant, dose dependent inhibition of control PBMo and PEM phagocytosis, comparable to those in TAM, indicating that a soluble factor(s) plays a prominent role in this alteration. Next, we investigated the potential of cancer patients mononuclear phagocytes to produce nitric oxide (NO). It was found that TAM produce fourfold lower levels of NO than PEM from control subject, whereas monocytes produce NO at levels comparable to those of corresponding controls. These data support the hypothesis that depressed TAM function may contribute to the mechanisms of tumor escape from immune destruction.

Key words: Macrophages, monocytes, phagocytosis, nitric oxide, cancer, ascitic fluid.

It has been known for long time that mononuclear cells (MNC) infiltrate tumor tissue. Macrophages (Mph), T cells and natural killer cells infiltrate tumors because they are chemoattracted by cytokines released by tumor cells [14]. The fact that MNC accumulate at the tumor sites does not, in it self imply that these cells can efficiently kill the malignant cells. As a matter of fact, in some cases the tumor cells can benefit from their presence. For example, macrophages produce angiogenic factors that favor neovascularisation, therefore increasing the possibility that the tumor will increase in size [15]. However, MNC also produce TNF, IFN-γ, IL-1, and reactive oxygen and nitrogen species, all of them having the potential for inhibiting tumor growth. Moreover, recent reports indicate that immune reaction involving neoplastic cell phagocytosis by macrophages plays an important role in the control of malignancies [9]. Despite infiltration by MNC, tumor cells can still escape from immune destruction. They can do this by changing microenvironment in which macrophages and other MNC may be affected and inhibited. Therefore, tumor-associated macrophages, strategically located at the very interface between tumor and host, represent target for experimental and therapeutical manipulation.

Material and methods

Patients. We analyzed a group of 10 patients with peritoneal carcinomatosis, none of them had received any chemotherapy or endocrine therapy during last three months. Control group consists of 10 healthy individuals and 10

Abbreviations: TAM – tumor-associated macrophages; PBMo – peripheral blood monocytes; PC – peritoneal carcinomatosis; Mo – monocytes; PEM – peritoneal macrophages; NO – nitric oxide; MNC – mononuclear cells; Mph – macrophages MNph – mononuclear phagocytes; AF – ascitic fluid; Pl – plasma; MDA – malonildialdehyde; Sn – supernatants; iNOS – inducible nitric oxide synthetase.