

Influence of tumor cell culture supernatants on macrophage functional polarization: *in vitro* models of macrophage-tumor environment interaction

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ABSTRACT

Aims and background. Macrophages are heterogeneous cells with extensive functional plasticity; they can change their functional profiles repeatedly in response to environmental changes anywhere between their extreme phenotypical programs (labeled as M1 and M2 polarization, respectively). In terms of antitumoral immune response, M1 macrophages are considered to be beneficial, while M2 macrophages supposedly promote tumor progression. Tumor-associated macrophages (TAMs) represent a major leukocyte population present in many tumors. Although many studies indicate that TAMs elicit several M2-associated protumoral functions, including promotion of angiogenesis, matrix remodeling and suppression of adaptive immunity, their role regarding tumor progression is still controversial. The aim of the present study was to develop an appropriate *in vitro* model to study the effect of tumor-secreted soluble factors on the functional phenotype of macrophages.

Methods and study design. THP-1 human monocytic line cells and peripheral blood mononuclear cells from healthy volunteers were used for macrophage differentiation; primary tumor cell culture supernatants or tumor cell line supernatants were employed along with various cytokines, growth factors and other stimuli to design different model variants and to better mimic the *in vivo* tumor microenvironment.

Results. The cytokine secretion patterns of these macrophages suggest that primary tumor cell culture supernatants are able to switch the macrophage phenotype or to induce functional polarization of macrophages toward a mixed M1/M2 phenotype.

Conclusions. These data support the hypothesis that TAM behavior is modulated by the tumor microenvironment itself.

Key words: macrophages, M1/M2 polarization, tumor-associated macrophages, TAMs, tumor progression, cytokine pattern.

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