Секция «Тезисы на английском языке»

Immunoregulatory cells of the innate and adaptive immune systems in the development of invasive cancer (by the example of carcinoma in situ and microinvasive carcinoma of the cervix)

Научный руководитель – Volkova Tatyana Olegovna

Kurmyshkina Olga Vadimovna
Кандидат наук
Московский государственный университет имени М.В.Ломоносова, Биологический факультет, Кафедра биоорганической химии, Москва, Россия
E-mail: olya.kurmyshkina@yandex.ru

Emergence and progression of a malignant tumor are believed to be the consequence of impaired mechanisms of immune response that attract increasing scientific interest in view of the rapid development of methods for cancer immunotherapy and immunoprevention. Immunoregulatory cells of the adaptive and innate immune systems (as well as cell populations that combine the features of both systems) are receiving considerable attention, as their activity results in the establishment of immunosuppressive environment and is proposed to serve as one of the driving forces of carcinogenesis. Exploration of the role of immune-regulation processes in the development of epithelial tumors, particularly at the very early stages preceding invasion and metastasis, is often complicated by the problem of early diagnostics. From this point of view, squamous cell carcinoma of the cervix that arises in a minor percentage of human papillomavirus (HPV) carriers as a consequence of inefficient immune response represents a unique natural model to study both local and systemic disorders. In this work, we used multicolor flow cytometry to perform immunophenotyping of peripheral blood samples taken from 57 patients of the Republic Oncological Dispensary diagnosed with cervical intraepithelial neoplasia grade 3 (including carcinoma in situ) and microinvasive cancer (stage IA, with invasion of stroma $\leqslant$3 mm in depth), infected with high-risk HPV; 30 healthy age-matched women, who were negative for HPV, constituted the control group. We analyzed the frequencies of the following immune cell populations: a) regulatory CD4 and CD8 lymphocytes (CD4 and CD8 Tregs described by CD25+/highCD127dim/negFoxP3+ phenotype); b) subsets of natural killers (NK cells, including regulatory NKreg identified as CD16dim/negCD56bright population), and c) CD3bright population (including CD3briCD56+ and CD3briCD8dim cells that may constitute subpopulations of NK-like (NKT) or gammadelta (T[U+F067][U+F064]) T-lymphocytes). According to the results, initial stages of invasive cervical cancer formation can be accompanied by the increased percentage of not only CD4 Tregs, but also CD8 cells that have Treg phenotype (CD8+CD25+FoxP3+) and are known to display high immunosuppressive activity. At the same time, CD3CD8/Treg ratio was decreased in patients with pre- and microinvasive cancer relative to the control group; importantly, data analysis revealed a correlation between the number of circulating Tregs and the expression of apoptotic markers in effector T cells in the patient group. The frequencies of circulating regulatory NK cells and NKT-lymphocytes recognized as potent producers of IFN[U+F067], showed a tendency to decrease in patients; furthermore, we observed the change of CD56dim/CD56bright NK ratio, which may reflect the change of the balance between effector and regulatory cell subsets. Comparison of data obtained for patients with preinvasive (in situ) and microinvasive cancer suggests that the described trends can amplify during neoplastic progression. In sum, the development of cervical cancer, and the induction of invasive growth in particular, are associated with early activation of specific mechanisms that inhibit the organism's immune function, and further investigation into these mechanisms will contribute to the improvement of immunomodulatory

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