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Tumor microenvironment associated immune suppression mediated disease progression

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Tumor microenvironment consists a lot of various cell types and plays a key role for tumor survival. These different cells, such as Myeloid-Derived Suppressor Cells (MDSCs), Tumor-Associated Macrophages (TAMs), Cancer-Associated Fibroblasts (CAFs), express different function-associated molecules which are involving in mediating tumor progression. CD39/CD73-adenosine pathway has been recently defined as an important tumor-induced immunosuppressive mechanism. We here documented a fraction of CD11b+CD33+ MDSCs in peripheral blood and tumor tissues from Non-Small Cell Lung cancer (NSCLC) patients expressed surface ectonucleotidase CD39 and CD73. Tumor TGF- β stimulated CD39 and CD73 expression, thereby inhibited T cell and NK cell activity and protected tumor cells from the cytotoxic effect of chemotherapy through ectonucleotidase activity. Moreover, CD39+CD73+ MDSCs expressed higher levels of typical MDSC-associated suppressive factors and were significantly associated with disease progression and the poor response to chemotherapy. Our further studies for the reduction of CD39 and CD73 expression by Metformin could block the suppressive function. CD39 and CD73 on MDSCs, therefore, link their immunosuppressive and chemo-protective effects to cancer progression, providing novel targets for chemo-immunotherapeutic intervention.

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