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Lung cancer cell-derived EDA-containing fibronectin induces an inflammatory response from monocytes and promotes metastatic tumor microenvironment

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Abstract

Tumor-associated macrophages (TAMs) play a pivotal role in facilitating tumor growth and metastasis. This tumor-promoting propensity of TAMs sets in as a result of their complex cross-talk with tumor cells mediated primarily by tumor cell-secreted proteins in the tumor microenvironment. To explore such interactions, we employed an immunoscreening approach involving the immunization of Balb-c mice with model human lung carcinoma cell line, A549. From serological examination combined with

mass spectrometric analysis, EDA-containing fibronectin (EDA_{FN}) was identified as a conspicuous immunogenic protein in A549 cell secretome. We showed that A549 secreted EDA_{FN} engages TLR-4 on THP-1 monocytes to drive the proinflammatory response via NF-κB signaling cascade. Conversely, A549 derived EDA_{FN} potentiates their metastatic capacity by inducing epithelial-mesenchymal transition through its autocrine activity. In conclusion, the study proposes a possible mechanism of cellular cross-talk between lung cancer cells and associated monocytes mediated by lung cancer-derived EDA_{FN} and resulting in the establishment of proinflammatory and metastatic tumor microenvironment.