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ПОВЫШЕННАЯ ЭКСПРЕССИЯ ГЕНОВ СИСТЕМЫ ПРОЦЕССИНГА АНТИГЕНОВ ГЛАВНОГО КОМПЛЕКСА ГИСТОСОВМЕСТИМОСТИ (MHC) КЛАССА I В КЛЕТКАХ РАКА МОЛОЧНОЙ ЖЕЛЕЗЫ ПОД ДЕЙСТВИЕМ ТРИХОСТАТИНА A[#]

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Ранее показано, что ассоциированные со злокачественными опухолями эпигенетические альтерации облегчают туморогенез и индуцируют метастазирование. При изучении механизмов метастазирования обнаружили, что эпигенетика играет решающую роль в уклонении опухоли от распознавания иммунной системой. В результате эпигенетические препараты рассматривают в качестве потенциальных агентов, активирующих противоопухолевый иммунный ответ и “отменяющих” иммунологическую толерантность опухоли. Все больше данных свидетельствует о том, что аберрантная экспрессия молекул, процессирующих антигены главного комплекса гистосовместимости (major histocompatibility complex, MHC) класса I, и их активация – потенциальные индикаторы противоопухолевого иммунитета. В проведенном исследовании продемонстрировано, что эпигенетический препарат трихостатин A (Trichostatin A, TSA), ингибитор гистондеацетилазы, восстанавливает экспрессию генов системы презентации антигенов (antigen presentation machinery, APM) MHC I в клетках рака молочной железы человека (MCF-7). Обработка TSA приводила к усилению экспрессии генов MHC I, *B2M* и *PSMB9* в монослое клеток MCF-7 и MHC I, *B2M*, *PSMB9*, *PSMB8*, *TAP1* и *TAP2* в сфероидных клетках MCF-7. Интересно, что обработка TSA также увеличивала экспрессию *CD274* в этих клетках и усиливала инвазивную способность сфероида MCF-7. Это агрессивное поведение подтверждено повышенной экспрессией генов, ассоциированных с метастазами: *SCN5A* (белок nNav1.5) и *MMP1*. Таким образом, под действием TSA в клетках рака молочной железы, с одной стороны, происходит восстановление экспрессии генов APM MHC I, с другой – активируется экспрессия метастатических генов и *CD274*, что усиливает инвазивную способность клеток. Эти результаты свидетельствуют о необходимости глубокого изучения вопроса о возможности применения эпигенетических препаратов в терапии рака молочной железы.

Ключевые слова: главный комплекс гистосовместимости класса I, трихостатин A, рак молочной железы, инвазия, метастазирование, эпигенетика, PD-L1, nNav1.5, MMP1

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Upregulation of MHC I Antigen Processing Machinery Gene Expression in Breast Cancer Cells by Trichostatin A

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Epigenetic alterations associated with cancer have been shown to facilitate tumorigenesis and promote metastasis. In the study of cancer metastasis, epigenetics has been revealed to play a crucial role in supporting tumour immune evasion. As a result, epigenetic drugs have been identified as potential agents to activate anti-tumour immune responses and reverse tumour immunologically tolerant states. Mounting evidence is showing aberrant expression of MHC class I antigen processing molecules in cancers and their upregulation as a potential indicator for anti-tumour immunity. In this study, we demonstrate that the epigenetic drug Trichostatin A (TSA), a histone deacetylase inhibitor, can restore MHC I antigen presentation machinery (MHC I APM) genes in human breast cancer cells (MCF-7). Treatment with TSA resulted in the upregulation of MHC I, *B2M*, and *PSMB9* in MCF-7 monolayer cells, and MHC I, *B2M*, *PSMB9*, *PSMB8*, *TAP1*, and *TAP2* in MCF-7 spheroid cells. Interestingly, treatment with TSA also increased *CD274* expression in these cells and enhanced the invasion ability of the MCF-7 spheroid. This aggressive behaviour was confirmed by increased expression of metastatic-related genes, *SCN5A* (nNav1.5 protein) and *MMP1*. In summary, although the restoration of MHC I APM expression was achieved by TSA, the upregulation of metastatic genes and *CD274* also enhanced the invasion ability of breast cancer cells. These findings suggest the need for careful consideration when utilizing epigenetic drugs for breast cancer therapy.

Keywords: MHC I, Trichostatin A, breast cancer, invasion, metastasis, epigenetics, PD-L1, nNav1.5, MMP1