

Microfabricated platforms for cancer immunotherapy

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Cancer immunotherapy has recently been successful in the treatment of various types of tumors. Cytotoxic lymphocytes, including cytotoxic T lymphocytes (CTLs), natural killer (NK) cells, and T cells, play an essential role in elimination of tumors by directly killing tumor cells. Therefore, evaluation of lymphocyte cytotoxicity against tumor cells is critical for the improvement of cancer immunotherapy. Lymphocyte cytotoxicity is a strictly regulated function requiring a multi-step “checkpoint” to minimize normal cell damage. First, cytotoxic lymphocytes migrate to tumor sites and make close contact with tumor cells (trafficking). Second, cytotoxic lymphocytes recognize distinct signatures of tumor cells and make stable contact with tumor cells (recognition). Third, cytotoxic lymphocytes exert cytotoxicity by exocytosis of lytic granules containing cytotoxic molecules, including perforin and granzyme B, to lysis tumor cells (execution). Lastly, cytotoxic lymphocytes successfully performed cytolysis of tumor cells detach from dead cells and re-engage tumor cells to perform further cytotoxicity (detach and re-engage). However, current cytotoxicity assays mostly provide information about final outcomes of cytotoxicity. To overcome this limitation, we are developing new assays that allow “stepwise” evaluation of lymphocyte cytotoxicity using dynamic imaging and microfabrication techniques.