Author's response to reviews

Title: Immunotherapy using slow-cycling tumor cells prolonged the overall survival of mice bearing colon carcinoma

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Author's covering letter for initial submission

Title: Immunotherapy using slow-cycling tumor cells prolonged the overall survival of mice bearing colon carcinoma

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Comments:

Despite a lot of progress has been made in the development of anticancer therapies, the mortality caused by the relapse and metastasis of cancer is still progressing. And dormant or slow-cycling residual tumor cells are thought to be a source of tumor relapse and metastasis and obstacle in tumor therapy.

For the first time we found that:

1. Slow-cycling tumor cells induced anti-tumor immune response especially tumor specific CTL with enhanced killing of drug-resistant tumor cells. And vaccination with slow-cycling tumor cells could distinctly prolong the overall survival of tumor bearing mice. Till now, the primary therapy of eliminating slow-cycling tumor cells is to induce them into cell cycle and then kill them through traditional methods. However, our therapy not only kills normal tumor cells but also selectively targets the slow-cycling tumor cells, thus reduces the risk of cancer metastases and relapses. Moreover, this vaccine has excellent histocompatibility as slow-cycling tumor cells are isolated from tissues of recipient own, thus, no severe side-effects will appear. All the findings suggest us that immunotherapy with inactivated slow-cycling tumor cells could become a possible strategy complementing to traditional therapy.

2. Cancer stem cells were enriched in the slow-cycling population. More importantly, we found that slow-cycling tumor cells may take some time to exit quiescent state, and then expand to establish tumors. This finding have a indication that if we could understand the mechanism that cause the re-cycling of quiescent cells and inhibit the critical point of the pathway, we may prevent their re-cycling in order to obviate tumor relapses and metastases.

3. Slow-cycling cells expressed a higher level of MHC class II and costimulatory molecules CD80 and CD86, and this finding may explain their increased induction of immune response.