Cross-presentation of Tumor Antigens Is Increased by UVC Light Tumor Treatment

To the Editor: Renal carcinoma is a disease for which both positive involvement of the immune system and immunoevasive mechanisms have been described. In the dendritic cell (DC) vaccine-based protocol described by Schwaab et al. (1), steps to overcome dysfunctional immune pathways have been taken. Interleukin-2 was introduced to enhance the in vivo function of arising cytotoxic T cells, and IFN-α to increase the MHC class I antigen-presenting molecules on tumor targets.

As for the vaccine-induced lymphocyte boosting, significant enlargement of the tumor specific CD8+ T lymphocyte compartment was observed, but only the increase of CD4+ cells was correlated with the clinical outcome. A major point to be raised in face of a disappointing CD8+ boosting is if the vaccine was strong enough. DCs were aptly injected intranodally. However, this clever strategy was not coupled with an attentive preparation of the source of tumor antigen, an issue often neglected during DC vaccine preparation. The use of the whole tumor as source of antigens is the gold standard for renal cancer, for which no strong antigens are available. However, defining the number of DCs (107 in Schwaab et al.’s article) is not sufficient to describe the potency of a vaccine, which is instead dictated by the number of tumor-derived molecules cross-presented within the MHC class I groove. Schwaab et al.’s use of tumor lysate to load DCs may have not been most advantageous. There is in fact mounting evidence that the way a tumor dies decides its immunogenicity (2, 3). Live renal carcinoma cells significantly suppress the maturation and the ensuing cross-priming activity of DCs (4), and secondary necrotic cells (i.e., UVC treated), but not primary necrotic (freezing/thawing), lysate, or apoptotic (irradiated) cells (4), could rescue the DC function. Secondary necrotic UVC-treated cells are engulfed with higher efficiency by DCs (4, 5), and the UVC-induced environment promotes cross-presentation of tumor-derived antigens by properly matured DCs (Fig. 1). In the study by Schwaab et al., excellent analysis of the clinical and immune outcome was done. However, only by using effectual consensus procedure for DC preparation can the effects of cancer vaccine trials be firmly assessed. I believe that in this well-designed and well-executed study, this limitation should have been mentioned.

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No potential conflicts of interest were disclosed.

References

Fig. 1. A, K562 cells become secondary necrotic (i.e., expose phosphatidylserine and are permeable to the DNA staining PI) after UVC treatment. B, 35S-labeled MHC class I-immunoprecipitated molecules are increased in DC loaded with 35S methionine/cysteine K562 in the presence of a supernatant of unlabeled UVC-treated (UVC-SN) vs untreated (un-SN) K562 cells. The amount of radioactivity was evaluated by a gamma-counter.
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