

Correction: Macrophage Inflammatory Protein Derivative ECI301 Enhances the Alarmin-Associated Abscopal Benefits of Tumor Radiotherapy

In this article (Cancer Res 2014;74:5070–8), which appeared in the September 15, 2014, issue of *Cancer Research* (1), the authors have corrected two sentences in the abstract so that it more accurately reflects the rest of the article. The corrected abstract is below.

Radiotherapy can produce antitumor benefits beyond the local site of irradiation, an immune-based phenomenon known as the abscopal effect, but the mechanisms underlying these benefits are poorly understood. Preclinical studies of ECI301, a mutant derivative of macrophage inhibitory protein-1 α , have shown that its administration can improve the antitumor effects of radiotherapy in a manner associated with a tumor-independent abscopal effect. In this article, we report that i.v. administration of ECI301 after intratumoral injection of tumor cell lysates can inhibit tumor growth, not only at the site of injection but also at nontreated sites. Effects of the tumor lysate were further recapitulated by intratumoral injection of the alarmins HSP70 or HMGB1, but not HSP60, and i.v. administration of ECI301 + HSP70 was sufficient to inhibit tumor growth. Although i.v. administration of ECI301 + HMGB1 did not inhibit tumor growth, we found that administration of a neutralizing HMGB1 antibody neutralized the cooperative effects of ECI301 on tumor irradiation. Moreover, mice genetically deficient in TLR4, an immune pattern receptor that binds alarmins, including HMGB1 and HSP70, did not exhibit antitumor responses to irradiation with ECI301 administration. Although ECI301 was cleared rapidly from peripheral blood, it was found to bind avidly to HSP70 and HMGB1 *in vitro*. Our results suggest a model in which sequential release of the alarmins HSP70 and HMGB1 from a tumor by irradiation may trap circulating ECI301, thereby licensing or restoring tumor immunosurveillance capabilities of natural killer cells or CD4⁺ and CD⁺ T cells against tumor cells that may evade irradiation.

Reference

1. Kanegasaki S, Matsushima K, Shiraishi K, Nakagawa K, Tsuchiya T. Macrophage inflammatory protein derivative ECI301 enhances the alarmin-associated abscopal benefits of tumor radiotherapy. *Cancer Res* 2014;74:5070–8.

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