1-SS-56 Student Sessions

Evaluation of cytotoxicity of bispecific antibody against mesothelioma

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Malignant mesothelioma is a fatal tumor caused by past exposure to asbestos. In Japan, mesothelioma due to asbestos exposure is a major public health problem. The prognosis for mesothelioma patients is very poor. Satisfactory recovery is often not possible with chemotherapy and/or radiotherapy. Therefore, a new effective anti-mesothelioma drug is urgently required. In previous study, we isolated a highly specific anti-mesothelioma mAb, SKM9-2. The specificity and sensitivity of SKM9-2 to mesothelioma reach 99% and 92%, respectively. SKM9-2 recognizes the sialylated protein HEG homolog 1 (HEG1), a novel mucin-like membrane protein.

In this study, we investigated the cytotoxic activity of bispecific antibodies (bsAbs) in which the antigen-recognition domains of SKM9-2 and anti-CD3 (OKT3) were linked. BsAbs were purified from the culture supernatant of stably expressed mammalian cell lines and were analyzed about the binding to SKM9-2 epitope and CD3. Some bsAbs strongly bound to SKM9-2 epitope but not CD3. In these bsAbs, two antigen recognition domains may interfere. A bsAb that bound to both SKM9-2 epitope and CD3 showed a strong T cell-dependent cytotoxicity against mesothelioma.

SKM9-2 binds to mesothelioma cells but not normal tissues. Thus, T cell-engaging bsAb including SKM9-2 may be a promising drug for mesothelioma.