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Development of antibody-drug conjugates that target vascular endothelial cells to promote anti-tumor activity

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Antibody drugs have revolutionised and strongly impacted therapy in the 21st century, especially in the field of cancer and inflammation-related diseases. Moreover, the development of bispecific antibodies as well as antibody-drug conjugates forms a new platform of antibody drugs by extending application range and by increasing efficacy. Although anti-cancer therapies pay much attention to the induction of cancer cell death, the cancer microenvironment and the functional roles of vascular endothelial cells in metastasis are also important to understand to regulate the growth of cancer cells.

We observed that anti-high mobility group box-1 antibody (HMGB1 Ab) was incorporated into vascular endothelial cells in culture under certain conditions. Moreover, Alexa Fluor 488 labeled anti-HMGB1 Ab was distributed and accumulated specifically in the vascular endothelial cells of melanoma inoculated in mice whereas not accumulated in normal vascular endothelial cells in the brain, lung and liver. Based on these results, we hypothesized that anti-HMGB1 Ab can be utilized as the anti-tumor drug carrier to improve the efficiency for cancer treatment. Therefore, we biosynthesized anti-HMGB1 Ab-doxorubicin conjugates and injected it into the melanoma-bearing mice. The tumor growth was significantly suppressed in HMGB1 Ab-doxorubicin conjugates treatment group compared with the group treated with doxorubicin alone. In conclusion, anti-HMGB1 Ab may function as a drug delivery molecule targeting the cancer vascular endothelial cells.