Development of a monoclonal antibody for CD44-expressing oral cancers

Junko Takei1,2, Mika K. Kaneko1, Tomokazu Ohishi3, Teizo Asano1, Manabu Kawada3, Hiroyuki Harada2, Yukinari Kato1,4


Purpose: CD44 is widely expressed on the surface of most tissues and all hematopoietic cells. CD44 plays important roles in cell proliferation, adhesion, and migration. Previously, we developed an anti-CD44 monoclonal antibody, C44Mab-5 (IgG1, kappa) by immunizing mice with CD44-overexpressing Chinese hamster ovary (CHO)-K1 cells. In this study, we converted the mouse IgG1 subclass antibody C44Mab-5 into an IgG2a subclass antibody, 5-mG2a, and further produced a defucosylated version, 5-mG2a-f and investigate its antitumor activities against oral cancers.

Methods: To generate 5-mG2a-f, appropriate VH cDNA of mouse C44Mab-5 and CH of mouse IgG2a were subcloned into pCAG-Neo vector, and light chain of C44Mab-5 was subcloned into pCAG-Ble vector. Vectors were transfected into BINDS-09 (FUT8-deficient ExpiCHO-S cells) using the ExpiCHO Expression System. Mouse xenograft models of HSC-2 and SAS (human oral cancer cell lines) were used for examining the antitumor activity.

Results: 5-mG2a-f demonstrated a sensitive and specific reaction against oral cancer cells in flow cytometry and immunohistochemical analyses. The sensitivity of 5-mG2a-f was similar with that of C44Mab-5. In vitro analysis demonstrated that 5-mG2a-f showed moderate ADCC and CDC activities against HSC-2 and SAS. 5-mG2a-f significantly reduced tumor development in HSC-2 and SAS xenografts in comparison to control mouse IgG.

Conclusion: 5-mG2a-f may be a useful antibody-based therapy for patients with CD44-expressing oral cancers.