Cancer-specific CD98 antibody

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Technology description

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Newly generated monoclonal antibody (R8H283) is specific to MM cells. Although CD98 is expressed broadly in normal hematpoietic cells, R8H283 recognizes MM-specific epitope of the CD98 molecules. The MM-specific epitope is formed under elevated ER stress presumably due to altered glycosylation of CD98.

Background

MM is a hematological malignancy with abnormal expansion of monoclonal plasma cells and production of monoclonal immunoglobulin. There are the malignant plasma cells observed in MM patient’ s bone marrow. MM is one of the major hematological cancer. Monoclonal antibody (mAb) drugs are desirable for the improvement of MM therapy. Cancer-specific cell surface antigens are ideal targets for therapies using mAb. Daratumumab (human anti-CD38 mAb) approved in 2015. However, CD38 are expressed on normal hematopoietic cells and target antigens that are more specific to MM cells are needed.
Inventors aimed to identify novel cancer-specific antigens formed by post-translational events, such as glycosylation, complex formation, or conformational changes. They identified MM-specific mAbs designated as R8H283 after screening more than 10,000 anti-MM mAb clones. Then, they identified CD98 as the antigen recognized by R8H283 using an expression cloning method. The R8H283 epitope is formed under elevated ER stress presunmably due to altered glycosylation.

Data

SCID mice were transplanted with MM cells subcutaneously, and then treated with R8H283 or control IgG (10mg/kg, n=5 for each). R8H283 treatment significantly suppressed tumor growth in vivo (figure).
R8H283 did not damage normal hematopoietic cells in vitro and in vivo.
R8H283 reacts with solid tumor cell lines.
Internalization of R8H283 is unverified.

Advantages

・Eliciting strong cytotoxic effects (ADCC/CDC) against MM cells
・Antibody therapy without side effects because it does not damage normal hematopoietic cells

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