The activated conformation of integrin β7 is a novel multiple myeloma–specific target for CAR T cell therapy

Cancer-specific cell-surface antigens are ideal targets for monoclonal antibody (mAb)-based immunotherapy but are likely to have previously been identified in transcriptome or proteome analyses.

Professor Kumanogoh and his research group show that the active conformer of an integrin can serve as a specific therapeutic target for multiple myeloma (MM). They screened >10,000 anti-MM mAb clones and identified MMG49 as an MM-specific mAb specifically recognizing a subset of integrin β7 molecules. The MMG49 epitope, in the N-terminal region of the β7 chain, is predicted to be inaccessible in the resting integrin conformer but exposed in the active conformation. Elevated expression and constitutive activation of integrin β7 conferred high MMG49 reactivity on MM cells, whereas MMG49 binding was scarcely detectable in other cell types including normal integrin β7+ lymphocytes. T cells transduced with MMG49-derived chimeric antigen receptor (CAR) exerted anti-MM effects without damaging normal hematopoietic cells. Thus, MMG49 CAR T cell therapy is promising for MM, and a receptor protein with a rare but physiologically relevant conformation can serve as a cancer immunotherapy target.