Cancer Immunotherapy with Chimeric Immune Receptors (CIRs): A Focus on Their Antitumor Activity

Hirotomo SHIBAGUCHI, Motomu KUROKI, Tetsushi KINUGASA,
Toshihiro TANAKA and Masahide KUROKI

Department of Biochemisty, Faculty of Medicine, Fukuoka University

Abstract: T cell immunotherapy is based on the assumption that tumor-associated antigen (TAA) peptides are correctly presented by HLA class I molecules on target tumor cells. However, human tumor cells are well known to often lose HLA class I molecules. This altered HLA class I expression constitutes the major tumor escape mechanism related to the tumor-specific cytotoxic T lymphocyte (CTL)-mediated response. This fact also indicates that it is not easy to eliminate the target tumors by only activating tumor-specific CTLs. On the other hand, it can be easily confirmed by immunostaining whether or not antibody-recognized TAAs, such as carcinoembryonic antigen, exist on the cell surface of target tumor cells. Recently, strategies which combine the advantages of antibody-based and T cell-based immunotherapy by grafting CTLs with chimeric immune receptors (CIRs) have been attempted to improve the efficacy of T cell immunotherapy for cancer. CIRs are usually made up of antibody fragments of anti-tumor antibody and cellular activation domains of antigen-recognizing receptors on CTLs. Current mouse experiment data using human tumor xenograft models suggest this CIR strategy to be a potentially useful new therapy for TAA-expressing tumors, and several phase I/II clinical studies have just been started to evaluate this CIR strategy.

Key words: **Chimeric immune receptor, Cancer immunotherapy, Tumor-associated antigen, Antitumor activity**