Cancer Immunotherapy with Chimeric Immune Receptors (CIRs): A Renewed Focus on Their Gene Constructions

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Abstract: The use of cellular immunotherapy has been limited to date mostly due to the poor immunogeneicity of tumor cells, based on a downregulation and/or dysfuncition of the major histocompatibility complex that is essential for tumor cell recognition by the cellular immune system. On the other hand, the application of tumor specific monoclonal antibodies have given rise to major obstacles in the effective cytolysis of tumor cells by the humoral immune system because of their slow tumor penetration and short half-life. In the past two decades, various strategies have been which combine the advantages of antibody-based and T cell-based immunotherapy by grafting cytotoxic T lymphocytes (CTLs) or natural killer (NK) cells with chimeric immune receptors (CIRs) in order to improve the efficacy of adoptive cellular cancer immunotherapy. CIRs are usually made up of antibody fragments of anti-tumor antibodies and cellular activation domains of antigen-recognizing receptors on CTLs or NK cells. Recently, the details of the intracellular signaling pathways of CTLs or NK cells has gradually become clear, and based on such information, modifications of the CIRs to enhance the effector function have thus been carried out.

Key words: **Chimeric immune receptor, Cancer immunotherapy, Activation signaling, Intracellular domain**