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MAIN FIELDS OF RESEARCH; ABSTRACT

IL-2 is a potent T cell growth factor. It exerts its actions on its target cells by binding to two different signaling IL-2 receptor (IL-2Rs) complexes. Dimeric IL-2Rs are comprised of the common gamma chain (γ_c) and the IL-2Rβ chain (also called CD122), whereas trimeric IL-2Rs consist of the γ_c, CD122 and the IL-2Rα chain (also termed CD25). The CD25 subunit is not involved for signaling but enhances the binding affinity of IL-2 to the receptor complex by 10-100 fold. Dimeric IL-2Rs are expressed by memory $CD8^+$ T and NK cells at high levels and by naïve $CD8^+$ T and memory $CD4^+$ T cells at intermediate levels. Following TCR stimulation, $CD8^+$ T cells transiently upregulate CD25, thus expressing the high affinity trimeric receptor. In steady state, the trimeric receptor is constitutively expressed by thymus-derived $CD4^+$ forkhead box p3 $(Foxp3)^+$ T regulatory cells (Tregs).

The use of IL-2 was the first successful cancer immunotherapy due to its potent T cell stimulatory activity. Despite promising results in the clinics, IL-2 immunotherapy has not been widely adopted because of several shortcomings such as short half-life, toxic adverse effects and stimulation of immunosuppressive Tregs. The biology of IL-2 as a therapeutic agent including improved IL-2 formulations have been widely studied by us and others. However, the effect of endogenous IL-2 has not been extensively investigated in the tumor setting. The studies conducted on various IL-2 deficient mice models using viral infections have shown IL-2 has a supporting effect rather than a crucial role in generation of the immune response. Although an overall anti-viral immune response was generated, several aspects were impaired such as effector function and memory formation. However, the immune responses during infections differ considerably from malignancies, creating the need of studying the relevance of these findings to the anti-tumor immune response.

SPECIAL TECHNIQUES AND EQUIPMENT

Flow cytomery, mouse models