Therapeutic approaches to enhance natural killer cell cytotoxicity: the force awakens

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Scientific insights into the human immune system have led to unprecedented breakthroughs in immunotherapy, and drugs and cell-based therapies that have been developed to bolster humoral and T cell immune responses represent an extended and expanded armamentarium of therapeutic alternatives. Although NK cells have long been known to have advantages over T cells in terms of their capacity to induce antigen-independent immune responses against cancer cells, their therapeutic potential in the clinic has been largely unexplored.

Here, we present different pharmacological and genetic strategies to bolster NK cell antitumour immunity. These approaches, as well as advances in our ability to expand NK cells ex vivo and manipulate their capacity to home to solid tumours, have now armed investigators with a variety of new strategies to harness the full potential of NK cell-based cancer immunotherapy in the clinic.

NK cell tumour killing

NK cells can mediate cytolysis through several distinct mechanisms. Despite the use of several pathways in which NK cells release cytotoxic granules upon interaction with target cells, this is controlled by NK cell intrinsic sensing of tumour cells, such as MHC, Dendritic Cells, and NKs, which are enhanced by cytokines and chemokine receptors. These mechanisms can be modulated by transduction of NK cell lines using adenoviral and lentiviral vectors, or using a variety of small molecules and antibodies that modulate the expression of L-selectin, which is required for the transduction of NK cell lines using adenoviral and lentiviral vectors. Additionally, there are several investigational strategies to manipulate the expression of target antigens. In a recent study of low-dose subcutaneous rIL-12 in healthy individuals reported an improved toxicity profile and a decrease in toxicity.

Cytokines to boost NK cell persistence, expansion, cytotoxicity and migration

Cytokines such as IL-2 and IL-15 have been shown to enhance the cytotoxicity and proliferation of NK cells, as well as suppressing NK cell fatigue and proliferation. Cytokines such as IL-2 and IL-15 are known to boost the cytotoxicity and proliferation of NK cells, as well as suppressing NK cell fatigue and proliferation. These cytokines induce cytotoxicity independent of NK cell education and signalling from receptors controlling NK cell degranulation.

Drugs to augment NK cell cytotoxicity and tumour targeting

Immunoconjugates. The use of immunoregulatory, lymphoablative and oncoimmunology. In our study of low-dose subcutaneous rIL-12 in healthy individuals reported an improved toxicity profile and a decrease in toxicity.

References