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Autore	Vincent Vieillard
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Sommario/riassunto

NK cells are lymphocytes of the innate immune system that share some features with adaptive immune cells like T cells. They are well known for their importance to control viral infections and tumor development, but also intracellular bacterial and parasitic infections. A balance between negative and positive signals transmitted via germ line-encoded inhibitory and activating receptors controls the function of NK cells. Activated NK cells respond by killing the infected or tumor cells without prior sensitization, and by producing cytokines and chemokines. It has been shown that NK cells cross-talk with other immune cells, such as dendritic cells and macrophages, can shape T cell and B cell immune responses through direct interactions as well as by virtue of their cytokine/chemokine production. NK cells can also regulate immune responses by killing other immune cells, including activated T cells, or by producing anti-inflammatory cytokines upon excessive inflammation. However, NK cells are not friends in all situations. Indeed, it has been shown in LCMV-infected murine models that, depending on the viral inoculation load, NK cells may either help fight infection or can promote chronic infection. Moreover in cancer models, it has been shown that NK cells can kill anti-tumoral T cells. Recent studies of NK cells in patients with cancer support the notion of detrimental roles of NK cells. Furthermore, studies implicate NK cells in contributing to both graft rejection and tolerance to an allograft. In some autoimmune diseases, like rheumatoid arthritis, NK cells may

promote disease pathogenesis. The scope of this Research Topic is to present and discuss knowledge on the role of NK cells in various diseases settings: viral infections as well as other infections, cancer, transplantation, and autoimmunity. The aim is to discuss how NK cells respond during disease and specifically when, why and how NK cells can be harmful and if they exert different functions (production of specific cytokines, inhibition of other immune cells through other mechanisms beside cytotoxicity) in these situations. Which are the NK cell subsets that play beneficial or deleterious roles in these diseases? Are there different phenotypes associated with protective NK cells (e.g. antiviral, antitumoral) and NK cells involved in disease pathogenesis? How are these diverse NK cells activated and do they function primarily through direct cytotoxicity, ADCC or cytokine and chemokine production? What are the signals or interactions that can change and shape the NK cell response shifting them from protective to harmful? We thank the authors that submitted reviews and original research manuscripts that help to better understand these questions, with the aim that this will help the scientific community to determine what could be the main future research directions to better understand the role of NK cells in disease protection or development.