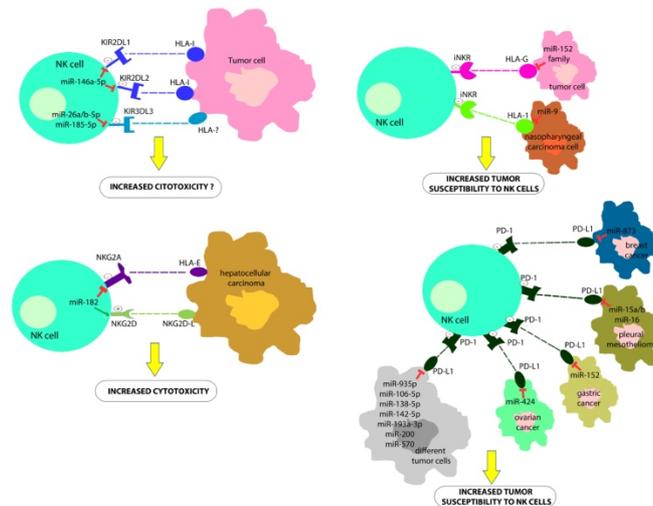


CITOLOGY AND HISTOLOGY



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NK Cell Checkpoints as Promising Therapeutic Targets in Cancer Immunotherapy

Natural killer (NK) cells are cytotoxic lymphocytes of the innate lymphoid cell (ILC) family that play an essential role against cancer and virus-infected cells. NK cell function is regulated and maintained by a balance between signals deriving from inhibitory and activating receptors. The balance between these signals is responsible for maintaining the proper homeostasis of NK cells. It is well known that the presence of tumor-infiltrating NK cells represents a positive prognostic factor, however it is also known that tumors implement mechanisms that can lead to a malfunction of NK cells in the tumor microenvironment, such as an increase in the expression of inhibitory receptors (called immune checkpoints). In fact, if in physiological conditions these receptors serve to recognize the self and prevent autoimmune reactions, in pathological conditions they can be exploited by tumors to escape the control of the immune system and prevent an attack by the latter. It has been shown, in fact, that the immune checkpoints, following the recognition of their own ligand on tumor cells, generate an inhibitory signal that leads to a functional block of NK cells and the consequent uncontrolled proliferation of the tumor.

For this reason, the research group is involved in the identification of new strategies for blocking the functioning (and / or expression) of the immune checkpoints most expressed by NK cells in the tumor microenvironment in order to reactivate these cells against the tumor. In this context, a new transfection protocol is being developed using specific siRNAs for the main immune checkpoints of NK cells, as well as a molecular approach involving miRNA mimics, which would lead to a modulation of their expression and therefore to a block of their functioning. These approaches will be studied in different tumor types (solid and hematological).

Therefore, this project aims to examine the mechanisms that regulate the expression and functioning of NK immune checkpoints expressed in the tumor microenvironment in order to propose new tailored anti-tumor therapeutic approaches that reflect both the characteristics of the patient and those of the tumor.

Keywords: NK cells, cancer, immune checkpoints, immunotherapy

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