

Killer cells that prevent metastasis

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Treatment of a tumor does not always succeed in eliminating cancer cells that have migrated to other organs and have the potential to form metastases. Recent research shows that these residual cancer cells can be kept in a dormant state by promoting the growth of so-called natural killer immune cells.

A major obstacle to the lasting cure of many cancers is the presence of residual cancer cells that spread from the primary tumor and establish themselves in distant organs. These cancerous cells are present in a stationary state and are clinically undetectable, but can reappear unpredictably, sometimes several years later, in the form of metastases which compromise the survival of patients.

Since these metastases are the main cause of death of cancer patients, understanding the factors responsible for this awakening of residual cancer cells is of considerable clinical importance.

INHIBITORY MICROENVIRONMENT

Cancer cells that are disseminated throughout the body contain multiple genetic abnormalities and should therefore, in theory, be able to progress rapidly to form metastases.

The long period of dormancy which is often observed before the appearance of these metastases (sometimes more than ten years for breast cancer, for example) therefore suggests that the tissue microenvironment in which these cancer cells are found acts as a brake on this growth.

One of these brakes is the immune surveillance carried out by a class of lymphocytes called natural killer cells or NK lymphocytes. These cells, which are very abundant in the blood (5 to 16% of all lymphocytes), have the particularity of being able to attack and quickly destroy abnormal cells, such as cancer cells, without requiring the activation of cellular immunity by an antigen.

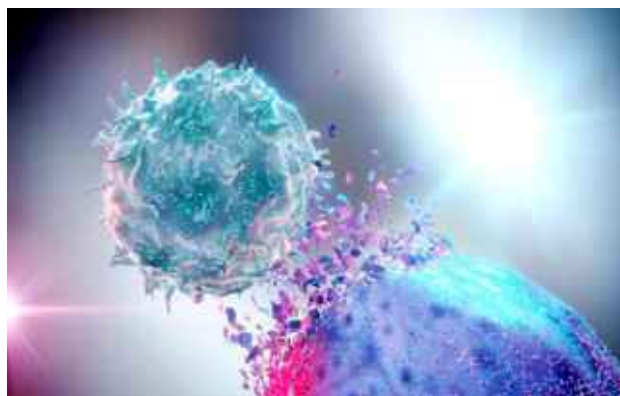
Several observations suggest that NK lymphocytes are particularly reactive towards metastatic cells (1), which makes them prime candidates for maintaining residual cancer cells in a dormant state and preventing the development of metastases.

NK CELL RESERVOIR

The results of a recent study support this view and suggest that the presence of a reservoir of NK lymphocytes manages to block the development of metastases from breast cancers in the liver, an organ frequently colonized by these cancer cells (2).

The researchers observed that the presence of metastatic cells is accompanied in parallel by an increase in NK lymphocytes in this organ, which keeps cancer cells in a dormant state and prolongs survival.

However, they surprisingly discovered that certain liver cells can reduce this population of NK cells, which allows cancer cells to progress rapidly in the form of metastases.



These antagonistic mechanisms are at work in human cancers, since the analysis of biopsies has revealed that the quantity of these permissive cells is closely correlated with the presence of metastases in this organ.

One of the most important points of the study is that the researchers observed that the administration of a molecule which preserves the reservoir of killer cells at high levels keeps cancer cells in a latent state and thus blocks the formation of metastases.

These results therefore open the door to a new revolutionary form of immunotherapy, in which the maintenance of the population of NK lymphocytes in the organs colonized by cancerous cells would make it possible to maintain these residual cancerous cells in a dormant state, without danger for the patient survival.

- (1) López-Soto A et al. Control of metastasis by NK cells. *Cancer Cell* 2017 ; 32 : 135-154.
- (2) Correia AL et al. Hepatic stellate cells suppress NK cell-sustained breast cancer dormancy. *Nature* 2021 ; 594 : 566-571.