Pushing our defense system to move faster
Receptor dynamics at the Natural Killer Cell receptors

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Our immune (defense) system constantly works to protect us from any foreign invaders tirelessly. This system is broadly divided into two, innate and adaptive, referring to those that immediately respond and do not need any previous information about the invader and those that need information to better prepare and act vigorously. Natural killer (NK) cells are one of the innate immune cells that have the ability to directly kill virus-infected cells or cells that are abnormal, including cancer cells. These cells have molecules on their surfaces, called receptors, used for detecting the surrounding cells to check whether they are healthy or diseased. There are two types of receptors on NK cells that help the cell regulate its function, inhibitory and activating receptors. The inhibitory receptors detect the presence of structures, called "Major Histocompatibility Complex class I" (MHC-I), that are normally present on all healthy cells. Up on binding to the MHC-I, these receptors transmit inhibitory signals to the NK cell. Therefore, it protects the healthy cells from being killed by the NK cell, and this is called self-tolerance. On the other hand, the activating receptors detect the presence of abnormal structures, either those normally found in a very low level but increase in diseased/stressed conditions or those are not normally present at all.

Some cancer cells decrease the availability of the MHC-1 molecule on the cell surface. In this case the NK cell detects the absence or abnormally low level of the MHC-I molecule through its inhibitory receptor. Some viruses, cell damage or transformation cause cells to have surface structures that are not normally present, which the activating receptors detect. The lack of inhibitory signal and the presence of activating signal activates the NK cell to kill the target (infected/transformed) cell.

An NK cell needs to make a cell-to-cell contact in order to be able to determine the status of a target cell. The contact area is called an immunological synapse (IS). The IS is a complex structure where many molecules and cellular structures are involved. The NK cell inhibitory and activating receptors are also the key players in this contact. Therefore, they should be able to move along the cell surface and make it to the IS. Cytokines are messenger proteins (chemicals) secreted by cells of the immune system to regulate different activities of other immune cells. They can also activate immune cells to do their functions. The use of these chemicals for the treatment of different diseases, including some cancers, is increasing. Therefore, knowledge of how they affect the immune cells helps in better targeting them and enhancing the outcome. In this study we investigated how these cytokines change some aspects of the NK cell inhibitory and activating receptors movement using mouse and human NK cells.

Using cell surface imaging/visualization technique called Total Internal Reflection Fluorescence (TIRF) microscopy we were able to obtain data that help us understand how fast these receptors move, how long they stay stand-still (bound) and the size of area where they are bound among other things. Accordingly, we found out that cytokines can enhance the rate at which the mouse inhibitory receptors move along the cell membrane and also that they spent less time bound at stationary phase, which could mean that they can provide the NK cell with the necessary information for faster action.

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