How killer -T-cells migrate towards virus-infected cells

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Joost Beltman (LACDR, Leiden University) has provided novel insights in the way T-killer cells migrate towards virus-infected cells. This was accomplished by a combination of experimental research in the group of Ton Schumacher (Dutch Cancer Institute, NKI) and computer simulations in collaboration with Rob de Boer (Utrecht University). The results have been published in the December edition of the *Journal of Immunology*.

Killer cells of our immune system are continuously searching for malignous cells or pathogens that need to be destructed. From the bloodstream they move into surrounding tissues and interact with other cells. It is well known that chemokine receptors are important for the movement and localization of immune cells. Recently, researchers discovered that the presence of the chemokine receptor CXCR3 on the killer cell promotes their binding with virus-infected cells. However, it remained unclear through which migration process the killers arrive at the infected cells, which could be either through random migration or through directed migration (chemotaxis).

In the study by Beltman and co-workers, epidermal skin was infected with fluorescent Herpes Simplex Virus. Subsequently, both the infected skin cells and the killer cells were visualized by confocal microscopy. One day after infection, small groups of infected cells surrounded by killer cells could be observed.

At first sight, the killer cells appeared to migrate at random and to stop

close to the infected cells. However, the researchers used a detailed analysis to show that there was a slight migration preference towards the infected areas. In contrast, without the CXCR3 receptors the migration-behavior could no longer be discerned from a random walk. In conclusion, the killer cells used a very subtle form of chemotaxis to appprach infected cells and this depended on CXCR3.

Computer simulations

Nevertheless, the significance of the subtle migration towards the infected areas was as yet unclear. Therefore, the researchers designed computer simulations based on the cellular paths that were measured on short time-periods, to predict the paths for longer periods of multiple hours. For comparison, simulations were also created for totally random paths, but with equal cell speeds.

These computer simulations demonstrated that the cells with a small migration component in the direction of the infected area arrived more often and faster at the infected area than the randomly moving cells. Thus, althoughthe directed migration of the killer cells is very small and practically invisible, it did have a highly important biological effect in terms of increasing the odds of killer cell arrival at the infected areas, and thus in curing the infection.

Destruction of tumor cells

It is as yet unclear whether the directed migration of killer cells is a general phenomenon that also occurs for other infections or for cancers. Other research of Joost Beltman's research group at the LACDR focuses on modeling the migration behavior of killer cells and of tumor cells and on factors that affect the desctruction of tumor cells. This is important for cancer immunotherapies in which killer cells are exploited to destruct tumors, and for therapies aimed at counteracting cancer

metastasis.

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