Press Release



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NATURAL KILLER CELLS – THE BODY'S OWN PATROL AGAINST VIRUSES AND TUMOURS

SETTING THE STAGE FOR PERSONALISED MEDICINE, RESEARCHERS DECODE MAJOR IMMUNE CELL'S PROTEIN CONTENT

Scientists at the Helmholtz Centre for Infection Research (HZI) have analysed for the first time all the proteins inside natural killer (NK) cells of healthy individuals. The newly discovered "protein repertoire" shows that these immune cells cannot only defend us against acute viral infections but they can also store information about earlier infections. The researchers have identified new proteins that help to determine NK cell condition. These findings may improve the basis for personalized therapies.



A natural killer cell (top cell) encounters a cancer cell. Under the microscope the researchers are able to observe the high degree of expression of the newly discovered protein S10A6 (shown here in red) at the contact surface. © HZI/Scheiter

To effectively fight off different kinds of pathogens, the human immune system has become highly specialized. Defending us against viruses and tumour cells is the task of NK cells. Armed with small, enzyme-containing spheres capable of causing a damaged cell to burst, these sentinels with their vicious sounding name patrol our bodies. When prompted to do so, they fire their ammunition at other cells across a specialized contact surface. As we grow older, our NK cells also age and mature. Scientists at HZI, Braunschweig City Hospital, and Ostfalia University of Applied Sciences recently characterized what happens inside these cells during this process. They published their findings in the scientific journal Molecular & Cellular Proteomics.

"We have isolated NK cells at varying stages of maturation from the blood of healthy individuals. Using accurate mass spectrometry, we managed to analyse which proteins they produce," explains HZI scientist Maxi Scheiter. Since proteins have a key role in many of the cell's functions - as enzymes, signalling molecules, or building blocks, to name only a few - the researchers are now able to draw conclusions as to their jobs within the cell. "We discovered more than 3,400 proteins inside cells at different stages of maturation. They suggest that NK cell development in humans is highly similar to what was known before from experiments in mice," says Prof. Lothar Jänsch, head of HZI's Cellular Proteome Research unit. The massive amounts of data that have come out of this research were analysed with the help of biostatistical algorithms by Ostfalia University's Prof. Frank Klawonn.

Among the identified proteins were some whose role in natural killer cells was previously unknown. "We were very interested in identifying these proteins' functions inside the immune cells," explains Scheiter. "We therefore labelled two of the most promising candidates using a special dye and then examined them under the fluorescence microscope to localize them within the cell." The view through the microscope confirmed that two molecules with the cryptic names S10A4 and S10A6 appear in the contact zone as soon as the NK cells have become activated by direct contact with cancer cells. The little spheres filled with ammunition arrive at the scene at the same time. They contain for example a substance called perforin, which, as its name would imply, perforates the cancer cells' surface, essentially puncturing holes in them. "It is very likely that S10A4 and S10A6 contribute in an unknown way to the transport of these destructive molecules to their targets," presumes Scheiter.

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The HZI researchers were also able to support a current hypothesis in NK cell research at the level of the proteome: "The natural killer cells can do more than we had initially suspected," explains Scheiter. Until recently, scientists assumed that these cells were exclusively involved in the innate immune response, where they represent a first line of defence against viral attacks. However, for some time now, there have been clues as to their ability to adapt to their environment throughout the course of their lives – a property that was rather assigned to acquired immunity only, a different branch of the immune system. According to Jänsch, "our proteomic analyses have shown that the more mature a cell, the more virus-specific its surface molecules, suggesting they are able to recall prior viral infections. Here, the lines between innate and acquired immunity become somewhat blurred."

To know which proteins are normally found within healthy NK cells and how their composition changes during development is a major step forward in patient-specific sample analysis. Several diseases can be ascribed to defective NK cell proteins. In some cases the contact area to other cells is not correctly formed and the cell cannot perform its function. Consequences might be a weak immune system and recurring infections. In the future, we may be able to intervene using targeted drug therapy whenever a patient's NK cells deviate from this protein standard – a first step towards personalized medicine.

Original Publication

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Proteome Analysis of Distinct Developmental Stages of Human Natural Killer Cells Molecular & Cellular Proteomics 2013

The research group "**Cellular Proteome Research**" studies changes in the proteome, the sum total of a cell's proteins. These offer clues as to which processes are being switched on or off inside immune cells and which ones are being manipulated by pathogens.

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