New Tel Aviv University study sheds light on precise trigger of deadly melanoma

Published on August 4, 2015 at 3:05 AM

Skin cancer is the most common of all cancers, and melanoma, which accounts for 2% of skin cancer cases, is responsible for nearly all skin cancer deaths. Melanoma rates in the US have been rising rapidly over the last 30 years, and although scientists have managed to identify key risk factors, melanoma's modus operandi has eluded the world of medical research.

A new Tel Aviv University study published in *Molecular Cell* sheds light on the precise trigger that causes melanoma cancer cells to transform from non-invasive cells to invasive killer agents, pinpointing the precise place in the process where "traveling" cancer turns lethal. The research was led by Dr. Carmit Levy of the Department of Human Genetics and Biochemistry at TAU's Sackler School of Medicine and conducted by a team of researchers from TAU, the Technion Institute of Technology, the Sheba Medical Center, the Institut Gustave Roussy and The Hebrew University of Jerusalem.

If melanoma is caught in time, it can be removed and the patient's life saved. But once melanoma invades the bloodstream, turning metastatic, an aggressive treatment must be applied. When and how the transformation into aggressive invasion took place was until now a mystery.

Understanding the skin

"To understand melanoma, I had to obtain a deep understanding about the structure and function of normal skin," said Dr. Levy, "Melanoma is a cancer that originates in the epidermis, and in its aggressive form it will invade the dermis, a lower layer, where it eventually invades the bloodstream or lymph vessels, causing metastasis in other organs of the body. But before invading the dermis, melanoma cells surprisingly extend upward, then switch directions to invade.

"It occurred to me that there had to be a trigger in the microenvironment of the skin that made the melanoma cells 'invasive,'" Dr. Levy continued. "Using the evolutionary logic of the tumor, why spend the energy going up when you can just use your energy to go down and become malignant?"

After collecting samples of normal skin cells and melanoma cells from patients at hospitals around Israel, the researchers mixed normal and cancerous cells and performed gene analysis expression to study the traveling cancer's behavior. They found that, completely independently of any mutation acquisition, the microenvironment alone drove melanoma metastasis.

"Normal skin cells are not supposed to 'travel,'" said Dr. Levy. "We found that when melanoma is situated at the top layer, a trigger sends it down to the dermis and then further down to invade blood vessels. If we could stop it at the top layer, block it from invading the bloodstream, we could stop the progression of the cancer."

A new way of saving lives

The researchers found that the direct contact of melanoma cells with the remote epidermal layer triggered an invasion via the activation of "Notch signaling," which turns on a set of genes that promotes changes in melanoma cells, rendering them invasive. According to the study, when a molecule expressed on a cell membrane -- a spike on the surface of a cell, called a ligand -- comes into contact with a melanoma cell, it triggers the transformation of melanoma into an invasive, lethal agent.

"When I saw the results, I jumped out of the room and shouted, 'We got it!'" Dr. Levy said. "Now that we know the triggers of melanoma transformation and the kind of signalling that leads to that transformation, we know what to block. The trick was to solve the mystery, and we did. There are many drugs in existence that can block the Notch signalling responsible for that transformation. Maybe, in the future, people will be able to rub some substance on their skin as a prevention measure."

Dr. Levy is continuing to explore the research with the end goal of providing medical professionals with another tool of analysis of different stages of melanoma. "Melanoma is a cancer with a very long gestation period," said Dr. Levy. "If you can provide a simple kit with precise answers, you can catch it at the beginning stage and hopefully save

lives."

Source:
American Friends of Tel Aviv University