

Researchers reveal how immune cells can be harnessed to target melanoma

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Researchers at the Babraham Institute and the University of Catanzaro "Magna Graecia", Italy, co-ordinating an international network of scientists and clinicians from Europe, the USA and Japan, have identified new mechanisms through which the immune system recognises and responds to tumours like melanomas. This discovery may offer therapeutic approaches for tackling metastatic melanoma, an aggressive form of skin cancer responsible for around 2,000 deaths in the UK each year.

These exciting new findings, published in the online edition of the [Journal of Clinical Investigation](#), reveal how a type of white blood cell - Natural Killer (NK) cells - tackles tumours, characterising for the first time the molecular interactions that lead to melanoma destruction. This has advanced understanding of melanoma recognition by the immune system and has the potential to open up new avenues of research into the prevention of metastasis by harnessing NK cells' natural immunity.

Natural Killer cells are found in the blood, the lymph glands and in tissues such as the liver, the lungs and the uterus, where they participate in immune defences against infection, cancer, in reproductive success and in transplantation. They play a key role in the immune response that targets tumour cells, while sparing healthy cells; mouse models revealed that NK cells prevent and control tumour growth although, in the case of melanomas, the molecular interactions behind this and how NK cells control metastatic progression had until now remained elusive.

The team of researchers, led by Francesco Colucci, Group Leader at the Babraham Institute and Ennio Carbone, of the University of Catanzaro "Magna Graecia", Italy, studied both human metastatic melanomas - aggressive forms of [skin cancer](#) that have spread to other sites - and spontaneous mouse melanomas.

NK cells sense signs of infection and recognise abnormal cells, including tumours and their metastases, via receptors on their cell membrane. One such family are natural cytotoxicity receptors (NCRs), which act like cancer-detection antennae seeking out molecules associated with tumours. Two receptors have been identified that are critical for NK cell-mediated killing of [melanoma cells](#). Using cell lines from 18 melanoma patients, the team found that melanoma cell lines produce proteins that bind to natural cytotoxicity receptors (NCRs) and a receptor that activates NK cells called DNAX accessory molecule-1 (DNAM-1). These cell lines were susceptible to being destroyed by NK cells both *in vitro* and after being transplanted into mice. Consistent with these data from human cell lines, mouse spontaneous melanomas and melanoma cell lines also produced proteins that bind to DNAM-1 and NCRs.

“Interfering with the ability of DNAM-1 and NCRs to interact with proteins on melanoma cells, by either genetic means or by antibody-blockade, reduced NK cell-mediated killing of human and mouse melanoma cells lines both *in vitro* and *in vivo*,” explained Dr Francesco Colucci. “Informed by these findings, we explored the potential of NK cells in cell therapy of melanoma in “humanized” mice, which is a standard method to understand how human cells work in the whole organism. The results strikingly showed that human NK cells were able to prevent death of the mice by killing the transplanted human melanoma cells.”

He added, “We are now setting up the next stage of the research programme. DNAM-1 and NCRs are critical parts of the machinery

governing NK cell-mediated killing of melanoma cells and indicate that NK [cells](#) could be harnessed to prevent melanoma metastasis. We aim to translate these findings into the clinic by proposing new NK cell-based immunotherapeutic strategies to treat melanoma patients and will also continue our research to understand the fundamental mechanisms of how, when and where the immune system detects early signs of cancer.”

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More information: J. Clin. Invest. doi:10.1172/JCI36022, NCRs and DNAM-1 mediate NK cell recognition and lysis of human and mouse [melanoma](#) cell lines in vitro and in vivo.

Source: Babraham Institute

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