

## Cholesterol-like molecules switch off the engine in cancer-targeting 'Natural Killer' cells

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A distinct engine configuration, controlled by a switch called Srebp, powers our Natural Killers against cancer



A visualization of the natural killer cell engine and how the protein Srebp, works as a switch. Credit: Dr. David Finlay, Trinity College Dublin.

Scientists have just discovered how the engine that powers cancer-killing cells functions. Crucially, their research also highlights how that engine is fuelled and that cholesterol-like molecules, called oxysterols, act as a



"cut-off" switch making it hard for our 'Natural Killer' cells to win the war against cancer.

The scientists, led by Ussher Assistant Professor in Immunometabolism at Trinity College Dublin, Dr David Finlay, have just published their findings in leading journal *Nature Immunology*. They report a previously unknown metabolic switch, which is essential for initiating the antitumour actions of Natural Killer cells.

Natural Killer (NK) cells are immune cells that play an important role in our defence against cancer, as they can directly kill <u>tumour cells</u>. Once activated, NK cells increase their uptake of cellular fuel, which is converted into energy by a biochemical engine. These engines and their fuel thus power the all-important tumour-killing machinery of the NK cells.

The new research shows that activated NK cells use a very different engine configuration to that observed in other <u>immune cells</u> and that the key factor that switches NK cells to this engine configuration is a protein called 'Srebp.' When the scientists used oxysterols to prevent this switch from occurring, the NK cells failed to kill tumour cells.

Dr David Finlay said: "The function of Srebp—the key factor that controls the energy production in Natural Killer cells and thus fuels their activity—is known to be blocked by cholesterol and cholesterol-like molecules, called oxysterols. Therefore, our findings reveal a previously unknown way by which the cancer-killing functions of Natural Killer cells can be disrupted."

As tumour cells can produce oxysterols and cholesterol levels tend to be higher in people with obesity, the scientists believe they may now have part of the explanation for why NK cells typically perform poorly in patients living with cancer and obesity.



"The next step is to investigate whether the functions of Natural Killer <u>cells</u> are indeed impaired in individuals with <u>high cholesterol level</u>, and whether cholesterol lowering interventions can restore NK cell function in these individuals," added Dr Finlay.

**More information:** Srebp-controlled glucose metabolism is essential for NK cell functional responses, *Nature Immunology* (2017). DOI: 10.1038/ni.3838

Provided by Trinity College Dublin

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