

## Cellular metabolism arms T cells to battle viruses and tumours

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(Medical Xpress)—New research demonstrates thatpathology associated with a range of autoimmune the cellular metabolism of certain immune cells is diseases including Multiple Sclerosis and closely linked to their function, which includes protecting against viral infections and the work reveals the potential for novel therapeutic development of tumours. strategies to disrupt CTL migration and cytotoxic

Results recently published in the Journal of Experimental Medicine reveal the relationship between <u>glucose metabolism</u> in Cytotoxic T lymphocytes (CTL) and their ability to acquire the tools necessary to migrate and kill virally infected cells or tumour cells. CTL are generated in response to particular cues, which promote the acquisition of a range of cytotoxic tools that are used to kill target cells and provide the ability to migrate to the locations in the body where they are required, i.e. sites of inflammation. While glucose has often been considered simply as a fuel source, this work reveals that the nature of glucose metabolism in CTL is closely linked to key CTL functions.

"It was previously thought that high levels of glucose metabolism simply served to provide CTL with energy and the raw materials to facilitate cell growth," explains Dr Finlay, "but it is now clear that in CTL glucose metabolism can dictate the function of these important immune cells".

Dr David Finlay of the School of Biochemistry and Immunology, Trinity College Dublin, working with Prof Doreen Cantrell's laboratory in the University of Dundee, has established that the activities of two proteins, mTORC1 and HIF1, are essential to maintain CTL glucose metabolism and normal CTL function. Disruption of mTORC1 or HIF1 dramatically reduces glucose utilisation in CTL while also disrupting the levels of key molecules that are required for normal migration and target cell killing. This work affords new insight into the relationship between cellular metabolism and cellular function in immune cells.

Inappropriate activation of CTL contributes to the

Rheumatoid Arthritis. Dr Finlay and Prof Cantrell's function for the treatment autoimmune conditions.

More information: PDK1 regulation of mTOR and hypoxia-inducible factor 1 integrate metabolism and migration of CD8+ T cells, doi: 10.1084/jem.20112607

Provided by Trinity College Dublin



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