ANTIVIRAL IMMUNITY

# LGP2 rigs CD8$^+$ T cells for survival

The cytosolic RNA helicases of the RIG-I-like receptor (RLR) family are pattern-recognition receptors that recognize viral RNA. The roles of two RLRs (namely, RIG-I and MDA5) in the induction of innate antiviral immunity have been well described, but the function of the third family member, LGP2 (encoded by *Dhx58*), is not fully known. Reporting in *Immunity*, Suthar *et al.* describe a cell-intrinsic role for LGP2 in promoting the survival and effector functions of CD8$^+$ T cells in response to RNA viruses.

To examine the antiviral immune function of LGP2, the authors generated *Dhx58*$^{-/-}$ mice, for the first time on a pure C57BL/6 background. *Dhx58*$^{-/-}$ dendritic cells and macrophages that were infected *in vitro* with West Nile virus (WNV) showed similar control of virus replication to infected wild-type cells, but the level of interferon-β (IFNβ) produced by the *Dhx58*$^{-/-}$ innate cells was lower. These *in vitro* results suggest that LGP2 has a non-essential but positive regulatory role in innate antiviral immune responses.

However, infection of *Dhx58*$^{-/-}$ mice with WNV resulted in increased mortality compared with controls. No differences in tissue viral load, innate immune responses or viral neuroinvasion were observed between *Dhx58*$^{-/-}$ and wild-type mice. However, higher viral loads were observed in the brains of *Dhx58*$^{-/-}$ mice at later time points during infection. Furthermore, infected *Dhx58*$^{-/-}$ mice had greatly reduced numbers of CD8$^+$ T cells in the brain compared with controls.

> “LGP2 is required for the survival of virus-specific CD8$^+$ T cells”

Given that CD8$^+$ T cells are known to have an important role in controlling WNV-induced pathology in the central nervous system, the authors next assessed the role of LGP2 in regulating CD8$^+$ T cells. They found that LGP2 is required for the survival of virus-specific CD8$^+$ T cells. Furthermore, the frequency and number of virus-specific CD8$^+$ T cells producing effector cytokines at later time points were reduced in infected *Dhx58*$^{-/-}$ mice compared with infected wild-type mice. Similar results were observed following infection with the RNA virus lymphocytic choriomeningitis virus.

But is the role of LGP2 in CD8$^+$ T cell survival and function cell intrinsic or extrinsic? T cell receptor- and IFNβ-mediated signalling in CD8$^+$ T cells was shown to induce LGP2 expression. Furthermore, following the transfer of equal numbers of *Dhx58*$^{-/-}$ and wild-type CD8$^+$ T cells to lymphocyte-deficient mice and subsequent infection, only virus-specific *Dhx58*$^{-/-}$ CD8$^+$ T cells showed defects in survival and effector function, indicating that LGP2 functions in a T cell-intrinsic manner. Finally, LGP2 was shown to regulate CD8$^+$ T cell survival by regulating the sensitivity of these cells to CD95 ligand-mediated cell death during virus infection through the control of CD95 expression.

So, LGP2 promotes antiviral immunity through the cell-intrinsic regulation of CD8$^+$ T cell survival and effector function.

*Olive Leavy*

**ORIGINAL RESEARCH PAPER** Suthar, M. S. *et al.* The RIG-I-like receptor LGP2 controls CD8$^+$ T cell survival and fitness. *Immunity* 26 Jul 2012 (doi:10.1016/j.immuni.2012.07.004)
**FURTHER READING** Desmet, C. J. & Ishii, K. J. Nucleic acid sensing at the interface between innate and adaptive immunity in vaccination. *Nature Rev. Immunol.* **12**, 479–491 (2012)

Macmillan Australia