Immune cells promote or prevent cytomegalovirus activity in mice depending on location

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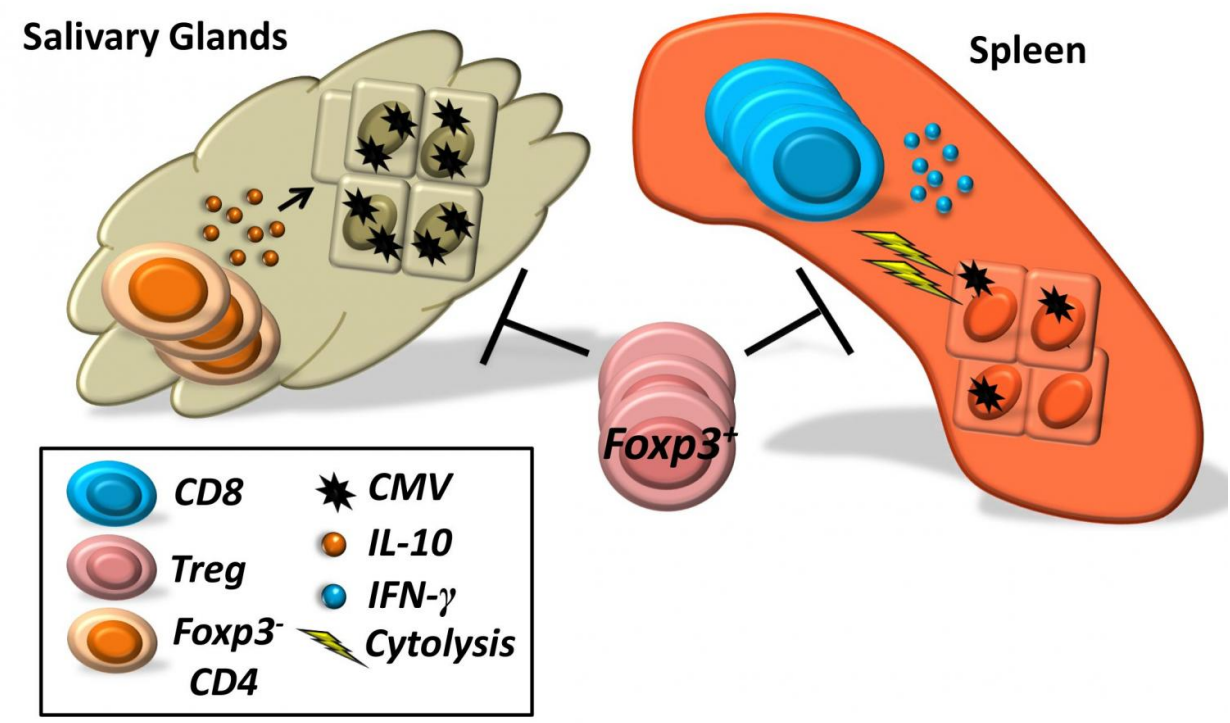

Treg have divergent control of MCMV infection depending upon the issue. In the spleen, Treg antagonize CD8+ effector function and promote viral persistence while in the salivary gland Treg prevent IL-10 production from Foxp3 - CD4+ T cells and limit viral reactivation and replication. Credit: Almana, et al. (2017)

Immune system cells called regulatory T cells appear to promote *cytomegalovirus* (*CMV*) latency in the spleen of mice, but suppress it in the salivary gland. Maha Almanan of the University of Cincinnati College of Medicine, Cincinnati Children's Hospital Research Foundation, and colleagues present this surprising finding in a new study in *PLOS Pathogens*.

CMV infects over half of adults by the time they reach the age of 40. Usually, it causes no signs or symptoms, but it can be dangerous for people with weakened immune systems and for babies who contract it before birth. In most people, *CMV* settles into a latent state; its genome exists in the cells of the infected person, but it does not replicate or cause harm unless it is reactivated.

Previous work has shown that immune system cells known as regulatory T cells are associated with reactivation of *CMV* in immune suppressed patients. Whether or not regulatory T cells were causal in this context was unclear. In the new study, the research team investigated this role in mice by infecting them with a mouse version of *CMV*.

Eight months after infection, *CMV* had established latent infection of the spleen, salivary gland, lung, and pancreas. The mice were of a recently developed strain that allowed the researchers to then trigger a decrease in levels of regulatory T cells and examine the effects.

The results suggest that regulatory T cells can either suppress or reactivate latent *CMV* depending on where in the body they are acting. In the spleen, depletion of regulatory T cells reduced viral load and enhanced the functionality of immune cells whose job is to eliminate viruses. But opposite effects occurred in the salivary gland, suggesting that regulatory T cells normally prevent *CMV* reactivation and replication in the salivary gland.

Future work could explore whether these findings hold true in humans and why regulatory T cells have opposing effects in different mouse tissues. Better understanding of the role of regulatory T cells could aid development of treatments that manipulate their activity. Such treatments may hold particular promise for preventing *CMV* reactivation in patients with suppressed immune systems (eg those with HIV or organ-transplants), and are already being investigated in such patients.

More information: Almanan M, Raynor J, Sholl A, Wang M, Chougnet C, Cardin RD, et al. (2017) Tissue-specific control of latent CMV reactivation by regulatory T cells. *PLoS Pathog* 13(8): e1006507. doi.org/10.1371/journal.ppat.1006507