Cytomegaloviruses deploy a novel stealth strategy to subvert immune surveillance

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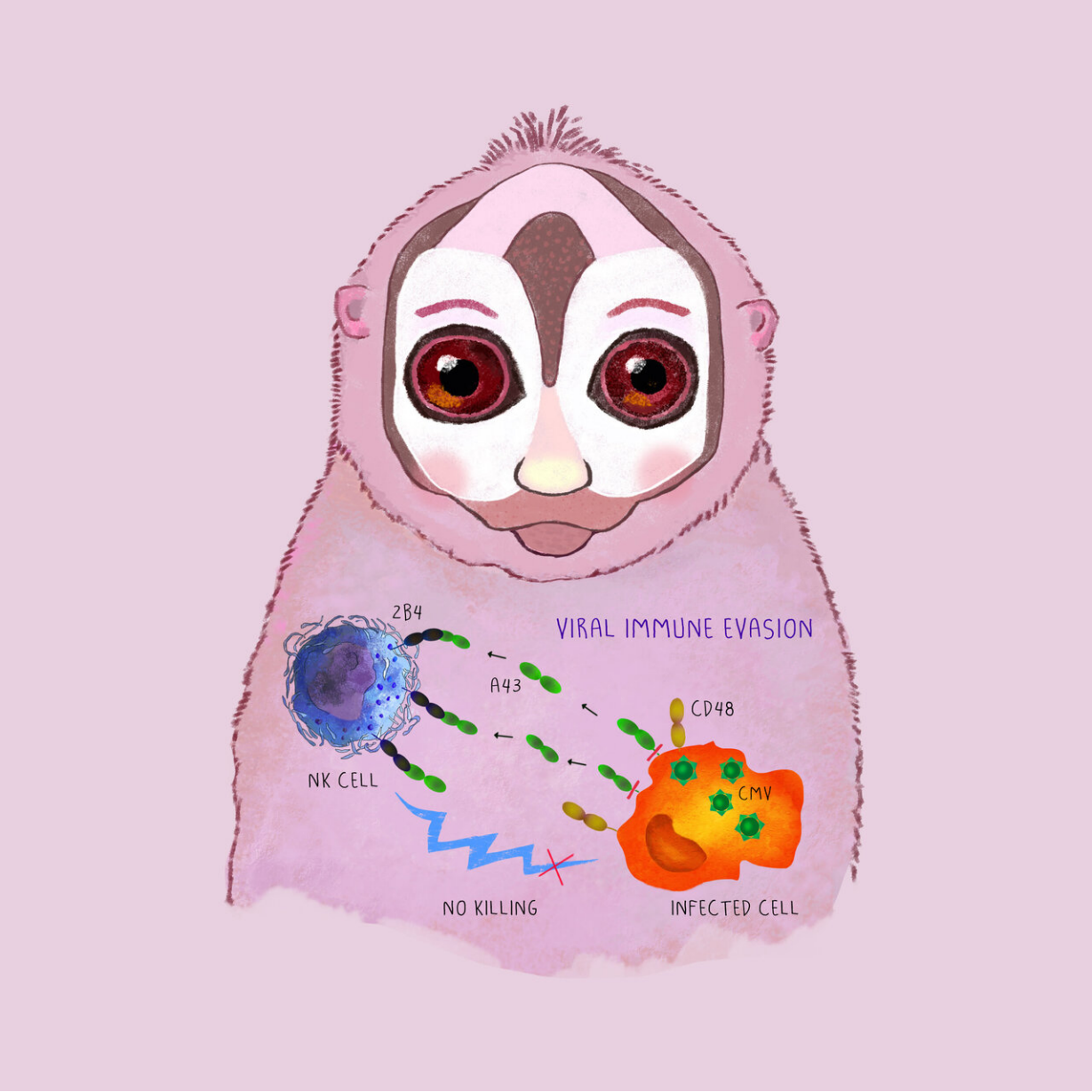

An ingenious viral immune evasion tactic used by the CMV protein A43. Credit: Maria Angulo

Owl monkey cytomegalovirus produces a decoy molecule A43 to evade detection and destruction by immune cells in their hosts, according to a study published April 4 in the open-access journal *PLOS Pathogens* by Ana Angulo of the University of Barcelona, and colleagues. As the authors note, the findings provide a novel example of an immune evasion strategy developed by viruses.

Throughout evolution, cytomegaloviruses (CMVs) have been capturing genes from their hosts, employing the derived proteins to dampen immune responses and successfully persist within their hosts. Certain CMVs encode homologs of CD48, a molecule found on the surface of most of the leukocytes of the body. CD48 binds to the 2B4 receptor on certain immune cells such as natural killer cells, which play a pivotal role in the rapid recognition and control of viral infections. But the properties and biological relevance of the viral CD48 homologs have not been explored. In the new study, Angulo and colleagues have investigated for the first time the immunomodulatory potential of one of these viral molecules: A43, a CD48 homolog encoded by owl monkey CMV.

The researchers show that A43 binds strongly to 2B4 and is capable of blocking its interaction with CD48. Moreover, the findings reveal how this viral protein interferes with the function of human natural killer cells. Taken together, these results not only underscore the importance of 2B4-mediated immune responses in controlling CMV infections, but also unveil CD48 as a new viral counteract mechanism for subverting immune surveillance. The authors propose that A43 may serve as a CD48 decoy receptor by binding and masking 2B4, thereby impeding effective immune control by cytotoxic lymphocytes during viral

infections. According to the authors, the research highlights the potential of using the inhibitory molecule A43 to develop novel therapeutic tools to manipulate aberrant immune responses, such as those linked to autoimmune diseases.

More information: Martínez-Vicente P, Farré D, Sánchez C, Alcamí A, Engel P, Angulo A (2019) Subversion of natural killer cell responses by a cytomegalovirus-encoded soluble CD48 decoy receptor. *PLoS Pathog* 15(4): e1007658. doi.org/10.1371/journal.ppat.1007658