Resistant mice provide clues about successful immune response to retroviruses

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Although our body's defense mechanisms are usually capable of detecting and destroying many types of pathogens, some viruses are able to evade the immune system and make us sick. In particular, "retroviruses," such as human immunodeficiency virus (HIV), are notorious for eluding host immune defenses and causing disease. Now, a new study published by Cell Press online on June 30th in the journal *Immunity* identifies a key virus-sensing mechanism that is necessary for a successful immune response against infection with this particularly deadly type of virus. The research may help to guide the future design of more effective antiretroviral vaccines.

"The demand for producing highly efficient vaccines against HIV is great and the approaches currently available for making vaccines may not be relevant to retroviruses, as none of the trials conducted to date have been successful," explains the senior study author, Dr. Tatyana V. Golovkina, from the University of Chicago. "It is critical that we achieve a basic understanding of how the immune system detects and responds to retroviruses in order to apply this knowledge to the production of anti-retrovirus vaccines."

To examine exactly what steps in the viral invasion and replication (copying) process are necessary and sufficient to trigger a successful virus-specific immune response in the host, Dr. Golovkina and colleagues used special strains of mice that are resistant to retroviruses. The mice used in the study become infected when exposed to retrovirus, but mount a powerful antivirus immune response that eliminates or controls the virus, making them a superior choice for studies examining successful antiretroviral immunity. The researchers discovered that of all the steps in the viral replication process, the ability to enter the host cell was sufficient to induce successful immune responses. In fact, complete viral replication was dispensable for triggering virus detection. A protein called endosomal Toll-like receptor 7 (TLR7), known for a role in the detection of viral single-chain RNA, was identified as the critical retrovirus-sensing receptor.

Taken together, the findings suggest that an efficient and sustained immune response to retroviruses is induced by sensing of the early stages of retroviral infection. "Although the precise mechanism of retroviral exposure to TLR7 is yet to be identified, our results provide definitive evidence that TLR7-dependent recognition is required for an efficient immune response against retroviruses," concludes Dr. Golovkina. "An understanding of the genetic mechanisms underlying retroviral resistance will help to drive design anti-retroviral vaccines that utilize inactivated viruses combined with targeting the immune pathways employed successfully in resistant organisms."

More information: Kane et al.: "Innate Immune Sensing of Retroviral Infection via Toll-like Receptor 7 Occurs upon Viral Entry."

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