Dendritic cells efficiently induce protective antiviral immunity

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Cytotoxic T lymphocytes (CTL) are essential for effective immunity to various viral infections. Because of the high speed of viral replication, control of viral infections imposes demanding functional and qualitative requirements on protective T-cell responses. Dendritic cells (DC) have been shown to efficiently acquire, transport, and present antigens to naive CTL in vitro and in vivo. In this study, we assessed the potential of DC, either pulsed with the lymphocytic choriomeningitis virus (LCMV)-specific peptide GP33-41 or constitutively expressing the respective epitope, to induce LCMV-specific antiviral immunity in vivo. Comparing different application routes, we found that only 100 to 1,000 DC had to reach the spleen to achieve protective levels of CTL activation. The DC-induced antiviral immune response developed rapidly and was long lasting. Already at day 2 after a single intravenous immunization with high doses of DC (1 x 10^5 to 5 x 10^5), mice were fully protected against LCMV challenge infection, and direct ex vivo cytotoxicity was detectable at day 4 after DC immunization. At day 60, mice were still protected against LCMV challenge infection. Importantly, priming with DC also conferred protection against infections in which the homing of CTL into peripheral organs is essential: DC-immunized mice rapidly cleared an infection with recombinant vaccinia virus-LCMV from the ovaries and eliminated LCMV from the brain, thereby avoiding lethal choriomeningitis. A comparison of DC constitutively expressing the GP33-41 epitope with exogenously peptide-pulsed DC showed that in vivo CTL priming with peptide-loaded DC is not limited by turnover of peptide-major histocompatibility complex class I complexes. We conclude that the priming of antiviral CTL responses with DC is highly efficient, rapid, and long lasting. Therefore, the use of DC should be considered as an efficient means of immunization for antiviral vaccination strategies.