

Measurement of long-term virus-specific CD8⁺ T cell memory in mice challenged with unrelated pathogens

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The consequence for the long-term maintenance of virus-specific CD8⁺ T cell memory have been analyzed experimentally for sequential respiratory infections with readily eliminated (influenza) and persistent (□HV68) pathogens. Sampling a broad range of tissue sites established that the numbers of CD8⁺ T cells specific for the prominent influenza D^bNP₃₆₆ epitope were reduced by about half in mice that had been challenged 100 days previously with □HV68, though the prior presence of a large CD8⁺D^bNP₃₆₆⁺ population caused no selective defect in the □HV68-specific CD8⁺K^bp79⁺ response. Conversely, mice that had been primed and boosted to generate substantial □HV68-specific CD8⁺D^bp56⁺ populations did not show any decrease in prevalence for this set of CD8⁺ memory CTL at 200 days after respiratory exposure to an influenza A virus. However, in both experiments, the total magnitude of the CD8⁺ T cell pool was significantly diminished in those that had been infected with □HV68 and the influenza A viruses. The broader implications of these findings, especially under conditions of repeated exposure to unrelated pathogens, are explored using a mathematical model which emphasizes that the immune effector and memory “phenome” is a function of the overall infectious experience of the individual.