Abstract


Vitamin D receptor signals regulate effector and memory CD8 T cell responses to infections in mice.

Yuzefpolskiy Y, Baumann FM, Penny LA, Studzinski GP, Kalia V, Sarkar S.

Center for Molecular Immunology and Infectious Diseases, Department of Veterinary and Biomedical Sciences, and The Huck Institutes of Life Sciences, The Pennsylvania State University, University Park, PA; Department of Pathology and Laboratory Medicine, Rutgers New Jersey Medical School, Newark, NJ; Center for Molecular Immunology and Infectious Diseases, Department of Veterinary and Biomedical Sciences, and The Huck Institutes of Life Sciences, The Pennsylvania State University, University Park, PA.

BACKGROUND: Vitamin D insufficiency is associated with broad-ranging human disease sequelae such as bone disease, cancer, cardiovascular disease, allergy, autoimmune disorders, diabetes, and infectious diseases. Disease risk and severity of a large proportion of the nonskeletal disorders heavily involve the cytotoxic cluster of differentiation (CD) 8 T lymphocyte (CTL) arm of cellular adaptive immunity. Considering the importance of vitamin D in CTL-dependent diseases, there is a critical need for systematic in-depth explorations into the role of vitamin D deficiency in generation and maintenance of CTL immunity during infections and vaccinations.

OBJECTIVE: With the use of wild-type (WT) vitamin D-sufficient mice and the vitamin D receptor knockout (Vdr(-/-)) mouse model of in vivo deficiency of vitamin D signaling, we systematically analyzed the impact of vitamin D deficiency on antigen-specific effector and memory CD8 T cell responses to acute viral and bacterial infections.

METHODS: WT and Vdr(-/-) mice were infected with lymphocytic choriomeningitis virus, a natural mouse pathogen, and antigen-specific CTL responses were analyzed during priming, expansion, contraction, and memory phases. Magnitude, breadth, cytokine production, and localization of antiviral effector and memory CTLs to lymphoid and nonlymphoid tissues were specifically assessed.

RESULTS: The absence of vitamin D signals led to 1) aberrant CD8 T cell effector differentiation (~2-fold lower granzyme B and reduced B cell lymphoma 2; P ≤ 0.05) and enhanced contraction (~15% increase; P ≤ 0.05) in antigen-specific CTLs; 2) a significantly restricted (P ≤ 0.05) breadth of the antigen-specific CD8 T cell effector and memory repertoire; and 3) preferential localization of effector (~2.5-fold increase; P ≤ 0.01) and memory (~5-fold increase; P ≤ 0.001) CD8 T cells to the lymph nodes compared to nonlymphoid tissues.

CONCLUSION: Our data show a previously unrecognized impact of vitamin D deficiency on the quantity, quality, breadth, and location of CD8 T cell immunity to acute viral and bacterial infections.

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