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A quantitative understanding of the balance between pathologic and protective T-cell responses during viral infection

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T-cell responses have the potential for efficient protection against a wide range of virus infections. However, T-cell responses also have the potential for mediating severe pathological responses. Understanding this balance is key to the development of vaccines that maximize protection while minimizing the potential for immune-mediated pathology. As pathology arises as a consequence of the complex interplay between the dynamics of rapidly changing populations of pathogen, immune cells and the cytokines that they secrete, understanding pathology compels the joint use of animal models and mathematical modeling. We have previously described the development of quantitative mathematical models to explain the pathology observed during LCMV infection in mice, due to narrow vaccination against a single virus epitope that is most severe when intermediate numbers of naive antigen-specific CD8 T-cells are present prior to infection. We have used these models to make predictions regarding how key attributes of the T-cell response, such as cell phenotype and polyclonality affect this balance. We found, as predicted, increased pathology during LCMV infection due to an intermediate precursor frequency of memory CD8 T-cells was independent of the breadth of the memory T-cell response, but was dependent on T-cell production of TNF. In particular, abrogation of TNF signaling resulted in decreased pathology but no change in viral clearance, suggesting that TNF-blockade may be useful for minimizing pathology while maintaining protection following virus infection.

Biography

Joseph N Blattman has completed his PhD in Immunology and Molecular Pathogenesis from Emory University and Postdoctoral studies at the University of Washington and Fred Hutchinson Cancer Research Center. He is an Assistant Professor of Infectious Diseases and Vaccinology in the School of Life Sciences at Arizona State University. He actively teaches immunology courses and has more than 38 peer-reviewed publications in highly cited journals.

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