Chronic immune reactivity against persisting microbial antigen in the vasculature exacerbates atherosclerotic lesion formation

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OBJECTIVE: The purpose of this study was to examine the relative contribution of different immunopathological mechanisms during murine cytomegalovirus (MCMV)-mediated acceleration of atheroma formation in apolipoprotein E-deficient (apoE-/-) mice. METHODS AND RESULTS: To distinguish between the effects of systemic activation and cognate immune reactivity against a pathogen-derived persisting antigen in the vasculature, we used hypercholesterolemic transgenic mice constitutively expressing the beta-galactosidase (beta-gal) transgene in the cardiovascular system (apoE-/- x SM-LacZ). After infection with beta-gal-recombinant MCMV-LacZ, apoE-/-, and apoE-/- x SM-LacZ mice mounted comparable cellular immune responses against the virus. Beta-gal-specific CD(+) T cells expanded rapidly and remained detectable for at least 100 days in both mouse strains. However, compared with apoE-/- mice, apoE-/- x SM-LacZ mice developed drastically accelerated atherosclerosis. Moreover, atherosclerotic lesions in MCMV-LacZ-infected apoE-/- x SM-LacZ but not apoE-/- mice were associated with pronounced inflammatory infiltrates. CONCLUSIONS: Taken together, our data indicate that chronic immune reactivity against pathogen-derived antigens persisting in the vasculature significantly exacerbates atherogenesis.