Latent cytomegalovirus infection causes substantial alterations in cardiac cell composition and confers poorer left ventricular function after experimental myocardial infarction in a murine model

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Introduction: In recent decades, physiological and pathological processes in the heart have been increasingly looked upon through the lens of the immune system, giving birth to the new field of cardioimmunology[1]. Several lines of research have indicated that latent cytomegalovirus infection (CMV) can have major impact on the functioning of the immune system of mammals. Human data have shown that cytomegalovirus serostatus was a single largest non-genetic determinant of an immune phenotype of an individual[2]. Importantly, strong epidemiological signal exists associating CMV seropositivity with increased incidence of cardiovascular mortality[3], yet the causal relationship has hitherto not been established.

Methods: To investigate the long-term effects of latent CMV infection on cardiac tissue, we used murine cytomegalovirus (MCMV) as a model. C57BL/6J mice were infected intravenously with MCMV or left uninfected. Immune cell composition within the heart was determined by flow cytometry and bulk RNA sequencing of cardiac tissue was performed during acute and latent viral infection. Myocardial infarction was induced using the standard surgical LAD ligation procedure. Left ventricular function was assessed with echocardiography.

Results: During acute infection there was a large increase in the number of T cells in the hearts of infected mice which remained substantially elevated during the latent infection. Majority of them were MCMV specific and, importantly, some of them expressed the markers of tissue residency. Bulk RNA sequencing of cardiac tissue from infected animals revealed 500 deferentially expressed genes with considerable increase in transcripts associated with interferon signaling and T cell activation. Furthermore, transcripts associated with oxidative phosphorylation and ATP synthesis were extensively down regulated in latently infected mice. Crucially, mice latently infected with CMV showed poorer left ventricular function after experimental myocardial infarction.

Conclusion: Latent viral infection with murine cytomegalovirus causes long term alterations in the composition and phenotype of the immune cells within the heart, which is associated with worst cardiac function after experimental myocardial infarction.

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LITERATURE

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