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Hydroxychloroquine cures autoimmune myocarditis by inhibiting innate immune via the CXCL16-CXCR6 axis between macrophages and T cells

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Background: Myocarditis is a lift-threatening inflammatory disease of the heart and is lack of effective treatment measures. Hydroxychloroquine (HCQ), a classic antimalarial drug, has been widely used in the treatment of rheumatic diseases. This study investigated whether HCQ can treat chronic autoimmune myocarditis..

Methods and Results: Murine autoimmune myocarditis was induced, and therapeutic effects of oral HCQ on acute and chronic myocarditis were evaluated using echocardiography, cardiac catheterization, and analysis of inflammatory scores in cardiac tissue. Results showed that HCQ treatment significantly improved cardiac function, inhibited ventricle enlargement and reduced cardiac inflammation. Single-cell transcriptomic analysis in the heart showed that HCQ treatment significantly reduced infiltration of macrophage, neutrophiles and T-cells, inhibited inflammatory pathway, especially the secretion of CXCL16 from macrophages, thereby reducing the chemotaxis of T cells, especially NKT cells and Th17 cells. Finally, both in vitro and in vivo experiments confirm the inhibitory effect of HCQ on CXCL16-CXCR6 axis between macrophages and T cells. Additionally, treatment with anti-CXCL16 antibody can also improve cardiac function and attenuate cardiac fibrosis in myocarditis.

Conclusion: HCQ treatments clinically cure mice with autoimmune myocarditis through inhibiting innate immune and infiltration of macrophages majorly via CXCL16-CXCR6 axis.

Keywords: Hydroxychloroquine, Autoimmune myocarditis, monocyte/Macrophage and T cells, CXCL16

Biography

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