一般口演

[O2-6]Picornavirus

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14:35 〜 14:50

[O2-6-4]血小板はウイルス性心筋炎の動物モデルでは増悪因子として働く

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[Objectives] Myocarditis is an inflammatory disease of the heart and mainly caused by infections with a variety of viruses, including SARS-CoV-2. Although the precise pathomechanism of viral myocarditis is unclear, viral replication and immune responses in the heart have been proposed to contribute to cardiac damage. We aimed to determine the role of platelets in myocarditis, since platelets can modulate immune responses and bind various viruses. We used a murine model for myocarditis induced by Theiler' s murine encephalomyelitis virus (TMEV), which belongs to the family *Picornaviridae*. TMEV inoculation in mice induces myocarditis similar to human myocarditis, where viral replication and anti-viral immune responses cause inflammation in the heart during the acute stage [days 4 and 7 post-infection (p.i.)], leading to cardiac fibrosis during the chronic stage (1–2 months p.i.). [Methods] We infected mice with TMEV and harvested the heart, whole blood, as well as platelets, separately during the acute and chronic stages. For platelet depletion, we injected mice with the platelet-specific anti-GPIbα antibody (4 μ g/g bodyweight). [Results] Although we did not detect the live virus or viral genome in platelets at any time, we detected them in the heart during the acute, but not chronic, stage. In transcriptome analyses, platelet-related genes were among the top upregulated genes in whole blood samples during the chronic stage. We also found up- and down-regulation of distinct sets of genes in separated platelet samples at each time point. Then, we conducted a mechanistic experiment by injecting TMEV-infected mice with the platelet-depletion antibody on days 0 and 5 p.i. (" early" group) or on days 18 and 22 p.i. (" late" group). During the chronic stage, we harvested the samples from the mice. We found that all groups of mice developed myocarditis composed of inflammation and fibrosis by picrosirius red staining; the late group had substantial suppression of the cardiac pathology. Immunologically, the late group had significantly lower anti-TMEV whole IgG and IgG1 titers. On the other hand, we found that all groups of mice had similar levels of TMEV-specific lymphoproliferative responses, and productions of interleukin (IL)-4, IL-10, IL-17, and interferon-γ. [Discussion] This study suggested that platelets could play a detrimental role in myocarditis by modulation of anti-viral humoral immune responses.