

7. SUMMARY

The role of CD8⁺ T lymphocytes in the murine model of Coxsackievirus B3 induced myocarditis

Enteroviruses, from the family of the Picornaviruses, are known to induce acute as well as chronic myocarditis in humans. From investigations in the murine model of the CVB3-myocarditis which mimic human myocarditis it can be concluded that, in addition to virus-specific factors, the host's immune response influence the outcome and the course of the enteroviral heart disease.

In order to gain further insight into the role of the cellular immunity in murine CVB3-myocarditis, we have compared the course of the disease in immunocompetent C57BL/6J mice with perforin knock out and with β_2 microglobulin knock out mice. The immunocompetent C57BL/6J mice as well as the immunodeficient Perforin knock out mice revealed a nearly identical course of the disease. Both mouse strains developed a mild acute myocarditis with virus clearance during the acute stage of infection. In contrast, the CVB3 infection of the β_2 microglobulin knock out mice which are deficient in CD8⁺ T lymphocytes and CD4⁺NK1.1⁺ cells was characterized by a severe inflammatory response with massive myocardial damage. These mice were not able to eliminate the virus and thus developed a chronic myocarditis consistently associated with virus persistence.

From these results it can be concluded, that perforin-mediated cytotoxicity is neither required for virus resolution from the heart nor responsible for myocardial damage during the course of the disease. The analysis of the different immune deficiencies of the β_2 microglobulin knock out mice indicates, that expression of β_2 microglobulin is important for the protection against the development of chronic myocarditis. There is firm evidence that in addition to defective antiviral effector mechanisms induced by CD8⁺ T lymphocytes, e. g. via expression of interferon- γ , an ineffective humoral immune response contributes to the failure of these mice to reduce initial viral load in the organism during acute infection, thus resulting in the development of chronic myocarditis.