Role of 14-3-3ζ in the Activation-Induced Cell Death

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Introduction: Immune cell dysfunction is a critical step in the pathogenesis of autoimmune diseases. Activation-induced cell death (AICD) occurs in various immune cells, especially T cells, following antigen receptor ligation. AICD plays a significant role in maintaining peripheral immune tolerance. We showed that 14-3-3ζ is an autoantigen in human aortitis.

Methods: To investigate the immunological functions and role in autoimmune conditions, we generated 14-3-3ζ knockout Lewis rats. Under two distinct experimental models, 14-3-3ζ knockout rats showed their crucial role in alleviating inflammatory arthritis (IA). To elucidate the mechanisms underlying 14-3-3ζ anti-inflammatory action, we studied its role in the AICD of immune cells. We investigated the CD3/CD28 activation of primary splenocytes isolated from wild-type and 14-3-3ζ knockout rats.

Results: Our data showed that the viability of primary splenocytes upon T cell receptor activation is reduced in the presence of 14-3-3ζ. We extended these results to explore whether 14-3-3ζ modulates AICD in macrophages, employing various inducers such as TNF-a, LPS, and IFN-g. Preliminary results suggest that the AICD in macrophages operates independently of 14-3-3ζ.

Conclusion: This study is innovative in demonstrating that 14-3-3ζ is implicated in the AICD of T cells but not in macrophages, signifying cell-type-specific effects. Ongoing research is directed at understanding how AICD influences the pathogenesis of inflammatory arthritis and the potential implications of 14-3-3ζ -regulated cell death in its anti-inflammatory role.

