A Study on cellular requirements for apoptotic cell death of activated T cells in EBV infection

1994 Fiscal Year Final Research Report Summary

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Research Project

Project/Area Number

05454284

Research Category

Grant-in-Aid for General Scientific Research (B)

Allocation Type

Single-year Grants

Research Field

Pediatrics

Research Institution

Kanazawa University

Principal Investigator

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Keywords

Apoptosis / EBV / Infectious mononucleosis / Activated T cells / IMN3.1 / Fas antigen / Bcl-2 / p53

Research Abstract

We employed EBV-induced infectious mononucleosis (IM) as a model of activated T cell death to elucidate cellular requirements for induction of T cell death by activation with viral infection. Obtained results are as follows :
1)Both activated T cells in acute IM patients and memory T cells in normal persons express CD45RO and Fas antigen, which can mediate apoptosis. Unlike memory T cells, activated T cells in IM easily undergo apoptotic cell death after on a simple incubation in vitro. By immunizing mice with IM cells, we obtained a novel mouse monoclonal antibody, termed IMN3.1, which was marked to react with apoptosis-prone T cells. Molecular cloning of IMN3.1-identified antigen is in progress.
2)Seemingly supporting their susceptibility to apoptosis, activated T cells in IM lacked expression of Bcl-2, which have a preventive function against apoptotic cell death. Low or absent expression of Bcl-2 was observed on granulocytes and monocytes, both of which have shorter life-spans. The

important finding was that anti-Fas antibody could accelerated apoptotic cell death in granulocytes and monocytes. These observations suggest that the Fas antigen/ligand system may play a key role in resolution of inflammatory and immune responses.
3)The mutation of the p53 oncogene is thought to lead to oncogenosis in human malignancies. Expression of p53 was not found in activated T cells in IM patients, although they were sucseptible to apoptosis. Ionizing irradiation could induce p53 expression on the whole population of peripheral blood lymphocytes, concomitant with marked apoptosis. However, we found a marked difference of lymphocyte subpopulations regarding p53 induction. Induction of p53 in CD4^+ T,CD8^+ T and B cells after irradiation was prominent. In contrast, neither TCR-gamma/delta^+ T cells nor NK cells showed identifiable levels of p53. The results suggest that radiation-induced lymphocytic apoptosis may be mediated by p53-dependent or-independent mechanisms.

Research Products (14 results)

All | Other

All | Publications (14 results)

[Publications] Uehara,T.et al.: "A novel T-cell activation antigen identified by monoclonal IMN3.1 antibody and expressed preferentially on human T cells susceptible to apoptotic cell death." J.Immunol.150. 3243-3253 (1993)

[Publications] Tamaru,Y.et al.: "Absence of bcl-2 expression by activated CD45RO^+T lymphocytes in acute infectious mononucleosis supporting their susceptibility to programmed cell death" Blood. 82. 521-527 (1993)

[Publications] Hasui,M.et al.: "Mature helper T cell requirement for immunoglobulin production by neonatal naive B cells injected intraperitoneally into severe combined immunodeficient(SCID)mice" Clin.Exp.Immunol.95. 357-361 (1994)

[Publications] Tsuji,T.et al.: "Efficient induction of immunoglobulin production in neonatal naive B cells by memory CD4^+T cell subset expressing homing receptor L-selectin" J.Immunol.152. 4417-4424 (1994)

[Publications] Iwai,K.et al.: "Diffrential expression of bcl-2 and suscebtibility to anti-Fas-mediated cell death in peripheral blood lymphocytes,monocytes and neutrophils" Blood. 84. 1201-1208 (1994)

[Publications] Seki,H.et al.: "Ionizing radiation induces apoptotic cell death in human TcR-γ/δ^+ T and NK cells without detectable p53 protein." Eur.J.Immunol.24. 2914-2917 (1994)

[Publications] 宮脇利男(共著): "Annual Review 血液1993" 中外医学社, 241 (1993)

[Publications] 宮脇利男(共著): "周産期の感染と免疫" 南江堂, 194 (1994)

[Publications] Uehara, T.et al.: "A novel T-cell activation antigen identified by monoclonal IMN3.1 antibody and expressed preferentially on human T cells susceptible to apoptotic cell death." J.Immunol.Vol.150. 3243-3253 (1993)

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