

show that in patients with ATLL, a high frequency of CD4⁺FoxP3⁺Tax⁻ cells is associated with a significant reduction in the rate of lysis of autologous HTLV-1-expressing cells, and with the capacity to suppress T-cell proliferation.

Acknowledgements

We thank Dr. Tao Dong for the gift of the anti-TCRVβ monoclonal antibodies.

References

- Uchiyama T, Yodoi J, Sagawa K, Takatsuki K, Uchino H. Adult T-cell leukemia: clinical and hematologic features of 16 cases. *Blood* 1977;50:481-92.
- Miyoshi I, Kubonishi I, Yoshimoto S, Akagi T, Ohtsuki Y, Shiraishi Y, Nagata K, Hinuma Y. Type C virus particles in a cord T-cell line derived by co-cultivating normal human cord leukocytes and human leukaemic T cells. *Nature* 1981;294:770-1.
- Kalyanaraman VS, Sarngadharan MG, Nakao Y, Ito Y, Aoki T, Gallo RC. Natural antibodies to the structural core protein (p24) of the human T-cell leukemia (lymphoma) retrovirus found in sera of leukemia patients in Japan. *Proc Natl Acad Sci U S A* 1982;79:1653-7.
- Kawano F, Yamaguchi K, Nishimura H, Tsuda H, Takatsuki K. Variation in the clinical courses of adult T-cell leukemia. *Cancer* 1985;55: 851-6.
- Shimoyama M. Diagnostic criteria and classification of clinical subtypes of adult T-cell leukaemia-lymphoma. A report from the Lymphoma Study Group (1984-87). *Br J Haematol* 1991;79:428-37.
- Akagi T, Ono H, Shimotohno K. Characterization of T cells immortalized by Tax1 of human T-cell leukemia virus type 1. *Blood* 1995;86: 4243-9.
- Matsuoka M, Jeang KT. Human T-cell leukaemia virus type 1 (HTLV-1) infectivity and cellular transformation. *Nat Rev Cancer* 2007;7:270-80.
- Roncador G, Garcia JF, Maestre L, Lucas E, Menarguez J, Ohshima K, Nakamura S, Banham AH, Piris MA. FOXP3, a selective marker for a subset of adult T-cell leukaemia/lymphoma. *Leukemia* 2005;19: 2247-53.
- Chen S, Ishii N, Ine S, Ikeda S, Fujimura T, Ndhlovu LC, Soroosh P, Tada K, Harigae H, Kameoka J, Kasai N, Sasaki T, et al. Regulatory T cell-like activity of Foxp3⁺ adult T cell leukemia cells. *Int Immunopharmacol* 2006;18:269-77.
- Kohno T, Yamada Y, Akamatsu N, Kamihira S, Imaizumi Y, Tomonaga M, Matsuyama T. Possible origin of adult T-cell leukemia/lymphoma cells from human T lymphotropic virus type-1-infected regulatory T cells. *Cancer Sci* 2005;96:527-33.
- Bach JF. Regulatory T cells under scrutiny. *Nat Rev Immunol* 2003;3: 189-98.
- Fontenot JD, Rudensky AY. A well adapted regulatory contrivance: regulatory T cell development and the forkhead family transcription factor Foxp3. *Nat Immunol* 2005;6:331-7.
- Cross SL, Feinberg MB, Wolf JB, Holbrook NJ, Wong-Staal F, Leonard WJ. Regulation of the human interleukin-2 receptor alpha chain promoter: activation of a nonfunctional promoter by the transactivator gene of HTLV-I. *Cell* 1987;49:47-56.
- Inoue J, Seiki M, Taniguchi T, Tsuru S, Yoshida M. Induction of interleukin 2 receptor gene expression by p40x encoded by human T-cell leukemia virus type 1. *Embo J* 1986;5:2883-8.
- Ziegler SF. FOXP3: of mice and men. *Annu Rev Immunol* 2006;24: 209-26.
- Toulza F, Heaps A, Tanaka Y, Taylor GP, Bangham CR. High frequency of CD4⁺FoxP3⁺ cells in HTLV-1 infection: inverse correlation with HTLV-1-specific CTL response. *Blood* 2008;111:5047-53.
- Yano H, Ishida T, Inagaki A, Ishii T, Kusumoto S, Komatsu H, Iida S, Utsunomiya A, Ueda R. Regulatory T-cell function of adult T-cell leukemia/lymphoma cells. *Int J Cancer* 2007;120:2052-7.
- Lee B, Tanaka Y, Tozawa H. Monoclonal antibody defining tax protein of human T-cell leukemia virus type-I. *Tohoku J Exp Med* 1989; 157:1-11.
- Asquith B, Mosley AJ, Barfield A, Marshall SE, Heaps A, Goon P, Hanon E, Tanaka Y, Taylor GP, Bangham CR. A functional CD8⁺ cell assay reveals individual variation in CD8⁺ cell antiviral efficacy and explains differences in human T-lymphotropic virus type 1 proviral load. *J Gen Virol* 2005;86:1515-23.
- Kannagi M, Harashima N, Kurihara K, Ohashi T, Utsunomiya A, Tanosaki R, Masuda M, Tomonaga M, Okamura J. Tumor immunity against adult T-cell leukemia. *Cancer Sci* 2005;96:249-55.
- Kannagi M, Sugamura K, Kinoshita K, Uchino H, Hinuma Y. Specific cytotoxicity of fresh tumor cells by an autologous killer T cell line derived from an adult T cell leukemia/lymphoma patient. *J Immunol* 1984;133:1037-41.
- Arnulf B, Thorel M, Poirot Y, Tamouza R, Boulanger E, Jaccard A, Oksenhendler E, Hermine O, Pique C. Loss of the ex vivo but not the reinducible CD8⁺ T-cell response to Tax in human T-cell leukemia virus type 1-infected patients with adult T-cell leukemia/lymphoma. *Leukemia* 2004;18:126-32.
- Harashima N, Kurihara K, Utsunomiya A, Tanosaki R, Hanabuchi S, Masuda M, Ohashi T, Fukui F, Hasegawa A, Masuda T, Takaue Y, Okamura J, et al. Graft-versus-Tax response in adult T-cell leukemia patients after hematopoietic stem cell transplantation. *Cancer Res* 2004;64:391-9.

