

# IMMUNOSPOT<sup>®</sup>

## Our Publications Establishing ImmunoSpot<sup>®</sup> as the Validated ELISPOT Technology for Direct Ex Vivo T Cell Monitoring at Single Cell Resolution.

Cellular Technology Ltd.'s founder, Dr. Paul V. Lehmann, together with a network of closely collaborating scholars and scientists pride themselves in having elevated ELISPOT to an exact science in a series of peer reviewed publications.

### ***Single Cell Resolution/Exact Frequency Measurements of Antigen-Specific T cells Ex Vivo.***

- ▶ Helms, T., B. O. Boehm, R. J. Assad, R. T. Trezza, P. V. Lehmann, and M. Tary-Lehmann. 2000. Direct visualization of cytokine-producing, recall antigen-specific CD4 memory T cells in healthy individuals and HIV patients. *J. Immunol.* 164: 3723-3732.
- ▶ Karulin, A. Y., M. D. Hesse, M. Tary-Lehmann, and P. V. Lehmann. 2000. Single-cytokine-producing CD4 memory cells prevail in vivo, in type 1/type 2 immunity. *J. Immunol.* 164: 1862-1872.
- ▶ Hesse, M. D., A. Y. Karulin, B. O. Boehm, P. V. Lehmann, and M. Tary-Lehmann 2001. A T cell clone's avidity is a function of its activation state. *J. Immunol.* 167: 1353-1361.
- ▶ Targoni, O. S., J. Baus, H. H. Hofstetter, M. D. Hesse, A. Y. Karulin, B. O. Boehm, T. Forsthuber, and P. V. Lehmann. 2001. Frequencies of neuroantigen-specific T cells in the CNS versus the immune periphery during the course of EAE. *J. Immunol.* 166: 4757-4764.

### ***Measuring Type 1/Type 2 Immunity***

- ▶ Helms, T., B. O. Boehm, R. J. Assad, R. T. Trezza, P. V. Lehmann, and M. Tary-Lehmann. 2000. Direct visualization of cytokine-producing, recall antigen-specific CD4 memory T cells in healthy individuals and HIV patients. *J. Immunol.* 164: 3723-3732.
- ▶ Forsthuber, T., H. C. Yip, and P. V. Lehmann. 1996. Induction of TH1 and TH2 immunity in neonatal mice. *Science.* 271: 1728-1730.
- ▶ Chu, R. S., O. S. Targoni, A. M. Krieg, P. V. Lehmann, and C. V. Harding. 1997. CpG oligodeoxynucleotides act as adjuvants that switch on T helper 1 (Th1) immunity. *J. Exp. Med.* 186: 1623-1631.
- ▶ Yip, H. C., A. Y. Karulin, M. Tary-Lehmann, M. D. Hesse, H. Radeke, P. Heeger, R. T. Trezza, F. P. Heinzel, T. Forsthuber, and P. V. Lehmann. 1999. Adjuvant guided type 1 and type 2 immunity: Infectious/non-infectious dichotomy defines the class of response. *J. Immunol.* 162: 3942-3949.
- ▶ Karulin, A. Y., M. D. Hesse, H. C. Yip, and P. V. Lehmann. 2002. Indirect IL-4 pathway in Th1 immunity. *J. Immunol.* 168: 545-553.
- ▶ Guerkov, R. E., O. S. Targoni, C. R. Kreher, B. O. Boehm, M. T. Herrera, M. Tary-Lehmann, P. V. Lehmann, and S. K. Schwander. 2003. Detection of low-frequency antigen-specific IL-10-producing CD4(+) T cells via ELISPOT in PBMC: cognate vs. nonspecific production of the cytokine. *J. Immunol. Methods.* 279: 111-121.

### ***Cognate Cytokine Production by T Cells vs Bystander Cytokine Production***

- ▶ Helms, T., B. O. Boehm, R. J. Assad, R. T. Trezza, P. V. Lehmann, and M. Tary-Lehmann. 2000. Direct visualization of cytokine-producing, recall antigen-specific CD4 memory T cells in healthy individuals and HIV patients. *J. Immunol.* 164: 3723-3732.
- ▶ Karulin, A. Y., M. D. Hesse, M. Tary-Lehmann, and P. V. Lehmann. 2000. Single-cytokine-producing CD4 memory cells prevail in vivo, in type 1/type 2 immunity. *J. Immunol.* 164:1862-1872.

- ▶ Karulin, A. Y., M. D. Hesse, H. C. Yip, and P. V. Lehmann. 2002. Indirect IL-4 pathway in Th1 immunity. *J. Immunol.* 168: 545-553.
- ▶ Guerkov, R. E., O. S. Targoni, C. R. Kreher, B. O. Boehm, M. T. Herrera, M. Tary-Lehmann, P. V. Lehmann, and S. K. Schwander. 2003. Detection of low-frequency antigen-specific IL-10-producing CD4(+) T cells via ELISPOT in PBMC: cognate vs. nonspecific production of the cytokine. *J. Immunol. Methods.* 279: 111-121.

## **Measurements of Functional T Cell Avidity**

- ▶ Hesse, M. D., A. Y. Karulin, B. O. Boehm, P. V. Lehmann, and M. Tary-Lehmann. 2001. A T cell clone's avidity is a function of its activation state. *J. Immunol.* 167: 1353-1361.
- ▶ Targoni, O. S. and P. V. Lehmann. 1998. Endogenous myelin basic protein inactivates the high avidity T cell repertoire. *J. Exp. Med.* 187: 2055-2063.
- ▶ Yip, H. C., A. Y. Karulin, M. Tary-Lehmann, M. D. Hesse, H. Radeke, P. Heeger, R. T. Trezza, F. P. Heinzl, T. Forsthuber, and P. V. Lehmann. 1999. Adjuvant guided type 1 and type 2 immunity: Infectious/non-infectious dichotomy defines the class of response. *J. Immunol.* 162: 3942-3949.
- ▶ Karulin, A. Y., M. D. Hesse, M. Tary-Lehmann, and P. V. Lehmann. 2000. Single-cytokine-producing CD4 memory cells prevail in vivo, in type 1/type 2 immunity. *J. Immunol.* 164: 1862-1872.
- ▶ Hofstetter, H. H., O. S. Targoni, A. Y. Karulin, T. G. Forsthuber, M. Tary-Lehmann, and P. V. Lehmann. 2005. Does the frequency and avidity spectrum of the neuroantigen-specific T cells in the blood mirror the autoimmune process in the central nervous system of mice undergoing experimental allergic encephalomyelitis? *J Immunol* 174:4598-4605.

## **Cytokine Co-Expression/Two Color ELISPOT**

- ▶ Karulin, A., M. Hesse, M. Tary-Lehmann, and P. V. Lehmann. 2000. Single-cytokine-producing CD4 memory cells prevail in vivo, in type 1/type 2 immunity. *J. Immunol.* 164: 1862-1872.
- ▶ Heeger, P. S., T. Forsthuber, C. Shive, E. Beikert, C. P. Genain, H. H. Hofstetter, A. Y. Karulin, and P. V. Lehmann. 2000. Revisiting tolerance induced by autoantigen in incomplete Freund's adjuvant. *J. Immunol.* 164: 5771-5781.
- ▶ Karulin, A. Y., M. D. Hesse, H. C. Yip, and P. V. Lehmann. 2002. Indirect IL-4 pathway in Th1 immunity. *J. Immunol.* 168: 545-553.

## **Spot Size Distribution**

- ▶ Karulin, A. Y., M. D. Hesse, M. Tary-Lehmann, and P. V. Lehmann. 2000. Single-cytokine-producing CD4 memory cells prevail in vivo, in type 1/type 2 immunity. *J. Immunol.* 164: 1862-1872.
- ▶ Hesse, M. D., A. Y. Karulin, B. O. Boehm, P. V. Lehmann, and M. Tary-Lehmann. 2001. A T cell clone's avidity is a function of its activation state. *J. Immunol.* 167: 1353-1361.
- ▶ Guerkov, R. E., O. S. Targoni, C. R. Kreher, B. O. Boehm, M. T. Herrera, M. Tary-Lehmann, P. V. Lehmann, and S. K. Schwander. 2003. Detection of low-frequency antigen-specific IL-10-producing CD4(+) T cells via ELISPOT in PBMC: cognate vs. nonspecific production of the cytokine. *J. Immunol. Methods.* 279: 111-121.

## **Determinant Mapping/High Throughput Screening**

- ▶ Targoni, O. S. and P. V. Lehmann. 1998. Endogenous myelin basic protein inactivates the high avidity T cell repertoire. *J. Exp. Med.* 187: 2055-2063.
- ▶ Yip, H. C., A. Y. Karulin, M. Tary-Lehmann, M. D. Hesse, H. Radeke, P. Heeger, R. T. Trezza, F. P. Heinzl, T. Forsthuber, and P. V. Lehmann. 1999. Adjuvant guided type 1 and type 2 immunity: Infectious/non-infectious dichotomy defines the class of response. *J. Immunol.* 162: 3942-3949.
- ▶ Heeger, P. S., A. Valujskikh, and P. V. Lehmann. 2000. Comprehensive assessment of determinant specificity, frequency, and cytokine signature of the primed CD8 cell repertoire induced by a minor transplantation antigen. *J. Immunol.* 165: 1278-1284.
- ▶ Pelfrey, C. M., R. A. Rudick, A. C. Coteleur, J. C. Lee, M. Tary-Lehmann, and P. V. Lehmann. 2000. Quantification of self-recognition in multiple sclerosis by single-cell analysis of cytokine production. *J. Immunol.* 165: 1641-1651.

- ▶ Anthony, D. D., H. Valdez, A. B. Post, N. L. Carlson, P. S. Heeger, and P. V. Lehmann. 2002. Comprehensive determinant mapping of the hepatitis C-specific CD8 cell repertoire reveals unpredicted immune hierarchy. *Clin.Immunol* 103:264-276.
- ▶ Kleen, T. O., R. Asaad, S. J. Landry, B. O. Boehm, and M. Tary-Lehmann. 2004. Tc1 effector diversity shows dissociated expression of granzyme B and interferon-gamma in HIV infection. *AIDS* 18:383-392.
- ▶ Anthony, D. D., and P. V. Lehmann. 2003. T-cell epitope mapping using the ELISPOT approach. *Methods*. 29: 260-269.

## **Assay to Assay Reproducibility of Ex Vivo Measurements on PBMC**

- ▶ Helms, T., B. O. Boehm, R. J. Assad, R. T. Trezza, P. V. Lehmann, and M. Tary-Lehmann. 2000. Direct visualization of cytokine-producing, recall antigen-specific CD4 memory T cells in healthy individuals and HIV patients. *J. Immunol.* 164: 3723-3732.
- ▶ Gebauer, B. S., D. E. Hricik, A. Atallah, K. Bryan, J. Riley, M. Tary-Lehmann, N. S. Greenspan, B. O. Boehm, B. J. Hering and P. S. Heeger. 2002. Evolution of the Enzyme-Linked Immunosorbent Spot Assay for Post-Transplant Alloreactivity as a Potentially Useful Immunme Monitoring Tool. *The American Journal of Transplantation*. 9: 857-866
- ▶ Anthony, D. D., and P. V. Lehmann. 2003. T-cell epitope mapping using the ELISPOT approach. *Methods*. 29: 260-269.
- ▶ Kreher, C. R., M. T. Dittrich, R. Guerkov, B. O. Boehm and M. Tary-Lehmann M. 2003. CD4+ and CD8+ cells in cryopreserved human PBMC maintain full functionality in cytokine ELISPOT assays. *J. Immunol. Methods*. 278: 79-93.

## **Fresh vs. Cryopreserved Human PBMC**

- ▶ Gebauer, B. S., D. E. Hricik, A. Atallah, K. Bryan, J. Riley, M. Tary-Lehmann, N. S. Greenspan, B. O. Boehm, B. J. Hering and P. S. Heeger. 2002. Evolution of the Enzyme-Linked Immunosorbent Spot Assay for Post-Transplant Alloreactivity as a Potentially Useful Immunme Monitoring Tool. *The American Journal of Transplantation*. 9: 857-866.
- ▶ Kreher, C. R., M. T. Dittrich, R. Guerkov, B. O. Boehm and M. Tary-Lehmann M. 2003. CD4+ and CD8+ cells in cryopreserved human PBMC maintain full functionality in cytokine ELISPOT assays. *J. Immunol. Methods*. 278: 79-93.

## **CD8+ T cells and Granzyme B ELISPOT**

- ▶ Rininsland, F. H., T. Helms, R. J. Asaad, B. O. Boehm and M. Tary-Lehmann. 2000. Granzyme B ELISPOT assay for ex vivo measurement of T cell immunity. *J. Immunol. Methods* 240: 143-155.
- ▶ Kleen, T. O., R. Asaad, S. Landry, B. O. Boehm and M. Tary-Lehmann. 2004 . Tc1 effector cell diversity in HIV infection: dissociated expression of IFN-G and of granzyme B by peptide-specific CD8 cells. *AIDS*, 18: 383-392.

## **ELISPOT With Cells Other than Human PBMC, or Murine Lymph Node/Spleen Cells**

- ▶ Targoni, O. S., J. Baus, H. H. Hoffstetter, M. D. Hesse, A. Y. Karulin, B. O. Boehm, T. Forsthuber, and P. V. Lehmann. 2001. Frequencies of neuroantigen-specific T cells in the CNS versus the immune periphery during the course of EAE. *J. Immunol.* 166: 4757-4764. (lymphocytes isolated from murine CNS, peritoneal cavity)
- ▶ Schwander, S. K., M. Torres, C. C. Carranza, D. Escobedo, M. Tary-Lehmann, P. Anderson, Z. Toossi, J. J. Ellner, and E. Sada. 2000. Pulmonary mononuclear cell responses to antigens of *Mycobacterium tuberculosis* in healthy household contacts of patients with active tuberculosis and healthy controls from the community. *J. Immunol.* 165: 1479-1485 (human bronchoalveolar lavage cells)
- ▶ Gebauer, B. S., D. E. Hricik, A. Atallah, K. Bryan, J. Riley, M. Tary-Lehmann, N. S. Greenspan, B. O. Boehm, B. J. Hering and P. S. Heeger. 2002. Evolution of the Enzyme-Linked Immunosorbent Spot Assay for Post-Transplant Alloreactivity as a Potentially Useful Immunme Monitoring Tool. *The American Journal of Transplantation*. 9: 857-866. (Human spleen cells, B cells and different APC subpopulations)
- ▶ Aung, H., J. Sherman, M. Tary-Lehmann, Z. and Toossi. 2002. Analysis of transforming growth factor-beta 1 (TGF-b1) expression in human monocytes infected with *Mycobacterium Avium* at a single cell level by ELISPOT assay. *J. Immunol. Methods* 259: 25-32. (human macrophages)

## **Vaccine and Adjuvants**

- ▶ Forsthuber, T., H. C. Yip, and Lehmann P. V. 1996. Induction of TH1 and TH2 immunity in neonatal mice. *Science*, 271: 1728-1730.
- ▶ Chu R. S., O. S. Targoni, A. M. Krieg, P. V. Lehmann, and C. V. Harding. 1997. CpG oligodeoxynucleotides act as adjuvants that switch on T helper 1 (Th1) immunity. *J. Exp. Med.* 186: 1623-163.
- ▶ Yip, H. C., A. Y. Karulin, M. Tary-Lehmann, M. D. Hesse, H. Radeke, P. S. Heeger, R. P. Trezza, F. P. Heinzl, T. Forsthuber, and P. V. Lehmann. 1999. Adjuvant-guided type-1 and type-2 immunity: infectious/noninfectious dichotomy defines the class of response. *J Immunol* 162:3942-3949.
- ▶ Heeger, P. S., T. Forsthuber, C. Shive, E. Beikert, C. P. Genain, H. Hofstetter, A. Karulin, and P. V. Lehmann. 2000. Revisiting tolerance induced by autoantigen in incomplete Freund's adjuvant. *J. Immunol.* 164: 5771-5781 .
- ▶ Gottwein J. M., T. G. Blanchard, O. A. Targoni, J. G. C. Eisenberg, B. M. Zagorski, R. V. Redline, J. G. Nedrud, M. Tary-Lehmann, P. V. Lehmann and S. J. Czinn. 2001. Protective anti-Helicobacter immunity is induced with aluminium hydroxide or complete Freud's adjuvant by systemic immunization. *J. Infect. Dis.* 184: 308-314.
- ▶ Stern B. V., B. O. Boehm, M. Tary-Lehmann. 2002. Vaccination with tumor peptide in CpG adjuvant protects via IFN-G dependent CD4 cell immunity. *J. Immunol.* 168: 6099-6105.
- ▶ Eisenberg, J., J. S. Czinn, C. A. Garhard, R. W. Redline, W. C. Bartholomae, J. Gottwein, J. G. Nedrud, S. E. Emancipator, B. O. Boehm, P. V. Lehmann, T. G. and Blanchard. 2003. Protective efficacy of anti-Helicobacter pylori immunity following systemic immunization of neonatal mice. *Infection and Immunity*, 71: 1820-1827.
- ▶ Ott, P. A., Berner, B. R., Herzog, B. A., Guerkov, R., Yonkers, N. L., Durinovic-Bello, I., Tary-Lehmann, M., Lehmann, P. V., Anthony, D. D. 2004. CD28 costimulation enhances the sensitivity of the ELISPOT assay for detection of antigen-specific memory effector CD4 and CD8 cell populations in human diseases. *J. Immunol. Methods.* 15;285(2):223-35

## **Tumor Immunology**

- ▶ Stern, B. V., B. O. Boehm, and M. Tary-Lehmann. 2002. Vaccination with tumor peptide in CpG adjuvant protects via Interferon-G dependent CD4 cell immunity. *J. Immunol.* 168: 6099-6105.
- ▶ Lonsdorf, A. S., H. Kuekrek, B. V. Stern, B. O. Boehm, P. V. Lehmann and M. Tary-Lehmann. 2003. Intratumor CpG-oligodeoxynucleotide injection induces protective antitumor T cell immunity. *J. Immunol.* 171: 3841-3946.
- ▶ Bartholomae W. C., Rininsland F. H., Eisenberg J. C., Boehm B. O., Lehmann P. V., Tary-Lehmann M. 2004. T cell immunity induced by live, necrotic, and apoptotic tumor cells. *J. Immunol.* 173(2):1012-22.

## **Transplantation Immunology**

- ▶ Lehmann, P. V., Matesic D, Benichou G, Heeger, P. S. 1997. Induction of T helper 2 immunity to an immunodominant allopeptide. *Transplantation.* 64(2): 292-296.
- ▶ Matesic, D., P. V. Lehmann, and P. S. Heeger. 1998. High resolution characterization of cytokine producing alloreactivity in naive and allograft primed mice. *Transplantation.* 65: 906-914 .
- ▶ Tary-Lehmann, M., D. Hricik, A. C. Justice, N. S. Potter and P. S. Heeger. 1998. Enzyme-linked immunosorbent assay spot detection of interferon-G and interleukin 5 producing cells as a predictive marker for renal allograft failure. *Transplantation.* 66: 219-224 .
- ▶ Heeger, P. S., N. Greenspan, S. Kuhlenschmidt, C. Dejele, D. E. Hricik, J. Schulak and M. Tary-Lehmann. 1999. Pretransplant frequency of donor specific, IFN-G producing lymphocytes is a manifestation of immunologic memory and correlates with the risk of posttransplant rejection episodes. *J. Immunology.* 163: 2267-2275.
- ▶ Heeger, P. S., A. Valujskih and P. V. Lehmann. 2000. Comprehensive assessment of determinant specificity, frequency, and cytokine signature of the primed CD8 cell repertoire induced by a minor transplantation antigen. *J. Immunol.* 165: 1278-1284 .
- ▶ Gebauer, B. S., D. E. Hricik, A. Atallah, K. Bryan, J. Riley, M. Tary-Lehmann, N. S. Greenspan, B. O. Boehm, B. J. Hering and P. S. Heeger. 2002. Evolution of the Enzyme-Linked Immunosorbent Spot Assay for Post-Transplant Alloreactivity as a Potentially Useful Immunme Monitoring Tool. *The American Journal of Transplantation.* 9: 857-866.
- ▶ Hricik, D. E., V. Rodriguez, R. N. Jocelyn Riley, K. Bryan, M. Tary-Lehmann, N. Greenspan, C. Dejele, J. A. Schulak, and P. S Heeger. 2003. Enzyme linked immunosorbent spot (ELISPOT) assay for Interferon-G independently predicts renal function in kidney transplant recipients. *Am. J. Transplantation.* 7: 878-884.

## Autoimmunity

- ▶ Herzog, B. A., Ott P. A., Dittrich, M. T., Quast, S., Karulin, A. Y., Kalbacher, H., Karges, W., Tary-Lehmann, M., Lehmann, P. V., Boehm, B. O., Durinovic-Bello I. 2004. Increased in vivo frequency of IA-2 peptide-reactive IFN $\gamma$ +/IL-4- T cells in type 1 diabetic subjects. *J. Autoimmun.* 23(1):45-54.
- ▶ Ott, P. A., Dittrich, M. T., Herzog, B. A., Guerkov, R., Gottlieb, P. A., Putnam, A. L., Durinovic-Bello, I., Boehm, B. O., Tary-Lehmann, M., Lehmann, P. V., 2004. T cells recognize multiple GAD65 and proinsulin epitopes in human type 1 diabetes, suggesting determinant spreading. *J. Clin. Immunol.* ;24(4):327-39.
- ▶ Ott, P. A., M. R. Anderson, M. Tary-Lehmann, and P. V. Lehmann. 2005. CD4(+)CD25(+) regulatory T cells control the progression from perinsulinitis to destructive insulinitis in murine autoimmune diabetes. *Cell Immunol* 235:1-11.
- ▶ Ott, P. A., B. A. Herzog, S. Quast, H. H. Hofstetter, B. O. Boehm, M. Tary-Lehmann, I. Durinovic-Bello, B. R. Berner, and P. V. Lehmann. 2005. Islet-cell antigen-reactive T cells show different expansion rates and Th1/Th2 differentiation in type 1 diabetic patients and healthy controls. *Clin.Immunol* 115:102-114

## Infectious Diseases

- ▶ Gross, D. M., Forsthuber, T., Tary-Lehmann, M., Etling, C., Ito, K., Nagy, Z., Field, J. A., Steere, A. C. and Huber, B.T. 1998, Identification of LFA-1 as a candidate autoantigen in treatment-resistant Lyme arthritis. *Science* 281:703-706 (178 citations).
- ▶ Helms, T., B. O. Boehm, R. J. Assad, R. T. Trezza, P. V. Lehmann, and M. Tary-Lehmann. 2000. Direct visualization of cytokine-producing, recall antigen-specific CD4 memory T cells in healthy individuals and HIV patients. *J. Immunol.* 164: 3723-3732.
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- ▶ Schwander, S. K., M. Torres, C. C. Carranza, D. Escobedo, M. Tary-Lehmann, P. Anderson, Z. Toossi, J. J. Ellner, and E. Sada. 2000. Pulmonary mononuclear cell responses to antigens of *Mycobacterium tuberculosis* in healthy household contacts of patients with active tuberculosis and healthy controls from the community. *J. Immunol.* 165: 1479-1485.
- ▶ Gottwein J. M., T. G. Blanchard, O. A. Targoni, J. G. C. Eisenberg, B. M. Zagorski, R. V. Redline, J. G. Nedrud, M. Tary-Lehmann, P. V. Lehmann and S. J. Czinn. 2001. Protective anti-*Helicobacter* immunity is induced with aluminium hydroxide or complete Freud's adjuvant by systemic immunization. *J. Infect. Dis.* 184: 308-314.
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- ▶ Guerkov, R. E., O. S. Targoni, C. R. Kreher, B. O. Boehm, M. T. Herrera, M. Tary-Lehmann, P. V. Lehmann, and S. K. Schwander. 2003. Detection of low-frequency antigen-specific IL-10-producing CD4(+) T cells via ELISPOT in PBMC: cognate vs. nonspecific production of the cytokine. *J. Immunol. Methods.* 279: 111-121 .
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- ▶ Eisenberg, J., J. S. Czinn, C. A. Garhard, R. W. Redline, W. C. Bartholomae, J. Gottwein, J. G. Nedrud, S. E. Emancipator, B. O. Boehm, P. V. Lehmann, T. G. and Blanchard. 2003. Protective efficacy of anti-*Helicobacter pylori* immunity following systemic immunization of neonatal mice. *Infection and Immunity*, 71: 1820-1827.
- ▶ Anthony, D. D., and P. V. Lehmann. 2003. T-cell epitope mapping using the ELISPOT approach. *Methods.* 29: 260-269.
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- ▶ Darabi K., Karulin, A. Y., Boehm, B. O., Hofstetter, H. H., Fabry, Z., LaManna, J. C., Chavez, J. C., Tary-Lehmann, M., Lehmann, P. V. 2004. The third Signal in T cell-mediated autoimmune disease. *J. Immunol.*173(1):92-9.



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