

Tra autoimmunità e immunoterapia: vaccinazione con antigeni tumore associati nel melanoma.

G.C. Spagnoli e colleghi

**Institute for Surgical Research and Hospital
Management
University of Basel**

Common receptor γ chain cytokines

	α -chain	β -chain	γ -chain
IL-2	CD25	CD122	CD132
IL-7	CD127	none	CD132
IL-15	IL-15α	CD122	CD132

Knock out mice

Phenotype

Reference

IL-2

**Autoimmune
syndrome**

**Sadlak B et
al., 1993**

IL-7

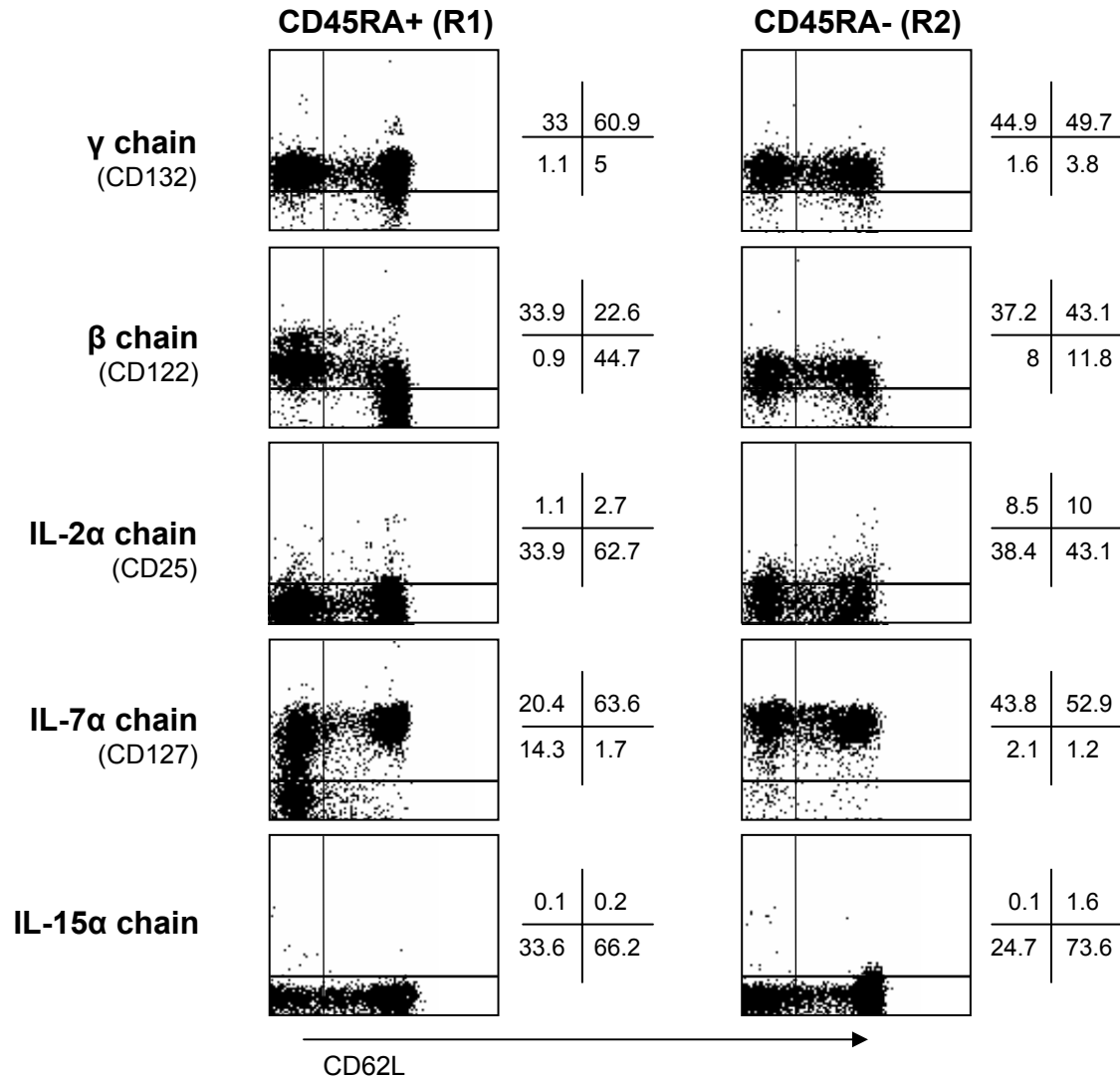
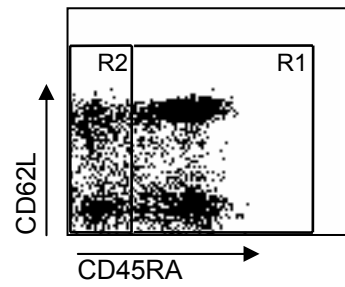
**Altered Thymic
development and B
lymphopoiesis**

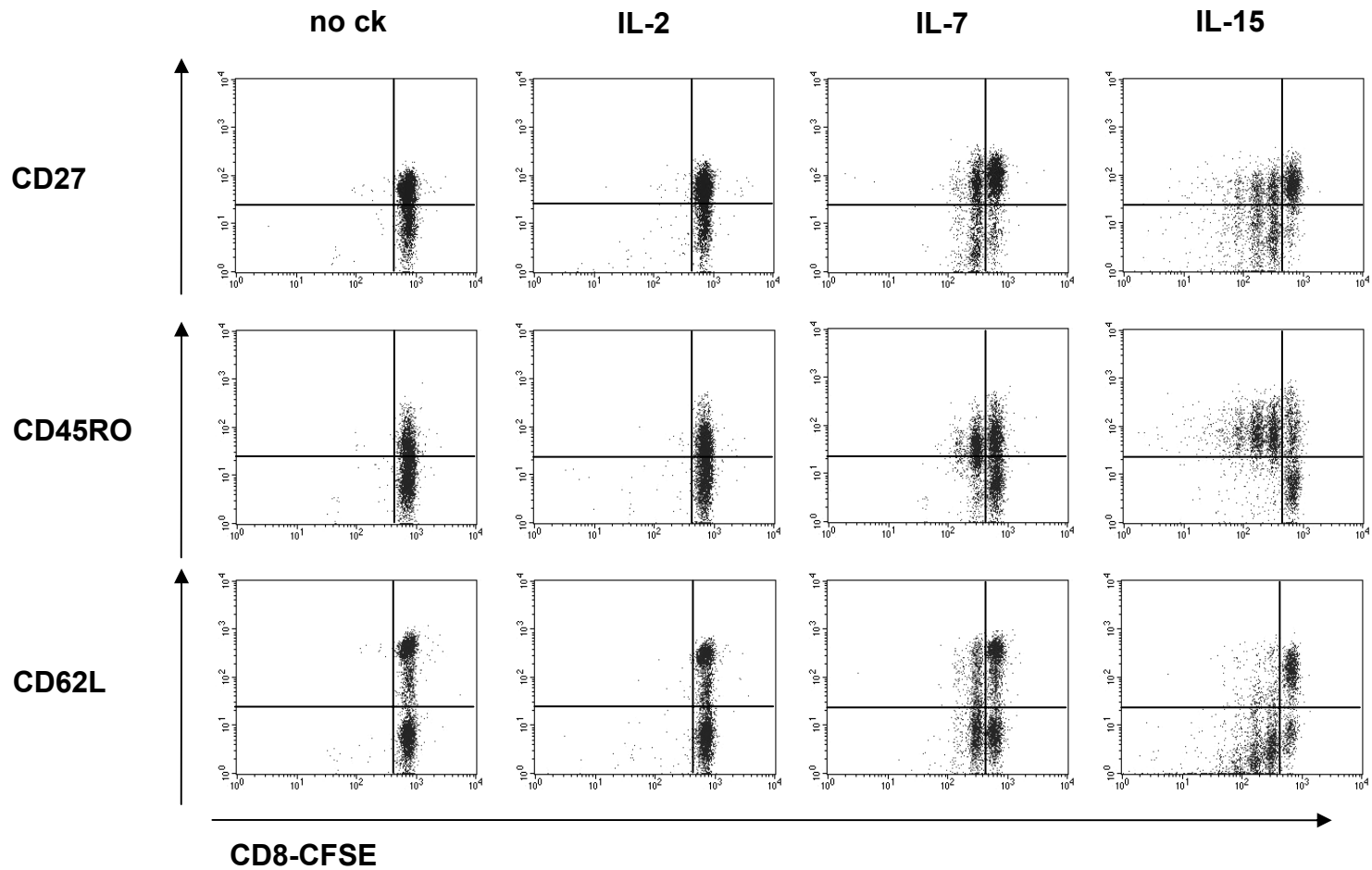
**von Freeden-
Jeffry U et
al., 1995**

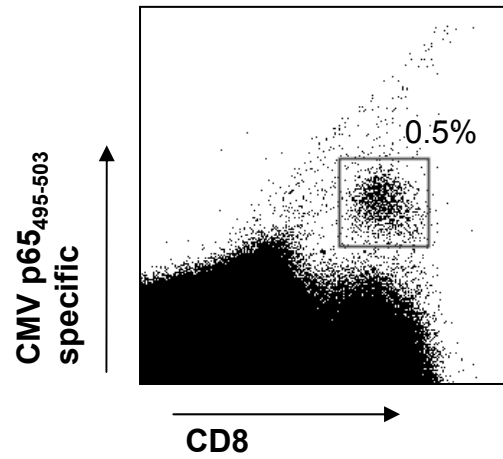
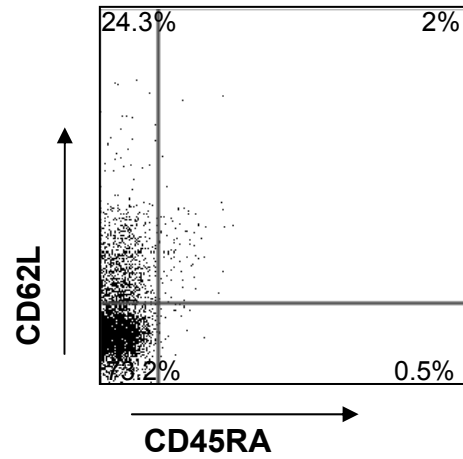
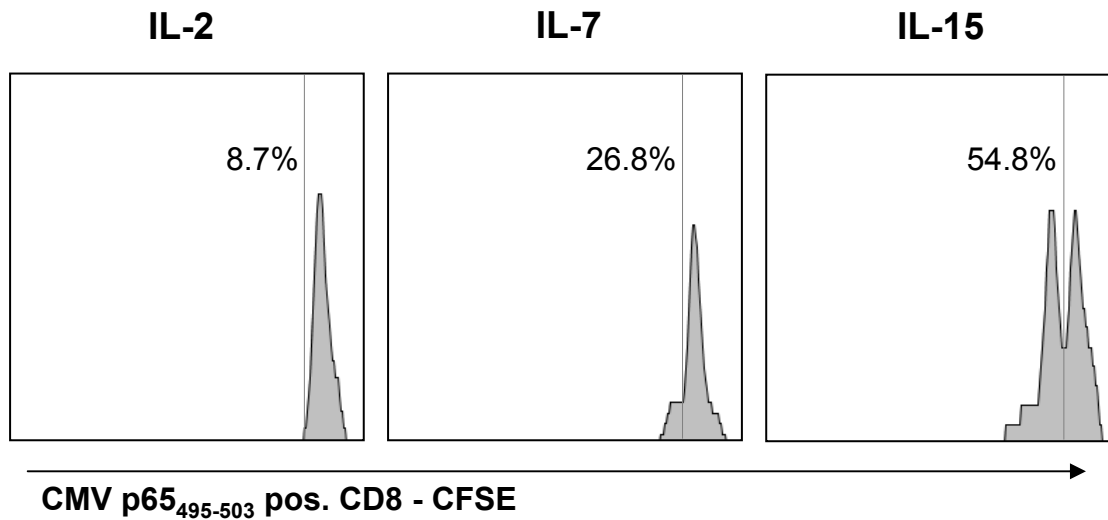
IL-15

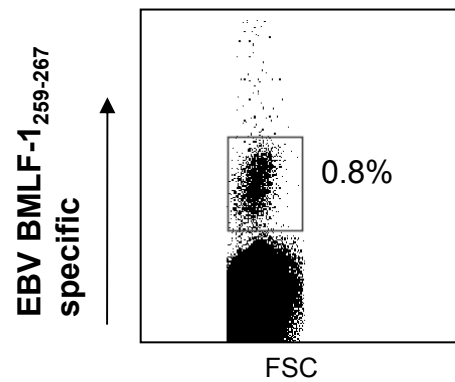
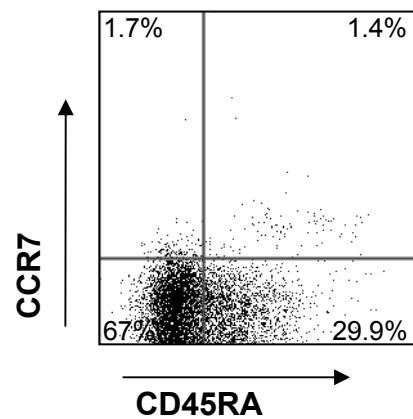
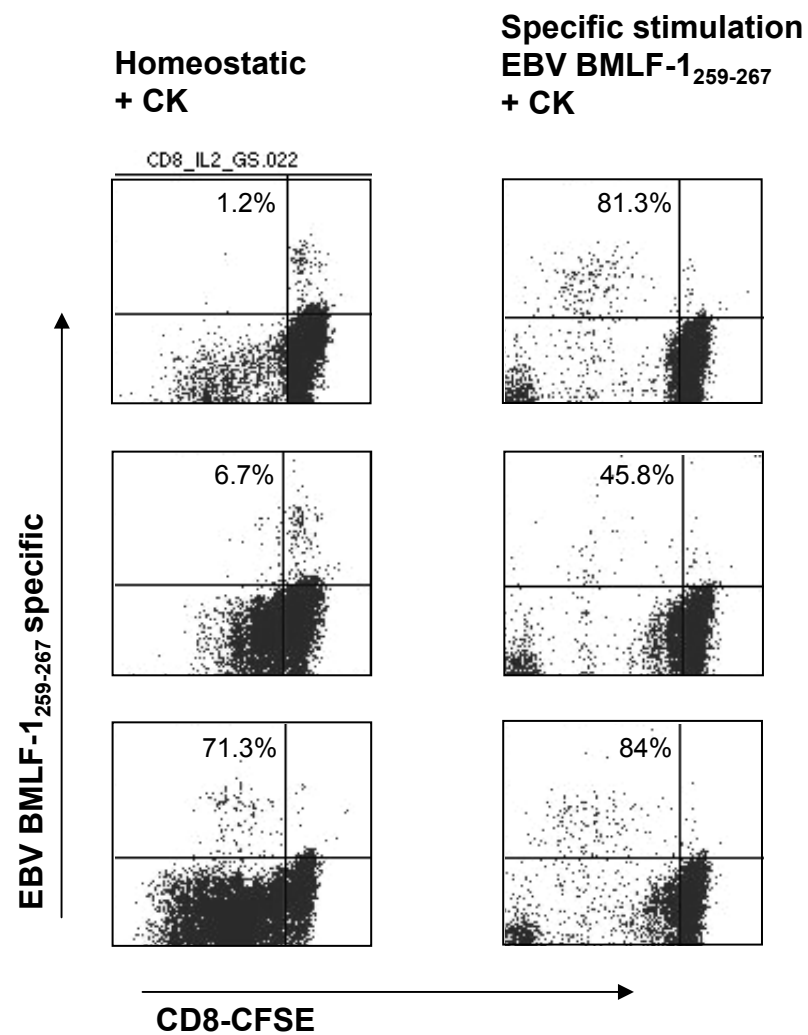
**Defective NK and
memory CD8+ T
cell development**

**Kennedy MK
et al., 2000**



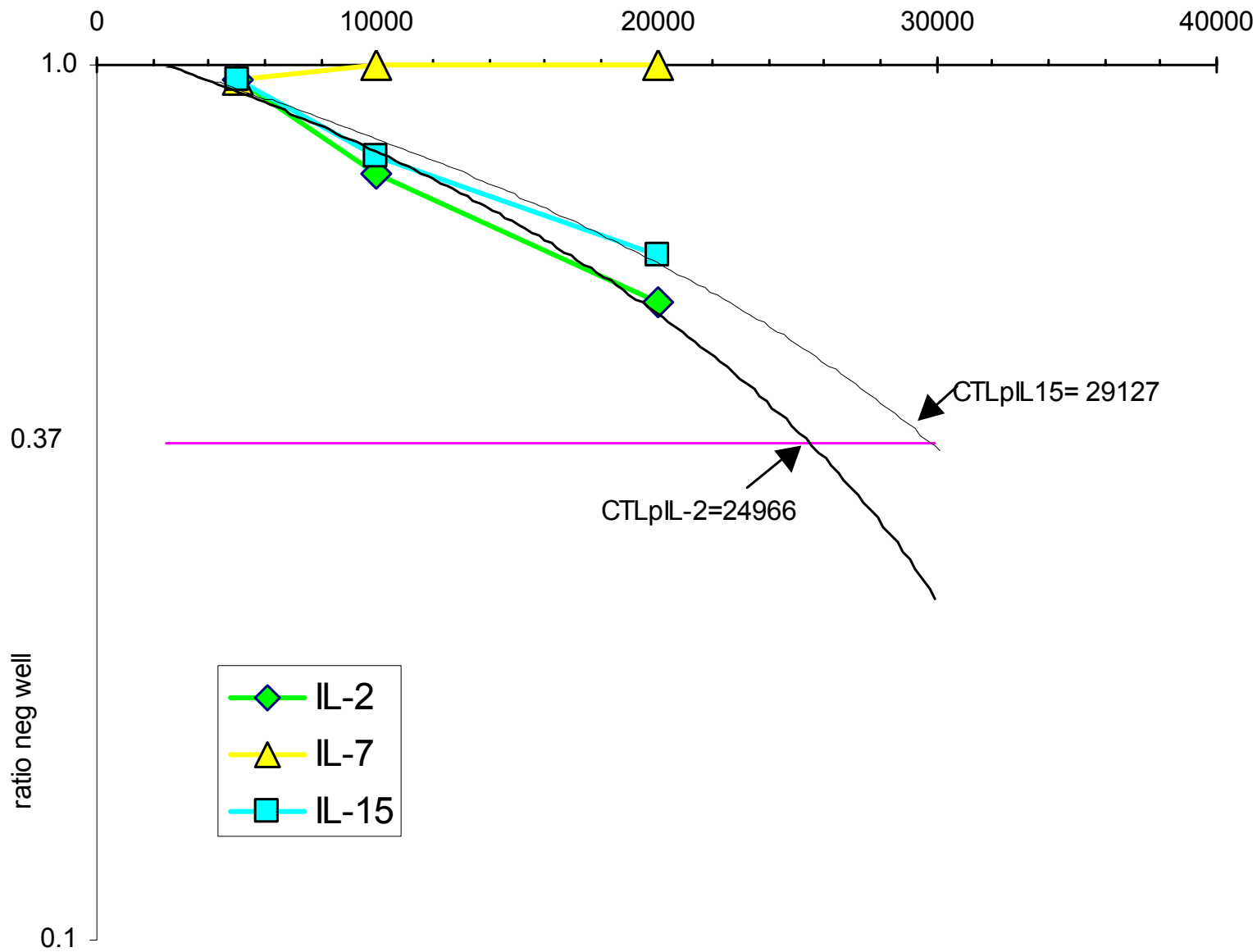


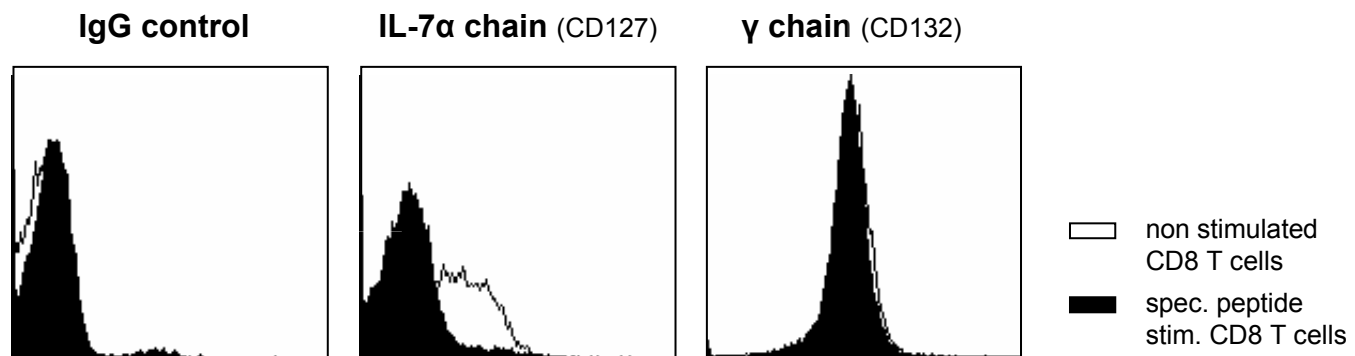
A**B****C**

A**B****C**

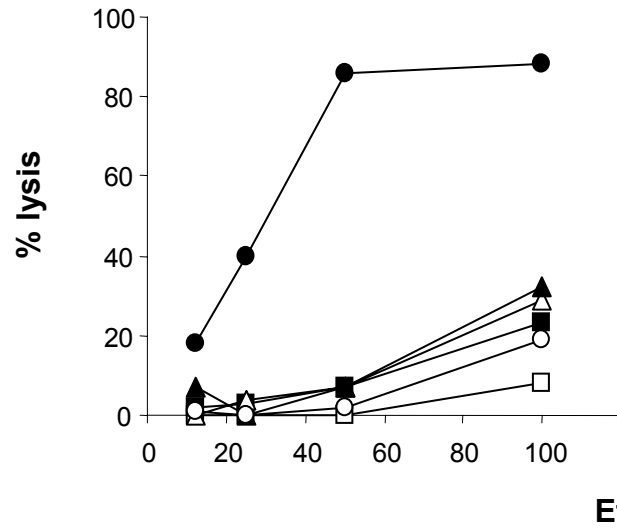
FLU CTLp

cell/w ell

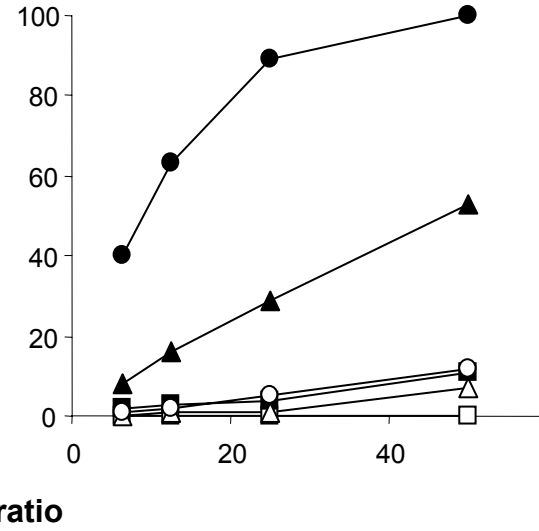




A EBV seropositive donor



B Melanoma patient



C

	pre-incubation	IL-2	IL-7	IL-15
A	EBV BMLF-1 ₂₅₉₋₂₆₇ pos, %	1.5	2	3.3
B	VV H3L ₁₈₄₋₁₉₂ , B22R ₂₉₋₃₇ and C7L ₇₄₋₈₂ pos, %	1	1.3	16.3

Medullary Epithelial Cells of the Human Thymus Express a Highly Diverse Selection of Tissue-specific Genes Colocalized in Chromosomal Clusters

Jörn Gotter,¹ Benedikt Brors,² Manfred Hergenhahn,³ and Bruno Kyewski¹

¹Tumor Immunology Program, ²Intelligent Bioinformatic Systems, and ³Genetic Alterations in Carcinogenesis, German Cancer Research Center, D-69120 Heidelberg, Germany

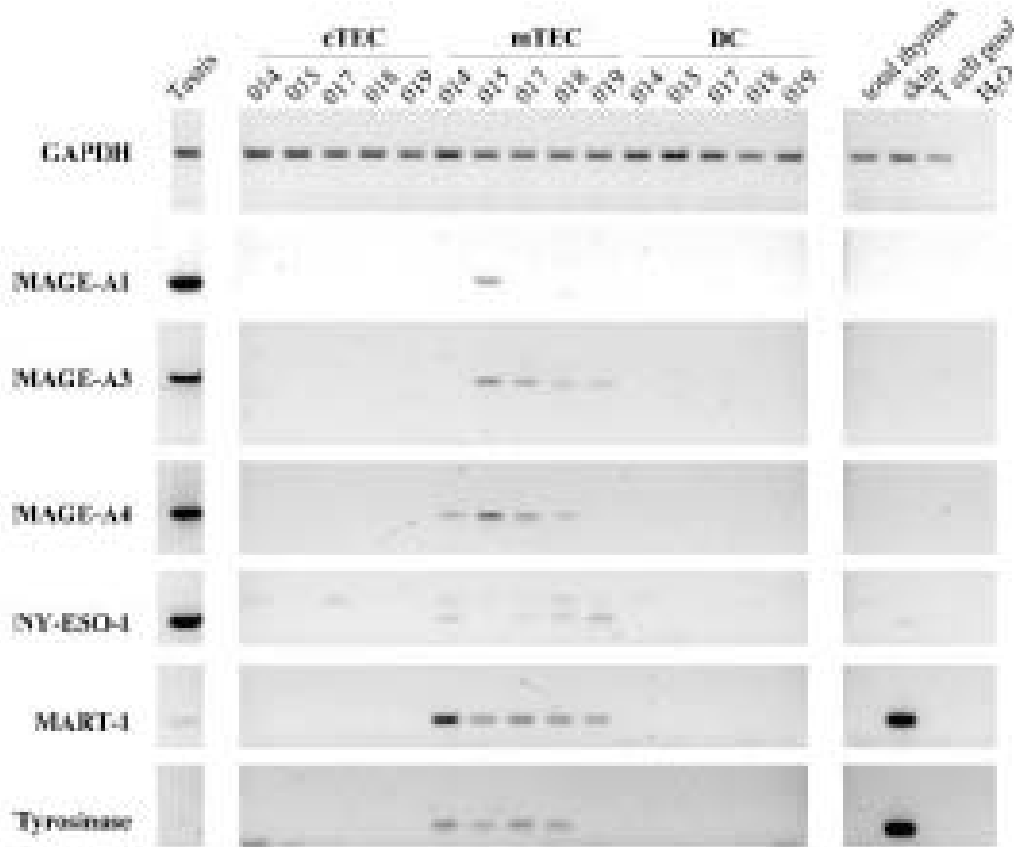
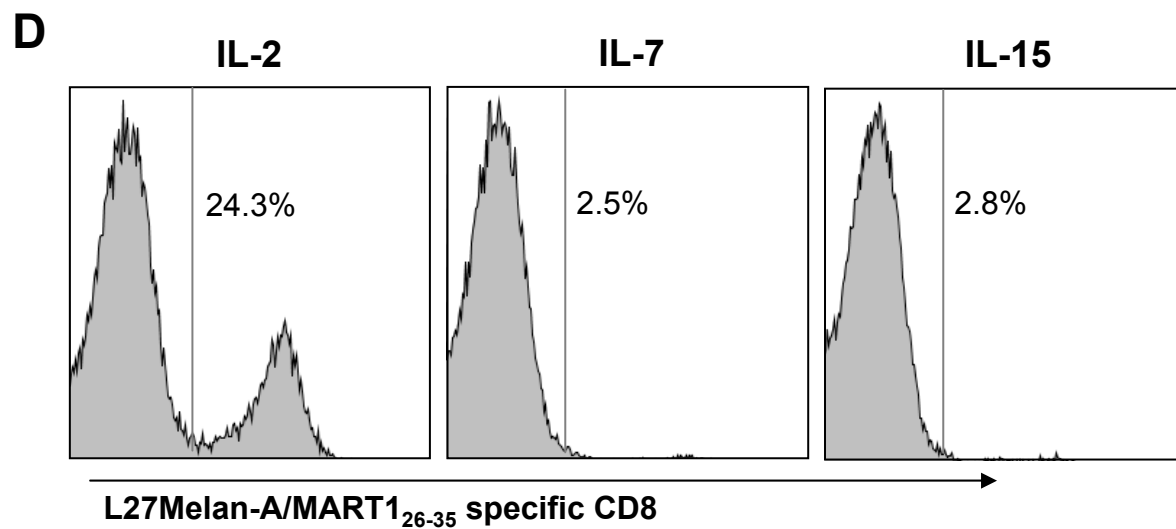
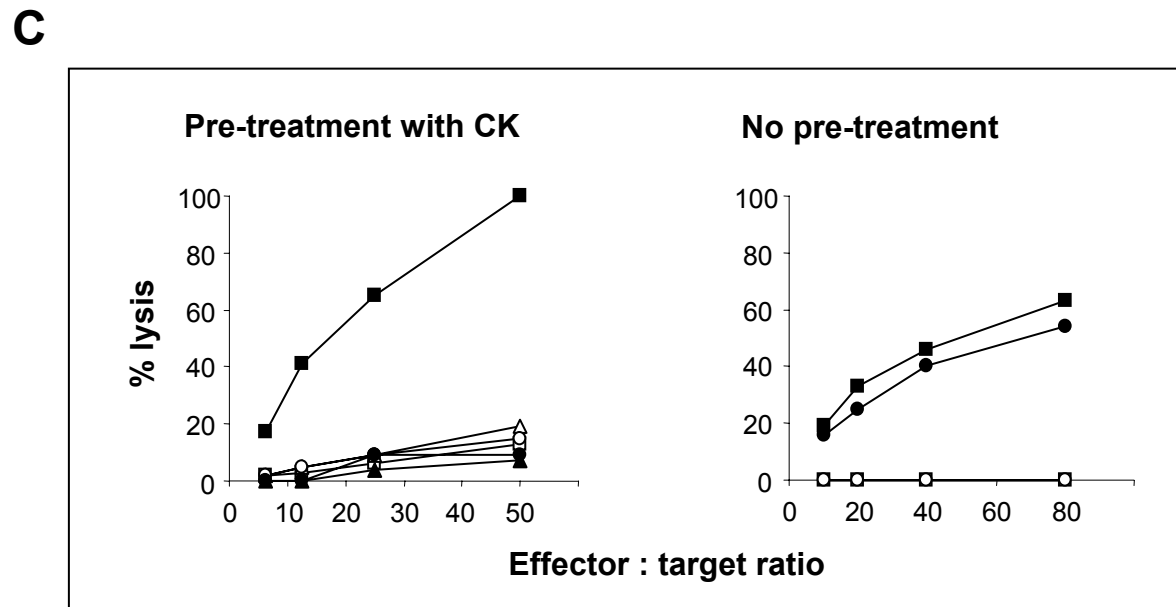
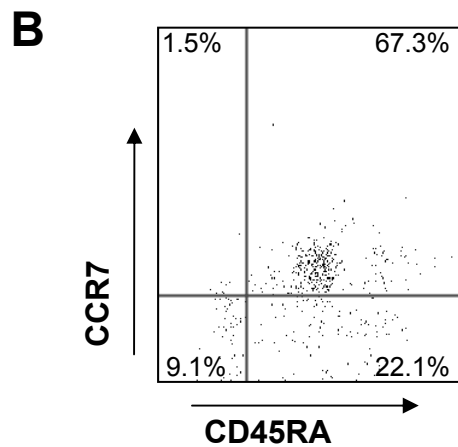
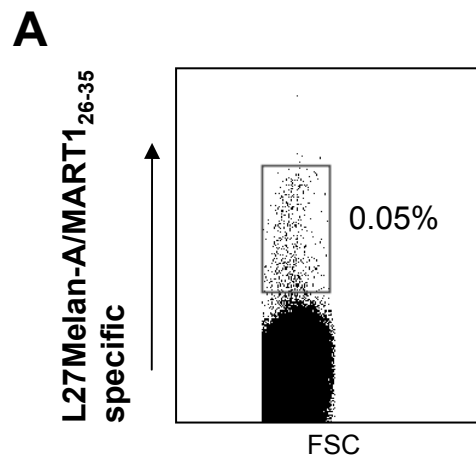
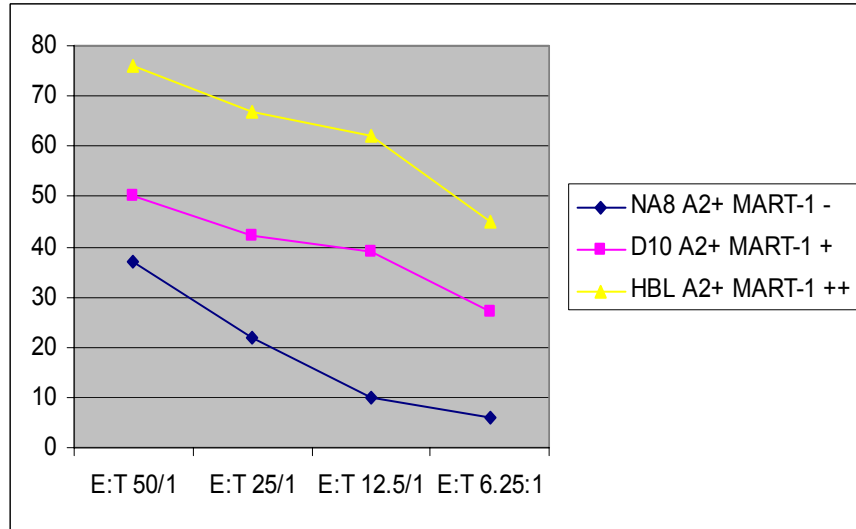


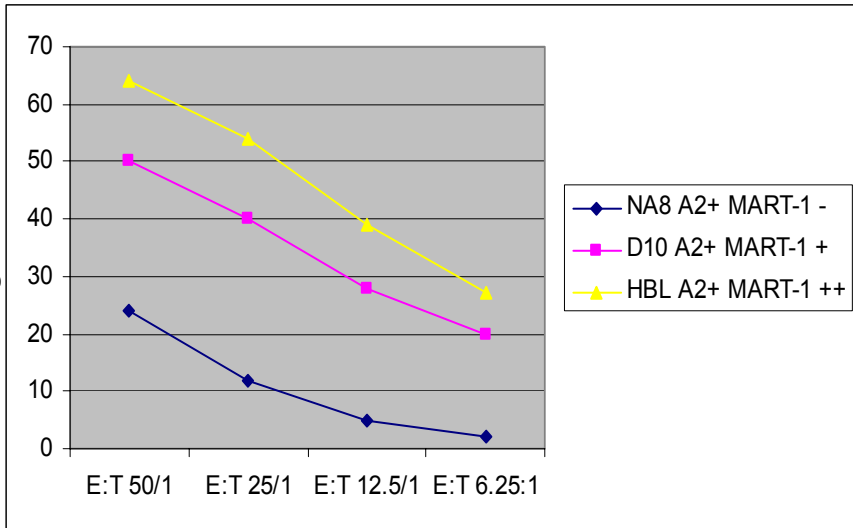
Figure 2. Thymic expression of tumor-associated antigens. Expression of selected tumor-associated antigens in thymic stromal cells of five thymi was assessed by RT-PCR. Expression in each case was confined to mTECs. Note inter-individual variations and the difference in signal strength compared with control tissues. The amount of input cDNA was normalized according to signals obtained for GAPDH in a titration experiment (not depicted).



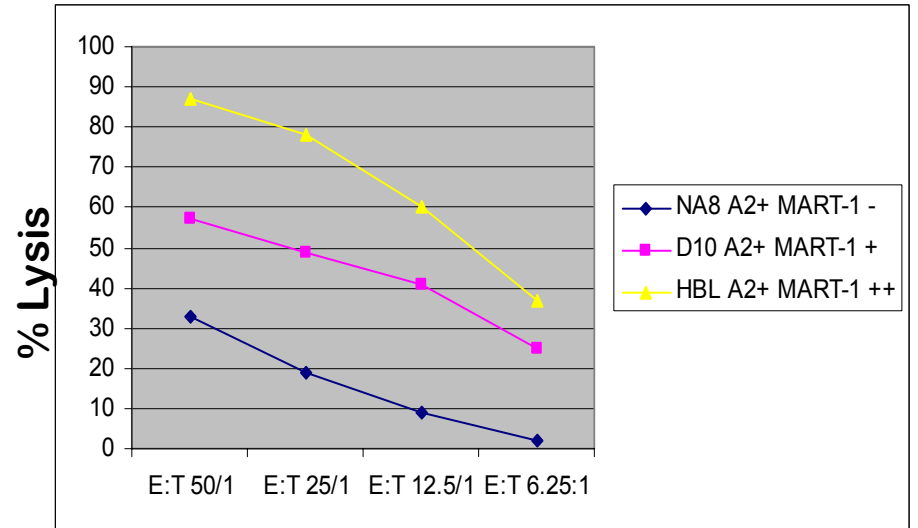
A



B



C



LETTERS TO NATURE

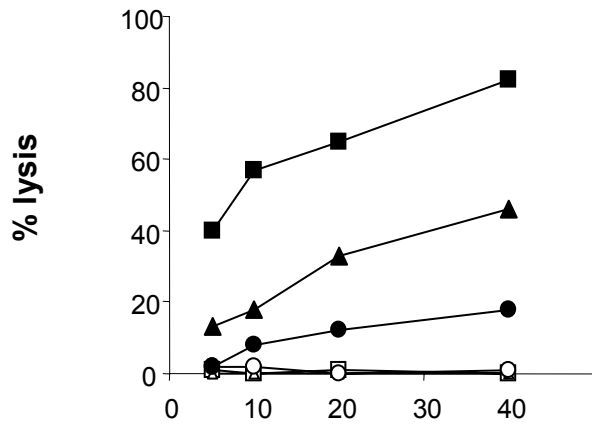
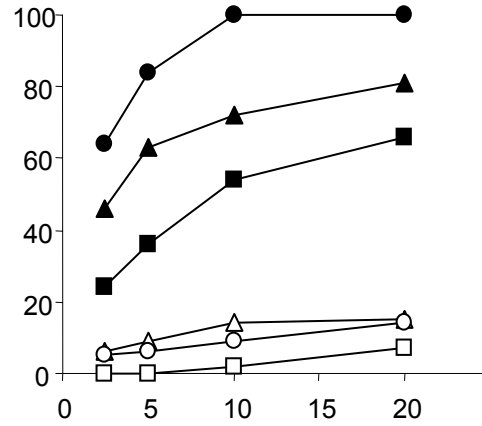
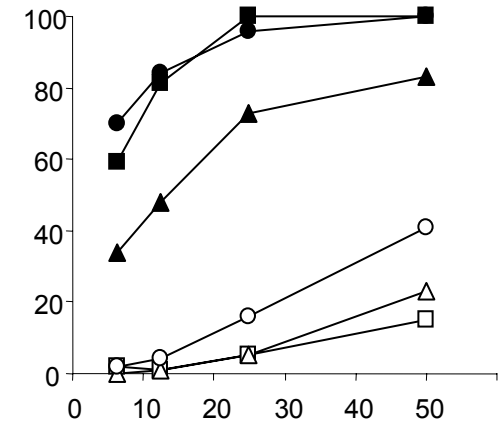
Autoimmune diabetes as a consequence of locally produced interleukin-2

William R. Heath*, **Janette Allison***,
Matthias W. Hoffmann*, **Günther Schönrich†**,
Günter Hämmerling†, **Bernd Arnold†**
& **Jacques F. A. P. Miller*‡**

* The Walter and Eliza Hall Institute of Medical Research, Post Office,
The Royal Melbourne Hospital, Parkville, Victoria 3050, Australia

† Institut für Immunologie und Genetik, Deutsches
Krebsforschungszentrum, Im Neuenheimer Feld 280,
D-6900 Heidelberg 1, Germany

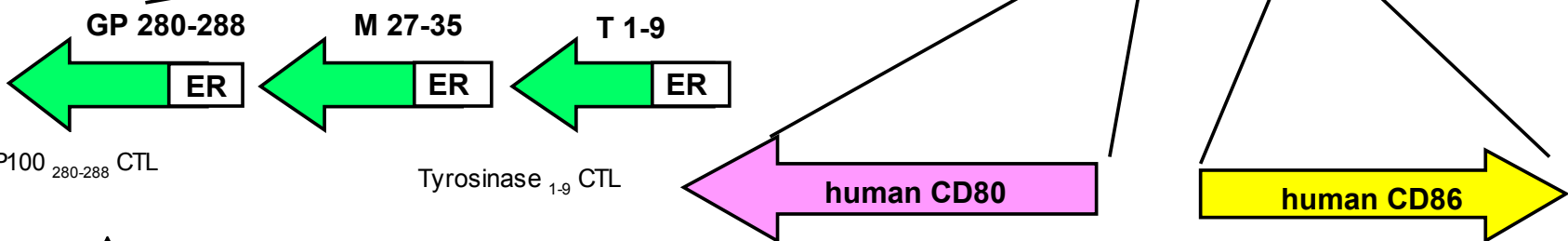
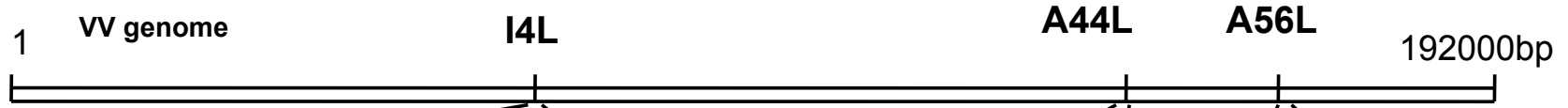
Nature, 1992

A**B****C****Effector : target ratio**

IL-2: squares

IL-7: triangles

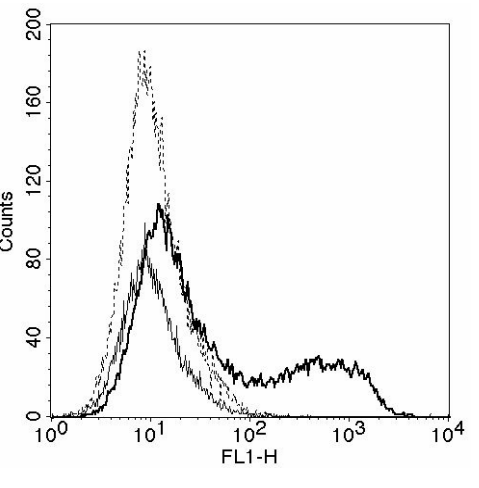
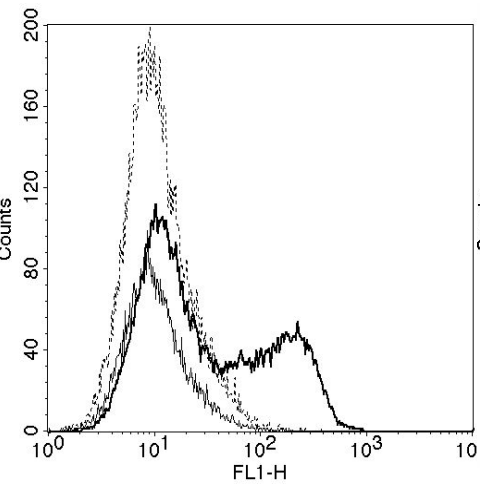
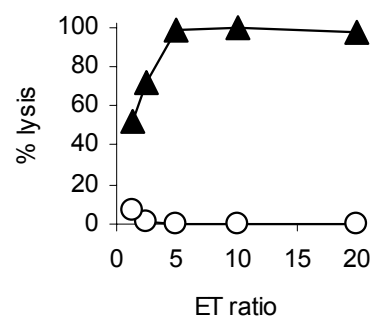
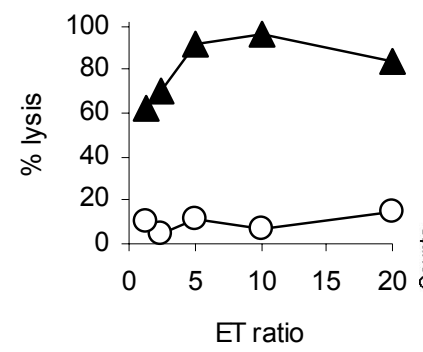
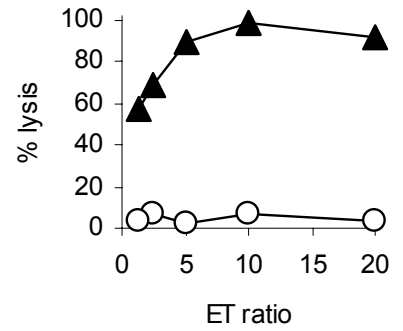
IL-15: circles



GP100₂₈₀₋₂₈₈ CTL

Tyrosinase₁₋₉ CTL

MART-1₂₇₋₃₅ CTL



Quality control: expression of the transgenes

Methods: Immunization schedule

Cycle 1

Cycle 2

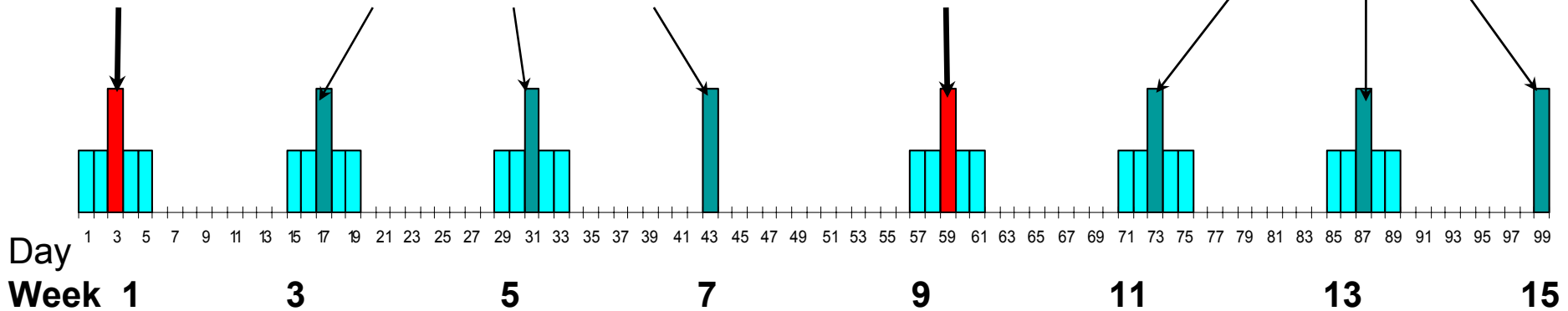
GM-CSF 5ug/kg/day (s.c)

10e7pfu
rec.vv

100ug of each peptide
M₂₇₋₃₅+ Gp₂₈₀₋₂₈₈+T₁₋₉

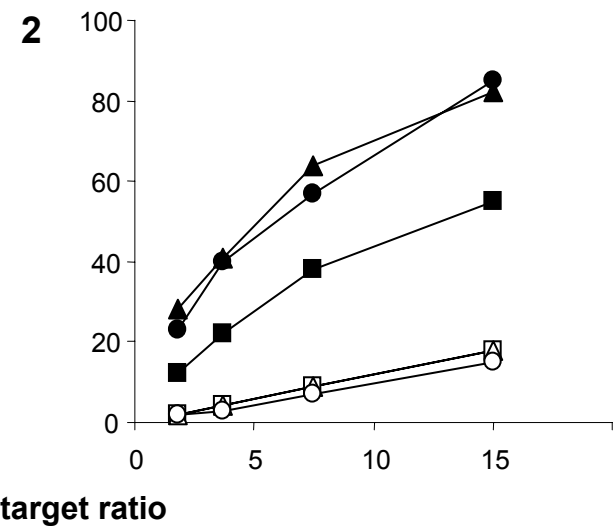
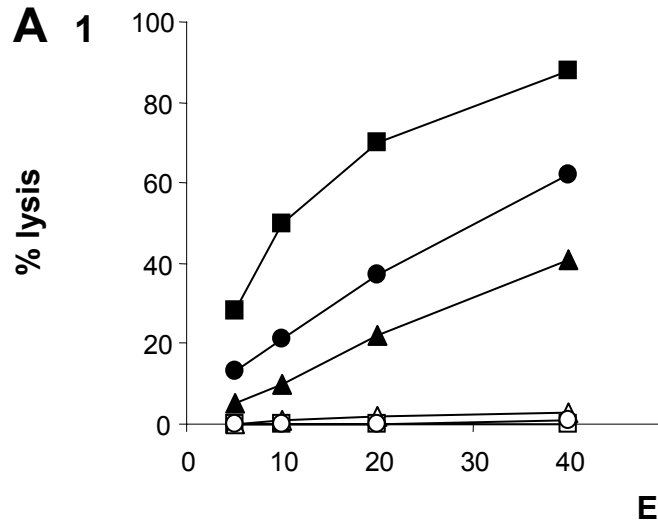
10e8 pfu
rec.vv

100ug of each peptide
M₂₇₋₃₅+ Gp₂₈₀₋₂₈₈+T₁₋₉



before immunization

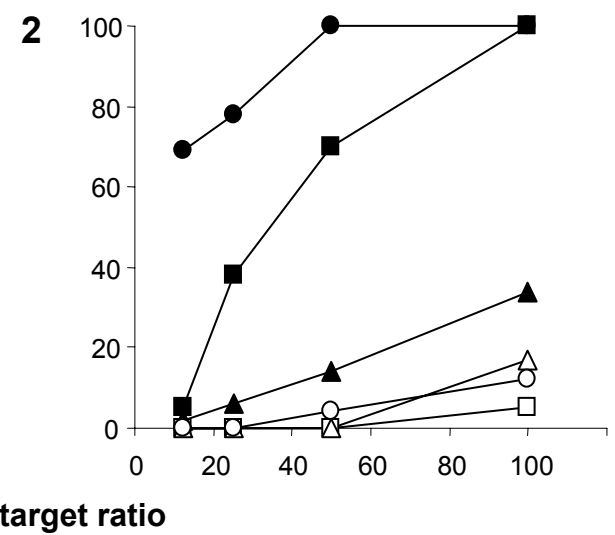
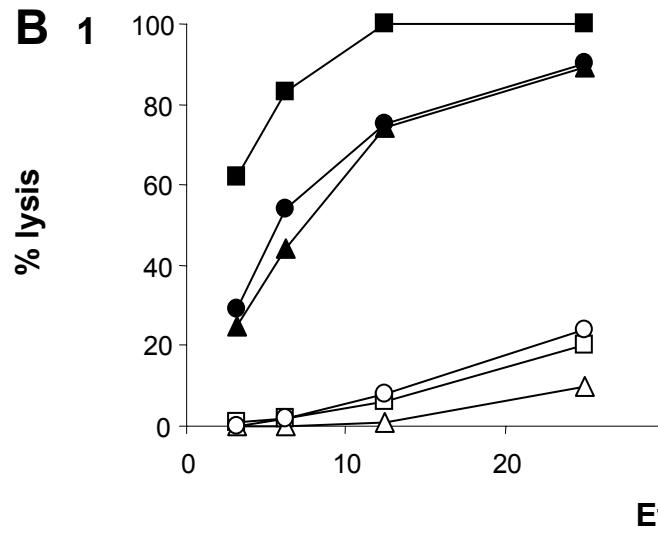
after immunization



IL-2: squares

IL-7: triangles

IL-15: circles



An intense form of homeostatic proliferation of naive CD8⁺ cells driven by IL-2

Jae-Ho Cho,^{1,2} Onur Boyman,^{1,3} Hee-Ok Kim,^{1,2} Bumsuk Hahm,¹
Mark P. Rubinstein,¹ Chris Ramsey,¹ David M. Kim,¹ Charles D. Surh,¹
and Jonathan Sprent²

¹Department of Immunology, The Scripps Research Institute, La Jolla, CA 92037

²Garvan Institute of Medical Research, Darlinghurst, New South Wales 2010, Australia

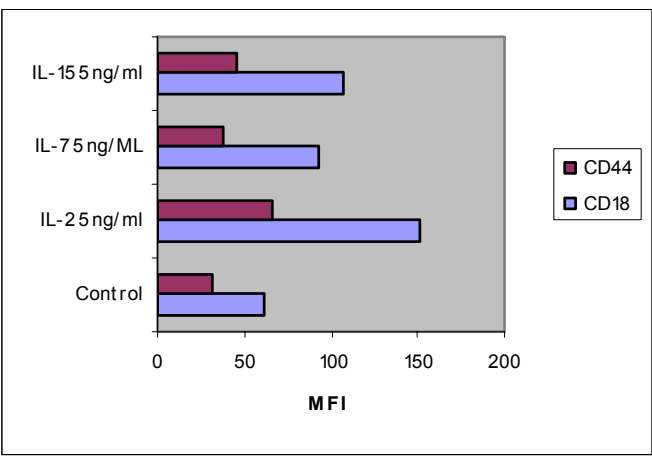
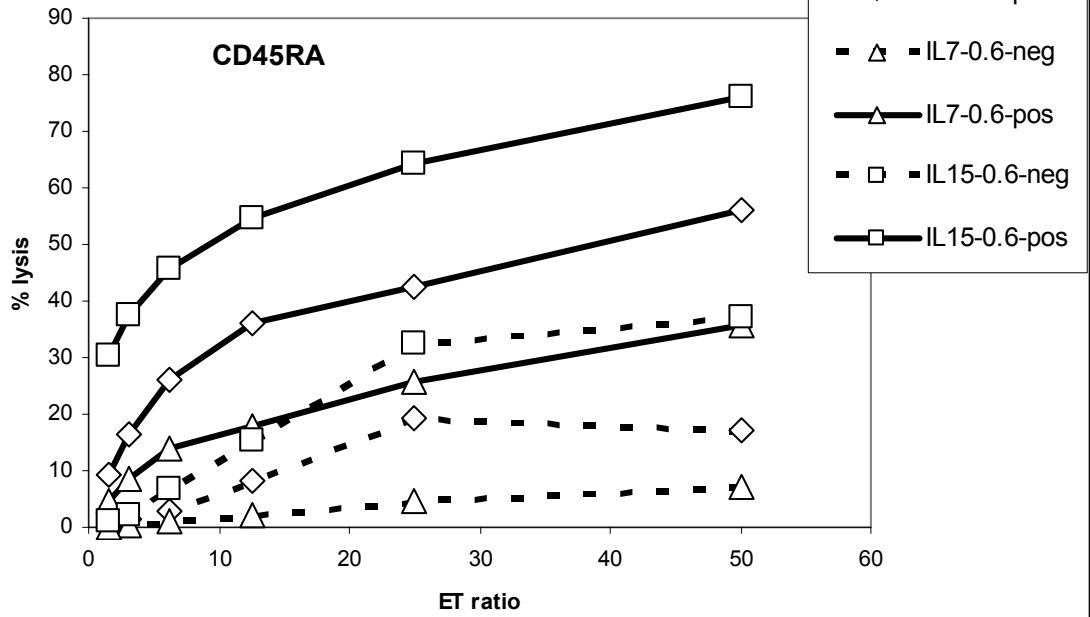
³Division of Immunology and Allergy, University Hospital of Lausanne, Centre Hospitalier Universitaire Vaudois, 1011 Lausanne, Switzerland

Naive CD8⁺ T cells differentiate into protective memory-like cells after IL-2–anti-IL-2 complex treatment in vivo

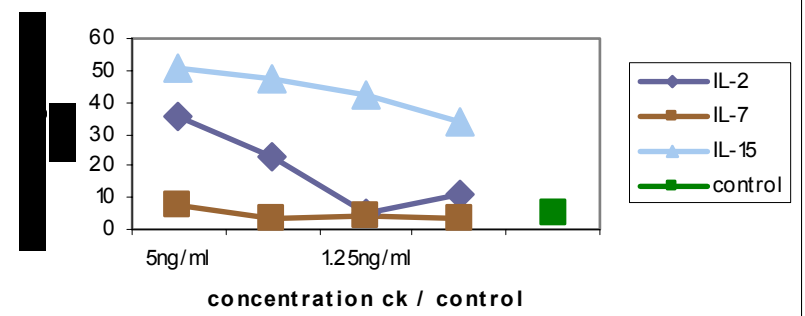
Daisuke Kamimura and Michael J. Bevan

Department of Immunology and Howard Hughes Medical Institute, University of Washington, Seattle, WA 98195

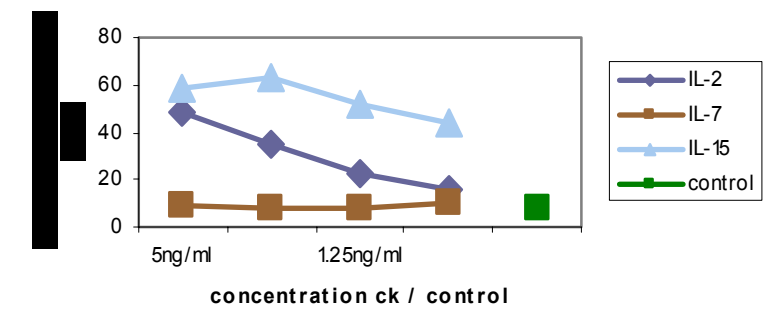
CD45RA



CD45RApos. % Perforin positive cells



CD45RAneg. % Perforin positive cells



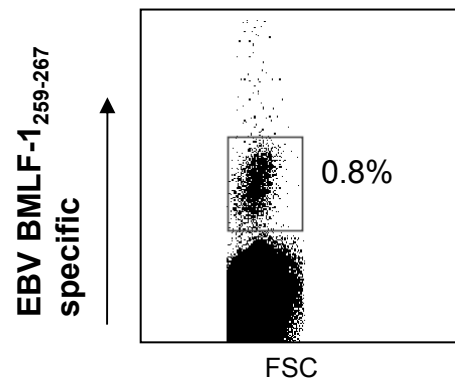
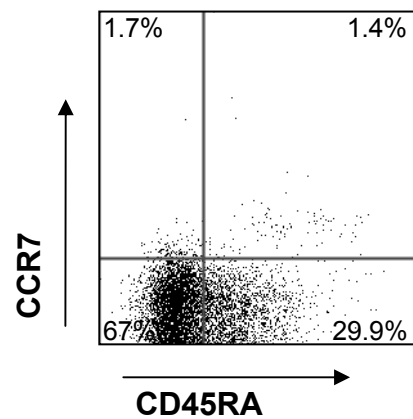
Outlook

- Effects of CK pre-treatment on generation of HLA class I restricted CD8+ T lymphocytes specific for melanoma differentiation TAA other than Melan-A/MART-1 and CTA in cells from healthy donors and from patients bearing melanoma or lung cancers.
- Effects of CK pre-treatment on generation of HLA class II restricted CD4+ T lymphocytes specific for viral antigens or for melanoma differentiation TAA and CTA in cells from healthy donors and from patients bearing melanoma or lung cancers.
- Mechanisms underlying differential responsiveness to antigen specific stimulation in naïve or memory T cell subsets following treatment with α - γ CKs.

Institute for Surgical Research and Hospital Management University of Basel

Daniel Oertli
Walter R. Marti
Martin Bolli
Michel Adamina
Ulrich Güller
Walter P. Weber
Rachel Rosenthal
Franco Gambazzi
Stephan Wyler
Carsten Viehl
Daniel Frey

Michael Heberer
Giulio Spagnoli
Elke Schultz-Thater
Paul Zajac
Maurizio Provenzano
Laura Bracci
Reto Schumacher
Celia Groeper
Chantal Feder
Sourabh Ghosh
Giovanni Sais

A**B****C**