Anne-Marie SCHMITT-VERHUSLT, PhD

Group leader:
Molecular basis of the anti-tumor functions of T cells

Background

1968	B.S. Chemistry at Université Libre de Bruxelles (ULB), Bruxelles, Belgium
1972	Ph.D. Dpt of Molecular Biology, ULB.
1972	Post-doc, Dpt Chemical Immunology, Weizmann Institute of Science, Rehovot, Israel
1974	Visiting fellow, then «Cancer-Expert-NCI», Immunology Branch, NCI, NIH, Bethesda, MD, USA
1978	INSERM tenured position. Head of team, CIML, Marseille
1985	Visiting Scholar, Dpt of Pathology, Stanford Medical School, Stanford, CA, USA
1986	Head of team at CIML; Associate Director of CIML (1990 – 1994)
1998	Visiting Scientist, DNAX, Palo Alto, CA (October – December).
1999	Head of team, CIML.

Membership

Editorial Boards:

- Eur J Immunol (1984 - 2007); Immunogenetics (1982 - 1987);
- Cellular Immunology (1990-1995);
- Chemical Immunology;
- Review Editorial Board of Frontiers in Immunological Tolerance (2010-)

Present committee:

- Scientific committee of Association pour la Recherche sur le Cancer.

Main achievements

Studying the mechanistic basis for MHC-restriction in antigen-recognition by CD8 T cells, we demonstrated that recognition of « modified-self » did not require covalent modification of the MHC molecules (Schmitt-Verhulst et al. 1978).

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The continuing interest of our group in defining the molecular basis for activation of alloantigen reactive CD8 T cells led to the identification of essential early signaling events mediated via the T cell receptor (TCR) in differentiation and in effector function of cytolytic T lymphocytes (CTL) (Truneh et al. 1985 ; Schmitt-Verhulst et al. 1987 ; Poenie et al. 1987) and in sustained maintenance of an effector program (Verdeil et al. 2006).

This interest had led us to develop transgenic mice expressing the TCR of CTL clones allowing us to establish some rules for thymic selection on distinct MHC class I T cell lineages (Curnow, Boyer et al. 1995). It also led us to identify the peptides recognized in association with MHC class I molecules by the TCR of alloreactive CTL clones allowing for the direct demonstration of the contribution of the peptide to the peptide-MHC-TCR interaction in alloreactivity by crystallography with the group of B. Malissen and of its consequence on the differentiation program of CD8 T lymphocytes (Guimezanes et al. 2001; Reiser et al. 2000; Mazza et al. 2007).

A mouse model of inducible melanoma expressing a known tumor antigen was established as a preclinical model of inflammatory melanoma (Soudja et al. 2010).

Selected publications

- Soudja, S.M., M. Wehbe, A. Mas, L. Chasson, C. Powis de Tenbossche, I. Huijbers, B. Van den Eynde, and A.M. Schmitt-Verhulst. 2010. Tumor-initiated inflammation overrides protective adaptive immunity in an induced melanoma model in mice. *Cancer Res* 70:3515-3525.
- Mazza, C., N. Auphan-Anezin, C. Gregoire, A. Guimezanes, C. Kellenberger, A. Roussel, A. Kearney, P.A. van der Merwe, A.M. Schmitt-Verhulst, and B. Malissen. 2007. How much can a T-cell antigen receptor adapt to structurally distinct antigenic peptides? *Embo J* 26:1972-1983.
- Verdeil, G., D. Puthier, C. Nguyen, A.M. Schmitt-Verhulst, and N. Auphan-Anezin. 2006. STAT5 mediated signals sustain a TCR-initiated gene expression program toward differentiation of CD8 T cell effectors. *J Immunol* 176:4834-4842.
- Reiser, J.B., C. Darnault, A. Guimezanes, C. Gregoire, T. Mosser, A.M. Schmitt-Verhulst, J.C. Fontecilla-Camps, B. Malissen, D. Housset, and G. Mazza. 2000. Crystal structure of a T cell receptor bound to an allogeneic MHC molecule. *Nat Immunol* 1:291-297.
- Guimezanes, A., G.A. Barrett-Wilt, P. Gulden-Thompson, J. Shabanowitz, V.H. Engelhard, D.F. Hunt, and A.M. Schmitt-Verhulst. 2001. Identification of endogenous peptides recognized by in vivo or in vitro generated alloreactive cytotoxic T lymphocytes: distinct characteristics correlated with CD8 dependence. *Eur J Immunol* 31:421-432.
- Curnow, S.J., *C. Boyer, M. Buferne, and A.M. Schmitt-Verhulst. 1995. TCR-associated zeta-Fc epsilon RI gamma heterodimers on CD4-CD8- NK1.1+ T cells selected by specific class I MHC antigen. *Immunity* 3:427-438. (* first authors).
- Poenie, M., R.Y. Tsien, and A.M. Schmitt-Verhulst. 1987. Sequential activation and lethal hit measured by [Ca2+]i in individual cytolytic T cells and targets. *Embo J* 6:2223-2232.
- Schmitt-Verhulst, A.M., A. Guimezanes, C. Boyer, M. Poenie, R. Tsien, M. Buferne, C. Hua, and L. Leserman. 1987. Pleiotropic loss of activation pathways in a T-cell receptor alpha-chain deletion variant of a cytolytic T-cell clone. *Nature* 325:628-631.

- Truneh, A., F. Albert, P. Golstein, and A.M. Schmitt-Verhulst. 1985. Early steps of lymphocyte activation bypassed by synergy between calcium ionophores and phorbol ester. *Nature* 313:318-320.
- Schmitt-Verhulst, A.M., C.B. Pettinelli, P.A. Henkart, J.K. Lunney, and G.M. Shearer. 1978. H-2-restricted cytotoxic effectors generated in vitro by the addition of trinitrophenyl-conjugated soluble proteins. *J Exp Med* 147:352-368.