

This Week's Citation Classic®

Moretta L, Webb S R, Grossi C E, Lydyard P M & Cooper M D. Functional analysis of two human T-cell subpopulations: help and suppression of B-cell responses by T cells bearing receptors for IgM or IgG.

J. Exp. Med. 146:184-200, 1977. [Cellular Immunobiology Unit, Lurleen B. Wallace Tumor Inst., Depts. Pediatrics and Microbiology, Univ. Alabama, Birmingham, AL]

This paper describes the first dissection of human T lymphocytes into phenotypically and functionally distinct subpopulations. The finding that peripheral T lymphocytes express either receptors for the Fc portion of IgM or for the Fc portion of IgG made it possible to separate cells exerting helper or suppression functions on antibody production. [The SCI® indicates that this paper has been cited in over 1,300 publications since 1977.]

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This paper represents an extension of studies that were performed in collaboration with Manlio Ferrarini and Maria Cristina Mingari during the period I was a post-doctoral assistant at the Institute of Microbiology, University of Genoa. At that time (1973), several functional capabilities had already been attributed to human T lymphocytes. However, no information was available on whether distinct T-cell subsets could be identified on the basis of expression (or lack thereof) of distinct surface markers. In this regard, we were investigating whether activation of T cells by different means could lead to expression of receptors for the Fc portion of IgG or receptors for C3b on identifiable subsets of cells.

After one year with no substantial success in this area, we made two basic observations, namely, that 5 to 20 percent of freshly drawn peripheral blood T lymphocytes expressed the IgG Fc receptor, while a larger proportion expressed "new" receptors for the Fc portion of IgM.¹ These two classes of

receptors were mutually exclusive and thus defined two distinct subsets (termed T_μ and T_γ) that could be isolated and analyzed for different functional capabilities.² In 1975 Carlo Grossi from the University of Genoa was spending his sabbatical year in the laboratory of Max Cooper at the University of Alabama in Birmingham. After having been made aware of our finding by Grossi, Cooper kindly invited me to spend a few months in his laboratory to undertake collaborative studies. Cooper and his coworkers had recently developed a culture system that allowed the analysis of the regulatory control exerted by T cells on the polyclonal B-cell responses to pokeweed mitogen. Thus, by applying his culture system, it was possible to demonstrate that important immunoregulatory activities such as help and suppression of antibody production were associated with T_μ and T_γ cells, respectively. Certainly, the successful and rapid development of this research was made possible by the joint effort and the enthusiasm of all the coauthors, namely Webb, Grossi, Lydyard, and Cooper.

I believe that our publication has been so highly cited because it allowed the first dissection of different functional capabilities of human T-lymphocyte subsets based on the expression of distinct surface markers. For several years the differential expression of Fc receptors represented the most reliable and the easiest means of identifying human T-cell subsets, and this criterion has been applied extensively in clinical immunology. More recently, other markers, namely, differentiation antigens recognized by monoclonal antibodies, have been utilized widely to define functional subsets of human T lymphocytes.³ In addition, the development in our laboratory of cloning techniques allowing proliferation of virtually 100 percent of human T lymphocytes⁴ has made possible a precise, quantitative analysis of the relationship existing between expression of cell-surface markers and given functional capabilities of human T cells.⁵

1. Moretta L, Ferrarini M, Durante M L & Mingari M C. Expression of a receptor for IgM by human T cells *in vitro*. *Eur. J. Immunol.* 5:565-9, 1975. (Cited 505 times.)
2. Moretta L, Ferrarini M, Mingari M C, Moretta A & Webb S R. Subpopulations of human T cells identified by receptors for immunoglobulins and mitogen responsiveness. *J. Immunology* 117:2171-4, 1976. (Cited 510 times.)
3. Reinherz E L & Schlossman S F. The differentiation and function of human T lymphocytes: a review. *Cell* 19:821-6, 1980.
4. Moretta A, Pantaleo G, Moretta L, Mingari M C & Cerottini J-C. Direct demonstration of the clonogenic potential of every human peripheral blood T cells: clonal analysis of HLA-DR expression and cytolytic activity. *J. Exp. Med.* 157:743-54, 1983.
5. Moretta A, Pantaleo G, Maggi E & Mingari M C. Recent advances in the phenotypic and functional analysis of human T lymphocytes. *Semin. Hematol.* 21:257-69, 1984.