

This Week's Citation Classic

Rosenau W & Moon H D. Lysis of homologous cells by sensitized lymphocytes in tissue culture. *J. Nat. Cancer Inst.* 27:471-83, 1961.

This investigation demonstrated that lymphocytes from one inbred-mouse strain, previously sensitized to cells from another strain with a background of different histocompatibility, would destroy the latter type of cells in tissue culture. The lymphocytes aggregated about the (homologous, allogeneic) target-cells, resulting in marked, progressive cytopathogenic changes, with extensive lysis of the targets. These events occurred without the demonstrable involvement of serum complement or antibody and permitted the direct study of cytolytic cellular immune reactions. [The *SCI*[®] indicates that this paper was cited 385 times in the period 1961-1977.]

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"This work was originally conceived to develop an *in vitro* model for studying cellular immune reactions to examine possible cellular autoimmunity in certain progressive liver diseases. However, having successfully produced an *in vitro* model of cellular immunity, we subsequently abandoned the study of hepatic disorders and turned our attention to details of lymphocyte/target-cell interaction, applying our findings to homograft immunity and additionally to tumor immunity in isogenic animals.

At first this work met with great skepticism, since cellular immunity was not a

popular field in the early '60's — its existence was even doubted by some scientists. Nevertheless, although I was at that time an unknown Assistant Professor, I was able to obtain grant support from the National Institutes of Health to extend this research.

"It was only natural that these earlier experiments with intact cells subsequently led to a search for cytotoxic chemical mediators of lymphocytes, an area pioneered in the late '60's by N. H. Ruddle and B. H. Waksman as well as G. A. Granger and associates. The isolation of highly purified cytotoxin from stimulated human lymphocyte or T-lymphocyte suspensions allowed us to study morphologic and biochemical alterations of target-cell membranes and also biochemical changes occurring within the cell. The role of lymphocyte toxins in cellular immune reactions in the intact organism remains to be conclusively proven, but evidence for their function(s) is increasingly accumulating. Now the field of cellular immunity has become deservedly respectable, and considerable progress has been made on many of its frontiers.

"Reflecting on the courage of the NIH in supporting an unknown Assistant Professor working in an area of then-dubious existence, I find it of interest to relate what recently happened to the same investigator when he tried to strike out into a new field on the basis of what he considered to be promising preliminary data. A majority critique by a granting agency concluded that 'the approach in this application is new and probably unreliable,' although a minority of the reviewers felt that the preliminary findings 'have already exceeded the results of many other studies.'

"How many new and potentially significant concepts are now lost to science because they are presented by an unknown researcher, an investigator unproven in a new field, or because they may be 'ahead-of-their-times'?"