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Claman H N & Chaperon E A. Immunologic complementation between thymus and marrow cells—a model for the two-cell theory of immunocompetence. *Transplant. Rev.* 1:92-113, 1969.
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This paper reviews and expands the idea that antibody production requires both thymus-derived cells (now called T cells) and bone marrow-derived (B) cells. [The *SCI*® indicates that this paper has been cited in over 480 publications since 1969.]

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"In the early-1960s, there was great excitement in immunology. The role of the thymus (one of the last 'mystery' organs in the body) was being unraveled. The work of J.F.A.P. Miller,[1] R.A. Good,[2] and A.J.S. Davies[3] and their colleagues showed that the presence of the thymus was needed for the proper development of the immune system. Nevertheless, it was quite clear that thymus cells themselves did not make antibody *in vivo*. Why not? At the same time, there were data to indicate a 'blood-thymus barrier' so that the failure to make antibody in the thymus might be due to the fact that antigen never got to the thymic lymphocytes. The critical experiments were done in 1965.[4]

"Using the then recently developed methods of cell transfer, we wondered if thymus cells could respond to antigen if they were removed from the thymus and injected (with antigen) into lethally irradiated syngeneic recipients (which had been irradiated to render them nonresponsive). This would bypass the blood-thymus barrier. The results were unequivocal. Normal spleen cells plus sheep rbc antigen given to irradiated mice produced antibody (showing that the spleen has all the necessary immunologic machinery), but transferred thymus cells plus antigen were inert.

"The important experiment involved pure serendipity. We felt that the transferred thymus cells might be either too immature or too 'sluggish' to respond, so we gave the recipients thymus cells and *two* injections of antigen. By the time there might possibly have been a response to the second dose of antigen, the recipients had died (from the radiation). We knew that bone marrow infusions would protect the recipients from irradiation death. When we added syngeneic bone marrow to thymus cells plus antigen, much antibody was made! By adjusting the cell and radiation doses, we showed that neither thymus cells nor bone marrow cells alone would respond to antigen by making antibody, but a *mixture* of both cell types would do so. We hypothesized that bone marrow cells made the antibody while thymus cells acted in some auxiliary fashion. We were unable to prove this, but, as G.F. Mitchell and Miller showed, this was correct.[5]

"I believe that this article has been highly cited for three reasons: (a) It reviews the first experiments showing cell-cell interactions in immunology. This concept has since become crucial in understanding immune responses. (b) It was clearly written and posed a number of simple questions for further research. (c) It appeared in the first volume of a series of publications together with three other articles on similar topics (by Miller and Mitchell,[6] by Davies,[7] and by R.B. Taylor[8]). Each of these papers explored (in different ways) the results of the interaction between antigen and thymus-derived cells.

"The precise nature of T-B cell interaction is still not quite clear. There have been hundreds of experiments, some of which are reviewed in the paper by R.N. Germain and B. Benacerraf."[9]

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2. **Good R A, Dalmasso A P, Martinez C, Archer O K, Pierce J C & Papermaster B W.** The role of the thymus in development of immunological capacity in rabbits and mice. *J. Exp. Med.* 116:773-96, 1962.
3. **Davies A J S, Leuchars E, Wallis V & Koller P C.** The mitotic response of thymus-derived cells to antigenic stimulus. *Transplantation* 4:438-51, 1966.
4. **Claman H N, Chaperon E A & Triplett R F.** Thymus-marrow cell combinations. Synergism in antibody production. *Proc. Soc. Exp. Biol. Med.* 122:1167-71, 1966.
5. **Mitchell G F & Miller J F A P.** Cell to cell interaction in the immune response. II. The source of hemolysin-forming cells in irradiated mice given bone marrow and thymus or thoracic duct lymphocytes. *J. Exp. Med.* 128:821-37, 1968.
6. **Miller J F A P & Mitchell G F.** Thymus and antigen-reactive cells. *Transplant. Rev.* 1:3-42, 1969.
7. **Davies A J S.** The thymus and the cellular basis of immunity. *Transplant. Rev.* 1:43-91, 1969.
8. **Taylor R B.** Cellular cooperation in the antibody response of mice to two serum albumins: specific function of thymus cells. *Transplant. Rev.* 1:114-49, 1969.
9. **Germain R N & Benacerraf B.** Helper and suppressor T cell factors. *Springer Semin. Immunopathol.* 3:93-127, 1980.