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LYMPHSPIRATION

DIRECT CONTACT BETWEEN MACROPHAGES AND PLASMA CELLS IN ANTIBODY PRODUCTION

A. F. Baradi, Ph. D.

Department of Anatomy, University of Otago Medical School, Dunedin, New Zealand

A current, though somewhat oversimplified view on antibody production holds that an antigen is phagocytized by neutrophils that subsequently die and are ingested by macrophages which deliver the antigen to B lymphocytes with the aid of helper T lymphocytes. B lymphocytes, in turn, differentiate into plasma cells which are responsible for synthesis of type-specific antibodies against that antigen (1). In this scheme, direct contact between macrophage and plasma cells is rarely considered (2).

During study of exudative immune peritonitis by transmission electron microscopy, I observed macrophages making direct contact with plasma cells through pseudopodia (Fig. 1A) and also by cytoplasmic continuity (Fig. 1B).

Exudative immune peritonitis was induced in mice by three intraperitoneal injections, one week apart, of 2mg bovine serum albumin in 0.5ml Freund's adjuvant. This antigen-adjuvant mixture produced large volumes of ascitic fluid rich in specific antibodies (3). Overt ascites was detectable on the average, 19 days after the third injection. Mice developed marked abdominal distention and yielded from 7 to 12ml of peritoneal fluid. Ascitic fluid was tested for antibody content by the ring method using a saline solution of the corresponding antigen containing 0.1mg/ml (3).

Foci of plasma cells appeared in the subserosal connective tissue approximately one week after the third injection, but inflammatory cells were mobilized much earlier in the peritoneal fluid and adjacent connective tissue. Peritoneal lining (mesothelial) cells retracted and separated thereby creating large gaps (stomata), measuring up to 8μ in width between cells. These gaps permitted direct communication between the peritoneal fluid and adjacent tissue.

The validity of the proposal that macrophages somehow establish direct contact with plasma cells during antibody production depends upon proper identification of both types of cells in ultrathin sections viewed by transmission electron microscopy. Cytological features of cells labeled macrophages and plasma cells in the electron micrographs presented here, leave little doubt as to the correct identity of these two cell types.

Whereas lymphocytes inhabit peritoneal fluid and adjacent connective tissue, plasma cells are not characteristically seen unless antibodies are being produced (4). Although the physiologic significance of plasma cell contact with macrophages has not been clarified, the observation in the setting of exudative immune peritonitis suggests a heretofore unrecognized immunoreactive role for circulating macrophages.

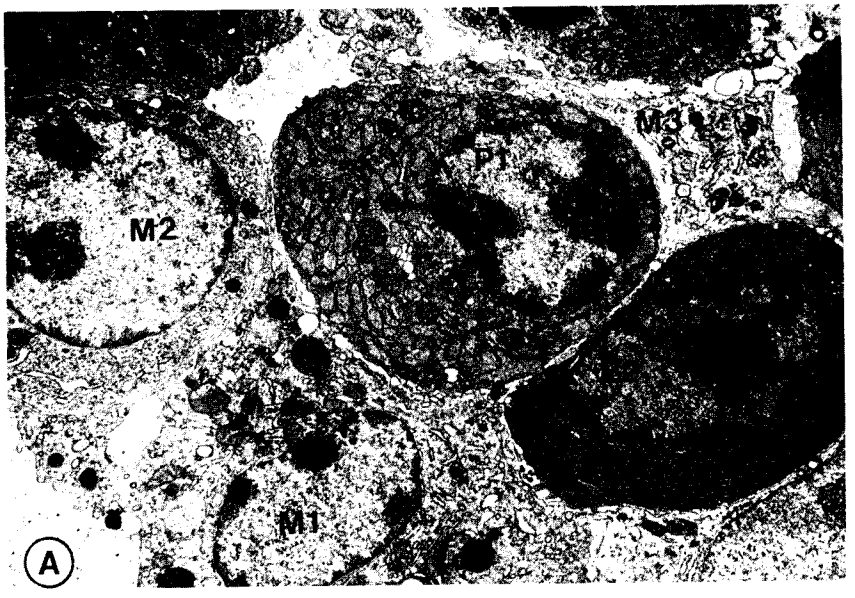

Fig. 1: A. Pseudopodia of a macrophage (M1) making several contacts with a plasma cell (P1) and, to a lesser extent, with another plasma cell (P2). A second macrophage (M2) seems also to be in contact with a plasma cell (P1). A third macrophage (M3) (which is barely seen in the top right corner of the picture) partially encircles a plasma cell (P1). Magnification x 5000.

B. A higher magnification of part of Fig. 1. Five arrows show point of contact (probably cytoplasmic continuity) between macrophage (M1) and a plasma cell (P1). Magnification x 10,000.

EDITORIAL COMMENT

An interesting observation that further suggests cooperative rather than independent immunologic function among circulating peripheral blood and tissue elements. The macrophage may yet turn out to be the most ubiquitous and underestimated white cell in disorders as diverse as fever, multiple sclerosis, regional ileitis, and lymphedema. (CLW)

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