toxic T cells (reactive to H-2 antigens) by the use of anti-Ia antiserum, which lyses the former, and also by anti-Ly-1.1, which lyses cytotoxic cells of the CBA strain. On the other hand, the precursors of suppressor cells are usually not lysed by anti-Ia antiserum[11], and thus the two cell types could still be closely related.

It is now clear, however, that the Ly-1 and Ly-2 populations belong to different lines of differentiation and are not sequential stages in a single lineage[12]. Cantor and his colleagues have shown that mice depleted of T cells (thymectomised, irradiated and bone-marrow-reconstituted mice or "B mice") and repopulated with Ly-1 T cells only were not able to perform any of the functions of Ly-2,3 cells, even many months later; and conversely "B mice" repopulated with Ly-2,3 cells could express cytotoxicity and suppression, but not other T cell functions.

There is great interest in the role of the major histocompatibility complex (MHC) in immune responses. One aspect which has attracted attention is the prohibition of cell interactions across allogeneic barriers where MHC differences are involved. This has been reported for T-B interactions by Katz and colleagues[13], for T-macrophage interactions by Rosenthal and Shevach[14] and Erb and Feldmann[15], and for T cell killing, by Zinkernagel, Blanden and Doherty[16]. Several explanations have been suggested for these restrictions. One is that a molecule controlled by the MHC must be "shared" or recognised for successful interactions to occur[13]. An alternative suggestion is that mixing histoincompatible cells may induce active suppression[9,17]. D. H. Katz (Harvard University), for example, found that suppressor cells are induced when $F_1$ thymocytes are primed in an irradiated parental mouse. These suppressor cells may explain the genetic restrictions on T-B collaboration found in earlier experiments[13]. Support for this possibility was discussed by H. Cantor and R. K. Gershon (Yale University) who have shown that removal of Ly-2,3 cell populations (which contain suppressor cells) permits the residual T cells to collaborate with histoincompatible B cells in the primary response *in vitro* to sheep red cells. Independently, Dutton and his colleagues[17] have obtained similar results using anti-Ly antisera and cell separation techniques, indicating that allogeneic effects can suppress interactions between histoincompatible T and B cells. Thus, there is no doubt that suppression explains some examples of the failure of histoincompatible T and B cells to interact. Whether all such failures can be attributed to suppression is not yet clear.

# EGF and viral transformation

*from Robin A. Weiss*

EPIDERMAL growth factor (EGF) was discovered by Stanley Cohen (*J. biol. Chem.*, **237**, 1555; 1962) when he was purifying nerve growth factor from the submaxillary salivary gland of male mice. Cohen noted that the factor stimulated the proliferation and differentiation of the epidermis, as reflected by precocious opening of the eyelids and eruption of the incisors in baby mice. Since that time it has been Cohen's remarkable achievement to purify and sequence murine EGF (Cohen and Savage, *Recent Progress in Hormone Research*, **30**, 551; 1974). It is a single-chain polypeptide containing 53 amino-acid residues with a molecular weight of 6,045. The molecule has been well conserved during evolution and human EGF extracted from urine shows only minor differences in amino-acid sequence to murine EGF. Recently it has become evident that EGF will stimulate proliferation of a variety of both epithelial and fibroblastic cells in culture. Its specific mitogenic action on non-proliferating cells in culture provides a much more convenient and quantitative assay than examining eyelid opening *in vivo*.

Last year Cohen's group showed that cells in culture which respond to the mitogenic action of EGF possess specific receptors for EGF on the cell surface (Carpenter, Lembach, Morrison and Cohen, *J. biol Chem.*, **250**, 4297; 1975). EGF receptors were assayed by measuring the binding of $^{125}$I-labelled EGF to the cell surface. Cells of many species bound EGF, but certain types, including a human lymphoblastoid line (NC-37) and rat cells transformed by mouse sarcoma virus (KNRK) and by Rous sarcoma virus (XC) apparently lacked EGF receptors. Reduction in the binding of other hormones to transformed cells has also been reported, for example, in a recent study of insulin receptors on BALB/3T3 cells by Thomopoulous, Roth, Lovelace and Pastan (*Cell*, **8**, 417; 1976). The binding of insulin varied with the level of proliferation in cell population and the reduction seen in transformed clones was not specific to the transforming agent. However, the presence of EGF receptors appears to be more specific. In this issue of *Nature* (page 26), Cohen, in collaboration with Todaro and De Larco, reports additional data on the binding of EGF to the same cell types transformed by different tumour viruses. For example, the A31 clone of mouse BALB/3T3 cells was transformed by SV40, two strains of mouse sarcoma virus (MSV) and Rous sarcoma virus (RSV). Only the MSV-transformed subclones failed to bind EGF. This remarkable specificity of binding was true for transformed subclones of other types of cell such as Swiss 3T3, NRK and Mink lung. In each case, only the subclones transformed by MSV or by feline sarcoma virus failed to bind EGF.

Solely on the basis of the specific failure to bind EGF, the authors postulate that MSV might transform cells by coding for an EGF-like molecule in part of its sarcoma-specific genetic sequences. This EGF analogue would then block the receptors and stimulate the cells to grow. This will hardly provide the whole explanation of viral oncogenesis, but it can be tested.

It now seems clear from the reports of several workers that suppression is mediated by products of the I region. T cell suppression in mice, for example, is mediated by an antigen-specific T cell factor with a molecular weight of about 50,000 and which does not operate across H-2 barriers[18,19] (T. Tada, Chiba University). This factor is absorbed by antisera reactive to products of the I-J subregion, which also seems to code for the receptor for the suppressive factor. The cells carrying the receptors (sometimes known in this context as acceptors) were found not to be helper T cells, but nylon-wool-adherent T cells which could be killed by anti-I-J serum and complement[18,19]. Allotype specific suppressor T cells can also be killed by antiserum containing antibody to I-J region products[20-22] (L. Herzenberg and D. B. Murphy, Stanford University).

Two generalisations seem to be possible on the basis of this and other work. First, that the I region is functionally specialised, the I-J subregion being involved in suppression and the I-A subregion in macrophage or T-cell helper functions. Second, the products of the I region act on target cells through receptors controlled by the same I subregion[23,24].

M. Taniguchi (Chiba University) discussed studies performed with Tada on a factor obtained from lysed antigen-primed spleen or thymus cells which augmented IgG antibody responses, provided that factor donor and recipient (in culture) were identical in the I-A region. This factor seems to be different from the helper factor described by

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