causing a 1.5-fold increase at 11.7 µg/ml. The monoclonal antibodies do not stimulate the purified NTPase, which suggests that another part of the translocation system is affected. Preliminary Scatchard plots have suggested an increased affinity for poly(A) in the presence of these monoclonal antibodies; it is therefore possible that they stimulate the NTPase in situ by stimulating dephosphorylation of the mRNA binding site.

Fig. 1(b) shows that the NTPase is inhibited by up to 50% by PMA. This is consistent with the view that the protein kinase involved in translocation is protein kinase C. Moreover, when poly(A) was added with the PMA, the inhibition of the NTPase was partially relieved as would be predicted from the current translocation model. These findings may be relevant to the increased rate of translocation seen in carcinogenesis (Clawson et al., 1984).

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Liposomes formed from polymerizable diacetylenic phospholipids and their potential as drug delivery systems

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Encapsulation of a drug within a liposome provides the potential for a controlled drug delivery system, whereby the drug can be released systemically in a sustained, time-dependent manner, or targeted to a specific site by attachment of a ligand to the liposomal surface (Juliano & Layton, 1980). A major constraint in the application of conventional liposomes as pharmacological carriers is the inherent physical and chemical instability of phospholipid membranes. In an effort to produce synthetic membranes of improved stability, many investigators have developed phospholipid analogues, containing polymerizable moieties in their acyl chains (Johnston et al., 1980, Regen et al., 1982). Here we report on the permeability characteristics of liposomes formed from polymerizable phospholipids containing diacetylenic groups in one or both acyl chains (Fig. 1a) (Johnston et al., 1983), to determine whether these novel membranes may find an application as drug delivery systems. Diacetylenic phospholipids form crystalline polymers upon irradiation with ultraviolet light. Clotting studies have shown that the vesicles retained their morphological structure after polymerization. C, idPC is atypical, forming irregular shaped monomorphic and polymeric vesicles (Leaver et al., 1983).

Rate constants of carboxyfluorescein leakage from C, idPC liposomes showed that polymerization affected a decrease in permeability at both 21 and 37°C. This effect was most pronounced at 21°C, with monomorphic and polymeric liposomes experiencing losses in latency of 18.5 and 4.6%, respectively, over 24 h. Liposomes formed from C, idPC, C, idPC, C, idPC or C, idPC, conversely, were found to be more permeable as a result of polymerization. In the latter instances, increases in permeability were attributed largely to disturbances in the packing of lipid molecules, the limited ability of small unilamellar vesicles to accommodate long polymers, and the extent of polymerization. The stability of liposomes in vivo is affected not only by their structural characteristics, but also by contact with the biological environment. Plasma high density lipoproteins (HDL) remove phospholipid from conventional liposome membranes, resulting in an accelerated release of entrapped solutes (Damen et al., 1981). The permeability of diacetylenic C, idPC liposomes, in their monomorphic and polymeric states, was investigated in the presence of human plasma, according to Kirby et al. (1980). Polymerization of C, idPC liposomes markedly decreased in their permeability in plasma at both 21 and 37°C. The permeability of C, idPC monomorphic liposomes was significantly greater in the presence of plasma, suggesting some HDL-mediated release of entrapped carboxyfluorescein. These data suggest that polymerization of C, idPC liposomes increases their resistance to the destructive actions of plasma HDL.

The permeability of C, idPC liposomes was also investigated by the release of [3H]insulin. C, idPC liposomes exhibited low permeabilities to insulin in both their monomorphic and polymeric states at 21 and 37°C. The large molec-
Polymerization of diacetylenic phospholipids and the permeability of C2-idPC liposomes to inulin in the presence of plasma

(a) Polymerization of diacetylenic phospholipids. Ultraviolet irradiation converts the monomer to a triple-bonded and double-bonded conjugate structure. The number of methylene groups between the methyl terminus and the diacetylenic group, n, can be altered to produce monomers of different chain length and phase transition. Diacetylenic lipids can be synthesized as either (A) mixed-chain lipids or (B) identical-chain lipids. (b) Dependence of inulin retention on time for C2-idPC liposomes, in their monomeric (○) and polymeric (●) states, incubated with fresh human plasma at a ratio of 1:5 according to the method described by Kirby et al. (1980).