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Short Communication

A Possible Mechanism for Cell to Cell Interaction Involving Phosphoryl Group Transfer at the Cell Surface

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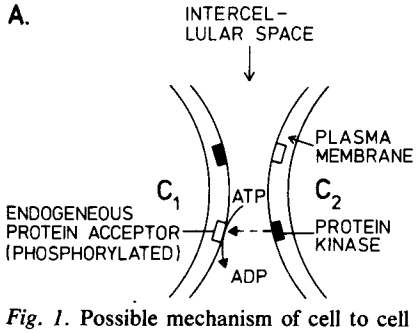
Some of the ATP formation of the cell takes place in the plasma membrane (10, 11, 14, 15, 17, 18, 19, 22, 23). Part of this membrane-bound activity is localized to the outer surface of the membrane (1, 2, 3, 16). A prerequisite condition for surface-located ATP synthesis to occur is the presence of all necessary substrates and cofactors in the external medium provided albumin is also included in the incubation medium as a membrane "stabilizer" (5).

However, we have found that if the albumin concentration of the incubation medium is below a critical concentration or totally omitted, ATP formation can occur at the cell surface also when one of the necessary cofactors is excluded from the incubation medium (9, 23). The critical albumin concentration in this connection seems to be around 0.1%. Thus, we have reasons to conclude that an intramembranous metabolic pool exists (9).

Protein kinase (ATP: protein phosphotransferase, E.C. 2.7.1.37) has also been established to be associated with the plasma membrane of different cells (4, 6, 8, 12, 13, 20, 21). At least part of this plasma membrane activity is located at the external surface of the plasma membrane (20). An endogenous surface-located acceptor protein for the terminal phosphoryl group of ATP has also been reported (6, 8, 12).

Furthermore, the endogenous protein kinase of the membrane surface can catalyse the transfer of the terminal phosphoryl group of ATP into extrinsic acceptor proteins (7, 20). The acceptor proteins used were histone and phosvitin. The molecular weights of the two proteins are about the same but the former has a nettopositive charge while the latter has a nettonegative one. Under the experimental conditions used, histone was a poor acceptor while phosvitin was readily phosphorylated. The phosphorylation was not further stimulated by cyclic AMP.

It is well known that practically all animal cells have a nettonegative surface charge. These results suggest a model for cell to cell interaction. Fig. 1



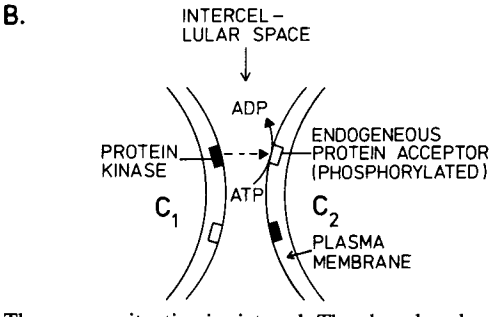


Fig. 1. Possible mechanism of cell to cell interaction by phosphoryl group transfer. *A*, The terminal phosphoryl group of ATP is transferred into the endogenous protein acceptor at the surface of one cell, C_1 by means of the protein kinase at the cell surface of an adjacent cell, C_2. *B*, The reverse situation is pictured. The phosphoryl group of ATP, which is available at the cell surface or in the intercellular space, is transferred into the endogenous protein of C_2 by means of the enzyme at the cell surface of C_1.

illustrates the model. Protein kinase at the surface of one cell (Fig. 1*A*) may catalyse the phosphorylation of the endogenous acceptor protein of the surface membrane of another cell using the ATP regenerating capacity of the outer part of the membrane as phosphoryl group donor (1, 3, 9). The albumin concentration in the intercellular space of the brain parenchyma *in vivo* and perhaps of other tissues might be around 0.1% or less, which may make available at the surface the necessary cofactors from the endogenous intramembranous metabolic pool (9). This type of phosphorylation might well represent a type of regulatory function (8) where two cells in a reciprocal way can influence each other (Fig. 1*A* and *B*).

We may discern another superior principle for the overall metabolic regulation of cells constituted in a multicellular organism. This principle could be exerted at the cell membrane autonomously of the genome.

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