Hypothesis

LECTINS AS MEMBRANE COMPONENTS: IMPLICATIONS OF LECTIN–RECEPTOR INTERACTION

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Received 8 March 1979

1. Introduction

There is increasing evidence that carbohydrate-containing components of cellular membranes play a role in recognition phenomena. Attention has centred on glycoproteins and glycolipids as cell membrane receptors for extracellular signals [1,2]. Although it is implied that these glycosylated species function in the transmission of signals across the surface membrane, the exact nature of this transmission and the means by which it influences cellular events is little understood [3]. Many investigations have shown that carbohydrate-binding proteins (lectins) are located within a wide variety of cells and membranes (reviews [4–6]). These results have raised the possibility that endogenous lectins could be involved in cellular communication. It would like to develop this suggestion further and put forward a model in which an underlying principle governing recognition events both between cells and within cells is the specific interaction of a membrane-bound lectin with its receptor.

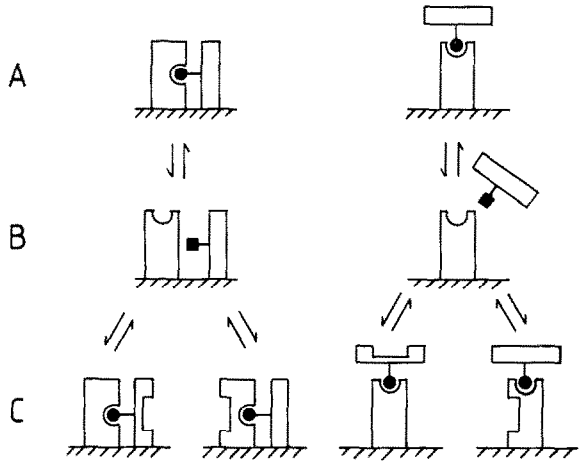

Fig.1. The reversible formation of a lectin–receptor complex can be used to regulate carbohydrate-binding activity and enzymatic activity. (A) The interaction of a lectin with endogenous receptors neutralizes its activity. (B) Modification of the receptor causes disruption of the pair complex and activation of the lectin. (C) Lectin–receptor complex formation causes an allosteric change in either partner that can be used to modulate enzymatic activity.

2. Parameter of the model

In the model as shown in fig.1, the lectin is a protein which exhibits specific, reversible carbohydrate-binding activity and can be either monovalent or multivalent. The receptor is the passive partner in the interaction and may be either a glycoprotein or glycolipid. The lectin is membrane-bound but the receptor(s) may be either membrane-bound or soluble. The carbohydrate-binding site of membrane lectins is always directed towards non-cytoplasmic surfaces of the membrane, that is, towards the lumen of the intracellular membrane system or towards the exterior of the cell. This directionality is dictated by the assymetric glycosylation of both the internal and surface membranes of the cell [7,8]. If the lectin and receptor are bound to the same membrane, it can be envisaged that the two interact in the plane of the membrane and exist as a 'self-neutralized pair complex'. The formation, maintenance and destruction of

this complex can be a means of regulation of the lectin activity Moreover, this interaction of a lectin with its receptor can be used not only to regulate the carbohydrate-binding potential of the lectin, but also other biochemical activities of either member of the pair The interaction of the lectin and receptor and modulation of pair complexes can occur both at the cell surface and within the cell

3 Cell surface interactions

When the interaction takes place at the plasma membrane, two main states can occur either the complementary pairs are 'closed', a state in which the cell surface copies of lectin and receptor are in self-neutralized complexes or alternatively, the pairs are 'open' and not complexed A lectin can be in a surface membrane throughout the cell cycle or developmental sequence either in an active (open) or inactive (closed) state Activation, visualized as the 'opening' of the endogenous pair complex, enables the cell to redirect the carbohydrate-binding activity towards the extracellular environment Regulation could occur by changes in the lectin-specific sugar residues on receptor molecules, which in turn are regulated by glycosyl transferases, glycosidases or proteases In this instance, the regulatory partner of the complex is the receptor, although modification of the sugars on the receptor molecule may be effected by more than one mechanism

The erythrocyte is an example of a cell type in which complementary pairs may be 'closed' in the surface membrane Glycophorin exhibits lectin activity which can only be expressed in a test assay if the lectin is separated from endogenous receptors by purification [9] It is likely that once the pair complex is formed in the erythrocyte membrane it is maintained However, platelets and lymphocytes are cell types in which the pair complex may be disrupted and the carbohydrate binding activity of the lectin utilized in physiological processes [10–12] For example, the process of haemostasis may involve the disruption of an endogenous complex, existent in plasma membranes of freely-circulating platelets, and the redirecting of lectin activity towards the extracellular space

However, the regulation of carbohydrate-binding potential is only one feature of the functional significance of pair-complexes An additional feature is that the complex may be used to regulate enzymatic activity In this instance, one would predict that the enzymatic activity would be affected by the glycosylated species that the lectin can recognize A recent finding that a surface-localized enzyme of *Limonium* can be stimulated by *N*-acetylgalactosamine provides support for this prediction [13] Theoretically, either the lectin or the receptor can possess the separate enzymatic activity in *Limonium* the lectin has been shown to be the enzyme Therefore, the regulatory partner must be the receptor and modulation of enzymatic activity may well be achieved by reversible binding of the lectin to the receptor molecule

4 Intracellular interactions

Lectin–receptor complexes also occur within cells lectins are components of intracellular membranes and have been found in isolated fractions of endoplasmic reticulum, Golgi apparatus, lysosomes and mitochondria [14–16]

A central problem associated with intracellular synthesis and transport of enzymes is regulation This regulation involves both the control of segregation to specific loci in the cell and the control of enzymatic activation Lectin–receptor complexes could form an ideal vehicle for such regulation In this respect, all the lysosomal enzymes so far investigated are glycosylated The carbohydrate moiety of the enzymes has been implicated to function in their segregation from the site of synthesis in the endoplasmic reticulum to the site of utilization in the lysosome [17,18]. Recently, carbohydrate-binding components of the surface and internal membranes that can recognize the enzymes have been demonstrated [19] Thus, candidates for complex formation are available If the complexes are involved in intracellular regulation, one would predict that alteration in sugar composition of the enzymes would lead to malfunctions, either in intracellular transport or enzymatic activation In these examples, unlike that of *Limonium*, the regulatory partner of the complex would be the membrane lectin

The basic feature of this model for lectin function lies in the emphasis on the interaction of lectins with

their endogenous glycosylated receptor molecules. This reversible interaction and the consequent formation and destruction of pair complexes provides the cell with a rapid and efficient means of regulation.

Acknowledgements

I would like to thank Colin Hughes and Martin Raff for their critical reading of the manuscript, and members of EMBL for many helpful discussions.

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