Synthetic membrane biology:
Reconstitution of cellular processes on artificial membrane systems

Specific interactions of lectins with glycosphingolipids lead to tubular plasma membrane invaginations and cellular uptake of pathogens and pathogenic products

Each cell produces a distinct array of cell surface glycans that carries rich structural information unique to that cell. It is not surprising that multiple carbohydrate-binding proteins ("lectins") have evolved to use glycans as receptors to mediate cell surface biology. Different pathogens or pathogenic factors, like simian virus 40 and polyoma virus, cholera and Shiga toxins, also exploit host cell plasma membrane glycans to enter and infect cells. After binding to the glycosphingolipids GM1, GD1a and Gb3, respectively, these molecules enter cells via endocytic routes that do not involve the elaborate network of clathrin.

These bacterial toxins and animal viruses can induce tubular plasma membrane invaginations without the help of the cytosolic protein machinery through the dynamic construction of protein-lipid nanodomains whose intrinsic properties lead to membrane bending and invagination. Depletion of cellular energy or direct inhibition of dynamin or actin function on cells allow to uncouple membrane invagination from the subsequent scission step suggesting that cellular factors are required not for the formation of the invaginations, but for their processing. The formation of deep membrane invaginations and tubules occurs not only in the plasma membrane of cells, but can also be reconstituted in giant unilamellar vesicles. These studies have uncovered a previously unknown mechanism for generating negative membrane curvature, and they have created a new paradigm that allows conceptualizing why endocytic coats are not detected at many sites of clathrin-independent endocytosis.

Lectin-induced tubular membrane invaginations are poised in a membrane environment whose lipid and protein composition supports domain formation. The scission of these plasma membrane invaginations is preceded by cholesterol-dependent membrane reorganization, and correlates with the formation of membrane domains on model membranes, suggesting that domain boundary forces are driving tubule membrane constriction. Actin triggers scission by inducing such membrane reorganization processes that may function independently from or in synergy with pinchase activity.

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