CHAPTER - 1

INTRODUCTION
It is well established that surface oligosaccharides play a vital role in a variety of cell functions such as cell differentiation and cell regulation, membrane transport, secretion of proteins, as receptors for enzymes, hormones, toxins and lectins (Montreuil, 1980). Increasing evidence tends to suggest that many viruses (Dimmock, 1982), bacteria (Jones and Isaacson, 1983), bacterial toxins (Eidels et al., 1983) and protozoa (Inge et al., 1988) specifically recognize and bind to cell surface carbohydrates and this interaction is necessary to cause an infection or produce a toxic effect.

The digestion of food is completed in the small intestine and its hydrolytic products are absorbed into the blood stream. The complex nutrients are progressively degraded into simpler compounds by enzymes present in the intestinal lumen. The absorption of these simple compounds is carried out by mucosa of the small intestine, which projects into the lumen to form finger-like or tongue-shaped structures called villi. In between the villi are depressions called crypts. A single layer of epithelial cells covers the villi. On the luminal side, enterocytes are lined with a characteristic brush border consisting of microvilli. The microvillus membrane (MVM) covering the microvilli is a mosaic of structural and functional proteins intercalated in lipid bilayer. Chemically, proteins, lipids and carbohydrates comprise 60%, 30% and 10%, respectively of the membrane constituents on dry weight basis (Kenny and Booth, 1978). Among lipids, the molar ratio between cholesterol, phospholipids and glycolipids is 1:1:2 in rats (Forstner et al., 1968) and 1:1:1 in mice (Kawai et al., 1974). At least seven
monosaccharides have been identified in MVM glycopeptides and glycolipids (Kim and Perdomo, 1974). The saccharidic structures of the enterocytes are believed to be implicated in receptor-mediated endocytosis and in the adhesion of microorganisms to epithelial surface in intestine (Kim et al., 1984).

It is likely that alterations in glycosylation of microvillus surface may influence the expression of receptors for regulation of cell growth and differentiation and for colonization of luminal pathogens in the small intestine. Conversely, the glycosylation processes could possibly be influenced by intestinal microflora. Observations on conventionalized mice compared to germ-free mice have shown that the synthesis of sugar chains in MVM-associated glycoproteins is affected by the introduction of intestinal microorganisms and that fucosyltransferase activity is modified (Umesaki et al., 1982). All the evidence points to an important role of glycosylation in receptor-ligand interactions on the cell surface.

The regulatory mechanisms and environmental influences can help us to understand better the pathophysiology of selected gastrointestinal diseases. The clinical disorders in which the intestinal epithelium histologically appears normal, may in reality possess deranged oligosaccharide structures on the microvillus surface. In fact, aberrated glycosylation pattern has been demonstrated in sucrase-isomaltase deficiency (Lloyd and Olsen, 1987; Trugnan et al., 1987), cystic fibrosis (Dische et al., 1959) and chronic inflammatory bowel disease (Neutra and Forstner, 1987). The detection of such abnormal
oligosaccharide structures by usual histological techniques may not be feasible.

Carbohydrates, fats and proteins in diet are three major sources of energy. Intake of these constituents below minimum requirements results in deficiency disorders. Excessive consumption of these nutrients may also be harmful because toxic symptoms develop when safe levels of these are surpassed. Malnutrition is an important environmental condition that affects gastrointestinal functions. Alterations in nutritional regimen and nutritional stress have been shown to affect the normal functioning of the adult intestine (Firmansyah et al., 1989). The adaptive changes in brush border enzymes to dietary manipulations include those of disaccharidases and peptidases in response to the changes in carbohydrate and protein contents of the diet, respectively (McCarthy et al., 1980). Changes in dietary fat content affect intestinal enzymes as well as MVM lipid composition (Brasitus et al., 1985). In addition, intestinal glycosyltransferase activities have been found to be altered by quality as well as quantity of the diet (Biol et al., 1984; 1987a; 1991). Recently, surface carbohydrates in suckling rats nursed on lactating mothers subjected to dietary manipulations have also been found to be modified (Babbar et al., 1990; Jaswal et al., 1990b). However, there is no report on the effect of such dietary changes on cell surface carbohydrates in adult mice.

Furthermore, intestinal tissue constitutes an interesting system for studying the events of cell differentiation, where the epithelial
cells lining the villi undergo replication in crypt base and immature cells migrate to the villus tip (Messier and Leblond, 1960). It is known that the progression of cells across the length of the villi is accompanied by alterations in brush border enzymes (Webster and Harrison, 1969), membrane fluidity (Brasitus and Dudeja, 1985), lectin binding characteristics (Etzler and Branstrator, 1974) and fucose and sialic acid contents (Gupta et al., 1988b; Jaswal et al., 1988). The level at which enterocytes are capable of responding to various dietary regimens with respect to enzymatic and terminal sugar alterations, needs further explorations to integrate different findings into a general description of enterocyte differentiation.