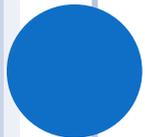


TYPES OF PREBIOTICS



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Prebiotic sources:

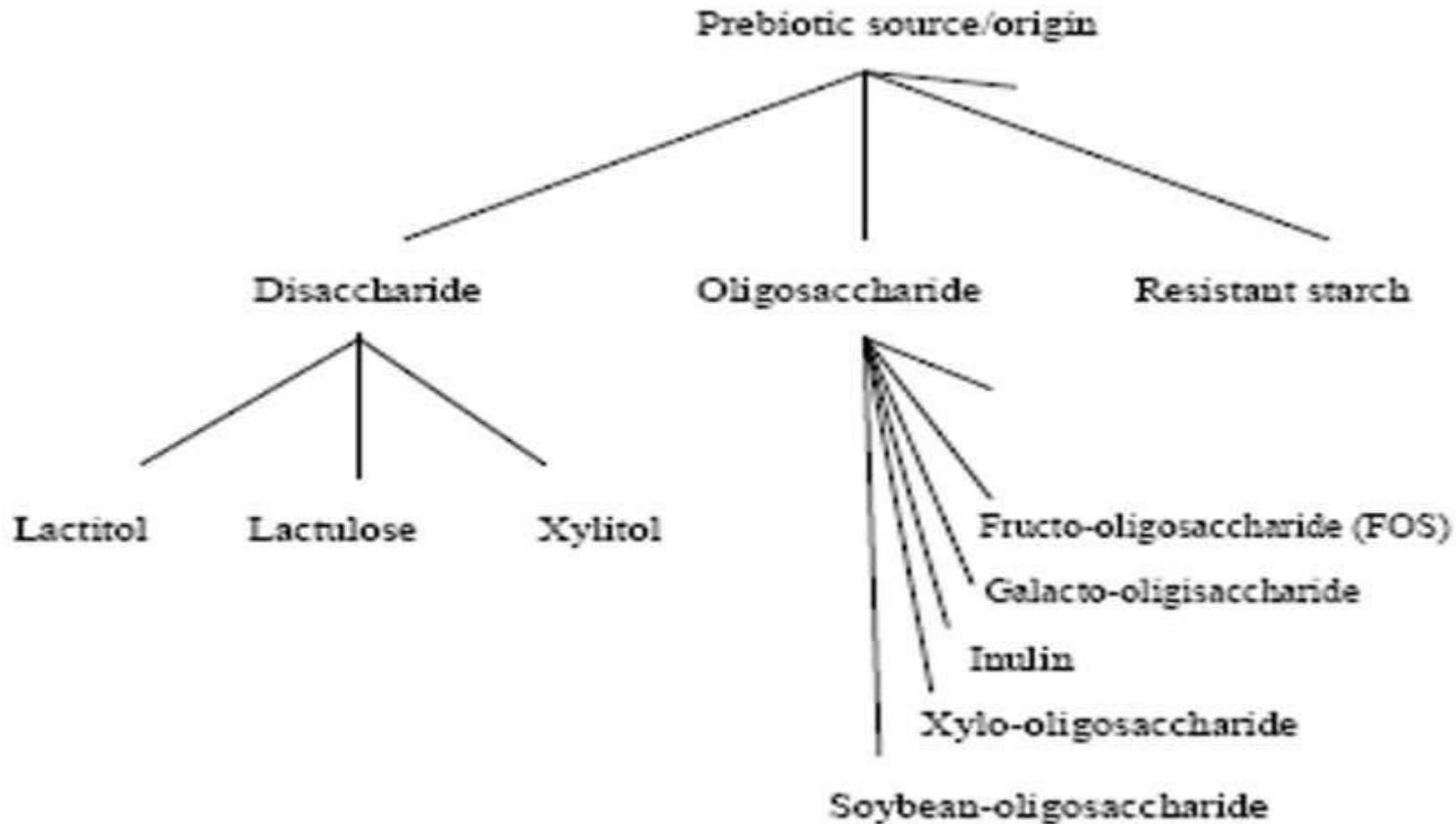


FIGURE 4. Prebiotic origin. Adapted from Magalhães *et al.* (23). / *Origen de los prebióticos. Adaptado de Magalhães et al. (23).*

- Only two particular prebiotics then fully met the refined definition of prebiotics: Inulin(IN) and Trans-galactooligosaccharide (Roberfroid, 2007).
- Other authorities also classify resistant starch, fructooligosaccharide (FOS) and lactulose as prebiotics. Mannan Oligosaccharides (MOS) have been termed as prebiotics but would more correctly be termed **immunosaccharides** (Roberfroid, 2007).
- Carbohydrates including gluco-oligosaccharides, isomalto-oligosaccharides, nigero-oligosaccharides, oat b-glucans, raffinose, soyabean oligosaccharides (SOS), and xylo-oligosaccharides are considered as **candidate prebiotics**.

MECHANISM FOR THE EFFECT OF PREBIOTICS ON IMMUNITY

- The underlying mechanisms of how prebiotics modulate the immune system are not known at present.
- However, experimental data suggests that these compounds exert effects in the GALT and also point to a few different mechanisms that might explain these effects:
 1. Selective changes in bacterial composition and bacterial products which modulate cytokine and antibody production;
 2. Production of SCFAs and their interactions with leukocytes
 3. Modulated mucin production
 4. Interaction with carbohydrate receptors of pathogens inhibiting their enhancement to epithelial cells as well as receptors on immune cells.

A. SELECTIVE CHANGES IN BACTERIAL COMPOSITION AND BACTERIAL PRODUCTS:

- It is well known that prebiotics increase the no. of beneficial bacterial (i.e bifidobacteria and lactobacilli).
- Probiotics when administered orally are known to increase the secretion of IgA in the small intestine and the feces and to stimulate PP B lymphocyte IgA production.
- They are also known to exert effects on systemic immune functions and various immune parameters in the lungs, spleen and peritoneal cells.

- Intestinal epithelial cells are involved in both innate and adaptive immune responses and act by transducing signals from luminal pathogens to adjacent immune cells of the intestinal immune system, via specific germinal-encoded pattern-recognition receptors, such as **Toll-like receptors (TLRs)** and **cytoplasmic receptors**.
- TLRs are able to discriminate between the normal commensal biota and pathogens and induce the transcriptional activation of a no. of genes mediating immune and inflammatory responses.

- **Pathogen-associated molecular pattern (PAMPs)** [eg., endotoxin(lipopolysaccharide), lipoproteins, lipopeptides and imidazoquinolines] present on diverse microbes are initially recognized by TLRs and their interaction result in the activation of intracellular signaling pathways, nuclear translocation of transcription factor NF- κ B and the transcription of pro-inflammatory cytokines.
- The changes that occur in the composition of the intestinal microbiota due to prebiotic fermentation could potentially reduce the presence of PAMPs and thereby exert a positive effects on the immune system.

- Prebiotics also promote an increase in the bacterial cell-wall components that are recognized by TLRs and in DNA derived from luminal bacteria that, in turn, stimulate the intestinal immune system.
- Cytoplasmic components and cell-free extracts of probiotics have also been demonstrated to produce some of the same immune effects (eg, IgA production by PP and macrophage stimulation) as live bacteria.

B. PRODUCTION OF SCFAs:

- The major end products of carbohydrate fermentation are SCFAs, of which acetate, propionate and butyrate are quantitatively the most important in the human colon.
- The production of SCFAs in the colon averages 400 mmol/day, with a range of 150-600 mmol/day.
- All SCFAs are rapidly absorbed from the large intestine and stimulate salt and water absorption: principally, the gut epithelium, liver and muscle metabolize them, with virtually none appearing in the urine and only small amounts appearing in the feces.

- The three major SCFAs are trophic when infused into the colon and these trophic properties have important physiological implications in addition to maintaining the mucosal defense barrier against invading organisms.
- Butyrate is known to suppress lymphocyte proliferation, inhibit cytokine production of Th1-lymphocytes and upregulates IL-10 production.
- It also suppresses expression of the transcription factor NF- κ B and upregulates TLR expression.
- Butyrate is also believed to protect against colon cancer as it inhibits DNA synthesis and induces cell differentiation.

- It has been demonstrated in a rat model that supplementing total parenteral nutrition with a SCFA mixture results in increased NK cell activity(Pratt et al.,1996).
- Pharmacological doses of acetate administered intravenously to both healthy individuals and cancer patients also increased NK cell activity and peripheral blood antibody production.
- In addition, it has been shown that serum glutamine levels are raised following lactulose administration and suggested that increased SCFA levels were responsible for this (glutamine is a preferred substrate for lymphatic tissue).
- Therefore, SCFA production in the large intestine could potentially reduce the requirement of epithelial cells for glutamine, making it available to the cells of the immune system.

C. MUCIN PRODUCTION:

- The first line of defense of the mucosa against luminal contents is the mucous layer, which is mainly composed of high-molecular-weight glycoprotein (mucins) that are secreted by goblet cells.
- The effect of prebiotics on mucin production has been reported in a study, where it was shown that inulin administration resulted in increased mucin production in rats.
- Greater mucin production was found to be associated with a lower incidence of bacterial translocation across the mucosa following dietary fibre supplementation.

- It has been shown in a perfused rat colon model that the production of acetate and butyrate from the fermentation of dietary fibre stimulates mucin secretion, but fibers do not have the same effect on their own.
- Pathogens and beneficial commensal bacteria are able to modulate mucin synthesis by regulating some of the mucin genes.
- Currently there are 16 identified mucin genes, but further work is needed to fully explain the function of each of them and to identify new genes.