

SHORT CHAIN FATTY ACIDS ACETATE, PROPIONATE, BUTYRATE ARE THE MEDIATORS OF THE HEALTH MESSAGE DELIVERED BY MICROBIOTA TO HOST.

Long standing epidemiological studies over the past 40 years associating **cardiovascular protection** and **fiber consumption**, and the recent discovery, at the beginning of this century, of FFR2 and FFR3, specific receptors of SCFAs which are the primary end products of microbiota fermentation of non-digestible carbohydrates have designed this compound **directly linked to health**. SCFAs are produced by the interplay of non-digestible carbohydrates, microbiota diversity and Gut Lumen environment.

SCFAs promote healthy effects in many physiological conditions and several diseases:

1. Butyrate, and in a lesser extent **Propionate**, ensure gut mucosa integrity by two mechanisms

- **Reduction** of inflammatory T Cell CD3c and Macrophages CD68 margination of the gut lamina propria.
- **Reinforcement** of Tight-Junction (TJ) adherence and solidity by enhancing its constitutive proteins Claudine and Occludine synthesis.

These two actions lead to reduction of gut derived whole body inflammation load.

2. SCFA mainly **Propionate** prevents liver steatosis by reducing hepatocyte "de novo lipogenesis" (DNL) and adipocyte derived circulating FFA reesterification into triglycerides. SCFA **Propionate** and to a minor degree **Butyrate**, prevent steato-hepatitis (NASH) which is a harmful complication of steatosis, reducing Kupffer Cells activation through inhibition of NFkB which lead to fibrogenic IL-1b, Il-6 and TNFa inflammatory cytokines.

By these conjugated activities, **Propionate** and **Butyrate** prevent cirrosis and its complication, hepato-carcinoma.

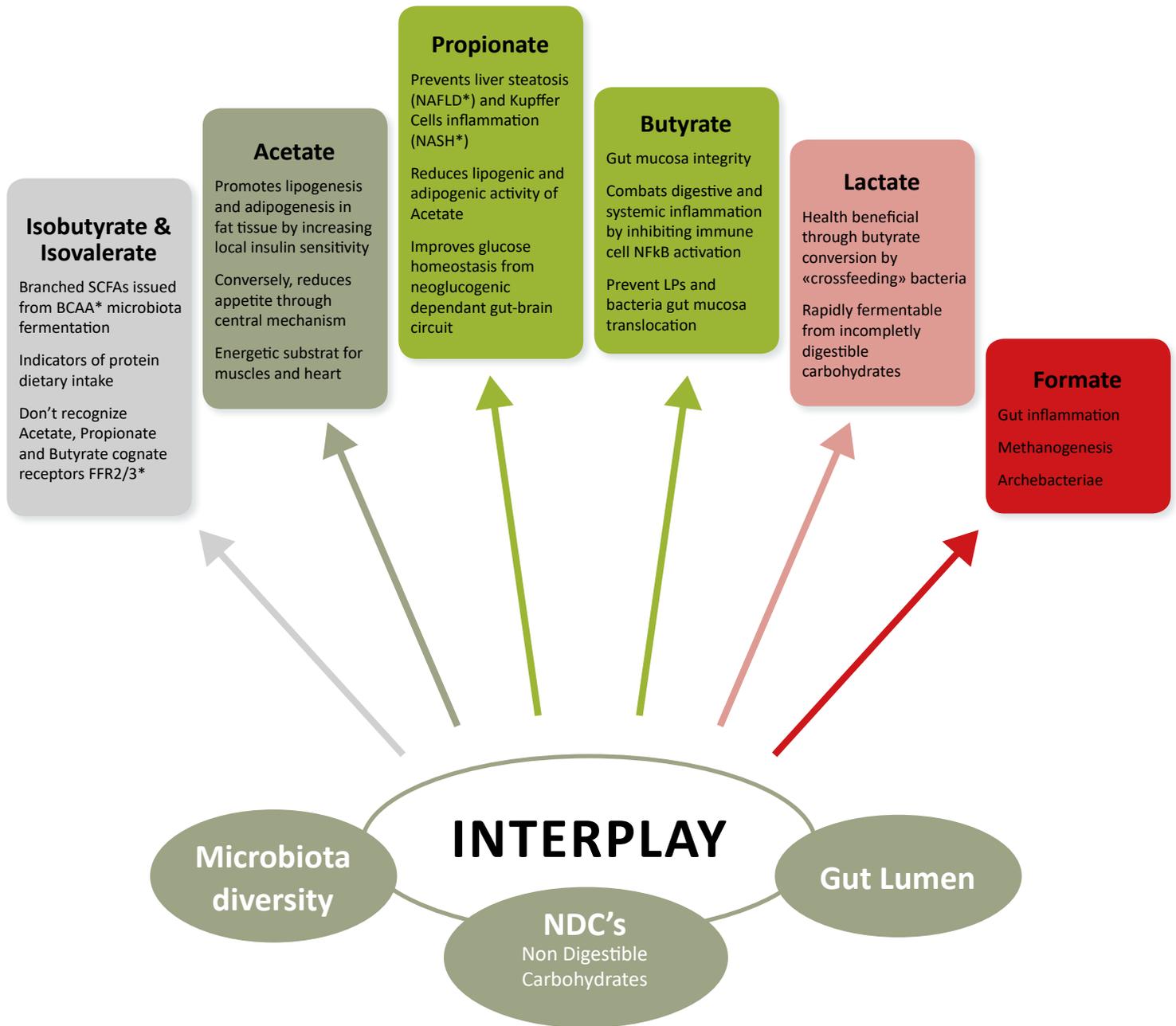
3. SCFA **Propionate** and, in a minor part, **Acetate** prevent weight gain by reducing lipogenesis and adipogenesis and enhancing insulin sensitivity in adipose tissue. And, in another hand, increasing pancreas beta-Cell insulin secretion by sensitization of glucose control. A second potent mechanism of weight control is the **reduction of appetite**, in a first step, by **Propionate** which initiates gut anorectic peptides GLP-1 and Pyy secretion by L-endocrine cells of digestive crypt. In a second step, **Acetate** activates directly satiety neurons of arcuate nucleus in hypothalamus.

4. SCFAs and particularly **Propionate**, improve diabetes through regulation of glucose homeostasis via a Gut-Brain circuit fed by intestinal neoglucogenesis, insulin sensitization in muscles, fat and beta islets and weight reduction.

5. SCFAs, mainly **Propionate**, reduce severity and incidence of many inflammatory diseases including arthritis, and bowel inflammatory diseases, by inactivating NFkB and reducing lipopolysaccharides toll like receptor downstream signaling through gut mucosa integrity restoration.

So 60 to 80 non-digestible carbohydrates daily consumption promote, in several months, microbiota diversity and enrichment in propiogenic and butyrogenic species capable of improving the most widespread pathological conditions of our western societies.

PHYSIOLOGICAL ROLES OF SCFAs ON METABOLISM AND IMMUNITY HOMEOSTASIS



Sources

1. The role of short chain fatty acids in appetite regulation and energy homeostasis, CS Byrne, ES Chambers, DJ Morrison and G Frost, *International Journal of Obesity* (2015) 39, 1331–1338
2. Douglas J. Morrison & Tom Preston (2016) Formation of short chain fatty acids by the gut microbiota and their impact on human metabolism, *Gut Microbes*, 7:3, 189–200, DOI: 10.1080/19490976.2015.1134082
3. Miller TL, Wolin MJ. Pathways of acetate, propionate, and butyrate formation by the human fecal microbial flora. *Appl Environ Microbiol* 1996; 62:1589–92; PMID:8633856
4. Flint HJ, Duncan SH, Scott KP, Louis P. Links between diet, gut microbiota composition and gut metabolism. *Proc Nutr Soc* 2015; 74:13–22; PMID:25268552; [http:// dx.doi.org/10.1017/S0029665114001463](http://dx.doi.org/10.1017/S0029665114001463)

* NAFLD : Non Alcoholic Fatty Liver Disease
 NASH : Non Alcoholic Steato-Hepatitis
 BCAA : Branched Chain Amino Acid (Len, Ile, Val)
 FFR2/3 : Free Fatty Acid Receptor 2 and 3