

Format for ANSWERING REVIEWERS

September 23, 2015



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 19961-Review.doc).

Title: New-found link between microbiota and obesity **Author:** Chandra Kanti Chakraborti

Name of Journal: *World Journal of Gastrointestinal Pathophysiology*

ESPS Manuscript NO: 19961

The manuscript has been improved according to the suggestions of reviewers:

Reviewer Number	Comments	Answering to the Comments
2441737	Explain more about the link of SCFA-microbiota- induced fermentation products and the lipopolysaccharides of Gram negative microorganisms with obesity (regarding Abstract).	Due to the grave pathological role of obesity, worldwide research is being continued to find out the causative factors involved in it. Recent advances in this field reveal a possible relationship between the compositional pattern of gut microbiota and genesis of obesity. Several study results have shown that short-chain fatty acids (SCFAs - microbiota-induced fermentation products) and lipopolysaccharides (LPS - an integral component of Gram negative microorganisms) play the key role in linking the two. Though several SCFAs are

produced as microbiota-fermentation products, three of them, i.e., butyrate, propionate and acetate have been found to be definitely involved in obesity; though individually they are neither purely obesogenic nor antiobesogenic. Out of these, butyrate and propionate are predominantly antiobesogenic. Butyrate, though a major energy source for colonocytes, has been found to increase mitochondrial activity, prevent metabolic endotoxemia, improve insulin sensitivity, possess anti-inflammatory potential, increase intestinal barrier function and protect against diet-induced obesity without causing hypophagia. Propionate has been found to inhibit cholesterol synthesis, thereby antagonizing the cholesterol-increasing action of acetate, and to inhibit the expression of resistin in adipocytes. Moreover, both these SCFAs have been found to cause weight regulation through their stimulatory effect

		<p>on anorexigenic gut hormones and to increase the synthesis of leptin. Unlike butyrate and propionate, acetate, which is substantially absorbed, shows more obesogenic potential, as it acts as a substrate for hepatic and adipocyte lipogenesis. High fat diet increases the absorption of LPS, which, in turn, has been found to be associated with metabolic endotoxemia and to induce inflammation resulting in obesity. Multiple independent and interrelated mechanisms have been found to be involved in such linking processes which are discussed in this review work along with some possible remedial measures for prevention of weight gain and obesity. (Yellow coloured portion has been added considering the comments)</p>
2441737	To draw up a table showing the family of each group of bacteria, and present both positive and negative outcomes associated with obesity	Two tables (Tables 1 and 2) have been incorporated.
2441737	Develop a scheme to explain mechanisms by which the microbiota can influence the genesis of obesity.	Gross mechanisms involved in SCFA-induced obesity have been mentioned in Table 3.
2445033	The description of the relationship between SCFA and obesity, both	Since repetitions in the discussion of SCFA seem to be

	protective and causal, is commented in the introduction, the SCFA section, and in the role of SCFA section. The author should shorten and summarize some of these sections.	necessary to explain their positive and negative role in obesity, shortening of those sections has not been done.
2445033	Perhaps adding some tables (for instance, for the different effects of SCFAs on obesity and their mechanisms would make the article friendlier for the reader.	Three tables (Tables 1-3) have been incorporated.
2445033	There are some typos to be fixed.	Typographical errors have been corrected.