Hypothetical epigenetic fingerprint in Nutritional-Neural-microbiota connection

Olaposi I. Omotuyi1,2

1Department of pharmacology and Therapeutic innovation, Graduate School of Biomedical Sciences, Nagasaki University, Japan
2Center for Bio-computing, Adekunle Ajasin University, Akungba-Akoko, Ondo State, Nigeria

Correspondence: Olaposi Omotuyi
E-mail: omotuyi@nagasaki-u.ac.jp
Received: June 05, 2015
Published online: June 23, 2015

A medical case was reported by Neha and Colleen of a 32-year-old female who had received Fecal microbial transplantation (FMT) as a consequent of recurring Clostridium difficile infection (CDI). Following this procedure, the recipient began to experience significant weight comorbid with constipation and dyspepsia episodes. The weight gain is unamendable by strict protein diet and exercise regimen, thus, leading the authors to hypothesize nutritional-neural-microbiota connection [1]. This hypothesis is further reinforced as animals were transformed into obese phenotypes following fecal transplant from obese human [2].

To begin to make the connection, we have to dive a bit into the current body of knowledge about the molecular basis of obesity. Alteration in effective circulating leptin/ghrelin balance and their cognate receptors is one of the leading causes of obesity. One of the major sites of leptin and gherlin receptors expression is the hypothalamus, making obesity arguably a brain disease. Over-expression of leptin receptor is associated with leanness, while the converse is true for gherlin receptor over-expression as well reported during pregnancy [3] and provides a scientific basis for obese phenotypes induced in animal model when treated with leptin receptor antagonists [4]. Obesity episode in the animals was preceded by increased food consumption, similar to what is expected when animals were treated with appetite stimulants such as gherkin, orexin and neuropeptide-Y, succinctly making the connection between food/energy intake (nutritional) and the neural circuitry.

How does the nutritional-neural axis link up with the microbiota and what is the epigenetic connection? These two questions represent the core of this write-up and since our knowledge of this interaction is premature, we must necessarily fall back to our current understanding of host-pathogen interaction and draw valuable epigenetic lessons from this relationship. Microbes have at least two important epigenetic modifying factors in their arsenal to alter gene expression; first, they have surface signals, which rely on coupling to receptor on host cells for onward intracellular transmission of epigenetic information like classical paracrine factors. Then, they can produce secondary metabolites, which behave like classical endocrine factors, crossing through physical barriers and dispersing in serum and reaching distant targets like the brain. For instance, Campylobacter rectus and Helicobacter pylori infection cause insulin-like growth factor (igf2) [5] and Runx-related transcription factor 3 (runx3) [6] promoter hypermethylation respectively. A few metabolites such as cysteine, propionate, sulforaphane and spermidine have been characterized as epigenetic modulators and of note is the p21 expression modulation by short chain fatty acids via Histone-deacetylase 1 inhibition [7].
Some of the low-hanging fruits of the diffuse connection between epigenetics and nutritional-neural-microbiota system would be to understand how microbe-derived factors alter epigenetics landscape of ghrelin/leptin precursor and cognate receptors expression. A co-culture of microbiota and cell-lines expressing the receptors and precursor proteins will be the unavoidable plain to begin the process of illuminating the hidden chemical connection between the two cellular environments. It is then we can begin to reconstruct the connection and building knowledge for possible clinical applications.

References