

## Editorial

# The human microbiome: a public health approach

Csaba Varga, István Kiss

*Institute of Public Health Medicine, Faculty of Medicine, University of Pécs, Hungary*

---

## Introduction

Accelerated alteration of the global environment generates urgent need for adaptation of human societies to the *chemosphere* (chemicalization) and *infectosphere* (emerging infections), involving preventive measures at population level. The novel trends and discoveries in relation to human health – e.g. epigenetics, nanotechnology, regenerative stem-cell medicine or the human microbiome research – generate new attitudes in public health as well. We should inevitably and urgently integrate the innovations into our research and activities at all levels of prevention. In these columns We try to outline the public health concern of the ongoing microbiome research as a revolutionary new field in medicine and biology.

---

## Environmental toxicology and the microbiome

In the early 1970's a genotoxicity test called host-mediated assay became very popular in genetic toxicology.<sup>1</sup> The main innovation of the test was that the particular exposing agents were metabolized by the host (rodent) organism, but finally the end-point (reverse gene mutations) could be studied on the standard *Salmonella typhimurium* strains. The bacteria injected to the peritoneal cavity of the treated animal were finally retrieved, plated and their mutation frequency was measured. That is, the target (bacterial) cell – the object – of the toxicity study and the subject of the study (rodent) were two different entities. Later, continuing this principle lower and higher eukaryotic (yeast, mouse lymphoma) cells were also applied for this purpose.<sup>2,3</sup> In other words, what it was changed is the philosophy of testing.

Nowadays, investigations on the gut microbiome seem to propose a brilliant similar opportunity to develop novel, highly specific and selective toxicity tests. As we also see in the recently published papers on environmental health, more and more well-known environmental toxicants have been proven *microbiome disruptor* as well, altering the species-distribution of this very sophisticated microbial community.<sup>4-6</sup> Actions of environmental toxic agents are followed by disturbances in these bacterial populations, affecting their size and growth characteristics. Some of them disappear, others overgrow. The marked alterations can be exactly detected at the metagenome level. Of course, the metagenome analysis is not an everyday routine examination. Not yet.

On other hand, a toxicity test requires a well quantifiable parameter to be tested, because finally we should decide if the compound is toxic or not. If toxicologist perform several tests with many compounds, then it would be possible to develop a quantitative evaluation system hand-in-hand with the statisticians. This requires hard and highly interdisciplinary work as the microbiome is not only a human *organ* but rather an ecological system involving specific features, trends, interests and evolutionary strategies of its elements.<sup>7,8</sup> This is what biologists call as

*emerging properties*.<sup>9</sup> That is why neglecting the ecological (super-individual) approach would be a fatal error.

New, simple, reliable and standardized toxicity tests are urgently needed. Let us remember that the number of chemical agents (registered by the CAS) has reached the 102 million.<sup>10</sup> About 1% of them finally appear in the human environment. In case of vast majority of these compounds we do not know anything on their toxicity profile. Let us take this new chance without hesitation.

---

## Nutrition and the microbiome

Another crucial link from gut microbiome research to public health is the issue of nutrition. Safe, healthy and nutritionally adequate diet is not available for every population on the Earth.

Over two billion humans suffer from the limited intake of micronutrients, 26% of the children on the Earth are stunted as a consequence of malnutrition.<sup>11</sup>

In the so called *developed* countries people may also be malnourished. It is called as *quality starvation* because the calorie intake is even higher than optimal, but the quality of food is very low. Typical examples for this phenomenon are the transient (the post-communist) countries. Even after a quarter-century of the democratic change deprivation is still highly characteristic to the average population in these countries. In addition to socioeconomic factors, the consumption of low-price *junk* food in these countries is a consequence of the lack of knowledge on healthy nutrition, and the pressure exerted by the food industry which tries to maximize its profit. This food is full of artificial additives, sometimes contaminants or pollutants, as well. And this is only one in the long line of problems with the dietary habits in the industrial countries.

On the basis of the principles of primary prevention we should prohibit/discourage consuming food containing constituents of potentially hazardous or adverse effects. But it seems to be very difficult under the present financial circumstances. Theoretically health promotion should be able to handle these problems, but it takes decades to substantially change the dietary habit of population level, while the efforts might not be effective enough in the lack of socio-economic conditions, and due to the deeply embedded unhealthy eating patterns in the society. What policy can be made then in this situation?

Let us consider the other side of this issue. The estimated costs of malnutrition, in all forms amount to 5% of the world's GDP, about 500 USD/earthling.<sup>12</sup> If the diet of the population cannot be optimal, we should find an additional modifiable factor in this process. And this may be the gut microbiome. Distribution and composition of the microbiota is changeable, probiotics are popularly used in the developed countries to reconstruct the microflora e.g. after an antibiotic therapy. Assuming that microbiologists can engineer new strains of bacteria carrying specific features, like rapid decay of toxic, carcino-

genic, atherogenic, etc. constituents, important characteristics and toxicological features of the food could be substantially changed. The diet-microbiome interactions may be moderators of human metabolism.<sup>13</sup> Does this mean that with the ingestion of a capsule with the mix of relevant bacterial strains we can colonize our gut with beneficial organisms that prevent us from cancer, cardiovascular or metabolic diseases as type 2 diabetes, etc.? What a perspective! What a brilliant opportunity for decreasing incidences of public diseases! The history, however, has taught an important lesson to those working in the field of disease prevention. There are no miracles! People cannot expect to take one miracle capsule per day, and solve their health problems without further efforts. Vitamin C, resveratrol, and several potentially cancer preventing/curing dietary supplements made from exotic plants, just to mention some such attempts. After extensive research these compounds found their appropriate roles in disease prevention, but not as miracle molecules, not as replacements of health lifestyle.

Utilizing the preventive – and even possible therapeutic – power of modifications of the gut microbiome has to find its place as well. There are enormous opportunities in this area, and to explore them extensive research must be focused on this recently developed *new organ* inside the human body, including its homeostasis, connections with other organs and organ systems, safe ways and health consequences of its modification, and possible hazards and side effects associated to these modifications. This may open a new, bright and promising chapter in the health research of the 21<sup>st</sup> century.

## Sesquitary prevention?

Looking at the revolutionary development of medical and pharmaceutical technologies, this idea is not a science fiction. In case of its realization, however, a theoretical question is also arisen. Namely: what level of prevention are we talking about? This intervention is neither primary nor secondary preventive measure. It can rather be referred as another new level between them: the *sesquitary level of prevention*.

Correspondence: Csaba Varga, Institute of Public Health Medicine, Faculty of Medicine, University of Pécs, Szigetű út 12. 7624 Pécs, Hungary.

E-mail: chemsafety@freemail.hu

Key words: Public Health, Microbiome, Toxicology.

Conflict of interest: the author declares no potential conflict of interest.

Acknowledgments: the present scientific contribution is dedicated to the 650<sup>th</sup> anniversary of the foundation of the University of Pécs, Hungary.

Received for publication: 29 September 2016.

Accepted for publication: 29 October 2016.

©Copyright C. Varga and I. Kiss, 2016

Licensee PAGEPress, Italy

Journal of Public Health Research 2016;5:764

doi:10.4081/jphr.2016.764

This work is licensed under a Creative Commons Attribution NonCommercial 4.0 License (CC BY-NC 4.0).

## References

1. Gabridge MG, Legator MS. A host-mediated microbial assay for the detection of mutagenic compounds. *Exp Biol Med* 1969;130:831-4.
2. Fahrig R. Metabolic activation of arylalkyltriazenes in the mouse: induction of mitotic gene conversion in *Saccharomyces cerevisiae* in the host-mediated assay. *Mutat Res* 1971;13:436-9.
3. Fischer GA, Lee SY, Calabresi P. Detection of chemical mutagens using a host-mediated assay (L 517 8Y) mutagenesis system. *Mutat Res* 1974;26:501-11.
4. Choi JJ, Eum, SY, Rampersaud E, et al. Exercise attenuates PCB-induced changes in the mouse gut microbiome. *Environ Health Perspect* 2013;121:725-30.
5. Potera C. POPs and gut microbiota: dietary exposure alters ratio of bacterial species. *Environ Health Perspect* 2015;123:A187.
6. Zhang L, Nichols RG, Correll J, et al. Persistent organic pollutants modify gut microbiota – host metabolic homeostasis in mice through aryl hydrocarbon receptor activation. *Environ Health Perspect* 2015;123:7679-88.
7. Walter J, Ley R. The human gut microbiome: ecology and recent evolutionary changes. *Ann Rev Microbiol* 2011;65:411-29.
8. Rózsa L, Apari P, Müller V. The microbiome mutiny hypothesis: can our microbiome turn against us when we are old or seriously ill? *Biol Direct* 2015;10:3.
9. Odum EP, Barrett GW. *Fundamentals of ecology*. Vol. 3. Philadelphia: Saunders; 1971.
10. CAS Registry. The gold standard for chemical substance information. Available from: [www.cas.org/content/chemical-substances](http://www.cas.org/content/chemical-substances)
11. FAO. *The state of food and agriculture. Food systems for better nutrition*. Rome: FAO; 2013.
12. Bonaccorsi G. Food and human behaviour: consumption, waste and sustainability. *J Public Health Res* 2015;606:133-4.
13. Sonnenburg JL, Bäckhed F. Diet-microbiota interactions as moderators of human metabolism. *Nature* 2016;535:56-64.