Fasting and engineered diets as powerful tool in the medical practice: an old approach in the new era

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Fasting and dietary restriction have been practiced for millennia for different purposes spanning from religious, philosophical to medical. Only in recent times it has been scientifically demonstrated that dietary restriction is associated with major health benefits such as: amelioration of cardiovascular diseases, immune disorders, slowing of the aging processes, diabetes, insulin resistance and reduced risk of cancer (1). Moreover, cutting-edge studies, taking advantage of in vivo and in vitro models, unveiled a potential link between short-term starvation and improved efficacy of chemotherapy for some types of cancer (2,3) accompanied by a decrease of side effects of chemotherapy in patients (4).

Previous animal studies by Dr. Longo’s group, who is a pioneer in this field, have shown that fasting or diets that mimic fasting condition (FMD) extend lifespan, ameliorate cognitive functions, reduce inflammation and relieve the symptoms of diseases such as multiple sclerosis and cancer (5,6). In a very recent study published by Dr. Longo and colleagues (7), a randomized controlled trial was conducted on humans, in order to evaluate the effects of a fasting-mimicking diet on markers and risk factors for aging, cancer, metabolic syndrome and cardiovascular diseases. This study enrolled 100 healthy participants without a diagnosed medical condition in the previous 6 months, which were randomly assigned to either a control group maintaining a normal diet for 3 months or a FMD group following three consecutive cycles of a fasting-mimicking diet for 5 days/month. First interesting thing to consider is that the fasting-mimicking diet has been proved to be safe and produced no serious adverse effect. This represents a step ahead of fasting which can cause deleterious nutritional deficiencies, when prolonged, in spite of its potential beneficial health effects. At the end of the 3-month period, the participants belonging to FMD group presented reduced body weight, trunk and total body fat, lowered blood pressure and lower levels of the hormone insulin-like growth factor 1 (IGF-1), whose implication in aging and cancer is well documented (8-10). The participants of the control group were then shifted to the FMD regimen for another 3 months: a post hoc analysis was performed on both FMD arms, replicating the aforementioned results and moreover showing decreased body mass index, glucose, triglycerides, cholesterol, and C-reactive protein upon fasting-mimicking diet. The study by Longo and colleagues is undoubtedly well conceived and the results are exciting and encouraging. This work convincingly contributes to promote a healthier lifestyle in a society in which metabolic and aging-related diseases represent a major health burden. In industrialized countries, indeed, the diffusion of the Western diet (high in animal protein and fat, low in fiber) and of the “fast food culture” is responsible for high calorie intake (11) and, together with sedentary behavior, increases the risk of obesity, metabolic syndrome, cardiovascular diseases and cancer.

“A new food culture, based on limiting dietary surplus and on preferring healthier foods, is then essential.”

However, it should be taken into account that in the
Moreover, in very recent years, a growing body of evidence has been produced highlighting the prominent role of the diet in shaping gut microbiota composition, which in turn plays a major role in the pathogenesis of several diseases (16,21). These studies suggest that not only the calories intake is important but also the type of dietary compounds. More studies on diet compounds and/or supplements are needed in order to better understand the relationship between diet and disease. It has been demonstrated that certain types of foods selectively enhance some microbial groups which in turn can shape the profile of the whole gut microbiota thus affecting the onset and the progression of several diseases, including cancer. Fiber-rich food regimens significantly decrease pro-inflammatory microorganisms such as Bacteroides acidifaciens, Escherichia coli, Ruminococcus gnavus and Clotrumodium cockeatum (16), supporting the indication that engineered diets able to perturb gut microbial community can be synergistically used together with the current chemotherapeutic approaches. Administration of probiotics and prebiotics represents the most common measure to shape gut microbiota in order to slow cancer progression, improve response to therapy or limit toxic side effects (22). As for cachexia, for instance, it has been recently demonstrated that administration of Lactobacillus reuteri in drinking water to mice with colon cancer predisposed to cachexia, has beneficial effects on gastrocnemius muscle masses and body weight that are increased as compared to untreated mice, together with reduced neutrophil counts, a marker of systemic inflammation (23).

In conclusion, in agreement with what has been stated elsewhere by Dr. Longo (24), dietary restriction effects on aging and health are not necessarily the result of a reduced caloric intake but also a consequence of changes in diet composition. Therefore, though recognizing the remarkable scientific value of the benefits provided by the fasting-mimicking diet, it is advisable to pursue less demanding strategies that would be more easily tolerated by healthy people and particularly by patients. Longo’s studies undoubtedly play a pivotal role in the prevention and/or cure of aging-related diseases and also paved the way for further nutritional manipulations.

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Page 2 of 3
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**Footnote**

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