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Changes in the intestinal microbiota from adulthood through to old age

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Abstract

The human intestinal microbiota comprises a complex community whose composition has been resolved in fine detail by recent culture-independent methodologies. The adult intestinal microbiota is stable within individuals, and individual specific when examined at high resolution. Infants and older persons, however, represent stages of life in which the microbiota is in flux. Since changes in the intestinal microbiota are associated with certain diseases or health issues, we have examined the composition and function of the intestinal microbiota in 500 subjects over 65 years of age in Ireland. Medical, biochemical and immunological parameters were measured for all subjects. Faecal microbiota was measured by amplicon pyrosequencing. The data revealed significant inter-individual variation, especially in the proportions of some major bacterial phyla, and significant differences in the microbiota compared with younger adults. These data support the notion of modulating the intestinal microbiota of older people to promote enhanced nutrition utilization and to improve general health

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Introduction

The development of culture-independent methods for microbial community composition determination, originally for environmental samples, has revolutionized our ability to study the human intestinal microbiota [1]. Application of these methods circumvents the poor laboratory culturability of a large proportion of the relevant species. The human infant is born essentially sterile, and is colonized in a series of establishment and succession events to ultimately move towards a more stable adult-like microbiota [2]. The intestinal microbiota of the healthy adult is stable and individual specific [3], and contains a set of microbial genes and functions that are largely shared between individuals [4]. The microbiota has an important role in releasing nutrition content from the diet, synthesizing vitamins and co-factors, and regulating the mucosal immune system [5]. Furthermore, there is a body of evidence (reviewed in [6]) that variations in the microbiota are linked to diseases including bowel dysfunction and obesity. Thus the study of the microbiota associated with humans, at various body sites but especially in the intestine where highest bacterial numbers are found, has become an important branch of health research.

Composition of the intestinal microbiota

Data based on culture-based analyses of the intestinal microbiota have presented a conflicting picture of trends in major phylum and species proportions [7]. More recently, phylochip analysis reported stability of the microbiota over time in older subjects [8], and distinctive compositional patterns of phylum Firmicutes in elderly subjects and centenarians compared with young adults [9]. There are few other longitudinal studies of the intestinal microbiota of older persons, so it is not clear if the state of microbiota flux expected from older culture-dependent analyses is actually due to technical variation compounded by inter-individual variation. There are compelling physiological and immunological factors that change dramatically in old age [10–12] and for which plausible scientific links with variation in the intestinal microbiota can be proposed. The ELDERMET study that commenced in Ireland in 2008 is therefore focusing on health–diet–microbiota

interactions in 500 elderly subjects. These subjects were selected from stratified community residence groups—community dwelling, outpatients, rehabilitation and institutionalized. As well as determining the microbiota composition in faeces as a surrogate for the distal intestine, all subjects are phenotyped (full blood biochemistry), urine and serum are collected for metabolomics, a food frequency questionnaire is completed, and measures of frailty and cognition are taken. The 16S rRNA gene, variable region V4, is amplified and analysed by pyrosequencing [13,14].

The intestinal microbiota of elderly subjects

As part of the ELDERMET study, we have recently analysed microbiota composition data from over 100 individuals [15]. The core microbiota of these subjects was distinct from that of younger subjects at phylum, genus and *Clostridium* cluster level. There was striking variability between individuals, represented by an enormous range of the Bacteroidetes : Firmicutes ratio [15]. We also noted significant variations in the proportions of butyrate-producing Firmicute genera, in the Proteobacteria, Actinobacteria (which includes *Bifidobacterium* spp.) and genus *Faecalibacterium* (which includes the anti-inflammatory species *F. prausnitzii* [16]). Butyrate-producing bacteria such as *Ruminococcus* sp. are known to be sensitive to dietary composition; butyrate produced by intestinal bacteria is a major energy source for intestinal epithelial cells. Thus this represents an important food–health link mediated by the microbiota. There was no correlation between the Bacteroidetes : Firmicutes ratio and body mass index in the subjects studied to date, questioning the association of Firmicutes proportion and obesity in this elderly cohort. In the majority of 29 patients for whom a 3-month follow-up faecal sample was analysed, the microbiota was more like the time-zero sample than any other microbiota sample, indicating temporal stability. However, analysis of the wider ELDERMET cohort over a long time-frame will be required to corroborate this finding.

Concluding remarks

The data obtained from the ELDERMET study thus far provide significant insights into the intestinal microbiology of older persons. They also provide support for the notion of using dietary intervention to alter the microbiota in a health-promoting direction (Fig. 1), because the proportions in the core microbiota of bacteria related to modification of dietary ingredients, including butyrate-producing *Clostridia*, are

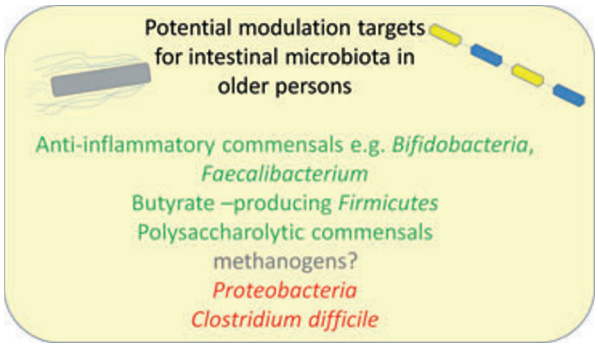

FIG. 1. Potential modulation targets for intestinal microbiota in older persons. Modulation could be by way of dietary supplementation or probiotic supplementation. Desirable elements in the microbiota are in green; status unclear in grey; microbiota components to be reduced are in red.

different to younger adults [15]. Such intervention modalities could include probiotics (live microorganisms that confer health benefits, either directly or indirectly [10]) or prebiotics, which are dietary ingredients, usually polysaccharides, that promote the growth of particular microbiota components [10]. However, one can envisage novel functional foods for elderly consumers that also alter physical conditions in the bowel to promote for example calcium and micronutrient uptake facilitated by altered pH or induction of uptake mechanisms by microbiota components [12].

Further analysis of microbiota–health associations, in multiple countries with different baseline microbiota composition and different diets, will identify additional targets and mechanisms.

Transparency Declaration

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