society for general Microbiology

THE HUMAN MICROBIOTA

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- The human microbiota is the community of micro-organisms that live on and in the body.
- Changes in the microbiota are linked to diseases such as type II diabetes and Crohn's disease.
- The microbiota is currently the subject of intensive medical research.

OVERVIEW

The human microbiota is the community of trillions of micro-organisms that live on and in the body. It may play a vital role in regulating our health and is therefore under intensive scientific investigation. Research efforts focus on identifying how changes in the microbiota might cause diseases such as inflammatory bowel disease, diabetes and atherosclerosis, how these changes might be prevented or reversed, and how we can screen the microbiota to predict disease susceptibility.[1]

WHAT IS THE MICROBIOTA?

The microbiota is the community of micro-organisms in a (usually) complex environment such as soil and body surfaces. Micro-organisms in the human microbiota outnumber human cells 10:1. They colonise parts of our body such as the gastrointestinal tract and skin, share nutrients, 'communicate' by secreting chemicals, and compete for living space. Although they make up only about 1–3% of our body mass, they are an invisible 'ecosystem' that recent evidence indicates may regulate our health.[2]

EVIDENCE THAT THE MICROBIOTA MATTERS FOR HUMAN HEALTH

Alterations in the composition or function of the microbiota have been detected in more than 25 diseases, but the level of evidence presented for a causative link between these alterations and the actual development of disease ranges from very strong to very weak.[3] The strongest links are for Crohn's disease, irritable bowel syndrome and diabetes, and there is mounting evidence for links with autoimmune diseases, obesity and severe malnutrition.[4]

THE LATEST MEDICAL RESEARCH

Scientists study the microbiota using high-tech 'metagenomic' techniques. Robots may be used to extract and sequence the 'microbiome' (the total microbial DNA) in a sample such as a skin swab. Powerful computers analyse the resulting sequence data to identify and compare the micro-organisms present, and to map the biochemical traits they confer on the human host.

Over the past 5 years, governments across North America, Europe and Asia-Pacific invested at least US$167 million into this kind of work which is often referred to as microbiome research or simply, 'microbiomics'.[5]

The output of scientific papers referring to the microbiome has multiplied more than 150 times, from a handful in 2002 to over 1,000 last year.[6] US-based scientists publish the largest proportion of reports in the field.[7]

COMMERCIAL ACTIVITY

Companies in the 'microbiome' sector include Enterome, Metabiomics Corporation, Osel Inc., Second Genome, Seres Health, Vedanta Biosciences and ViThera Pharmaceuticals.[8] The Paris-based firm Enterome, supported by €6.5 million in funding and with a staff of six, investigates diagnostic markers for chronic conditions such as NAFLD (a liver condition) and inflammatory bowel diseases.[9]

Quoted in the scientific journal *Nature*, the human microbiota pioneer David Relman said that diagnostic medical tests may be the key practical application to emerge from such research in the short term. Diseases in the frame for microbiome-based diagnostics include type II diabetes, Crohn's disease and ulcerative colitis, according to the same *Nature* article.[10]

In the longer term, research on the microbiome may lead to the development of personalised medicines, and provide a source for bioactive compounds that could be turned into antibiotics.[11] There are also opportunities for food companies to develop personalised nutrition products for particular microbiota types, especially in infants and older people whose microbiota is in a state of flux.[12]

FUTURE PERSPECTIVES AND KNOWLEDGE GAPS

The greatest scientific challenge facing microbiota research is 'cause or consequence': does the altered microbiota detected in a disease sufferer merely represent a symptom, or did the altered microbiota cause the disease?

To address this question, large prospective clinical studies conducted over 1–4 years in human subjects are highly desirable. For some syndromes such as Crohn's disease, trials that reverse alterations in the microbiota should be performed and assessed for their capacity to alleviate symptoms. The molecular mechanisms that underlie microbiota-disease risk need to be fully elucidated.

Particular attention should be directed at studying the health consequences of variations in the microbiota of infants, the elderly, and 'at-risk' adults such as those with incipient diabetes. We need a greater understanding of the long-term effect of antibiotics on the microbiota, and how diet might be used to modulate the microbiota to promote health.

Details of references cited in this briefing can be found at ***www.sgm.ac.uk/news/hot_topics/Microbiota-references.pdf***

SGM BRIEFINGS

The Society for General Microbiology (SGM) aims to highlight the important issues relating to microbiology to key audiences, including parliamentarians, policy-makers and the media. It does this through a range of activities, including issuing topical briefing papers. Through its many members, the SGM can offer impartial, expert information on all areas of microbiology.

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REFERENCES

1 **Sokol, H. *et al.* (2008).** *Faecalibacterium prausnitzii* is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. *Proc Natl Acad Sci U S A* **105**, 16731–16736; **Hara, N., Alkanani, A.K., Ir, D., Robertson, C.E., Wagner, B.D., Frank, D.N. & Zipris, D. (2013).** The role of the intestinal microbiota in type 1 diabetes. *Clin Immunol* **146**, 112–119; **Wang, Z. *et al.* (2011).** Gut flora metabolism of phosphatidylcholine promotes cardiovascular disease. *Nature* **472**, 57–63.

2 **Anon. (2012).** NIH Human Microbiome Project defines normal bacterial makeup of the body. *NIH News* **http://1.usa.gov/X27YYw**

3 **de Vos, W.M. & de Vos E.A. (2012).** Role of the intestinal microbiome in health and disease: from correlation to causation. *Nutr Rev* **70**, S45–S56.

4 **de Vos W.M. & de Vos E.A.,** *ibid.*; **Trasande, L., Blustein, J., Liu, M., Corwin, E., Cox, L.M. & Blaser, M.J. (2013).** Infant antibiotic exposures and early-life body mass. *Int J Obes (Lond)* **37**, 16–23; **Smith, M.I. *et al.* (2013).** Gut microbiomes of Malawian twin pairs discordant for kwashiorkor. *Science* **339**, 548–554.

5 Blog post: *Metagenomes in Nature*. 2 June 2008. **http://bit.ly/12bjODz**

6 Search with 'microbiome' term in the PubMed database, January 2013. **www.ncbi.nlm.nih.gov/pubmed?term=microbiome**. For comparison, there were over 5,000 research papers published in 2012 containing the term 'influenza'.

7 Based on SGM analysis of the PubMed database in October 2012 for the G20 nations plus the Republic of Ireland; the USA accounted for 34% of published papers in the field; equivalent figures for the UK and Republic of Ireland were, respectively, 5 and 2%.

8 Based on search of FierceBiotech with 'microbiome' keyword; Google search with 'microbiome company' search terms; and reading company websites; for an overview, see **McBride, R. (2012).** Bugs living in humans breed biotech startups. *FierceBiotech* 14 June 2012.

9 **Anon. (2012).** Press release: Enterome raises EUR 5 million in series A funding round, 22 March 2012, p. 1. **http://bit.ly/Xvn8Wb**

10 **Yong, E. (2012).** Microbiome sequencing offers hope for diagnostics. *Nature News* 23 March 2012.

11 **Virgin, H.W. & Todd J.A. (2011).** Metagenomics and personalized medicine. *Cell* **147**, 44–56; **Shanahan, F. (2012).** The gut microbiota in 2011: translating the microbiota to medicine. *Nat Rev Gastroenterol Hepatol* **9**, 72–74.

12 **Claesson, M.J. *et al.* (2012).** Gut microbiota composition correlates with diet and health in the elderly. *Nature* **488**, 178–184.