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Review article

The human microbiome

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ABSTRACT

Until recently, human microbiology was based on the identification of single microbes, such as bacteria, fungi and viruses, frequently isolated from patients with acute or chronic infections. Novel culture-independent molecular biochemical analyses (genomics, transcriptomics, proteomics, metabolomics) allow today to detect and classify the diverse microorganisms in a given ecosystem (microbiota), such as the gastrointestinal tract, the skin, the airway system, the urogenital tract and others, and to assess all genomes in these ecosystems (microbiome) as well as their gene products. These analyses revealed that each individual has its own microbiota that plays a role in health and disease. In addition, they greatly contributed to the recent advances in the understanding of the pathogenesis of a wide range of human diseases. It is to be expected that these new insights will translate into diagnostic, therapeutic and preventive measures in the context of personalized/precision medicine.

Contents

1. Introduction

The basic aspects of molecular and cell biology are not only integral part of biomedical research but are also translated into patient care. Several global consortia have been launched and in part completed during the last decades. All of them continuously transform basic biomedical research and translate into medical applications and, after evaluation in randomized clinical trials, enter clinical practice with a tremendous potential to advance the diagnosis, treatment and prevention of human diseases.

More than 15 years ago, the international human genome organization (HUGO) project established the complete sequence of the ca. 3 billion base pairs that make up the human genome [1,2]. In order to utilize these data from the HUGO project for research as well as for clinical applications and to define the functions of newly identified genes, collectively termed ‘functional genomics’, strategies were developed to globally analyze genomic DNA sequences as well as their cell-, tissue- or organ-specific expression profile. Using chips, so-called 'microarrays',

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thousands or ten thousands of single-stranded DNA species, reverse transcribed RNA (cDNA) or oligonucleotides of known sequence can provide a global gene (genomics), gene expression (transcriptomics, proteomics) or metabolite (metabolomics) profile ('signature') that is characteristic for the disease of individual patients, including its natural course/prognosis and response to therapy.

In 2005 the international haplotype map (HapMap) project was initiated to identify, based on genome-wide association studies (GWAS) in ethnically different populations, single nucleotide polymorphisms (SNPs) and their association with specific human diseases and individual phenotypic characteristics, respectively [3,4]. Through GWAS an increasing number of gene loci have been identified that are associated with individual (future) phenotypic traits, such as hair or eye color, height, body mass index and others as well as with the disposition to develop a specific disease [3,4]. Further, genetic variants are associated with the individuals' response to drug treatment, e.g., to lithium [5]. Overall, GWAS allow an increasingly better understanding of disease pathogenesis and a more accurate assessment of the individual risk to develop a specific disease. Clinically, this may eventually translate into clinical advances in disease prevention, early diagnosis and therapy. It should be cautioned, however, that the contribution of a defined SNP to the risk assessment for a given disease must be weighed against established clinical parameters and needs to be carefully evaluated before entering clinical practice.

2. Review

2.1. The human microbiome project

The human microbiome project (HMP) was established in 2007 as another global consortium [6–10]. The HMP and the 'Metagenomics of the Human Intestinal Tract (Meta-HiT) Consortium Europe' aim at the sequencing of all microbes (eukaryotes, archaea, bacteria, viruses) that inhabit specific body sites, such as the mouth, throat and airways, stomach and intestine, the urogenital system and the skin, respectively (Fig. 1A). Recent data demonstrate that specific compositions of the microbial community are associated with health and disease [6–10] and suggest that the detailed characterization, function and variation of the microbial community will reveal important commensal host-microbe as well as microbe-microbe interactions with diagnostic, therapeutic and preventive implications [11,12].

While the HMP has meanwhile developed into a major field of biomedical research, the intestinal microbial community in particular has turned out to play a major role in human health and disease pathogenesis as will be discussed in more detail below [13].

2.2. The intestinal microbial community

In recent years the intestinal microbial community has been studied in great detail. It represents a microbial ecosystem

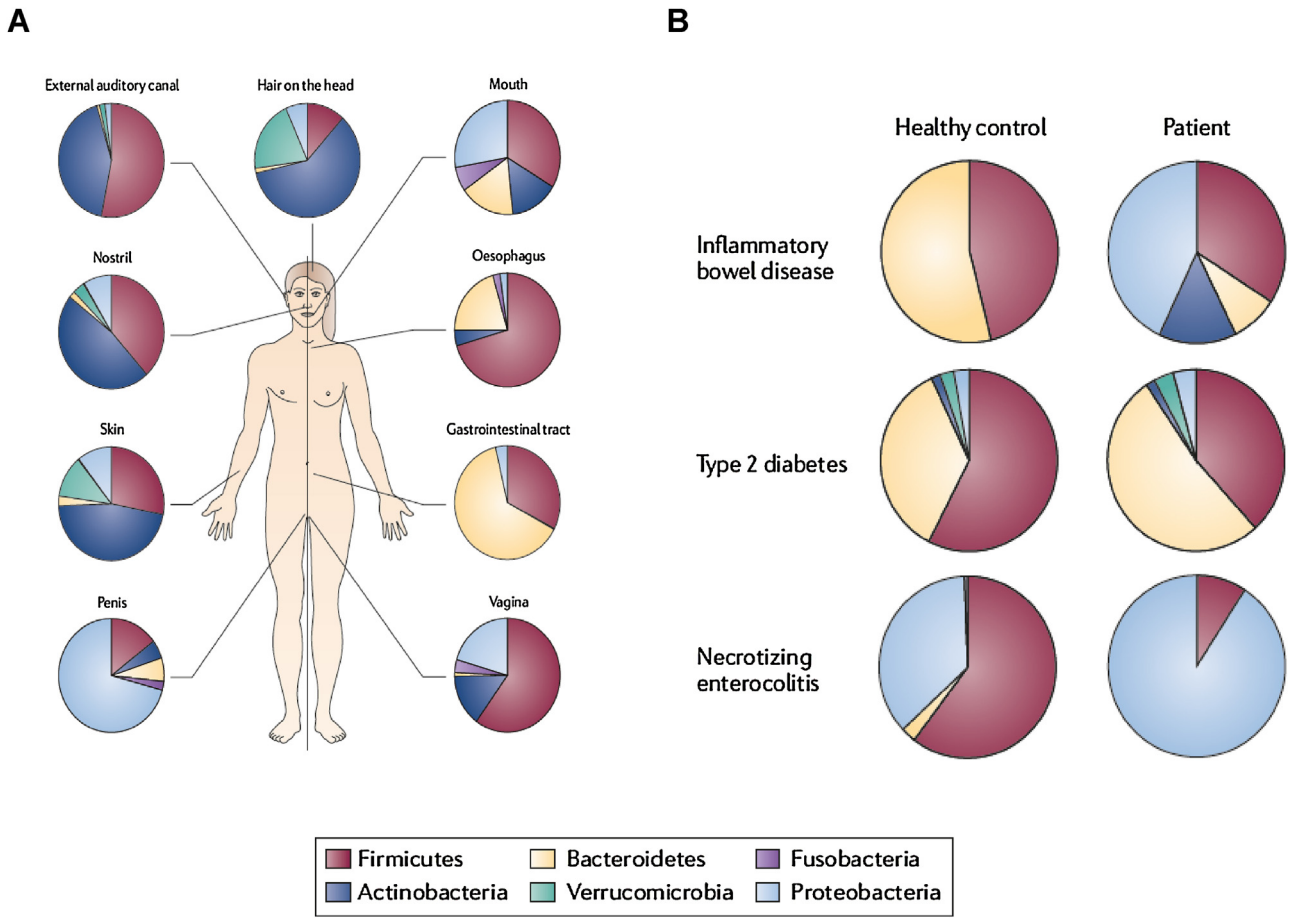

Fig. 1. (A) Different microbiomes in humans; (B) The intestinal microbiome in healthy individuals and patients [7].