Functional integrity of the host, the immune system and the gut microbiome

All multicellular eukaryotic organisms live together with beneficial bacterial communities in mutualistic or commensal association. They evolved in the presence of pro-caryocytes and acquired mitochondria and chloroplasts to help their physiological functions. The human microbiome involves several hundreds of various species, which outnumbers human somatic cells (10x) and genes (100x). The highly variable microbial communities share few conserved species, only and can be considered as a functional unit acting as a tissue. The microbiome is in continous contact with the immune- and nervous systems, food components and pathogens and thus it has an impact on host's physiology and defense mechanisms during all stages of life. Although several new high-through-put metagenomic approchases have recently been explored for studying the composition and functional attributes of complex ecosystems, the mapping of the human metagenome is far from complete. Recent studies revealed that the interaction of the nuclear genome, the cytoplasmic organelles and the microbiome supports the origin an the survival of new species and also promotes the development of protective mechanisms (*Brucker RM, Bordenstein SR Science 341:667,2013*). Based on the intimate link between the host, the microbiome and the environment the *hologenome* was introduced as a new term. The complexity of the microbiome acting as a functional unit is examplified by the modulatory role of retinoic acid, the metabolite of food-derived vitamin A, which plays an indispensable role in modulating the differentiation and functional activity of gut mieloid cell types ($CX3CR1^+$ macrophages and $CD103^+$ dendritic cells) and also in the regulation of T-lymphocyte polarization. In the special environment of the gut cells regulating innate and adaptive immunity acquire unique functions that support the growth of beneficial bacteria, while inhibit colonization by pathogens, prevent and decrease inflammatory reactions. The diversity and flexibility of the healthy microbiome is a pre-requisite of the development of the immune system as well as the induction and the maintenance of immunological tolerance. Vitamins, fatty acids, carbohydrates and food components play determining roles in our health, while changes in the microbiome causing dysbiosis may associate with chronic inflammation such as metabolic and cardiovascular diseases, diabetes, allergy, autoimmunity, inflammatory bowel diseases, coeliac disease, autism). Uncovering the extreme diversity of beneficial bacteria in the context of their functional attributes offers novel approaches for modulating the immune system and identifying innovative therapeutic targets.