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1. Developing an Artificial Bacterial Consortium to Modulate Microbiota of Frail Elderly

The microbial composition of the gut changes gradually with aging and is influenced by habitual diet and health status. In one cohort studied, frail elderly had a microbiota profile characterized by an increase in *Bacteroidetes* and a low microbiota diversity compared to healthy elderly. Paul W. O'Toole and colleagues (Cork, Ireland) developed a bacterial artificial consortium that mimics the healthy gut microbiota composition and potentially rectifies the gut microbiota of the frail elderly. More than 700 strains belonging to 90 bacterial species and one archaeon species were isolated in ore culture from the fecal samples of 7 healthy donors. 100 different commensal strains were finally selected from the initial collection, reflecting species with a range of abundance values in the gut microbiota based on the existing literature, and having considered the genetic similarity of the strains in order to maximize the genetic diversity of the consortium. To further investigate the safety of the 100 selected strains, the researchers determined their MIC values using a panel of 7 antibiotics. This rationally selected consortium of 100 commensal gut microbial strains could be used as a live biotherapeutic consortium for the modulation of the elderly gut microbiota.

2. Vaginal Microbiota-maternal Host Interactions and Their Influence on Pregnancy Outcomes

Vaginal bacterial communities dominated by *Lactobacillus* species are generally thought to promote healthy reproductive outcomes during pregnancy. Disturbance of these communities is associated with increased risk of poor outcomes, including preterm birth (PTB). David MacIntyre (London, UK) and colleagues showed that women with vaginal microbiota composition dominated by *Lactobacillus iners* species early in pregnancy are at increased risk of subsequent early PTB (before 34 weeks gestation). In contrast, early dominance of vaginal bacterial communities by *Lactobacillus crispatus* is associated with healthy term delivery. The researchers also showed that treatment interventions used for PTB prevention can impact upon vaginal microbiota composition. For example, while vaginal progesterone supplementation has minimal impact on community composition, cervical cerclage using braided suture material strongly promotes dysbiosis and is associated with activation of local inflammation and premature remodeling of the cervix. The use of erythromycin for treatment of women with preterm prelabor rupture of membranes (PPROM) also promotes dysbiosis, which may negatively impact both maternal and neonatal outcomes. The researchers then presented a novel application of the ambient mass spectrometry-based method, DESI-MS (Desorption Electrospray Ionization Mass Spectrometry) for assessment of vaginal mucosa metabolic profiles directly from medical swabs. This approach provides information about the composition of microbiota at different mucosal sites and their interaction with the host that could potentially be used to inform clinical decision making during pregnancy.

3. Role of Microbiome in Inflammatory Bowel Disease and Its Extra-intestinal Manifestations

A role for the microbiome in the initiation and maintenance of intestinal disease activity in patients with inflammatory bowel disease (IBD) is starting to emerge, with a decreased microbial diversity and an increased presence of *Proteobacteria* and *Actinobacteria* among the most often found dysbiotic components. Research by Gwenny Fuhler (Rotterdam, The Netherlands) and colleagues has shown that bacterial handling by innate immune cells is impaired in IBD patients. Furthermore, they showed that impaired host defense mechanisms in IBD patients can result in an increased presence of adherent invasive *Escherichia coli* species in the gut mucosa. IBD is associated with several extra-intestinal manifestations, including skin diseases such as psoriasis and hidradenitis suppurativa. The role of gut dysbiosis in IBD-associated diseases remains to be explored. The researchers therefore examined gut and skin microbiome of patients suffering from IBD, IBD and concomitant skin disease, or skin disease only. They showed a reduction in abundance of fecal *Faecalibacterium prausnitzii* and an increased abundance of *E. coli* in patients with IBD or psoriasis, compared to healthy controls, suggesting that a link between the gut microbiome and psoriasis might exist. However, the same was not observed for hidradenitis suppurativa. The authors went on to demonstrate that oral treatment of psoriasis with dimethylfumarates restores

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mycobiome dysbiosis in psoriasis patients. Whether or not UV treatment for skin diseases has an impact on the patients' gut microbiota is being investigated.

4. Cutaneous Microbiome in Inflammatory Skin Diseases

The skin acts as an important interface between the organism and the external environment, but also represents an ecosystem providing distinct niches for microbial communities. Next-generation-sequencing approaches used to characterize the cutaneous microbiome in healthy skin compared to lesional skin from psoriasis patients revealed significant differences in the composition of the microbiota. The vast majority of bacteria present in healthy human skin belong to the four phyla *Actinobacteria*, *Firmicutes*, *Proteobacteria* and *Bacteroidetes*. However, a marked decrease in the total diversity of microbial communities, an over-representation of *Proteobacteria* and an under-representation of *Actinobacteria* has been observed in lesional skin from psoriasis patients compared to corresponding non-lesional skin from the same individual. Karin Loser (Muenster, Germany) and colleagues characterized the cutaneous microbiota in lesional and corresponding non-lesional skin from psoriasis patients before and at different time points after the start of treatment with different biologics, including TNF-α blockade, IL-12/23 blockade, fumaric acid esters or phosphodiesterase inhibitors. The researchers found that clinical improvement as measured by Psoriasis Area Severity Index (PASI) correlated with alterations in the composition of the microbiome. Thus, successful treatment could help to "normalize" the microbiota in lesional skin of psoriasis patients.

5. Circulating Bile Acids as Biomarkers of Metabolic Health

The gut microbiota modulates bile acids (BA) enterohepatic circulation, and the profile of these potent cell signaling molecules in the blood. However, human data confirming dietary modulation of circulating BA profiles and subsequent regulation of physiological homeostasis remains elusive. The EU (ERA-HDHL) funded project CABALA_DIET&HEALTH, led by Fondazione Edmund Mach, Italy with partners in the UK (University of Reading), Italy (University of Insubria), Ireland (University College Cork) and Israel (Ben Gurion University of the Negev), aims to establish circulating BA profiles as biomarkers of health. Using samples from existing studies the researchers will correlate circulating BA profiles with adherence to the Mediterranean diet and measures of metabolic health (BMI, insulin/glucose and lipid homeostasis). In a short-term randomized controlled trial (RCT), they will measure the ability of probiotics, prebiotics and polyphenols to modulate post-prandial BA profiles. In a long-term (18-month), large-scale ($n = 300$) existing dietary and lifestyle RCT, they will also measure how polyphenol-rich foods and exercise, through BA signaling, promote metabolic health in susceptible individuals. Finally, the researchers will link BA profiles with microbiome signatures using high-resolution metagenomics and establish the molecular basis of BA regulation of immune and metabolic homeostasis by measuring the relative BA-metabotype receptor activation potential.

6. Genetically Modified Probiotics as Biotherapeutics

There is a strong interest in unraveling the molecular mechanisms involved in industrial robustness, cognate stress resistance and health-promoting phenotypes of food bacteria. This strategy, which involves the construction of genetically modified probiotics, can be divided into three distinct approaches: (i) delivery: engineering technological robustness; (ii) survival: improved competitiveness in the gut and other mucosa, and (iii) efficacy: improved therapeutic properties. During the past two decades, major health benefits of genetically modified probiotics have been demonstrated using animal models. The field has recently moved into the era of human clinical trials which showed biological containment, safety, and tolerability with preliminary data demonstrating positive efficacy in human subjects against oral mucositis. The potential of genetically modified probiotics as therapeutic tools for their safe and efficient use in human health was outlined. Catherine Daniel and colleagues (Lille, France) showed that a recombinant lactic acid bacterium producing a *Yersinia* protein has a dual potential in mice models: inhibition of experimental intestinal inflammation and protection against a pathogenic *Yersinia* challenge. Moreover, they developed multicolor bioluminescent bacteria for simultaneous visualization of different lactic acid bacterial strains by *in vivo* imaging in live mice.