were always in a state of perpetual change and self-overcoming. It depends on us to use any new technology for our benefit, establishing and adopting rules and behaviors under ethical and moral terms. In this way, it will not be 'appallingly obvious that our technology has exceeded our humanity' as it was through the eyes of Albert Einstein (1879–1955).

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Science & Society

Designer Probiotics: Paving the Way to Living Therapeutics

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Enhancing the functional repertoire of probiotics is a promising approach to cope with the inexorable rise of antibiotic-resistant pathogens and the rather slow development of new antibiotics. Probiotics that deliver novel therapeutics efficiently and with site specificity are emerging living therapeutics that may transform existing paradigms of disease diagnosis and prevention.

The normal microbiota are essential determinants of vital processes such as hematopoiesis, aging, immunity against infectious diseases, and behavior. Whereas the normal microbiota occasionally fails to protect the host against pathogens, a perturbed gut microbiota is associated with inflammation, obesity, insulin resistance, diabetes, cardiovascular diseases (CVDs), and neuropsychiatric disorders.

The WHO has recently released a list of 12 antibiotic-resistant families of pathogenic bacteria, described as 'priority pathogens', which pose a grave threat. Paradoxically, the development of new antibiotics has also slowed down, which increases the demand for alternative therapeutics. Expanding the efficacy of probiotics by introducing new genetic circuits to deliver drug biomolecules is crucial. These recombinant probiotics, informally called 'designer probiotics' or 'probiotics 2.0', are poised to reduce the gap between the mounting antibiotic resistance and the dearth of new antibiotics [1–4].

The science of probiotics, which was formerly confined to basic microbiology and food processing, has emerged in the postgenomic era of medicine and biology as a premier area of research towards functional nutraceuticals, gastroenterology, allergology, skin care, oncotherapy, psychoneuroendocrinology, and veterinary applications. The lactic acid bacteria (LAB), bifidobacteria, *Escherichia coli* Nissle 1917, and yeasts (*Saccharomyces cerevisiae*, *Saccharomyces boulardii*, *Kluyveromyces lactis*, and *Pichia pastoris*) are some of the prospective probiotics used for expressing heterologous genes encoding antimicrobial and anti-inflammatory biomolecules.

Designer Probiotics against Infectious Diseases

As the efficacy of orally administered antigens is reduced during passage through the alimentary tract, probiotic-mediated drug delivery could be a promising strategy for administering multiple therapeutics (cytokines, antibody fragments, antigens, peptides, etc.) *in situ* at the site of infection, therefore circumventing the side effects associated with the systemic administration of drugs.

For example, the vaccination of mice with recombinant *Lactobacillus gasseri* NM713 expressing streptococcal M6 protein (CRR6) protected them against streptococcus group A infections [5], and recombinant *Lactococcus lactis* (LL-Thy 12) expressing human interleukin-10 (IL-10) provided relief from Crohn's disease (CD) [1]. Furthermore, *L. lactis* strains that produce native (and pilin-deleted) immunomodulatory surface piliation appendages (SpaCBA) were found to activate Toll-like receptor 2-dependent signaling in cell lines and to modulate synthesis of anti-inflammatory cytokines (TNF-α, IL-6, IL-10, and IL-12) in human dendritic cells [6]. Another study reported recombinant *L. lactis* delivering therapeutic proteins at mucosal surfaces in murine models of human inflammatory bowel diseases (IBDs) and human papillomavirus type 16 (HPV-16) [7].

In addition, epidemiological, experimental, and clinical evidence convincingly shows that genitourinary microbiota dominated by LAB protect the host against bacterial vaginosis (BV) and sexually transmitted viral infections [9]. One contributor to host protection is a group of antimicrobial proteins including ribosomally-synthesized bacteriocins, microcins, peptides, and the type VI secretion