

MODIFYING THE HUMAN MICROBIOME

Human health is highly dependent upon the human microbiome—the microorganisms that live on and within us, especially those associated with the gut, oral cavity, nasopharyngeal space, and skin. These populations of microbes are likely far easier to manipulate than the human host itself, making the microbiome a potentially accessible vector for attack. The human microbiome is the focus of a great deal of academic and commercial research, and microbiome manipulation is an area that is rapidly developing, as also discussed in Chapter 5. Several possible ways the microbiome could be manipulated to cause harm were considered; these possibilities were analyzed, in aggregate, to determine the level of concern warranted.

Delivery of harmful cargo via the microbiome. As discussed in Chapter 5, the engineering of microorganisms to produce hazardous chemicals or biochemicals (including toxins) poses a medium to high level of concern and the potential for making chemicals or biochemicals in situ via the microbiome warrants a high level of concern. The microbiome could be used as a vector for other types of harmful cargoes, as well. For example, microbes could be modified to produce functional small RNAs (e.g., microRNAs [miRNAs]) that could be transferred to the host via the gut or skin microbiome¹ to cause a variety of health impacts.² Microbes also could potentially be engineered to horizontally transfer a genetic cargo to the native microbiome to, for example, cause a host's own well-established microbes to produce a harmful biochemical. In such a scenario the harmful agent would be manufactured by organisms in the established microbiome, so the engineered microbe would need to infiltrate and persist within the microbiome only long enough to transfer its cargo to a sufficient number of native microbes. Thus, this approach would circumvent the challenges associated with establishing engineered microbes in otherwise occupied niches. There are many known instances of natural horizontal transfer events that result in the production of toxins (Kaper et al., 2004; Strauch et al., 2008; Khalil et al., 2016). It may be possible to harm a population by enhancing the spread of vectors or phage (viruses targeting bacteria [Krishnamurthy et al., 2016]) carrying such genetic cargoes. Synthetic biology methods could advance such a capability, for example, through the engineering of toxin:antitoxin couples that would help ensure retention of plasmids. It is also conceivable that microbes could one day be engineered to horizontally transfer genes directly to human cells.