acetyltransferases (Barrett et al. 2008; Tsitovich et al. 2010) and directly monitoring antibiotic resistance (Disney and Childs-Disney 2007).

Not only the binding to the target but also the specificity, defined as the ability to discriminate between different RNA sequences, is critical for the development of new therapeutics. Several studies determined the specificity of rRNA interaction with different aminoglycosides. An advantage of the microarray approach is that the specificities can be estimated in a high-throughput manner by comparing relative intensities of each aminoglycoside binding to different RNA sequences. Importantly, the covalent aminoglycoside microarrays depicted in Figure 1.4b provided the basis for development, by Disney and colleagues, of a microarray-based two-dimensional combinatorial screening (2DCS) method for interactions of AGAs with RNA (Childs-Disney et al. 2007; Disney et al. 2008). In this method, ligand and RNA motifs are screened in parallel to identify selective interactions that can be used to target RNA. Later, this method was combined with a statistical analysis scoring method, designated structure–activity relationship through sequencing (StARTS) (Velagapudi and Disney 2013). This method scores RNA motif–ligand partners selected by 2DCS to map RNA/ligand interactions. The integration of the microarray-based 2DCS and computational StARTS methods led to the development of the Inforna technology, which has been applied in the identification of small molecules that bind to precursor miRNAs (pre-miRNAs) (Velagapudi et al. 2014).

With the development of microarray technology and the combination of chemoenzymatic synthesis, computational chemistry, and SAR-derived insight, new AGAs are anticipated to address effective antibacterial drugs.

1.4 Influence of the Human Microbiome in Aminoglycoside Resistance

In the quest for novel approaches to AGA usage, and to overcome factors that diminish the effectiveness of aminoglycoside therapy, the human gut microbiome has gained importance as it constitutes a reservoir of resistance genes and has a major potential to modulate the action of antibiotics in the human organism (Francino 2016; Langdon et al. 2016).

The human microbiota is a large microbial community primarily found on the skin and in gastrointestinal (GI), respiratory, and urogenital tracts that corresponds to 50% of the human body cells (Human Microbiome Project Consortium et al. 2012; Sender et al. 2016). Thus the human microbiome may be defined as the collection of all microbiota strains, genomes, metabolites, and host's by-products (Marchesi and Ravel 2015). This community carries a gene pool 150 times larger than the human's, including unique genes that expand our own metabolic abilities (Qin et al. 2010). The complex molecular