

Stable isotope labeling by amino acids in cell cultures (SILAC) is an alternative method, developed for quantitative proteomics, that has been applied successfully to detect resistance to various antibiotics in strains of *S. aureus* and *P. aeruginosa* (Sparbier et al. 2013; Jung et al. 2014). SILAC incorporates mass tags only into specific amino acids, such as lysine. To the extent that the tagged amino acids are selectively incorporated into biomolecules, changes to the isotope profile will be observed in the affected molecules. The labeling is limited in distribution and amount, so the changes are not easy to detect. While SILAC may produce less profound changes in the isotope profile, a significant advantage is that labeling can be done with easily obtainable isotope-labeled amino acids (Demirev 2016).

Metal oxide laser ionization (MOLI) MS, using cerium oxide as the catalyst, has also been proposed as a method for bacterial identification (Saichek et al. 2016). The use of *in situ* hydrolysis for applications involving pyrolysis MS of bacteria was pioneered by Basile et al. (1998); later a whole-cell MALDI-TOF MS method was modified to allow measurement of free fatty acids released from bacterial lipids (Voorhees et al. 2013). Laser ionization of extracted bacterial lipids on a CeO₂ surface (MALDI target) resulted in the release of free fatty acids for MS analysis (Cox et al. 2015). This technique now has been extended to include concurrent detection of antibiotic resistance (Saichek et al. 2016). Fatty acid profiles were used not only to identify *Staphylococcus* isolates but also to differentiate β -lactam-resistant and susceptible strains. Lipid profile differences reflected antibiotic susceptibility as well as bacterial species, but the resistance-related changes to the fatty acid profile were not profound. A combination of fuzzy rule building with expert system classification and self-optimizing partial least squares discriminant analysis was needed for data interpretation (Saichek et al. 2016). This approach clearly complements the whole-cell MALDI-TOF MS method, but the generality of the detection of antibiotic resistance as shown by fatty acids has not been proven.

Other MS methods that have shown feasibility for rapid detection of antibiotic resistance include surface-enhanced laser desorption ionization (SELDI)-TOFMS (Shah et al. 2011), high-performance liquid chromatography–electrospray ionization (LC-ESI) MS (Grundt et al. 2012; Schelli et al. 2017), and membrane electrospray ionization (MESI) MS (Fan et al. 2016).

Genomics-based MS methods that allow both identification and the concurrent determination of susceptibility show great promise. However, any omics approach will be much more complex than whole-cell MALDI-TOF MS (Lichtenwalter et al. 2000). While the complexity is similar for genomics and proteomics, proteins are generally more amenable to characterization by MS than DNA and RNA. Moreover, proteins more directly indicate phenotypic properties, such as resistance, whereas genomics addresses a potential that may or may not be expressed. Because of the difficulty of probing the genome