A New Understanding of Antibiotic Action via Solid-State NMR of Cells with Uniform Isotopic Labeling

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In this issue of the Biophysical Journal, Nygaard et al. (1) describe an exciting new solid-state NMR approach to probe the composition of whole bacterial cells and their cell-wall fractions. Use of uniform 13C and 15N labeling as well as magic-angle spinning and rotational-echo double-resonance (REDOR) selection of either Gly or non-Gly 13C signals allows for NMR detection of many chemical functionalities including polysaccharide and protein (2–5). In my view, the most exciting result is the striking differences among unfiltered 13C NMR spectra of whole bacterial cells grown with different antibiotics, as displayed in Fig. 7 in the article. Relative to control cells that were not treated with antibiotic, cells treated with fosfomycin antibiotic have a significantly smaller ratio of polysaccharide/protein 13C signal intensities whereas cells treated with chloramphenicol have a significantly greater ratio. This correlates with the known inhibition of cell-wall synthesis by fosfomycin and protein synthesis by chloramphenicol. It is therefore likely that this new method can rapidly and quantitatively discern the general mechanism of action of a new antibiotic. This should be very useful in development and comparison of new antibiotics.

The article by Nygaard et al. (1) builds on earlier whole-cell solid-state NMR studies by Cegelski et al. (6) and Kim et al. (7) with more selective isotopic labeling. The binding modes and mechanisms of action of antibiotics such as oritavancin were elucidated in this work. Other applications of whole-cell solid-state NMR include quantitation and analysis of folding of recombinant proteins in inclusion bodies (8,9). The use of uniform labeling and REDOR filtering described in the article by Nygaard et al. (1) highlights the power of solid-state NMR to address important questions in complex biological materials such as bacterial cell walls. There are many problems in medicine and biotechnology for which these approaches should provide great insight with potential application to cell types other than bacteria.

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REFERENCES


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