ACS Infectious Diseases

In This Issue

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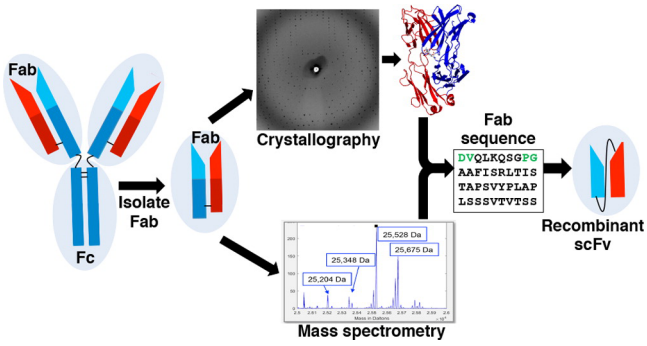
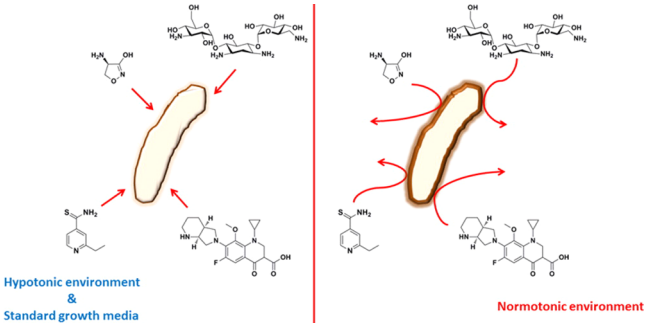
THE ANTIBODY IN THE FREEZER



Despite the critical need for diagnostic and therapeutic antibodies targeting infectious disease agents, development of clinically useful antibodies from previously identified mouse monoclonal antibodies is often hindered by the lack of antibody sequence information and/or loss of hybridoma cells that produce them. For example, a paper published over 20 years ago described the isolation of a mouse monoclonal antibody, PL-2, against human astrovirus; however, the hybridoma cells that produced the antibody have since been lost.

In this month's *ACS Editors Choice* article, Bogdanoff et al. (DOI: 10.1021/acsinfecdis.6b00026) perform X-ray crystallography and mass spectrometry using the remaining frozen PL-2 monoclonal antibody sample to determine the crystal structure and protein sequence of the antibody PL-2 Fab fragment. With the information gleaned from these experiments, the authors engineer a recombinant antibody that retains binding specificity to its virus antigen target. The human astrovirus-neutralizing antibody produced here holds the potential to be further developed as a diagnostic or therapeutic agent. Furthermore, these studies provide a blueprint for determining the sequences of previously developed antibodies against other infectious diseases and generating recombinant versions of these antibodies.

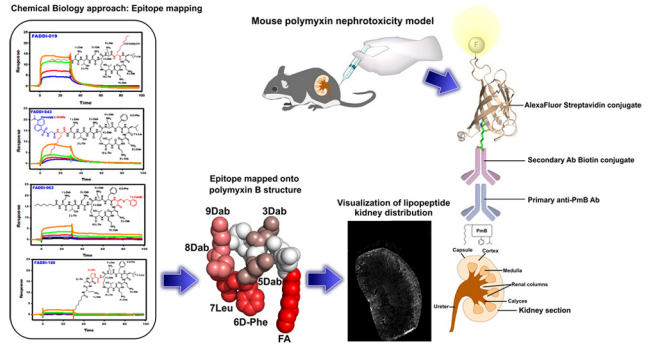
THE DANGERS OF SALT



The environment in which bacteria grow, be it within a culture flask or specific compartments within the body, plays a significant role in contributing to phenotypic antibacterial tolerance. In other words, antibiotic susceptible bacteria lacking defined resistance determinants may still persist upon antibiotic treatment as a result of bacterial adaptations to the environment. Indeed, activities of a number of antibiotics are known to be affected by salt concentration, and so susceptibility testing requires physiological concentrations of salts for these antibiotics. Although it is well established in several species that high salinity can affect the composition of the bacterial membranes, it is not established if salinity affects the cell envelope of *Mycobacterium tuberculosis*.

Here, Larrouy-Maumus et al. (DOI: 10.1021/acsinfecdis.5b00148) use state-of-the-art metabolomics and lipidomics to describe the discovery and characterization of the effects of physiologic salt concentrations on *M. tuberculosis* biology. The investigations reveal that osmotic stress induced multiclass antibiotic tolerance in *M. tuberculosis*. The authors found that rather than observing metabolic changes that are rapid and reversible, the antibiotic tolerance observed kinetically correlated to changes in the cell envelope. This work expands our understanding how *M. tuberculosis* drug tolerance may occur within the human body and has important implications for antibiotic treatment and development.

MOVING THE LINE ON POLYMYXIN SAFETY



As antibacterial resistance continues to increase and few new antibiotics reach the market, medical professionals are turning to "last-line" therapies such as polymyxin B and colistin for treatment of drug-resistant Gram-negative superbugs. These polymyxin lipopeptides are considered last-line therapeutics due to their nephrotoxicity, which limits their clinical utility. The major barrier to the development of novel safe polymyxin lipopeptides is a limited understanding of the complex structure–nephrotoxicity relationships for these drugs.

In this issue, Velkov et al. (DOI: 10.1021/acsinfecdis.6b00031) have employed a targeted chemical biology approach to map the polymyxin recognition epitope of a commercially available polymyxin monoclonal antibody. The authors demonstrate its utility for mapping the kidney distribution of a novel, less nephrotoxic polymyxin lipopeptide. This work presents a new platform for polymyxin structure–nephrotoxicity relationship studies that can be applied by drug development teams working on a new generation of safer polymyxin lipopeptide antibiotics.

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