Technical BULLETIN

ABRx™ Antibiotic Resistance Panel

Antibiotics are among the most commonly prescribed drugs in the world, and the invention of these "miracle drugs" have helped save millions of lives since their introduction in the 1940s. Unfortunately, the extensive use of antibiotics has led to development and worldwide spread of antibiotic resistance. Strategies to reduce antibiotic resistance have received an unprecedented amount of attention from the United Nations, WHO, White House, CDC, practicing physicians, and clinical scientists. Increasing numbers of key opinion leaders in the scientific community and political leaders worldwide are fearful that we are entering a "post-antibiotic era" in which previously dependable therapeutics are rendered useless, and common bacterial infections once again become untreatable and deadly.[1]

Bacteria possess naturally occurring antibiotic resistance mechanisms. They also acquire additional antibiotic resistance through the exchange of mobile genetic elements (plasmids) and/or partial chromosomal elements during conjugation (Figure 1). This exchange of genomic material frequently occurs within the rich microbiota of the upper respiratory and gastrointestinal tracts.[2] Furthermore, when bacteria causing an infection are exposed to therapeutic doses of antibiotics, genetic resistance mechanisms can be induced to be expressed. Unfortunately, patients are often started on empiric antibiotic therapy without the knowledge of a bacteria's underlying antibiotic resistance mechanisms.

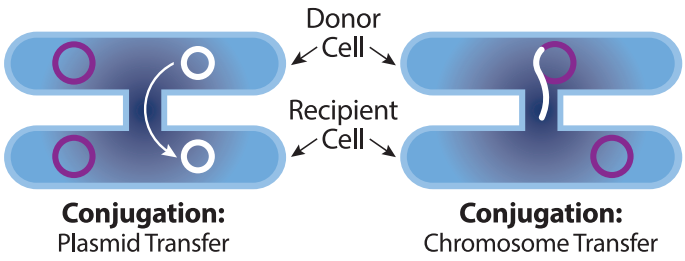

Figure 1. Exchange of antibiotic resistance genes in bacteria

Diatherix Laboratories has developed the ABRx Antibiotic Resistance Panel that tests for seventeen antibiotic resistance genes responsible for resistance to three major classes of antibiotics routinely prescribed: β-lactams (penicillins, cephalosporins, monobactams, and carbapenems), macrolides, and fluoroquinolones (Table 1). The ABRx Panel detects clinically relevant gene variants directly from clinical samples without the need for time-consuming bacterial isolation and identification. Direct detection of genetic resistance mechanisms is a novel and important concept of identifying potential failure in the treatment of infectious disease prior to isolation of the causative organism and subsequent antimicrobial sensitivity testing. The presence of a gene that codes for resistance is not always detected through conventional antibiotic susceptibility testing because resistance genes that are carried by bacteria may not be expressed at the protein level. Additionally, in the course of sample collection, transport, and workup in the laboratory, standard microbiological techniques can cause uncertainty as to whether or not the selected bacteria from the culture plate is the causative agent of infection.

The clear distinction between conventional antibiotic susceptibility testing and molecular resistance profiling is a difference of antibiotic inclusion versus antibiotic exclusion prescription strategy. Detecting genetic resistance provides information to clinicians so that they may avoid an antibiotic class for which a resistance gene may exert its effects during treatment of the infectious process. Left undetected, genetic drug resistance carries the threat of treatment failure. The laboratory report generated by the ABRx Panel will provide a list of antibiotic classes that may be minimally effective or contraindicated when gene resistance targets are detected.

With *One day results**, the ABRx Panel is designed to decrease turnaround time, improve diagnostic accuracy, and benefit both patient outcomes and hospital quality measures. Diatherix Laboratories provides physicians and pharmacists with clinically important information for antibiotic stewardship programs, preventing possible outbreaks, decreasing patients' lengths of stay and readmissions, and reducing healthcare costs.

Table 1. ABRx Panel Content [3,4,5,6]

Antibiotic Class	Mechanism of Gene Resistance Action	Molecular Class	Panel Target	Antibiotic Class Avoidance
β-Lactam	Breaks β-lactam ring through hydrolysis, deactivating the molecule's antibacterial properties	Class A β-lactamase	CTX-M Group 1	cephalosporins, penicillins, aztreonam
			CTX-M Group 2	
			CTX-M Group 8/25	
			CTX-M Group 9	
			KPC	carbapenems, cephalosporins, penicillins, β-lactamase inhibitors, aztreonam
		Class B metallo-β-lactamase	IMP-1	carbapenems, cephalosporins, penicillins, β-lactamase inhibitors
			VIM	
			NDM	
		AmpC β-lactamase	FOX	cephalosporins, penicillins, β-lactamase inhibitors
		Class D oxacillinase	OXA-1	cloxacillin, oxacillin, penicillins
			OXA-48	carbapenems, extended spectrum cephalosporins, penicillins, β-lactamase inhibitors
		Minor ESBL	PER	extended spectrum cephalosporins, penicillins, aztreonam
			VEB	
			GES	carbapenems, cephamycins, extended spectrum cephalosporins, penicillins
Macrolide	Methylation on 23S ribosome affects antibiotic binding	Erythromycin ribosomal methylase	*ermB*	macrolides (erythromycin, clindamycin, azithromycin)
Fluoroquinolone	Binds to and reduces affinity of DNA gyrase and topoisomerase to antibiotic	Pentapeptide repeat protein	*qnrA*	fluoroquinolones (ciprofloxacin, gemifloxacin, levofloxacin, moxifloxacin, norfloxacin, and ofloxacin)
			qnrS	

References:

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