Preventing antimicrobial resistance evolution by inactivating daptomycin in the gut

Clinical antibiotic use creates natural selection for antibiotic resistance, consequently fanning the flames of the antimicrobial resistance crisis. A key challenge, then, is to figure out how to use antibiotics therapeutically without driving the evolution of resistance. We recently discovered one way to do that: an adjunctive therapy that can prevent resistance evolution. We repurposed the drug cholestyramine, an FDA-approved bile acid sequestrant, as an ‘anti-antibiotic’ to disable intravenous (IV) daptomycin reaching the gastrointestinal (GI) tract. In mice, we demonstrated experimentally that co-administration of oral cholestyramine during systemic daptomycin treatment prevented the emergence of daptomycin resistance in gastrointestinal populations of patient-derived Enterococcus faecium. Thus, we prevented resistance emergence in transmissible populations of E. faecium colonizing the gut, while allowing antibiotic activity in the bloodstream, which is the target therapeutic site. Preventing resistance evolution in the gut is important because E. faecium spreads through fecal transmission. Therefore, gastrointestinal E. faecium are source populations for infection and transmission in healthcare settings. Preventing resistance emergence in GI populations thus protects treated patients from infection with resistant strains and prevents transmission of resistant pathogens. E. faecium is one of several pathogens listed as ‘Urgent’ or ‘Serious’ Resistance Threats by the US Centers for Disease Control and Prevention (CDC) that colonizes the GI tract asymptptomatically, so this approach has the potential to significantly combat antibiotic resistance in hospitals.

1. What is your pathogen? Multiple options possible (e.g. if working on coinfections)
   
   Bacteria : Enterococcus faecium

2. On a scale of 1-5 is your work mostly eco/epidemiological or evolutionary? 4

3. On a scale of 1-5 is your work mostly theoretical or experimental/empirical?
   5 (100% empirical)