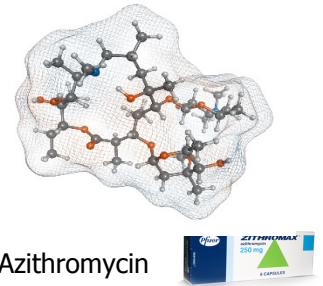


In vitro Pharmacology: Microbiology

- Long history in anti-infective drug discovery, culminating with the invention of the block buster macrolide antibiotic **azithromycin** (Zithromax™, Sumamed™)
- In house **strain collection**
 - >2000 bacterial and 800 fungal, fully characterized strains
 - Different resistance mechanisms against various antibiotic classes
 - Access to clinically relevant pathogens

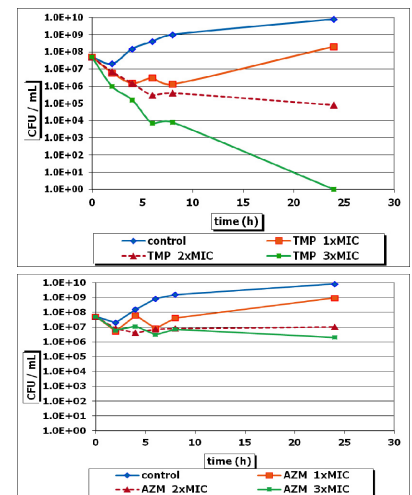


In vitro compound profiling

Over 20 years of experience in antimicrobial compound profiling, testing against a vast number of relevant pathogens bearing different resistance patterns in class 2 pathogen certified labs, ensures skilled and comprehensive *in vitro* compound profiling, in assays like:

- **Antimicrobial susceptibility testing** (CLSI/EUCAST guidelines compliant)
 - Microdilution, agar dilution, disk diffusion
 - MIC, MIC₅₀, MIC₉₀ and MBC determination
- **Drug combinations testing** for synergy effects
 - FIC index determination
- **Time-kill studies**
- **Resistance development propensity studies**

Fidelta is experienced in developing custom assays as well as **tailor-made assays** for non-conventional compounds and/or with clinical isolates provided by clients.

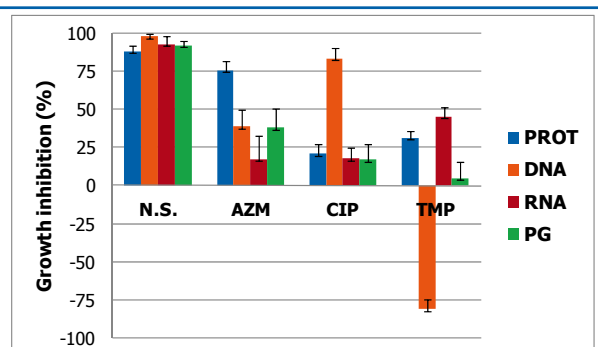


Time kill for azithromycin (AZM) and trimethoprim (TMP) on hyperpermeable *E. coli* strain.

Mechanism of action determination (MoA)

Based on experience with different classes of antimicrobials with diverse or unknown MoA and reverse pharmacology in general, Fidelta is confident to tackle any MoA demand with assays such as:

- **Macromolecular synthesis inhibition**
 - Differentiating inhibitors of DNA, RNA, protein and cell wall synthesis
- **Inhibition of transcription and translation**
- **Thymidine rescue**



Macromolecular synthesis. Cellular pathways analyzed by radioactive metabolite incorporation. *Thymidine rescue can be seen for trimethoprim. (N.S. – non specific, AZM – azithromycin, CIP – ciprofloxacin, TMP – trimethoprim).

References

Hasenoehrl et al. 2006, Antimicrob Agents Chemother, 50, 3011; Alihodzic et al. 2006, J Antibiot, 59, 753; Kapic et al. 2010, Bioorg Med Chem, 18, 6569; Pesic et al. 2012, J Med Chem, 55, 3216.