

Abstract

Antibiotic resistance is increasing rapidly world wide. Resistance determinants have evolved long before antibiotics were used. Though horizontal gene transfer and mutation play a major role in the dissemination of antibiotic resistance genes their evolutionary origins remain obscure. A model system was used to investigate how they might arise in the first case.

Plasmid borne erythromycin resistant clones were selected through marker rescue from genomic libraries of DNA from Gram positive organisms, maintained in *E. coli*. Ery^R determinants were recovered from nine libraries of 23 screened. Clone pMP1 (DNA from *Mycobacterium parafortuitum*) was the most resistant, with an MIC of 400 µg/ml for erythromycin and 12 µg/ml for azithromycin. Antibiotic resistance was not expressed in *Rhodococcus erythropolis*. Restriction maps were constructed for clones pMP1 and pMCX (DNA from *Mycobacterium avium*). Clone pMP1 was sub-cloned and the fragment carrying the Ery^R determinant (~2.4 kb) was sequenced. Analysis revealed 2 open reading frames (ORF1 and ORF2). ORF1 showed highest similarity to an FixB/FixA proteins and ORF2 showed similarity to a methyl transferase.

Key words: antibiotic resistance, erythromycin, Gram positive DNA