

**Over-expression of *patA* and *patB*, which encode ABC transporters,
is associated with fluoroquinolone resistance in clinical isolates of
*Streptococcus pneumoniae***

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Over-expression of the ABC transporter genes *patA* and *patB* has been shown to confer multi-drug resistance in laboratory strains of *Streptococcus pneumoniae*. However, to date, this resistance mechanism has not been observed in clinical isolates. In this study, fifty-seven clinical isolates of *S. pneumoniae* were tested for susceptibility to two fluoroquinolones and two dyes, and expression of *patA* and *patB* was determined by comparative RT-PCR. Over-expression of *patA* and *patB* was observed in 14 of the 15 isolates that were resistant to both fluoroquinolones and dyes, and in only 3 of 24 of those resistant to fluoroquinolones only. Isolates over-expressing *patA* and *patB* accumulated significantly less of the fluorescent dye Hoechst 33342 than wild type isolates, suggesting that PatA and PatB are involved in efflux. Inactivation of *patA* and *patB* by *in vitro* Mariner mutagenesis conferred hyper-susceptibility to ethidium bromide and acriflavine in all isolates tested, and lowered MICs of ciprofloxacin in the *patAB* over-producing and/or fluoroquinolone resistant isolates. These data represent the first observation of over-expression of *patA* and *patB* in clinical isolates and show that PatA and PatB play a clinically relevant role in fluoroquinolone resistance.