

**P1395 Is evolution towards resistance associated with virulence modification in *Pseudomonas aeruginosa* during ventilator-associated pneumonia?**

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**Background:** It is well known that treatment with broad-spectrum antibiotics leads to the selection of isolates with increased resistance. In this study, we wondered if the evolution towards resistance could be associated with changes in virulence, in the context of *P. aeruginosa* acute infections like ventilator-associated pneumonia (VAP).

**Materials/methods:** Four patients of intensive care units were retrospectively selected for this study because they had multiple episodes of VAP during a short period (12 days to 5 weeks), with emergence of resistance during antibiotic treatment. We performed Illumina whole genome sequencing of 12 *P. aeruginosa* isolated from bronchoalveolar lavages in these 4 patients. *Quorum sensing*-dependent virulence factors (pyocyanin and protease), serum resistance and cytotoxicity against the pulmonary cell line A549 were determined for all isolates. Twitching motility and biofilm production were studied for some isolates.

**Results:** Genetic events explaining evolution towards increased resistance to antibiotics were detected in *oprD*, *mexR*, or *ampD*. This evolution was associated in the same isolates with variations in genes known to be implicated in virulence in *P. aeruginosa* (*lasR*, *rhlR*, *pilM*, *groEL*, or *gacA*). Modifications in *lasR* correlated with decreased pyocyanin and protease production, but also with decreased serum resistance and cytotoxicity on A549 cells. A nonsense mutation in *pilM*, coding for a subunit of the type IV pili, correlated with enhanced twitching motility. The A201S substitution detected in the global activator GacA was associated with reduced biofilm formation.

**Conclusions:** We clearly show here that evolution of *P. aeruginosa* towards resistance is associated with modification of virulence, even in acute infections. The consequences of this short-term pathoadaptation still need to be explored.