

Impact of *per os* antibiotic treatments on the gastrointestinal colonization with a multi-resistant *Klebsiella pneumoniae* strain

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Introduction: Colonization resistance refers to the ability of microbiota to prevent expansion and persistence of exogenously acquired bacterial species. Previous research shows that changes in microbiota composition lead to multi-drug resistant bacteria domination of the gastrointestinal tract in antibiotic-treated mice.

In this study our goal was to determine the effect of different *per os* antibiotic treatments on colonization rate and resistance gene copy numbers in intestinally carried *K. pneumoniae* (KP5825) in mice. This strain expressed a PMQR gene (*aac(6')-Ib-cr*), an extended-spectrum β -lactamase enzyme (CTX-M-15) as well as a carbapenemase enzyme.

Methods: All experiments were carried out using 6- to 8 week-old C57BL/6 male mice. For colonization, 5×10^6 CFU of KP5825 was administered orally on the 14th and 15th days of ampicillin pretreatment. After the colonization mice were divided into 6 groups receiving the following antibiotic treatments for 15 days: 0.5g/L of ampicillin (AMP), ceftazidime (CAZ), and ciprofloxacin (CIP) and 0.1g/L of CAZ, CIP was administered in the drinking water (6th group: control). Throughout this period microbial DNA was extracted from freshly collected fecal pellets.

In the second phase of our experiments the V3-V4 region of the 16S rRNA gene was sequenced to determine the microbiota composition in the intestines of mice. We used the qPCR technique to determine the KP5825 DNA quantities and assess the resistance gene copy numbers.

Results: Our results show a significant perturbation in the intestinal microbiota. We could also observe that after 15 days KP5825 decreased significantly ($p < 0,004$) in the control group and in the CIP treatment groups ($p < 0,0001$, $p < 0,002$). Furthermore, our qPCR results show that the higher dose CAZ treatment lead to a 4-fold increase in quantities of plasmids with CTX-M.

Discussion and Conclusion: Thus, CAZ had higher power on the dissemination of resistance genes than CIP. This raises the possibility of *in vivo* plasmid transfer, which we intend to investigate in our future experiments.

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