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ePoster Viewing

Basic Science: animal models including experimental treatment

Effects of antibiotic on the microbiota of mice

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Background: We have previously shown (Boetius Hertz et al. AAC, 2014) that cefotaxime (CTX), cefuroxime (CFR), dicloxacillin (DCX) and clindamycin (CLI) significantly selected for ESBL-producing *E.coli* in the mouse intestine, while ciprofloxacin (CIP) did not. In the present study, we investigated the impact of these five antibiotics on the intestinal microbiome in mice.

Methods: Four weeks old, female NMRI mice (5/antibiotic) were treated with the antibiotics s.c. once daily for 3 days (mouse dose in mg/kg): (CTX; 60), (CFR; 120), (DCX;60), (CIP;15) and (CLI;50). Faeces were collected directly from each mouse at days 1, 3 and 5. The intestinal microbiotas were profiled by analysis of faeces samples by use of IS-pro, introduced by Budding et al. in 2010. IS-pro is based on the species-specific length and phylum-specific sequence polymorphisms of the IS region of 16S rDNA. All samples were analyzed by IS-pro with fluorescent probes binding to the phylum-specific rDNA. Thus high levels of rDNA present create high peaks of light absorbed. Therefore, IS profiles consist of a set of peaks with: (A) a specific length, measured in nucleotides reflecting lengths of IS fragments and (B) a specific height, measured in relative fluorescence units, reflecting quantity of PCR product. Specific optimizations were made for gut microbiota. DNA isolation, DNA amplification and electrophoresis were performed as described by Budding et al 2010. All data optimization and analysis was performed by IS Diagnostics Ltd. with in-house developed software in combination with the Spotfire software package (Tibco).

Results: These are given as the individual sums of three phyla: *Bacteroidetes* (Gram-negative anaerobic, including the *Bacteroides spp.*), *Firmicutes* (containing most Gram-positives including *Clostridia spp.*) and *Proteobacteria* (including *E.coli, Salmonella* and other spp.). The ratio between day 1 and day 3 are given when appropriate. CIP completely inhibited the *Proteobacteria* (ratio 0.026), with limited proliferation of other phyla. CLI inhibited the *Bacteroidetes* (ratio 0.00097) allowing for the two remaining phyla to proliferate. CTX allowed for some overgrowth of all three phyla while DIC seemed to inhibit the *Bacteroidetes* (ratio 0.66) during treatment leading to a subsequent increase in *Proteobacteria* (ratio 2.1). CLI and CIP had an impact on the flora which changed the phyla composition throughout the study. For the remaining antibiotics the flora normalized from day 3 to 5.

Conclusions: We found surprisingly few changes in the microbiota created by the cephalosporins. DIC and CLI exert their selective ability by inhibiting *Bacteroidetes* and changing the ratio between phyla. CIP had a major inhibiting impact on the *Proteobacteria*. We therefore identified the likely reasons for the selective abilities of CLI and to some extent DIC, while the lack of selection from CIP, as preciously found, remains unclear.