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An in vitro dynamic model of catheter-associated urinary tract infections to investigate the role of uncommon bacteria on the *Escherichia coli* microbial consortium

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About 9% of nosocomial infections are attributed to catheter-associated urinary tract infections (CAUTIs). Uncommon bacteria (*Delftia tusurhatensis*) have been isolated in CAUTIs in combination with well-established pathogenic bacteria such as *E. coli*. Nonetheless, the reason why *E. coli* coexists with other bacteria instead of outcompeting and completely eliminating them are unknown. As such, a flow cell reactor simulating the hydrodynamic conditions found in CAUTIs (shear rate of 15 s^{-1}) was used to characterize the microbial physiology of *E. coli* and *D. tsuruhatensis* individually and in consortium, in terms of growth kinetics and substrate uptake. Single-species biofilms showed that up to 48 h the CFU counts significantly increased for both species (p<0.05). After 48 h, both species stabilized with similar CFU values reaching log 6.24 $CFU.cm^{-2}$ for *E. coli* and log 6.31 $CFU.cm^{-2}$ for *D. tsuruhatensis* (p>0.05). The assessment of spatial distribution of dual-species biofilms by LNA/2´OMe-FISH revealed that *E. coli* and *D. tsuruhatensis* coexist and tend to co-aggregate over time, which implies that bacteria are able to cooperate synergistically. Substrate uptake measurements revealed that in artificial urine medium the bacteria metabolized lactic acid, uric acid (*E. coli* and *D. tsuruhatensis*) and citric acid (*D. tsuruhatensis*). In the consortium, *D. tsuruhatensis* consumed citric acid more rapidly, presumably leaving more uric acid available in the medium to be used by *E. coli*. In conclusion, metabolic cooperation between *E. coli* and

uncommon species seems to occur when these species share the same environment, leading to the formation of a stable microbial community.