Universität Basel

Research Project

EcoStrat: Interrogating the diversity of gut colonization strategies in multidrug-resistant E. coli to deduce robust competitive exclusion approaches

Third-party funded project

Project title EcoStrat: Interrogating the diversity of gut colonization strategies in multidrug-resistant E. coli to deduce robust competitive exclusion approaches
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Project start 01.01.2021
Probable end 31.12.2025
Status Active

The rise of multidrug-resistant bacteria limits the options to treat critically ill patients. In 2015, Escherichia coli producing Extended Spectrum β-Lactamases (ESBL) were the leading cause of death attributable to antibiotic resistant bacteria in Europe. The failure to address these infections using standard antibiotherapy calls for better understanding of how these bacteria evolve in order to develop new treatments.
Presence of resistance and virulence genes correlates with high prevalence in ESBL clones. Since the intestinal tract of mammals represents a major ecological niche for E. coli, gut colonization ability must have predisposed certain clones to evolutionary success during the antibiotic era. In particular, competition against the gut microbiota should select for colonization factors that predate the acquisition of resistance.
To test this hypothesis, we will compare strategies for gut colonization in ESBL clones of different prevalence in absence of antibiotics. Using mice, we will be able to modulate selective pressures exerted by the intestinal microbiota. We will compare gut colonization factors in ESBL clones by performing parallel high-throughput genetic screening in conventional mice (aim 1). We will analyze adaptability and the stability of resistance and virulence genes during long-term colonization (aim 2). Subsequent competitions in gnotobiotic mice harboring permissive microbiota will allow us to deduce functions needed for colonization in the presence of a competitive microbiota. In aim 3, we will measure the impact of competitors transmitted from cohabitant to infected mice on the duration of ESBL E. coli carriage and assess potential synergies with the adaptive immunity in vaccinated hosts.
Overall, we will unravel with unprecedented depth the general principles of intestinal colonization in ESBL E. coli, shed new light on the global success of prevalent clones and conceptualize robust antibiotic-free competition-based treatments.

Financed by
Commission of the European Union

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