



Cover page: The Synthetic Lethal Rosette

Aberrant mitotic phenotype found in BRCA1-deficient cells treated with the PLK1 inhibitor Volasertib. Cells become giant and multinucleated and acquire a flower shape, with nuclei arranging in a circular disposition around a cluster of centrosomes. Blue (DAPI: nuclei), Green (FITC-phalloidin: actin cytoskeleton), Red (γ -Tubulin: centrosomes).

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INCREASED PHOSPHATE SOLUBILIZATION BY RHIZOSPHERIC SUGARCANE INTERSPECIES INTERACTIONS

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Abstract: Plant-associated microbiota can enormously influence on plant traits. Manipulation of these microbial communities holds great potential as an effective way to improve crops, while contributing to a more environmentally benign agriculture. Revealing the chemical communication network in the rhizosphere will pave the way for the future production of bioinoculants using bacterial consortia. In this work, we isolated numerous microorganisms from the sugarcane rhizosphere, sequenced the 16S rDNA of a subset of isolates showing different cultural features and evaluated their ability to solubilize phosphate in NBRIP medium. Next, using only phylogenetically different isolates growing in solid medium containing salts, amino acids and sucrose, we tested interspecies interactions in pairwise combinations. Interactions were followed for 7 days and cultural traits such as growth inhibition, growth promotion, colony morphology changes and pigment production were registered. We focused in one peculiar interaction that involved isolate 258 promoting growth of isolate 214 while the latter inhibited growth of 258. In addition, 258 enhanced the ability of 214 to solubilize phosphate. To analyze if this phenomenon was due to a secreted metabolite, supernatants were tested. Interestingly, we observed that cell-free supernatants of isolate 258 were able to induce 214 phosphate solubilization. We are currently performing experiments to elucidate the chemical nature of the metabolites responsible for this phenotype.

MI-P14

STUDY OF GENOTOXICITY AND CITOTOXICITY OF MCCJ25 (G12Y)

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MccJ25 (G12Y) is an antimicrobial peptide active against *Escherichia coli* O157 H: 7 and other diarrheagenic *E. coli* strains. MccJ25 (G12Y) presents advantageous properties as a food preservative: it resists to extreme temperatures, is stable in a wide range of pH and exerts antimicrobial activity in food samples (egg yolk and milk). Our long-term aim is to develop a food preservative based on MccJ25 (G12Y). Therefore, we were interested in studying MccJ25 (G12Y) safety for humans. For this, we evaluated the geno- and cytotoxicity of MccJ25 (G12Y) on *Salmonella* Typhimurium and *Artemia salina* respectively and MccJ25 (G12Y) acute toxicity in mice. In addition, we performed an Ames test to test the mutagenic potential of the compound. Results obtained confirmed the absence of genotoxic effects of MccJ25 (G12Y) on *S. Typhimurium*. Furthermore, the *Artemia salina* assay, which determined the Medium Lethal Concentration (LC₅₀ value) of MccJ25 (G12Y), revealed that 0.31, 0.62, 1.25, 2.25 and 3 mg/mL of MccJ25 (G12Y) in the growing medium did not significantly affect the viability. In fact, the LD₅₀ was not reached with any of the MccJ25 (G12Y) concentrations tested. When MccJ25 (G12Y) citotoxicity was evaluated with *Galleria mellonella*, a low toxicity was observed with the concentrations studied (1500 and 2500 mg/kg). Finally, acute toxicity was studied in female BALB-c mice. Neither death nor symptoms of toxicity in animals were observed. In addition, macroscopic pathological studies showed that the organs of MccJ25 (G12Y)-treated animals did not present any morphological alteration. Taken together, results indicate that MccJ25 (G12Y) would be safe for humans. This finding is relevant in view of its application as a natural preservative to extend the shelf-life of foods.

MI-P15

QUORUM SENSING MEDIATED TRADEOFF LIMITS MUTATORS FIXATION DURING POLYMICROBIAL INFECTIONS

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Bacteria with elevated mutations rates (mutators) can reach high frequencies in cystic fibrosis (CF) chronic infections and are associated with treatment failure in chronic respiratory infections. The causes and consequences of bacterial elevated mutation rates have been widely studied and results suggest that mutators might be selected because their higher probability of generating beneficial mutations. However, it is notable that there are large between-patient differences in mutator frequency; even where the age and treatment protocols of patients are similar. Understanding this variation may provide opportunities for interventions that could minimize mutator evolution and the severity of infections. Possible drivers of variation in mutator frequencies are interactions with other bacterial co-infecting bacterial species. Ecological and evolutionary changes in populations of co-occurring species may result in continually changing selection pressures, potentially selecting for mutators. Alternatively, mutators may be selected against if competitors constrain adaptation to other components of the environment. Here, we used a combination of correlational *in vivo* data and *in vitro* experiments to determine the role played by co-occurring pathogens in driving variation in *Pseudomonas aeruginosa* mutation rate in chronic infections. By performing metagenomic analysis of CF sputum samples we show that mutation frequency in *P. aeruginosa* is negatively correlated with the frequency and diversity of co-infecting bacteria in chronic lung infections of CF patients. By competing *in vitro* *P. aeruginosa* mutators against wild-type in the presence and in the absence of the bacterial community we demonstrate that mutators have a fitness advantage in the absence of other CF-associated species, and that this was in part because mutations in the main Quorum-Sensing (QS) regulators that were beneficial in the absence of competitors but deleterious in their presence. These QS genes were also more likely to be mutated in *P. aeruginosa* CF populations showing elevated mutations frequencies *in vivo*. Our results demonstrate that interspecific competition constrains the evolution of mutation rates, and more generally highlights the crucial role of the community context in microbial evolution and virulence.