P2378

Characterization, Comparative Genomics and Genome Mining for Antibiotics and Secondary Metabolite of two Actinomycetales isolates.

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Actinomycetes are ubiquitous Gram (+) bacteria commonly found to have high G+C content and best known for their metabolic by-products and novel enzymes [1]. Isolates CCM*MD2014 & MR*MD2014 were co-cultured from soil impacted by a rusty fire hydrant in Woods Hole, MA. The *Streptomyces* sp. and *Curtobacterium* sp. isolates were identified by marker genes for 16S rRNA, rpoB, xylose isomerase, tryptophan synthase beta chain and Cytochrome P450 monooxygenase. Both isolates showed lactic acid fermentation and urease activity. The co-isolates were separated by selective culturing with antibiotics. In addition, whole genome sequencing revealed distinct inherent metabolic pathways in each culture that allowed for mutually exclusive selective culture conditions. Assembly was done using HGAP3 with Celera8 assembler using SMRT portal [2,3]. Annotation was done using the RAST server [4], with 7540 and 3969 CDS for *Streptomyces* sp. and *Curtobacterium* sp. respectively being revealed by AMIGene and BASys [5,6]. Subsequently, antiSMASH [7], was used to predict 52 and 26 secondary metabolite biosynthetic clusters that included genes for lantipeptides, terpenes, siderophores, polyketide synthases type I and II, bacteriocin and nonribosomal peptide synthase genes for *Streptomyces* sp. and *Curtobacterium* sp. respectively. The isolates have genes of potentially beneficial traits that could help study, among others, the role of fimbrial adhesins and iron in biofilm formation and investigation on natural products.

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P2379

Fitness profiling of yeast mutants reveal unique genetic responses to spaceflight.

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Many tumors have low redox potential, with local hypoxia and hypercapnia. The decreased convection-mediated transport of nutrients, gases, and metabolic products during spaceflight may offer a microenvironment for growing cells that mimics many of the metabolic features of tumors. We proposed that molecularly barcoded yeast deletion series can provide a quantitative assessment of the effects of spaceflight on a model organism. In liquid culture yeast have no requirement for substrate adhesion or physical cell-cell interactions and their responses during spaceflight can be quantified and compared to well-established databases of ground-based stressors to allow clear examination of features that are unique to microgravity as well as features that are shared with ground-based perturbations. We screened the complete collection of 4800 non-essential yeast homozygous alleles and a collection of 5900 yeast heterozygous alleles including 1200 alleles encoding essential genes in spaceflight and ground conditions, with and without stimulation by hyperosmolar sodium chloride as a second additive stressor. The genome-wide sensitivity profiles obtained from these treatments were queried for their similarity to a compendium of drugs whose effects on yeast have been studied by chemogenomics. Spaceflight has subtle but significant effects on core cellular processes including growth control via RNA and ribosomal biogenesis, metabolism, modification and decay pathways. Significant roles for DNA repair and replication, response to pH signaling, control of gene expression and mitochondrial function were observed. Our results strongly implicate DNA and RNA damage as the major ground based analogs of spaceflight. Given the unique, and substantial radiation exposure in space, this is consistent with major radiation-mediated effects. The high concordance to the profile induced by diallyl disulfide suggests increased glutathione S-transferase, binding of electrophilic toxins, increased reactive oxygen species and change in redox state. Identification of these vital pathways can guide future experiments by suggesting environmental modifications that can bolster cellular and organismal integrity by avoiding further stress to these pathways, and secondly, by identifying drug stresses that can exacerbate these pathway requirements in an effort to control pathological cell growth in the case of proliferative diseases. The performance of this platform is significant for spaceflight