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BIOLOGICAL RESPONSES OF STREPTOMYCETES EXPOSED TO SIMULATED MICROGRAVITY  
AND SPACEFLIGHT CONDITIONS**Abstract**

Streptomycetes are filamentous bacteria that produce a variety of bioactive natural products and have a complex life cycle. In this study, the model organism *Streptomyces coelicolor* A3(2) and isolated strain *Streptomyces* sp. C were exposed to simulated microgravity (SMG) on a ground rotating clinostat and microgravity (g) on the Shenzhou-8 spacecraft. The effects of SMG on growth of *S. coelicolor* indicated that similar growth curves were observed for the agar cultures of SMG and 1g control, but in liquid cultures, cells under SMG conditions grew more rapidly than the 1g control. Compared with the controls, its life cycle in agar medium was shortened relatively and the sporulation process was accelerated. The production of bioactive secondary metabolites from *S. coelicolor* was increased based on the results of bacteriostatic activity test by coculturing with *Bacillus subtilis*. The antibiotic assay results showed that spore pigment and undecylprodigiosin (RED) were produced earlier. Furthermore, the production of spore pigment in agar cultures increased, and production of RED increased in the early stage, while no difference in the last stage. Actinorhodin (ACT) was delayed to produce in agar cultures, and its production decreased. Global transcriptional analysis showed that some genes involved in morphological differentiation were upregulated under SMG conditions, notably the late *whi* genes (*whiD*, *sigF*, and *whiE*). The transcription of *whiE* cluster that coding spore pigment was upregulated; *act* cluster was downregulated and no difference with *red* cluster under SMG. The spaceflight experiment showed that the biomass of *S. coelicolor* was not different in agar cultures, while increased in liquid cultures. The morphological differentiation process was accelerated with more flourish aerial hyphae, thorough broken spore chains, short- and blunt-rod shape spores, and higher accumulation of the spore pigment. The bacteriostatic activity of *S. coelicolor* in agar and liquid cultures under g condition was stronger than the controls. Production of spore pigment in agar cultures was increased, while production of ACT and RED decreased. In liquid cultures, production of ACT was increased, while RED decreased. The transcription of genes/clusters involved in biosynthesis of secondary metabolites were influenced, notably those for PKS-II antibiotics. Meanwhile, the effects of SMG and spaceflight on Strain C were similar to those on Strain A3(2) in its growth, development and PKS-II biosynthesis. In conclusion, streptomycetes can perceive and respond to environmental change when exposed to SMG and spaceflight conditions. Our study provides new insights into the biological responses of streptomycetes to microgravity.