

# **DOTTORATO DI RICERCA IN BIOLOGIA CELLULARE E DELLO SVILUPPO**

**42° Cycle**

**Project proposal for a PhD scholarship**

**Main research line**

**Title of the research: Biotechnological applications of antimicrobial peptides against the *Bacillus cereus* group**

**Supervisor: Prof. Teresa Rinaldi (teresa.rinaldi@uniroma1.it)**

## **Summary**

*Bacillus cereus* sensu lato is a group of genetically closely related bacteria which includes *B. cereus*, *B. anthracis* and *B. thuringiensis*. They are spore-forming gram-positive bacteria, living in several different ecological niches, some strains can be pathogenic, *B. thuringiensis* is known for its pathogenicity against Lepidoptera and it is used as natural insecticide. *B. cereus* is responsible for food poisoning linked to toxin production. Moreover, *B. cereus* can also be responsible for more severe infections, called 'anthrax-like' diseases. *B. anthracis* is responsible for lethal animal and human infections, strains of *B. anthracis* cause lethal gastrointestinal, skin and systemic infections. Furthermore, these strains are monitored for their potential use as biological weapons. *Bacillus* spp. are mainly soil inhabitants, but they can persist in diverse environments and in harsh conditions because of spore production. Since their peculiar structural arrangement, spores can survive to conditions not compatible with vegetative bacteria. Consequently, they are resistant to many classical sterilization methods used in different fields. Of note, it is reported that many *Bacillus* species are present in the microbiota of the International Space Station (ISS) and that they are evolving on it, arising concerns for astronauts' health. To date, microbiological studies of interest to space exploration have focused on finding life forms capable of surviving a wide range of stresses, such as extreme temperatures, vacuum and lethal doses of UV and ionising radiation simulating cosmic radiation, or conditions simulated on the surface of Mars. However, there are no studies investigating the natural evolution of microorganisms in a confined environment, simulating the real interaction between microorganisms. It is of great importance to study strains common to both terrestrial and space environments, including pathogenic and/or technophilic species capable of causing human infections or damaging equipment in space bases. The project aims to evaluate the genomic evolution and pathogenic capacity of *Bacillus cereus* under conditions of altered gravity, controlled atmosphere and irradiation. Preliminary results have shown that, in the presence of chronic gamma radiation in a terrestrial environment, *B. cereus* undergoes profound genomic changes.

Chemical and physical methods, or a combination thereof, are currently used to inactivate spores, but unfortunately, they are not always effective or suitable for use in environments such as Space Stations. Given the importance of finding an effective and safe decontamination method, the aim of this project is to test and analyse the antimicrobial and sporicidal activity of synthetic peptides, safe and compatible with the substrate, environmentally friendly and non-toxic to humans. The physiology of spore production in three *Bacillus* species under space conditions will be evaluated and antimicrobial peptides will be tested in these species. The toxicity of these antimicrobials will firstly be assessed in *Saccharomyces cerevisiae*, a model organism for eukaryotic cells that was validated by our previous research.

## Pertinent Publications of the proponent (last 5 years)

1. Cirigliano, A., Amelina, A., Passarini, E., Ricelli, A., Balasco, N., Mori, M., Botta, B, De Stefano, M.E., Papotto, C., Guerriero, C., Tata A.M. & Rinaldi, T. (2025). The dual-site agonist for human M2 muscarinic receptors Iper-8-naphtalimide induces mitochondrial dysfunction in *Saccharomyces cerevisiae*. *Microbial Cell*, 12, 290. Doi: 10.15698/mic2025.12.862.
2. Cirigliano, A., Schifano, E., Ricelli, A., Bianchi, M.M., Pick, E., Rinaldi, T., Montanari, A. (2025). Csn5 depletion reverses mitochondrial defects in GCN5-Null *Saccharomyces cerevisiae*. *International Journal of Molecular Sciences*, 26(14), 6916; Doi: 10.3390/ijms26146916.
3. De Angelis, M., Primitivo, L., Sappino, C., Centrella, B., Lucarini, C., Lanciotti, L., Petti, A., Odore, D., D'Annibale, A., Macchi, B., Stefanizzi, V., Cirigliano, A., Rinaldi, T., Righi, G. & Ricelli, A. (2023). Stereocontrolled synthesis of new iminosugar lipophilic derivatives and evaluation of biological activities. *Carbohydrate Research*, 108984, Doi: 10.1016/j.carres.2023.108984.
4. Di Nisio, E.; Danovska, S.; Condemi, L.; Cirigliano, A.; Rinaldi, T.; Licursi, V.; Negri, R. (2023). H3 Lysine 4 Methylation Is Required for Full Activation of Genes Involved in alpha Ketoglutarate Availability in the Nucleus of Yeast Cells after Diauxic Shift. *Metabolites*, 13, 507. Doi: 10.3390/metabo13040507.
5. Quagliariello, A., Cirigliano, A., Rinaldi T. (2022). Bacilli in the International Space Station. *Microorganisms*, 10, 2309. Doi: 10.3390/microorganisms10122309.
6. Ourhizif, E.M., Ricelli, A., Cirigliano, A., Rinaldi, T., Bouissane, L., Saso, L., Chalard, P., Troin, Y., Khouili, M., Akssira, M. (2022). Antifungal and Cytotoxic Activity of Diterpenes and Bisnorsesquiterpenoids from the Latex of *Euphorbia resinifera* Berg. *Molecules* 27, 5234. <https://doi.org/10.3390/molecules27165234>.
7. Shahroor, M A., Lasorsa, F. M., Porcelli, V., Dweikat, I., Di Noia, M.A., Gur, M., Agostino, G., Shaag, A., Rinaldi, T., Gasparre, G., Guerra, F., Castegna, A., Todisco, S., Abu-Libdeh, B., Elpeleg, O., Palmieri, L. (2022). PNC2 (SLC25A36) deficiency associated with the hyperinsulinism/hyperammonemia syndrome. *The Journal of Clinical Endocrinology & Metabolism*, 107(5), 1346-1356. Doi: 10.1210/clinem/dgab932.
8. Changela, H. G.,..., Rinaldi, T.,..., Hallsworth, J. E. (2021). Mars: New insights and unresolved questions. *International Journal of Astrobiology*. 1–33. Doi: 10.1017/S1473550421000276.
9. Hallsworth, J. E., Mancinelli, R. L., Conley, C. A., Dallas, T. D., Rinaldi, T., Davila, A. F., Benison, K.C., Rapoport, A., Cavalazzi, B., Selbmann, L., Changela, H., Westall, F., Yakimov, M.M., Amils, R. and Madigan, M.T. (2021). Astrobiology of life on Earth. *Environmental Microbiology*. 23 (7), 3335-3344. Doi: 10.1111/1462-2920.15499.