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

**38° ciclo**

**Proposta di assegnazione di una borsa di Dottorato**

**Titolo della ricerca:**

***Saccharomyces cerevisiae* and *Bacillus cereus* group to study molecules of pharmaceutical interest**

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**Summary**

*S. cerevisiae* is the world’s most popular yeast, being essential in baking and brewing since ancient times. This yeast has also gained increasing interest among biotechnology researchers: thanks to several features that make it an easy-to-handle organism, this budding yeast has made possible the discovery of fundamental biological processes often shared with higher eukaryotic cells, at the point to be considered as an honorary mammal (Resnick & Cox, 2000). Many pathways are conserved from yeast to human and we are investigating the function of small molecules on yeast cells, specifically interested in the mitochondrial function. A simple test can predict if a molecule, with a possible pharmaceutical interest, has a negative effect on yeast mitochondria, opening the possibility of an early prediction of its toxicity in human cells. Our research line is based on two small molecules which act as inhibitors of the Csn5 enzyme, involved in the ergosterol/cholesterol pathway, but we are also studying some drugs with side effects in humans, already on the market.

Another type of molecules, synthetic peptides, are investigated in our laboratory, using as a model system the *Bacillus cereus* group. These bacteria are extraordinary from an

evolutionary point of view, and their extreme environmental resistance relies on spore

formation. Nevertheless, this characteristic is a huge problem because spore resistance is the main concern of contamination in food industry. The most famous species are *B. cereus*, *B. anthracis* and *B. thuringiensis*. Some of them are pathogenic for humans and *B. anthracis* is a potential biological terrorism threat because the spores are resistant to destruction and can be easily spread by release in the air. To investigate their peculiar characteristics, we are studying new *Bacillus cereus* strains selected from the environment during bioarchaeological studies and a simulant of *B. anthracis* to test new synthetic peptides with an antimicrobial activity.

**Research objectives**

The aim of this project is to study molecules of a pharmaceutical interest (small molecules and synthetic peptides) and to investigate drugs, already on the market, to study their side effects related to mitochondrial dysfunction.

**Lavori pubblicati negli ultimi 5 anni dal Docente Guida:**

1) Dinarelli, S., Mura, F., Mancini, C., La Penna, G., Rinaldi, T. and Rossi, M. Comparison of different correlative AFM-SEM workflows on calcite moonmilk (**2022**). In press.

2) M. A. Shahrour, F. M. Lasorsa, V. Porcelli, I. Dweikat, M. A. Di Noia, M. Gur, G. Agostino,

A. Shaag, T. Rinaldi, G. Gasparre, F. Guerra, P. Scarcia, A. Castegna, S. Todisco, F. Palmieri, B. Abu-Libdeh, O. Elpeleg, L. Palmieri. (**2022**). The PNC2 (SLC25A36) deficiency associated with the hyperinsulinism/hyperammonemia syndrome. *Journal of Clinical Endocrinology & Metabolism*; dgab932, Doi: 10.1210/clinem/dgab932.

3) Cirigliano A., Tomassetti M.C., de Kruif N.F., Cavallo I.F., Maras D.F., Mura, F. and Rinaldi T. (**2022**). Microbial recolonization of the mural paintings after restoration in the Etruscan Tomba degli Scudi in Tarquinia. In: *Biological Risk for Hypogea. Shared data among Italy and Republic of Korea*. Edited by Giulia Caneva & Yong Jae Chung. Editor Nardini, Florence.

4) Changela, H. G., Chatzitheodoridis, E., Anuntes, A., Beaty, D., Bouw, K., Bridges, J. C., Capova, K. A., Cockell, C. S., …. Waltemathe, M., and Hallsworth, J. E. (**2021**). Mars: New insights and unresolved questions. *International Journal of Astrobiology*. 1–33. Doi:

10.1017/S1473550421000276.

5) Cirigliano, F. Mura, A. Quagliariello, R. Negri and T. Rinaldi. (**2021**). Calcium carbonate of microbial origin in the Etruscan tombs of Tarquinia. 1st Italian Space Agency Workshop on Astrobiology. 27-29 October 2020. *Memorie della Società Astronomica Italiana/ Journal of the Italian Astronomical Society*. Fabrizio Serra Editore, Pisa-Roma. 92: 2, 64-66.

6) Mura, F., Cirigliano, A., Maras, D., & Rinaldi, T. (**2021**). Analysis of moonmilk nanofibers in the etruscan tombs of Tarquinia. In *AIP Conference Proceedings* (Vol. 2416, No. 1, p.

020014). AIP Publishing LLC. Doi: 10.1063/5.0068804.

7) Palermo, V., Stirpe, M., Bianchi, M.M., Rinaldi, T., Cirigliano, A., Ragnini-Wilson, A., Falcone, C., Mazzoni, C. (**2021**). The C-terminal region of yeast Ubiquitin-protein ligase Not4 mediates its cellular localization and stress response. *FEMS Microbiology Letters*. 368, fnab097. Doi:10.1093/femsle/fnab097.

8) Vapore, V., Mazzaglia, C., Sibilia, D., Del Vecchio, M., Fruhmann, G., Valenti, M., Miranda, E., Rinaldi, T., Winderickx, J., Mazzoni, C. (**2021**). Neuroserpin Inclusion Bodies in a FENIB Yeast Model. *Microorganisms*. 9, 1498. Doi:10.3390.

9) Giampaoli, S., De Vittori, E., Barni, F., Anselmo, A., Rinaldi, T., Baldi, M., Miranda, K.C., Liao, A., Brami, D., Vanni Frajese G. and Berti, A. (**2021**). DNA metabarcoding of forensic mycological samples. *Egyptian Journal of Forensic Sciences*. 11:7. Doi:10.1186/s41935-

021-00221-x.

10) Hallsworth, J. E., Mancinelli, R. L., Conley, C. A., Dallas, T. D., Rinaldi, T., Davila, A. F., Benison, K.C., Rapoport, A., … Amils, R. and Madigan, M.T. (**2021**). Astrobiology of life on Earth. *Environmental Microbiology*. 23 (7), 3335-3344. Doi: 10.1111/1462-2920.15499.

11) Nigro L., Gallo E., Mura F. and Rinaldi T. (**2021**). Teapot or milkpot? About the content of a small, spouted jar from eb iv (2300-2000 b.c.e.) Tell es-Sultan, ancient Jericho. *Mediterranean Archaeology and Archaeometry*. 21(1), 281-290. Doi:10.5281/zenodo.4575728.

12) Cirigliano, A., Mura, F., Cecchini, A., Tomassetti, M. C., Maras, D., Di Paola, F. M., Meriggi, N., Cavalieri, D., Negri, R., Quagliariello, A., Hallsworth J.E. and Rinaldi T. (**2021**). Active microbial ecosystem in Iron-Age tombs of the Etruscan civilization. *Environmental Microbiology*. 23 (7), 3957-3969. Doi:10.1111/1462-2920.15327.

13) Nigro L. and Rinaldi T. (**2020**). The divine spirit of bees. A note on honey and the origins

of yeast- driven fermentation. Vicino Oriente XXIV, pp. 185-196.

14) Mura, F., Cirigliano, A., Bracciale, M. P., Rinaldi T. (**2020**). Characterization of Nanostructured Calcium Carbonate found in two ancient Etruscan tombs. *AIP Conference Proceedings*. 2257 (1), 020011. Doi:10.1063/5.0023677.

15) Colotti, G. and Rinaldi, T. (**2020**). The central role of gut microbiota in drug metabolism and personalized medicine. *Future Medicinal Chemistry*. 12 (13), 1197-1200. Doi: 10.4155/fmc-

2020-0023.

16) Botta, L., Filippi, S., Zippilli, C., Cesarini, S., Bizzarri, B. M., Cirigliano, A., Rinaldi, T., Paiardini, A., Fiorucci, D., Saladino, R., Negri, R. & Benedetti, P. (**2020**). Artemisinin Derivatives with Antimelanoma Activity Show Inhibitory Effect against Human DNA Topoisomerase 1. *ACS Medicinal Chemistry Letters*. 11(5), 1035-1040. Doi:

10.1021/acsmedchemlett.0c00131.

17) Nigro, L., Gallo, E., Gharib, R., Mura, F., Macrì, M., Rinaldi T. (**2020**). An Egyptian green schist palette and an amazonite gemstone from the “Palace of the Copper Axes” at Batrawy, Jourdan. Vicino Oriente XXIV pp. 1-26.

18) Sinha, A., Israeli, R., Cirigliano, A., Gihaz, S., Trabelcy, B., Braus, G. H., Gerchman, Y., Fishman, A., Negri, R., Rinaldi, T., Pick E. (**2020**). The COP9 signalosome mediates the Spt23 regulated fatty acid desaturation and ergosterol biosynthesis. *The FASEB Journal*.

34:4870–4889. Doi: 10.1096/fj.201902487R.

19) Cirigliano, A., Amelina, A., Biferali, B., Macone, A., Mozzetta, C., Bianchi, M. M., Mori, M., Botta, B., Pick, E., Negri R. & Rinaldi, T. (**2019**). Statins interfere with the attachment of S. cerevisiae mtDNA to the inner mitochondrial membrane. *Journal of Enzyme Inhibition and Medicinal Chemistry.* 35(1), 129-137. Doi: 10.1080/14756366.2019.1687461.

20) Bramasole, L., Sinha, A., Gurevich, S., Radzinski, M., Klein, Y., Panat, N., E. Gefen, T.

Rinaldi, D. Jimenez-Morales, J. Johnson, N.J. Krogan, N. Reis, D. Reichmann, M.H. Glickman, E. Pick (**2019**). Proteasome lid bridges mitochondrial stress with Cdc53/Cullin1

NEDDylation status. *Redox biology*, 20, 533-543. Doi: 10.1016/j.redox.2018.11.010.

21) Bramasole, L., Sinha, A., Harshuk, D., Cirigliano, A., Sylvia, G., Yu, Z., Carmeli, R.L., Glickman, M.H., Rinaldi, T., Pick, E. (**2019**). The Proteasome Lid Triggers COP9

Signalosome Activity during the Transition of *Saccharomyces cerevisiae* Cells into

Quiescence. *Biomolecules*, *9*(9), 449. ISSN: 2218-273X.

22) Rinaldi, T. and Colotti, G. (**2019**). Use of Organoids in medicinal chemistry: challenges on ethics and biosecurity. *Future Medicinal Chemistry*, 11, 10. Doi: 10.4155/fmc-2018-0341.

23) Santomartino, R., Camponeschi, I., Polo, G., Immesi, A., Rinaldi, T., Mazzoni, C., Brambilla, L and Bianchi, M.M. (**2019**). The hypoxic transcription factor KlMga2 mediates the response to oxidative stress and influences longevity in the yeast *Kluyveromyces lactis*. *FEMS Yeast Research*. Volume 19, Issue 3, May, foz020. Doi: 10.1093/femsyr/foz020.

24) Cirigliano A., Macone M., Bianchi M.M., Oliaro Bosso S., Balliano, G., Negri R., Rinaldi T. (**2019**). Ergosterol reduction impairs mitochondrial DNA maintenance in *S.cerevisiae*. *BBA Molecular and Cell Biology of Lipids*. 1864. 290–303. Doi: 10.1016/j.bbalip.2018.12.002.

25) Cirigliano, M. C. Tomassetti, M. Di Pietro, F. Mura, M. L. Maneschi, M. D. Gentili, B.

Cardazzo, C. Arrighi, C. Mazzoni, R. Negri and T. Rinaldi. (**2018**). Calcite moonmilk of microbial origin in the etruscan *Tomba degli Scudi* in Tarquinia, Italy. *Scientific Reports*,

8:15839. doi:10.1038/s41598-018-34134-y.

26) Nigro L., Montanari D., Mura F., J. Yasine and Rinaldi T. (**2018**). A hoard of Nilotic nacreous shells from Egypt to Jericho (Early Bronze II, 3000-2900 BC): Their finding, content and historical archaeological implications. *Palestine Exploration Quarterly*, 150:2, 110-125. Doi:

10.1080/00310328.2018.1425957.

27) Cirigliano, A., Negri R., Rinaldi T. (**2018**). Dual-use Molecules from Yeast. *Biomedicine & Prevention.* vol.3 CBRNe safety. Special issue (PART1)- (114). Doi: 10.19252/000000072.