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Discovery of novel antibiotics from microbes: a project

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Background

- ✘ WHO named **antibiotic resistance** as one of the greatest threats to global health, predicting the advent of infections not responding to antibiotics. The humanity needs to pioneer disruptive technologies to regain the upper hand.
- ✘ Dense extracellular matrix prevents drugs from reaching bacteria inside **biofilms**. This limited exposure enhances development of antibiotic tolerance. PEST-BIN (the wider project we're involved in) will engineer magnetic nanoparticles spiked with antibacterial graphene coating which will be loaded with antibiotics. Such molecular "**nano-weapons**" will physically penetrate biofilms and ensure sustained delivery of antibiotics inside biofilms.

About a «rare» genus... *Microbispora*

- ✘ **Family:** *Streptosporangiaceae* – 12 child taxa
- ✘ **Type species:** *M. rosea* Nonomura and Ohara 1957
- ✘ **Morphology:** Two-spore chains disposed longitudinally on short aerial hyphae
- ✘ **Genome:** ~8.5 Mb & ~24 Biosynthetic Genes Cluster (geosmin, alkylresorcinol, desferrioxamine,...)
- ✘ **Naicons' library:** ~900 preidentified *Microbispora* strains

Objectives

- ✘ **Primary objective:** identification of new antibiotics
- ✘ **Secondary objectives:**
 - characterize «rare » or «talented» *Actinomycetes*
 - use & adapt state-of-the-art multi-omics techniques
 - characterize new antibiofilm molecules
 - load the newly discovered antibiotics on graphene-coated nanoparticles & assess their antibiofilm activity

Project overview

1. **«Rare» and/or «talented» strains identification**
 1. Selection (molecular networking)
 2. Culture conditions (metabolism optimization)
 3. Phylogenic affiliation (16S rRNA & genomics)
2. **Mass Spectrometry fingerprints library edition**
 1. Strains culture & Extraction (biofermentation)
 2. LC-MS² profiling (ESI-LC-MS²)
 3. MS profiles analysis (metabolomics)
3. **Promising metabolites characterization**
 1. Paired –omics (combined metabol- & genomics)
 2. Production (fermentation optimization)
 3. SAR elucidation (NMR & cheminformatics)