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NTERACTION

DYNAMIC







8th Congress of European Microbiologist

Activation of cryptic antimicrobial compounds by microbial co-cultures

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Introduction

The emergence of new multiresistant bacteria is nowadays a public health issue and the discovery of new antibiotics becomes crucial to overcome this threat. Bacteria (mostly actinomycetes e.g. Streptomyces) and fungi are one of the major source of antimicrobial compounds (secondary metabolites). However, most of the gene clusters coding for these secondary metabolites remain silent in standard lab conditions. Biotic interactions between microbes in nature constitute a signal to induce the production of specialized metabolites. Thus, co-cultures in lab, which mimick these interactions, can induce the production of cryptic natural products. The objective of this study is to perform cocultures between Streptomyces and fungi (e.g. Schizophyllum commune) for the production of new antimicrobial compounds.



GC-MS revealed the production of 10 metabolites during interaction

- \rightarrow 10 peaks specific of the interactions were identified
- 5 were common for the two interactions
- 3 were specific of the interaction with *Streptomyces* S1D4-23 and 2 with *Streptomyces* S1D4-11

30000000	—Fungus
250000000	—Interaction zone
<u> </u>	—Streptomyces
(UA	



 \rightarrow So far, negative mode EICs revealed at least the production of 4 new metabolites in interaction zones between *S. commune* 6601-A and *Streptomyces* S1D4-11





Illustration of the comparison of GC-MS metabolite profiles of one Streptomyces, the fungus and their

interaction zone. The metabolite profile of *Streptomyces* is in red, the one of the fungus is in green and the

interaction zone is in blue. New peaks induced during the interaction are framed by blue rectangles.

Conclusions and perspectives

- Two interaction models between S. commune and two Streptomyces strains showed an induced antimicrobial activity.
- The metabolite profiles of interactions are different from those of single cultures.
- > LC-MS and GC-MS peaks, potentially explaining these differences, were identified

Further experiments:

- To further analyse LC/MS (positive mode/second interaction) and GC/MS
- ✓ To correlate the antimicrobial effect with the production of new compounds
- To decipher the molecular mechanisms involved during the interactions