



HAL
open science

Screen the fungal diversity of Basidiomycota, the sister division of Ascomycota, could be efficient to find new antibiotics

Hajer Boutabouzi, Marc Maresca, Maxime Robin, Attilio Di Maio, David Navarro, Michaël Lafond, Stephane Greff, Charlotte Simmler, Marie-Noëlle Rosso, Anne Favel, et al.

► To cite this version:

Hajer Boutabouzi, Marc Maresca, Maxime Robin, Attilio Di Maio, David Navarro, et al.. Screen the fungal diversity of Basidiomycota, the sister division of Ascomycota, could be efficient to find new antibiotics. 8th International Symposium on Antimicrobial Peptides (AMP2024), Jun 2024, Marseille, France. hal-04607495

HAL Id: hal-04607495

<https://amu.hal.science/hal-04607495v1>

Submitted on 18 Dec 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Screen the fungal diversity of Basidiomycota, the sister division of Ascomycota, could be efficient to find new antibiotics



Hajer BOUTABOUZI¹; Marc MARESCA²; Maxime ROBIN²; Attilio DI-MAIO³; David NAVARRO^{1,4}; Michael LAFOND¹; Stephane GREFF⁵; Charlotte SIMMLER⁵; Marie-Noëlle ROSSO¹; Anne FAVEL^{1,2}; Quentin ALBERT^{1,2}

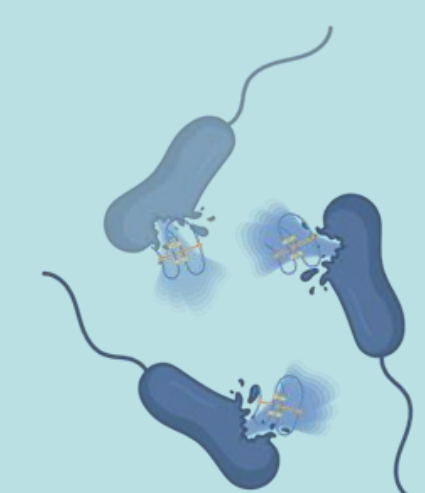
1) UMR1163, Biodiversité et Biotechnologie Fongique, Aix Marseille Université, INRAE, 13288 Marseille, France

2) Aix Marseille Univ., CNRS, Centrale Marseille, iSm2, 13013 Marseille, France

3) Aix Marseille Univ., Avignon Univ., CNRS, IRD, IMBE, Marseille, France

4) CIRM-CF, INRAE, Aix Marseille Université, UMR1163, 13288 Marseille, France

5) IMBE, Aix Marseille Université, Avignon Université, CNRS, IRD, Station Marine d'Endoume, 13007, Marseille, France

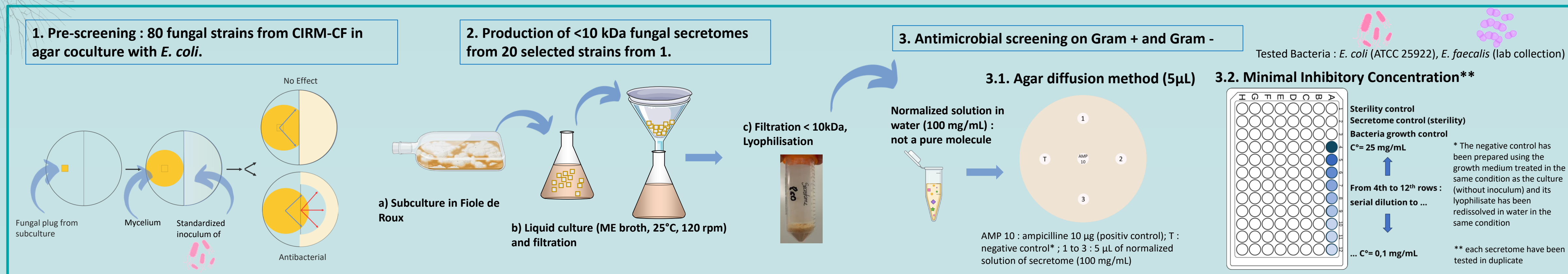


Context and Objectives

In the context of antibacterial resistance, finding new antibacterial molecules is an urgent need. The high potential of fungi to produce bioactive metabolites is well known, especially for Ascomycota (*Aspergillus*, *Fusarium* sp., *Xylaria* sp., ...). However, the few studies done with **Basidiomycota** (*Agaricus* sp., *Fomes* sp., *Pleurotus* sp., ...) were always based on sporophores (and mainly from *Ganoderma* species) harvests and extractions. This is a **bottleneck** for original metabolites discoveries and pressure environmental resources. In this purpose, we stressed Basidiomycota to trigger the production of secondary metabolites with potential antibacterial activities with a focus on fungal Antimicrobial Peptides (f-AMP). Indeed, genomic organization of f-AMP are not well known, and targeted and/or in silico studies are not efficient requiring the use of a non-targeted approach.

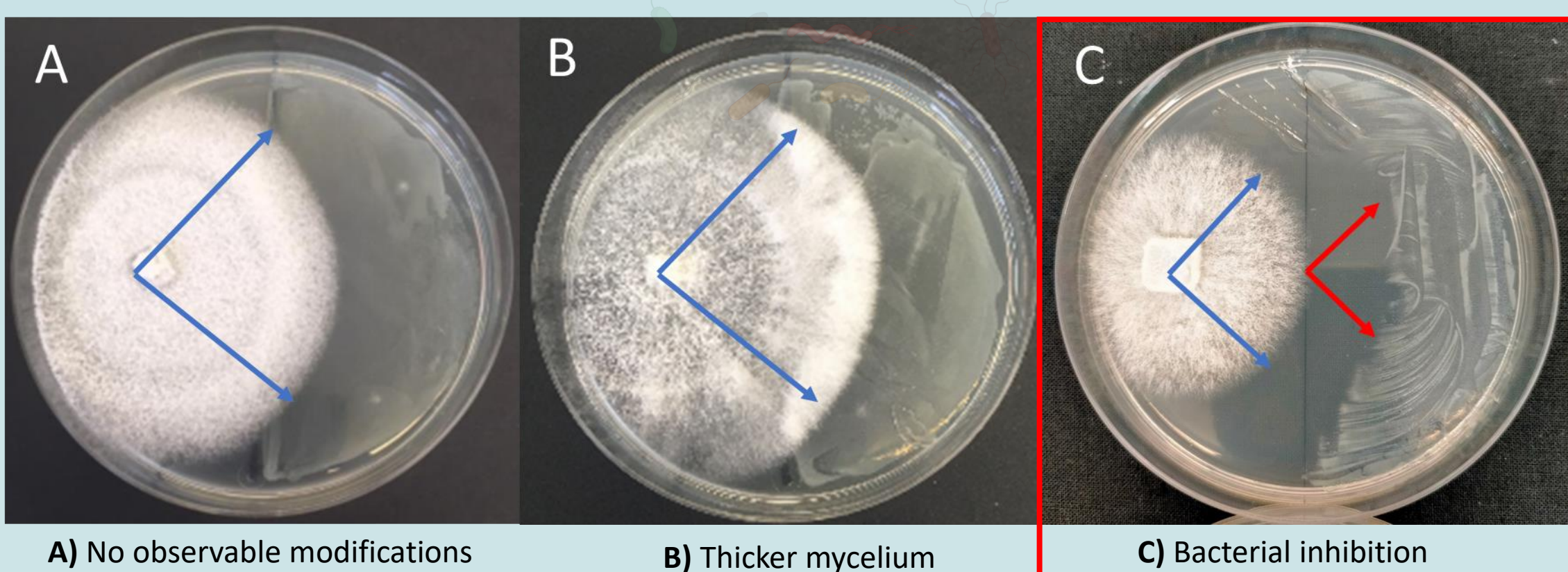
Briefly, after a prescreening of 80 fungal strains, we focused on the <10kDa fraction containing f-AMP of fungal secretomes from 20 strains to evaluate their antibacterial properties.

Material and Methods



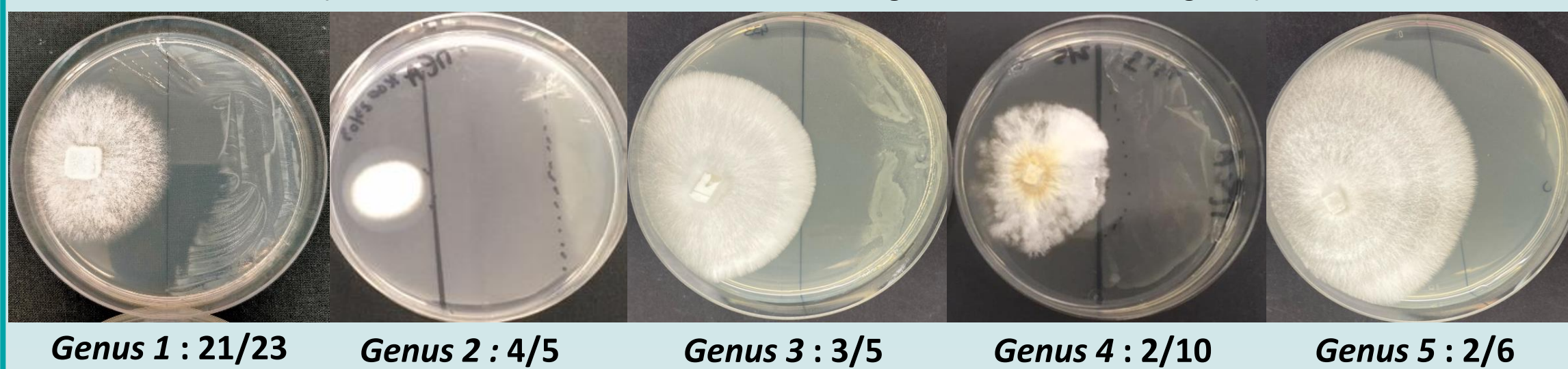
Results and Discussion

1. Pre-screening : 80 fungal strains in agar coculture with *E. coli*.



5/17 genres showed antibacterial activities
32/80 fungal strains with antibacterial activities

Examples of fungal genres with antibacterial activities
(with the number of antibacterial strains among tested strains for each genus)



Cheap, efficient, and fast method to screen antibacterial activities from Basidiomycota

2. Production of secretomes and Evaluation – global results

Table 1 : Global results of fungal secretomes's antibacterials activities on *E. coli* (ATCC 25922) and *E. faecalis* (lab collection).

N° BRFM	Agar Co-culture		Agar Diffusion Method		MIC (mg/mL)*	
	<i>E.coli</i>	<i>E.faecalis</i>	<i>E.coli</i>	<i>E.faecalis</i>	<i>E.coli</i>	<i>E.faecalis</i>
1	+	+	+	+	6,2	6,2
2	+	+	-	-	12,5	12,5
3	+	+	+	-	12,5	12,5
4	+	+	-	-	25	25
5	+	+	-	-	25	25
6	+	+	-	-	25	25
7	+	+	-	-	12,5	12,5
8	+	+	+	+	12,5	12,5
9	+	+	+	+	6,2	6,2
10	+	+	-	-	25	25
11	+	+	+	+	3,1	3,1
12	+	+	+	+	3,1	6,2
13	+	+	-	-	-	-
14	-	-	-	-	-	-
15	-	no data	-	-	-	-
16	+	no data	-	-	-	-
17	+	no data	-	-	-	-
18	+	+	-	+	12,5	12,5
19	+	+	+	-	12,5	12,5

* Since we tested secretomes and no pure molecules, the MIC are expressed in mg/mL, and not µg/mL.

Strains 11 and 12 showed the best antibacterial activity on both *E. coli* and *E. faecalis*. The metabolomic analysis showed an unknown molecule in Strain 11 (purification ongoing...)

Strains 14 and 15 were selected as 'negative control'.

Strains 16 and 17 were antibacterial in agar coculture (with *E. coli*) but not with classical approach. It is possible that the metabolite is > 10 kDa.

Antibacterial activity confirmed (except for 2 strains)
Promising data on Strain 11

Conclusions

- The agar coculture method is cheap, fast, and efficient to reveal new antibacterial activities from Basidiomycota.
- The antibacterial activity highlighted with agar coculture is confirmed with classical approach for 16/18 secretomes.
- Mycelium-based screening is relevant to mine new antibacterial activities from Basidiomycota.
- With 40% of antibacterial strains among the 80 tested strains, Basidiomycota is a highly promising reservoir for new antibacterial activities.



Perspectives

- Test the protease-treated fraction of the secretomes,
- Identify the antibacterial compounds.

References:

1 Fainaru, P.S.; Okoye, F.B.C.; Abiodun, O.O.; Kaimdem, R.S.T. and Ogbole, O.O. Editorial: Fungal Bioactive Metabolites of Pharmacological Relevance. *Front. Pharmacol.* **2022**, *13*, 912068. 10.3389/fphar.2022.912068

2 Vallavan, V.; Krishnasamy, G.; Zin, N.M.; Abdullatif, M. A Review on Antidiaphylocoical Secondary Metabolites from Basidiomycetes. *Molecules* **2020**, *25*, 5848. 10.3390/molecules25245848

3 Bertrand, S.; Böhm, N.; Schneid, S.; Schupp, O.; Gindro, K.; Wolfender, J.L. Metabolite induction via microorganism coculture: A potential way to enhance chemical diversity for drug discovery. *Biotechnology Advances*, **2014**, *32*, 6: 1180-1204. 10.1016/j.biotechadv.2014.03.001.

4 Robey, T.M.; Caesar, L.B.; Drott, M.T.; Keller, N.P.; Kelleher, N.L. An interpreted atlas of biosynthetic gene clusters from 1,000 fungal genomes. *PNAS*, **2020**, *118*, No. 19, e2020230118. 10.1073/pnas.2020230118

5 Lastovetsky, O.A.; Krasnovsky, L.D.; Qin, X.; Gaspar, M.L.; Gryganskiy, A.P.; Hurltemann, M.; Clum, A.; Pillay, M.; Palanisappan, K.; Varghese, N.; Mikhailova, N.; Stamatis, D.; Reddy, T.B.K.; Daum, C.; Shapiro, N.; Ivanova, N.; Kyriides, N.; Woyke, T.; Pawlikowska, T.E. Molecular dialogues between early divergent fungi and bacteria in an antiparasitism versus a mutualism. *mBio* **2020**, *11*, e02088-20. 10.1128/mBio.02088-20. Acknowledgement: Quentin ALBERT would like to thank Fabio MERRAHL.