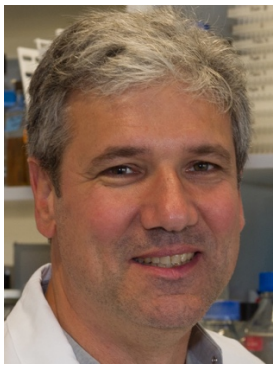

First Name / Last name: Christophe D'ENFERT
Contact : *Christophe.denfert@pasteur.fr*

Unit: Fungal Biology and Pathogenicity Unit – INRA USC2019
IP Department or IP: Department of Mycology
Secondary affiliation: Department of Genomes and Genetics

Main domain 1: Fungi

Main domain 2: mechanism of resistance and dissemination, new molecules, technological and methodological developments.

Attractive synopsis:
The Fungal Biology and Pathogenicity Unit explores different aspects of the biology of the fungal pathogens of humans *Candida albicans* and *Aspergillus fumigatus* with focuses on the mechanisms governing genome stability, biofilm formation and their tolerance to antifungals, and cell wall biogenesis.

Research projects in relation with AMR:
The Fungal Biology and Pathogenicity Unit has established new molecular resources, in particular a genome-wide collection of *Candida albicans* over-expression strains. These strains are leveraged in order to characterize the molecular mechanisms that control genome rearrangements underlying the acquisition of antifungal resistance. They are also leveraged to characterize the mechanisms that control the formation of biofilms and how these communities acquire tolerance to antifungals. These approaches shall reveal novel targets for the development of antifungals. In parallel, the Unit is exploring the biochemistry of cell wall biogenesis, which is essential for fungal cell viability. Enzymes that play key roles in the synthesis and cross-linking of cell wall polysaccharides are identified and characterized in details with the aim to use them as targets for novel antifungals.

3 Publications

- Denega I, d'Enfert C, Bachellier-Bassi S (2019) *Candida albicans* Biofilms Are Generally Devoid of Persister Cells. *Antimicrob Agents Chemother* 63: e01979-18.
- Cabral V, Znaidi S, Walker LA, Martin-Yken H, Dague E, Legrand M, Lee K, Chauvel M, Firon A, Rossignol T, Richard ML, Munro CA, Bachellier-Bassi S, d'Enfert C (2014) *PLoS Pathog* 10: e1004542.
- Henry C, Li J, Danion F, Alcazar-Fuoli L, Mellado E, Beau R, Jouvion G, Latgé JP, Fontaine T (2019) Two KTR Mannosyltransferases Are Responsible for the Biosynthesis of Cell Wall Mannans and Control Polarized Growth in *Aspergillus fumigatus*. *MBio* 10: e02647-18.

First Name / Last name: Françoise Dromer
Contact : dromer@pasteur.fr

Unit: Molecular Mycology
IP Department or IP: Mycology
Secondary affiliation: CNRS UMR2000

Main domains 1: Fungi

Main domain 2: surveillance and molecular epidemiology of resistance, technological and methodological developments.

Attractive synopsis:
The nationwide surveillance on invasive fungal infections (IFIs) together with centralized characterization of the isolates are unique assets for the investigation of single or clustered cases due to unusual fungal pathogens including those resistant to antifungal drugs.

Research projects in relation with AMR:
Beside expertise on all pathogenic fungi, the French National Reference Center for Invasive Mycoses & Antifungals has implemented since 2012 a secured website for active notifications of all invasive fungal infections (IFIs) nationwide to fulfill its mission of surveillance. The objective is to assess the IFIs' burden in France, but also to detect clusters/outbreaks due to species/isolates with decreased susceptibility to antifungal drugs such as *Candida auris*. We take advantage of our databases recording more than 11,000 cases and of our collection of more than 10,000 isolates of yeasts and molds (belonging to more than 120 different genera and more than 450 different species), all characterized at the reference center and collected since 2002 to analyze any unusual phenomenon. Cases can be compared with historical cases and isolates with epidemiologically-related and -unrelated isolates using whole genome sequencing. Tools for tracking resistant isolates and uncovering mechanisms of resistance can then be specifically developed.

3 Publications

- Vaux S, Criscuolo A, Desnos-Ollivier M, Diancourt L, Tarnaud C, Vandenbogaert M, Brisse S, Coignard B, Dromer Fand the Geotrichum investigation group (2014) Multicenter Outbreak of Infections by Saprochaete clavata, an Unrecognized Opportunistic Fungal Pathogen. *MBio* **5:** e02309–14
- Dellière S, Healey K, Gits-Muselli M, Carrara B, Barbaro A, Guigue N, Lecefel C, Touratier S, Desnos-Ollivier M, Perlin DS, Bretagne S & Alanio A (2016) Fluconazole and Echinocandin Resistance of Candida glabrata Correlates Better with Antifungal Drug Exposure Rather than with MSH2 Mutator Genotype in a French Cohort of Patients Harboring Low Rates of Resistance. *Front Microbiol* **7:** 2038
- Bretagne S, Renaudat C, Desnos-Ollivier M, Sitbon K, Lortholary O, Dromer FFrench Mycosis Study Group (2017) Predisposing factors and outcome of uncommon yeast species-related fungaemia based on an exhaustive surveillance programme (2002-14). *J. Antimicrob. Chemother.* **72:** 1784–1793

First Name / Last name: Thierry Fontaine
Contact : Thierry.fontaine@pasteur.fr

Unit: BPF
IP Department or IP: Mycology

Main domains 1: Fungi
Main domain 2: mechanism of resistance and dissemination, biomarkers and diagnostic.

Attractive synopsis:
The cell wall of fungal pathogens represents both an anti-fungal target and an essential armor to escape host defenses.

Research projects in relation with AMR:
The fungal cell wall is a complex and dynamic entity essential for the development of fungi. It has a prominent and dual role during the growth of fungal pathogens. It allows the pathogen to survive environmental challenges such as host tissue, and it also is central to polarized growth, which helps the fungus to invade host tissues. The aim of my project is the understanding of cell wall organization/biosynthesis and of cell wall-host interactions.

3 Publications

- Henry et al. Mbio 2019 Jan-Feb; 10(1): e02647-18.
- Fontaine et al. PLoS Pathog. 2011 Nov;7(11):e1002372.
- Li et al. J Fungi (Basel). 2018 Feb 2;4(1). pii: E19.

First Name / Last name: Guilhem Janbon
Contact : janbon@pasteur.fr

Unit: RNA Biology of Fungal Pathogens
IP Department or IP: Mycology
Secondary affiliation: Genomes and Genetics

Main domain 1: Fungi

Main domain 2: mechanism of resistance and dissemination, biomarkers and diagnostic, new molecules, alternative strategies.

Attractive synopsis:
Extracellular vesicles as a means to communicate an “antifungal” message of one cell to another

Research projects in relation with AMR:
Pathogenic fungi kill more than 1.5 million of persons every year. This is mostly due to the fact available antifungal treatment are very often not effective in patients whereas they seem to be active in vitro. As most organisms, pathogenic fungi produce extracellular vesicles. Published data and our preliminary results support the model that these extracellular vesicles could participate in cell-to-cell communication and antifungal tolerance. Here genetic screens, biochemistry assays and microscopy analyses are used to understand how an antifungal information can be transmitted from one cell to another.

3 (max) Publications

- Goebels C., et al.. (2013) Introns regulate gene expression in *Cryptococcus neoformans* in a Pab2p dependent pathway. *PLoS Genetics* 9, e1003686.
- Janbon G.,et al (2014) Analysis of the genome and transcriptome of *Cryptococcus neoformans* var. *grubii* reveals complex RNA expression and microevolution leading to virulence attenuation *PLoS Genetics* 10, e1004261.
- Gonzalez-Hilarion S, et al (2016) Intron retention-dependent gene regulation in *Cryptococcus neoformans. Scientific Reports* 6, 32252.

First Name / Last name: Jessica Quintin
Contact : jessica.quintin@pasteur.fr

Unit: Immunology Of Fungal Infections
IP Department or IP: Department of Mycology
Secondary affiliation: Department of Immunology

Main domains 1: Fungi

Main domain 2: alternative strategies

Attractive synopsis:
Understanding the modulation of innate immune responses for adjunctive immunotherapy

Research projects in relation with AMR:
Fungal infections caused by various fungal species affect billions of people every year and have become a leading cause of morbidity and mortality in the last decades. Even though most infections are "relatively" minor, there is an increasing body of evidence that fungal infections kill at least as many people as tuberculosis or malaria (Brown et al. 2012). The incidence of invasive fungal infections is rising as a result of modern medical interventions (heavy surgery, immunosuppressive therapy) and immunosuppressive diseases (such as AIDS). Despite the discovery in the last decade of novel and more potent antifungal drugs against the major fungal pathogens (*Candida*, *Aspergillus*, and *Cryptococcus* spp.), the mortality due to fungi remains high (in the range from 30 to 50%), as resistance to drug resistance became an emerging issue (increased incidence of naturally resistant/ emergence of resistance isolates due to large use of antifungal prophylaxis). It is believed that the combination of antifungal drugs with immunotherapy (termed adjunctive immunotherapy) would be the only potent approach to improve this outcome (van de Veerdonk et al. 2012).

Research in my group focuses on understanding how the innate immune responses, first line of defence against fungal infection (and functional in AIDS patient) can be improved and boosted with the fungal polysaccharide β-glucan, an approach coined as trained immunity. Training the innate immune responses of the host in combination with antifungal treatment could increase the efficacy of the treatment, minimizing the emergence of resistant isolates and help fighting antifungal resistant strains.

3 Publications
Quintin, J., Saeed, S., Martens, J.H.A., et al. (2012) Candida albicans infection affords protection against reinfection via functional reprogramming of monocytes. *Cell Host Microbe*. 12: 223-32.

Saeed, S., Quintin, J., et al. (2014) Epigenetic programming of monocyte-to-macrophage differentiation and trained innate immunity. *Science*. 345: 1251086.

Quintin, J. (2018) Fungal mediated innate immune memory, what have we learned? *Semin Cell Dev Biol*.