

Post doctoral fellow



Protein-protein interactions : Fungal Hsp90

Fungal Hsp90 chaperone is a major regulator of cell wall integrity and virulence. Genetic impairment of Hsp90 function reduces tolerance to stress and abrogates drug resistance to the two main classes of antifungals (azoles and echinocandins). Inhibition of Hsp90 by geldanamycin restores susceptibility of *C. albicans* strains resistant to azoles and echinocandins but such ATP inhibitors appear to have limited therapeutic potential on their own as they exhibit in vivo toxicity because of their non-selectivity.

This project proposes an innovative and original strategy in medical mycology to selectively inhibit yeast Hsp90 by targeting its interactions with associated proteins. The aim is to identify in silico and in vitro small molecules or hits able to disrupt the protein-protein interactions (PPIs). This approach will be carried out thanks to an interdisciplinary consortium, gathering biologists, organic and computational chemists. Therefore, the goal of the fundamental and multidisciplinary project will be the identification of new drug candidates with selective antifungal activity and being able to bypass resistance to the most widely used antifungal drugs.

The involved members/partners are P Le Pape (Medical Mycology), A. Laurent (Molecular modeling), P. Marchand and MA Bazin (Organic chemistry). Support from the IMPACT plateforme. This project is included in the PIRAMID consortium project supported by Pays de la Loire. The postdoctoral fellow will perform biological studies to produce *Candida* recombinant proteins and mutant strains to confirm the modelisation and biological concepts and to standardize *in vitro* methods to evaluate new compounds. The postdoc will work with Fungiline screen platform of the EA1155 IICiMed and Biogenouest Impact plateforme.

Contact: Patrice Le Pape 0635552728 patrice.lepape@chu-nantes.fr

IICiMed UPRES EA 1155, Institut de Recherche en Santé 2, Université de Nantes 22 Boulevard Bénoni Goullin, 44200 Nantes, France