Joint Postdoctoral Position available in Nuclear Magnetic Resonance in Grenoble (France)

In vitro and *in vivo* NMR investigation of the L,D-transpeptidase:peptidoglycan complex and of the mycobacterial cell-wall maturation

For over 50 years, peptidoglycan has played a pivotal role in the development of antibacterial chemotherapy. In the hunt for new drugs, the biosynthetic pathways of this ubiquitous cell wall polymer have been deciphered and essential peptidoglycan-synthesizing enzymes have been identified as antibacterial targets with high potentialand characterized *in vitro*. Nevertheless the efforts to develop drugs acting on these rationally chosen targets have largely proven disappointing due to the limited number of biophysical tools capable to produce static and dynamic structural views of the entire peptidoglycan polymer along the bacterial cell-life cycle and of its evolution under the selective pressure of antibiotics. Focusing on one important cell-wall synthesis and maturation reaction, the L,D-transpeptidation, the present project aims at combining information obtained on samples of different levels of complexity, ranging from purified enzymes in interaction with peptidoglycan fragments to the complete cell-wall synthesis machinery in bacterial cells. In this context, innovative spectroscopic approaches including high-field solution NMR, solid-state NMR as well as MAS-DNP will be conducted to provide a new view on the role of L,D-transpeptidases (Ldts) in the cross-linking of peptidoglycan peptide stems along the cell maturation.

To succeed in this integrative approach a joint postdoctoral position is proposed between two NMR research groups in Grenoble that already collaborated efficiently in the past. Structural and dynamical studies of peptidoglycan:L,D-transpeptidase complexes by liquid- and solid-state NMR spectroscopy will be mainly hosted in the Biomolecular NMR Spectroscopy group at Institut de Biologie Structurale (IBS, http://www.ibs.fr/) in the team directed by Dr Jean-Pierre Simorre. This group has a direct access to the state of the art NMR facility at IBS containing six high-field spectrometers (950 MHz, 850 MHz, 700 MHz, 3x600 MHz) equipped with latest solid-state NMR and cryogenic liquid-state probes. Furthermore, an innovative approach based on MAS-DNP will be developed, in particular for *in-vivo* studies. This part of the work will take place in the DNP group of the Institute for Nanosciences and Cryogenics at CEA Grenoble under the supervision of Sabine Hediger. This team, directed by Gaël De Paëpe, hosts a 400 MHz MAS-DNP spectrometer and is very active on instrumentation and methods developments in standard and ultra-low temperature MAS-DNP. The synergy between both groups is reinforced by the geographical proximity.

Applicants are expected to have a doctoral experience in liquid-state and/or solid-state biomolecular NMR spectroscopy. Knowledge about MAS-DNP will be considered as a plus. The successful candidate will be recruited for **18 months** and will benefit from an ANR postdoctoral fellowship. Interested candidates should send their application with a curriculum vitae, a letter of motivation, and 2 reference letters by **May 31st, 2017** via email to Jean-Pierre Simorre (jean-pierre.simorre@ibs.fr) and Sabine Hediger (sabine.hediger@cea.fr).

Selected related publications from our groups:

1. Schanda P, Triboulet S, Laguri C, Bougault CM, Ayala I, Callon M, Arthur M, **Simorre** JP. (2014) J. Am. Chem. Soc. 136(51):17852-17860.
2. Takahashi H1, Ayala I, Bardet M, De Paëpe G, **Simorre JP**, **Hediger S**. (2013) J Am Chem Soc. 135(13):5105-5110.