

## Post-Doctoral Research Associate Position - Development of Innovative Biochemical Methods for the NMR Studies of Therapeutics mAbs at Atomic Resolution

**Contract duration: 3 years**  
**funded by French National Research Agency**  
**Institut de Biologie Structurale – University of Grenoble (FR)**

Monoclonal antibodies (mAbs) have become the fastest growing class of therapeutics owing to their beneficial impacts in treating many life-threatening diseases. Development of protein pharmaceuticals (biologics) is challenging and requires overcoming various manufacturing hurdles such as purity, stability and structure characterization of the product. The 3D structure is unique to biologics and is directly related to their function. This is a key parameter to be assessed when evaluating the robustness of Therapeutic mAbs. Fragmentation and chemical modifications routinely encountered during production and long-term storage of mAbs, can potentially affect structure and alter therapeutics activities. The biophysical toolbox currently available (FT-IR, intrinsic fluorescence, DSC, CD) for the characterization of therapeutic mAbs in development does not have sufficient resolution to demonstrate subtle changes in mAb structure which nevertheless impact potency.

The IBS team, led by Dr. Jérôme Boisbouvier, develops and applies NMR and isotope labelling methods to study the structure, dynamics and mechanism of large biomolecular complexes. The team has developed in-house, new cell-free approaches to produce Fab fragments with optimized isotopic labelling for solution NMR studies of this new class of therapeutics. We are looking to strengthen the team and recruit a senior post-doctoral research associate who will be in charge of developing an innovative cell-free labelling method to simplify and accelerate the analysis of large protein complexes NMR spectra. The selected candidate will collaborate with the biophysicists, biochemists, post-doctoral fellows, PhD students and engineers of the team in order to apply the newly developed method to the study of interactions between therapeutic mAbs and human targets as well as the large molecular machines studied in the team. The research associate will participate in the management of the project, in the training of the young researchers of the team, and will be actively involved in the collaboration with the academic (Drs. P Barraud/ C. Tisné - IBPC-Paris) and industrial (Drs. C. Doyen & O. Frances - Sanofi R&D) collaborators.

### **Recent Relevant Publications of the team:**

Henot, Rioual, Favier, Macek, Crublet, Josso, Brutscher, Frech, Gans, Loison, Boisbouvier “*Visualizing the Transiently Populated Closed-State of Human HSP90 ATP Binding Domain*”. Nature Communications (2022). [doi: 10.1038/s41467-022-35399-8](https://doi.org/10.1038/s41467-022-35399-8)

Törner, Kupreichyk, Gremer, Colas Debled, Fenel, Gans, Willbold, Schoehn, Hoyer, Boisbouvier “*Structural Basis for the Inhibition of IAPP Fibril Formation by the Co-Chaperonin Prefoldin*”. Nature Communications (2022). [doi: 10.1038/s41467-022-30042-y](https://doi.org/10.1038/s41467-022-30042-y)

Gauto, Estrozi, Schwieters, Effantin, Macek, Sounier, Sivertsen, Schmidt, Kerfah, Mas, Colletier, Güntert, Favier, Schoehn, Schanda, Boisbouvier “*Integrated NMR and cryo-EM atomic-resolution structure determination of a half-megadalton enzyme complex*”. Nature Communications (2019). [doi: /10.1038/s41467-019-10490-9](https://doi.org/10.1038/s41467-019-10490-9)

Mas, Guan, Crublet, Colas Debled, Moriscot, Gans, Schoehn, Macek, Schanda, Boisbouvier “*Structural Investigation of a Chaperonin in Action Reveals How Nucleotide Binding Regulates the Functional Cycle*”. *Science Advances* (2018). doi: [10.1126/sciadv.aau4196](https://doi.org/10.1126/sciadv.aau4196)

Macek, Kerfah, Boeri Erba, Crublet, Moriscot, Schoehn, Amero, Boisbouvier “*Unraveling Self-Assembly Pathways of the 468 kDa Proteolytic Machine TET2*”. *Science Advances* (2017). doi: [10.1126/sciadv.1601601](https://doi.org/10.1126/sciadv.1601601)

**IBS Facilities:** The IBS is situated on the European Photon and Neutron (EPN) campus together with its European partners, the European Molecular Biology Laboratory (EMBL), the European Synchrotron Radiation Facility (ESRF), and the Institute Laue-Langevin (ILL). This unique site provides access to state of the art equipment to analyze biological systems at different scales of resolution. The EPN site, and the Grenoble scientific community in general represents a true hub of integrated structural and dynamic biology. The IBS itself employs 300 peoples and provides a lively international working environment with state-of-the-art NMR facilities, including 950, 850, 700 and 600MHz NMR spectrometers with both liquid-state cryoprobes and state-of-the-art solid-state technology, dedicated wet-lab facilities for cloning, in vivo and in vitro expression, isotope labelling and purification of proteins and state-of-the-art imaging facilities. Access to biophysical platforms is facilitated via the Integrated Structural Biology Grenoble (ISBG) platform (<http://www.isbg.fr/spip.php?lang=en>).

**Grenoble:** Capital of the French Alps, Grenoble is a world-renowned scientific hub with a strong international flavor. It is a pleasant city, situated at the foot of three mountain ranges offering many possibilities for cultural, outdoor and sporting activities throughout the year. Grenoble is close to the French riviera, Italy and Switzerland and is served by international and national airports and a high-speed rail network <https://www.ibs.fr/en/about-us/location>

**Position benefits:** The selected candidate will become an employee of the University of Grenoble. The gross salary ranges from €3,125 to €3,740 per month for full-time employment, depending on previous work experience. The total duration of the contract is 3 years and the starting date is expected between June 1 and September 1, 2023.

**Application:** Candidates should have a PhD in biology/biochemistry/biophysics or structural biology + a minimum of 3 years of post-doctoral experience with strong skills in biochemistry, expression and purification of challenging proteins and complexes for structural biology studies. Prior experience in cell-free protein expression and/or biomolecular NMR will be appreciated but is not required. Interested candidates should send a CV with a list of publications, a cover letter and the names and email addresses of two references. These documents should be submitted by email to [jerome.boisbouvier@ibs.fr](mailto:jerome.boisbouvier@ibs.fr) before April 16, 2023. Shortlisted candidates will be contacted for an interview in late April.