



Post-doctoral position to study *in vivo* transcriptional regulation at CBI Toulouse France

Project description: This position is offered in the context of the ANR project MEDNET untitled “The mediator complex: from a protein-protein interaction network to gene regulation *in vivo*”. Transcription initiation by RNA polymerase II (PolII) requires many protein-protein interactions, whose roles *in vivo* have been poorly investigated. One key element in this process is Mediator (MED), a conserved multisubunit complex serving as a physical as well as functional interface between DNA-bound transcription factors (TFs) and the basal PolII machinery. Despite a general role of Mediator in controlling transcriptional activation or repression, some MED subunits (SUs) display strikingly-specific functions, their molecular specificity and their functional roles *in vivo* in tissue-specific gene regulation, remains poorly understood. The present project aims to better understand the regulatory role of the CDK8 module, a separable MED sub-complex, involved in gene repression as well as activation. In particular, it will focus on the identification of protein domains required *in vivo* for CKM and anchorage to core MED. The successful candidate will address these questions in the *Drosophila* model, by generating CRISPR-CAS9 mutants affecting CKM-core MED interactions and analyzing their functional consequences in a living animal, through phenotypic, transcriptomic and chromatin immunoprecipitation analyses.

Keywords: transcriptional regulation, Mediator complex, *Drosophila* genetics, CDK8 module.

Selected references: Boube*, M, Hudry, B, Immarigeon, C, Carrier, C, Bernat-Fabre, S, Merabet, S, Graba, Y, Bourbon*, HM, and Cribbs*, DL (2014). *Drosophila melanogaster* Hox Transcription Factors Access the RNA Polymerase II Machinery through Direct Homeodomain Binding to a Conserved Motif of Mediator Subunit Med19. *PLoS Genetics* 10(5):e1004303. Baanannou, A, Mojica-Vazquez, LH, Darras, G, Couderc, JL, Cribbs, DL, Boube*, M, and Bourbon*, HM (2013). *Drosophila* Distal-less and Rotund Bind a Single Enhancer Ensuring Reliable and Robust *bric-a-brac2* Expression in Distinct Limb Morphogenetic Fields. *PLoS Genetics* 9(6):e1003581. Gobert, V, Osman, D, Bras, S, Augé, B, Boube, M, Bourbon, HM, Horn, T, Boutros, M, Haenlin, M and Waltzer, L (2010). A genome-wide RNA interference screen identifies a differential role of the mediator CDK8 module subunits for GATA/RUNX-activated transcription in *Drosophila*. *Mol Cell Biol.* 30, 2837-48. Bourbon H.M. (2008) Comparative genomics supports a deep evolutionary origin for the large, four-module transcriptional mediator complex *NAR*-36(12):3993-4008. Loncle, N., Boube, M., Joulia, L., Boschiero, C., Werner, M., Cribbs, D.L., and Bourbon, H.M. (2007). Distinct roles for Mediator Cdk8 module subunits in *Drosophila* development. *EMBO J* 26, 1045-1054

Toulouse and the CBI: Our research group is located in the Centre de Biologie du Développement (CBD). CBD is part of The Center for Integrative Biology in Toulouse (CBI-Toulouse) which unites five research departments and forms a strong pole in gene regulation and developmental genetics, with a total of about 400 researchers (<http://cbi-toulouse.fr>). It also benefits from several facilities/platforms: IBISA confocal microscopy, *Drosophila* housing, nursing and injection facilities. Nested in south western France, Toulouse, with around 1.2 million people in its metropolis, is the fourth biggest city in France (behind Paris, Lyon, and Marseille). Known to locals as “La Ville Rose” (the Pink City) after the pink stone used in many of its buildings, Toulouse is a city on the move. Boasting the world renowned University of Toulouse, the city ranked as the second best place in France to be a student this year.

Qualification and experience - Applicants should have a PhD in a relevant area of molecular and cellular life sciences. We are seeking a motivated candidate with strong experience in molecular biology, including NGS-based methods (RNAseq, ChIPseq) and *Drosophila* genetics. Experience in imaging technology would ideally complement this profile.

Funding: The position is available starting first of October 2018 for a one year fixed term contract twice renewable, funded by French ANR.

Application: Candidates are encouraged to send applications (cover letter, CV, and contact information of 3 references) to Muriel BOUBE muriel.boube-trey@univ-tlse3.fr and Henri-Marc BOURBON henri-marc.bourbon@univ-tlse3.fr, before July 15th 2018.