# PhD Program between the Freie Universität Berlin (FUB) and the China Scholarship Council (CSC)

## Open PhD position at FUB for CSC scholarship candidates 2018

***Please note: the PhD position is only offered to Chinese PhD candidates for application in the framework of the FUB-CSC PhD Program.***

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| **Department/Institute:** | Department of Biology, Chemistry, Pharmacy / Institute of Chemistry and Biochemistry |
| **Subject area:** | Gene Regulation, Transcription, Structural Biochemistry |
| **Name of Supervisor:** | Prof. Markus C. Wahl, PhD |
| **Number of open PhD positions:** | 2 |
| **Type of the PhD Study:** | Full-time |
| **Project title:** | Structural basis of bacterial transcription regulation |

**PhD Project description:**

In all free-living organisms, transcription is carried out by multi-subunit RNA polymerases (RNAPs). Bacteria harbor a single RNAP that receives regulatory inputs from the substrate DNA, nascent RNA and protein transcription factors1. The Escherichia coli RNAP core enzyme has a α2ββ'ω subunit composition and associates with a σ factor to form a holoenzyme that can initiate transcription at promoters. After promoter escape, σ is replaced by elongation factors NusA and NusG2, which together with core RNAP form a stable transcription elongation complex. During elongation, E. coli NusA enhances RNAP pausing at specific sites3, while NusG increases RNA chain elongation rate4. Transcription can be terminated via an intrinsic mechanism, elicited by a stable stem-loop structure followed by a stretch of uridine residues in the nascent RNA, which leads to conformational changes in RNAP, destabilization of the DNA:RNA hybrid and release of the transcript5. Alternatively, the ρ factor can terminate transcription by engaging nascent RNA via ρ-utilization sequences, translocating on the transcript in 5'-to-3' direction and, upon encounter of RNAP, extracting the transcript4,6. NusA facilitates intrinsic termination5 and can support or counteract ρ-dependent termination depending on the context6. NusG can directly contact ρ via its C-terminal domain and supports ρ-dependent termination4. Phages can hijack the host transcriptional machinery in diverse ways, and elucidation of such mechanisms also informs about regulatory principles underlying bacterial transcription7.

We use integrative structural biochemical approaches (including X-ray crystallography, single-particle electron cryo-microscopy and chemical cross-linking/mass spectrometry) and structure-guided mutational analyses to elucidate the functional organization of intact bacterial transcription complexes8 as well as of individual components and sub-complexes9,10. Recently, for example, we have worked out the functional architecture of a processive transcription antitermination complex, comprising RNA polymerase, DNA, RNA bearing a specific regulatory sequence, host transcription factors NusA, NusB, NusE and NusG and the phage protein λN8, revealing how the λN protein can launch a multi-pronged strategy to convert RNA polymerase into a termination-resistant form.

In the course of one of the proposed PhD projects, we plan to investigate the molecular mechanisms underlying other antitermination mechanisms, which depend on cis-acting RNA elements on the nascent transcript alone or on cis-acting RNA signals in combination with trans-acting proteins. The second project aims at elucidating the molecular bases of factor-dependent and intrinsic termination and the structural basis of co-transcriptional RNA folding1.

References

1. Zhang J, Landick R (2016) A two-way street: Regulatory interplay between RNA polymerase and nascent RNA structure. Trends Biochem Sci 41, 293–310.

2. Mooney RA, Davis SE, Peters JM, Rowland JL, Ansari AZ, Landick R (2009) Regulator trafficking on bacterial transcription units in vivo. Mol Cell 33, 97-108.

3. Yang X, Lewis PJ (2010) The interaction between RNA polymerase and the elongation factor NusA. RNA Biol 7, 272-275.
4. Tomar SK, Artsimovitch I (2013) NusG-Spt5 proteins-Universal tools for transcription modification and communication. Chem Rev 113, 8604-8619.
5. Nudler E, Gottesman ME (2002) Transcription termination and anti-termination in E. coli. Genes Cells 7, 755-768.
6. Ciampi MS (2006) Rho-dependent terminators and transcription termination. Microbiol 152, 2515-2528.
7. Casjens SR, Hendrix RW (2015) Bacteriophage lambda: Early pioneer and still relevant. Virology 479-480, 310-330.
8. Said N, Krupp F, Anedchenko E, Santos KF, Dybkov O, Huang YH, Lee TC, Loll B, Behrmann E, Bürger J, Mielke T, Loerke J, Urlaub H, Spahn CMT, Weber G, Wahl MC (2017) Structural basis for λN-dependent processive transcription antitermination, Nat Microbiol 2, 17062.
9. Luo X, Hsiao HH, Bubunenko M, Weber G, Court DL, Gottesman ME Urlaub H, Wahl MC (2008) Structural and functional analysis of the E. coli NusB-S10 transcription antitermination complex. Mol Cell 32, 791-802.
10. Burmann BM, Schweimer K, Luo X, Wahl MC, Stitt BL, Gottesman ME, Rösch P (2010) A NusE:NusG complex links transcription and translation. Science 328, 501-504.

**Language requirements:**

English is the working language in our lab. The doctoral thesis can be written in English or German. Proficiency in German is neither required in the lab nor for the thesis. English requirements: IELTS 6.5 or TOEFL 95 ibt.

**Academic requirements:**

We welcome applications from students holding a Bachelor's or Master's degree in Biochemistry or a related area of the Molecular Life Sciences. While students typically enter a PhD program with a Master's degree, in principle students can join after their Bachelor's degree. In the latter case, they may have to conduct some additional courses during the first year of the PhD.
Students need to have a strong theoretical background in Biochemistry and Molecular Biology. They need to have basic biochemical and molecular biological laboratory skills. For example, they should have practical experience with molecular cloning, recombinant protein production and protein purification. Additional background in Structural Biology or Bioinformatics is a plus.

**Information of the professor or research group leader:**

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**Please note:** In a first step, the complete application must be submitted to the Beijing Office for evaluation by January 4th, 2018. Please do not contact the professor before. He/She will get in contact with you after having received the complete application via the Beijing Office in January.