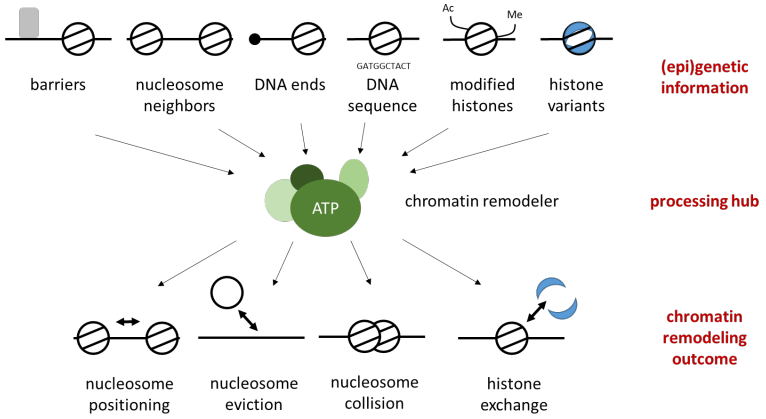
PhD Position (65%, TV-L E13)

Project A04: Genome-wide reconstitution of dynamics in nucleosome positioning, collision, eviction and histone exchange

(group leader: PD Dr. Philipp Korber)

Our Goals

Eukaryotes package their nuclear DNA into a complex protein-nucleic acid structure called **chromatin**. Chromatin structure regulates all DNA-templated processes, like transcription, replication, recombination and repair. Such regulation is often called "**epigenetic**" as it provides another and even heritable kind of information in addition to the genetic information in the DNA sequence. At the most basic level of chromatin, DNA is wrapped around histone octamers forming nucleosomes. The position of nucleosomes as well as their molecular make-up in terms of histone composition and modification influences DNA accessibility and co-factor recruitment/activity. As this offers a fundamental level of genome regulation, there is a keen interest in understanding the establishment, maintenance and modulation of chromatin structures.
We study how **ATP-dependent chromatin remodeling enzymes** shape the chromatin landscape as they mediate the **positioning, collision, eviction** and **histone exchange of nucleosomes.** We conceptualize chromatin remodeling enzymes as "information processing hubs" that read out molecular information of their substrates and their environment, contribute their own intrinsic information and thereby generate chromatin structures of specific functional relevance. Our particular strength and focus lie in the use of the only **genome-wide *in vitro* chromatin reconstitution** system currently available that allows to recapitulate and study the impact of chromatin remodeling enzymes and other factors (yeast and human) on nucleosome organization and dynamics. This protocol is published (Krietenstein et al., 2012, Meth. Enzymol.) and led to a successful series of papers (Zhang et al., 2011, Science; Krietenstein et al., 2016, Cell; Knoll et al., 2018, Nat. Struct. Mol. Biol.; Oberbeckmann, Krietenstein et al., 2021, Nat. Comm.; Oberbeckmann, Krietenstein et al., 2021, Nat. Comm.).



We offer

We are a **small, independent group** in the larger context of the department of Molecular Biology (chair Prof. Dr. Peter B. Becker) at the Biomedical Center, LMU Munich (http://www.molekularbiologie.abi.med.uni-muenchen.de/ueber_uns/korber/index.html). Together with more than 20 chromatin groups within the Molecular Biology department (http://www.molekularbiologie.abi.med.uni-muenchen.de/index.html) and other institutes of the LMU Munich, the Technical University of Munich, the Helmholtz Zentrum München and the Max Planck Institute of Biochemistry, we are members of the **Collaborative Research Center** (Sonderforschungsbereich, SFB) 1064 **"Chromatin Dynamics"** (https://www.sfb1064.med.uni-muenchen.de/about_sfb/index.html). The close proximity of so many groups that also study chromatin and gene regulation mechanisms provides an **exceptionally stimulating and collaborative working environment** and offers an extensive resource of expertise, materials and core facility services (e.g. bioinformatics,

mass spectrometry, high-throughput sequencing). Part of this is the **graduate program** of our Integrated Research and Training Group (IRTG 1064 http://www.sfb1064.med.uni-muenchen.de/irtg/index.html) that provides excellent opportunities, resources and networking for our graduate students (e.g. scientific writing/presentation/career orientation workshops, retreats). In addition to the connections within Munich, we also **collaborate with many groups internationally** (see "Networking/funding" on our home page).

We are looking for a PhD student who will pioneer new assays for histone exchange, generation of non-canoncial nucleosomal particles (e.g. nucleosome collision dimers), nucleosome eviction and DNA sequence-dependent nucleosome positioning in our genome-wide reconstitution system. This will involve **protein purification**, **enzymology** assays, **chromatin analysis** by nuclease digests and DNA methylation footprinting coupled to **high-throughput sequencing, especially single-molecule long-read sequencing (Oxford Nanopore, PacBio)** and **bioinformatic analyses**, and allow to address how chromatin remodeling enzymes process genetic (DNA sequence) and epigenetic (histone modifications, histone variants, chromatin environment) cues. The project will be in close collaboration with strong structural biology groups (Karl-Peter Hopfner, Gene Center, LMU; Sebastian Eustermann, EMBL Heidelberg).

Payment is guaranteed for 3 years and will be according to 65% TV-L E13. The project starts in May or June 2022.

You bring

Do you share our fascination for ATP-driven molecular machines? We are looking for a PhD student who brings a strong interest in **biochemistry** (protein purification and *in vitro* reconstitution) and **bioinformatics** (analysis of high-throughput sequencing data). Any prior experience in these fields is very welcome, but we also provide extensive training opportunities. A recent **degree** (Master or equivalent) in Biology, Biochemistry, Molecular Biotechnology, Pharmacology/Life Sciences with average grade of better than 2.3 is prerequisite. To take advantage of our well-connected local, regional and international research network we expect and encourage an **explorative** attitude and **good communication** skills, especially in English. Although we are a small group with extensive and frequent interaction between all members, an **independent** working attitude with strong problem-solving skills as well as strong **commitment** is expected.

For inquiries or more specific information, please feel free to contact the email below.

Applications should include a letter of motivation, an up-to-date CV, certificates of completed studies, letters of reference or contact information of former supervisors/tutors, and submitted by email to pkorber@lmu.de.

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The institutions contributing to the CRC 1064 are equal opportunity employers.