

The **Rudolf-Buchheim-Institute of Pharmacology (Prof. Dr. Michael Kracht)**, Department of Medicine, is inviting applications for a

PhD position (salary scale TV-H 13, 65 %)

The position is available for 3 years starting at 01.10.2018. The project entitled "Characterization of nuclear IL-1-regulated protein complexes that mediate chemokine gene expression" is part of the collaborative research center TRR81 "Chromatin Changes in Differentiation and Malignancies" as a DFG research grant. The position is provided for a promotion within the framework of the Giessen Graduate Center for the Life Sciences or the TRR81-associated graduate school. The TRR81 is a highly successful international research centre involving Dutch and German scientists (see www.uni-giessen.de/fbz/fb08/trr81).

The project: To date, there is still no cure for the major and common chronic inflammatory diseases that affect humans. During inflammatory reactions newly synthesized cytokines such as interleukin(IL)-1 and chemokines control both, activation and migration of infiltrating and resident tissue cells. Contrary to the prevailing view we postulate that the cytokine response is controlled by specific processes within the chromatin rather than by cytosolic signaling pathways. The identification of such points of nuclear control will open new avenues to modulate the biological activity of IL-1 and of chemokines in disease. Hence, the central aim of this project is identify such nuclear points of control and to reveal their dynamics at the molecular level. For this purpose, state-of-the art methods that are already established in our lab will be applied such as ChIP-seq, ATAC-seq, Chromosome Conformation Capture Assays (4C) and 3D RNA/DNA-FISH.

The applicant will use these approaches to investigate new mechanisms which control NF- κ B and IL-1-responsive genes at the level of chromatin. A focus will be the analysis of the composition of nuclear messenger ribonucleoprotein complexes (mRNP) which are assembled within so called transcription factories. For this, variants of the CRISPR-CAS9 system will be applied which enable PiTCH tagging and reversible knockouts (by the auxin degron system) of endogenous proteins.

Our goal is to study the functional interplay of all these factors at individual gene clusters but also at the genome-wide level in order to find new nuclear mechanisms of sterile inflammation in healthy and malignant epithelial cells and fibroblasts. The experiments involve a broad spectrum of biochemical, cell biology, molecular biology and bioinformatics approaches such chromatin immunoprecipitation, deep sequencing, CRISPR/CAS9-mediated genome engineering, protein purification and identification by mass spectrometry, substantial fluorescence microscopy work and reconstruction of signaling networks. The project is embedded within a highly active and experienced working group. This environment facilitates multiple social and scientific interactions as well as the acquirement of a broad repertoire of scientific methods and concepts. Further information and literature can be found at www.uni-giessen.de/cms/fbz/fb11/institute/rbi/forschung and in (Poppe et al., (2017) PLoS Pathog 13, e1006286; Tenekeci et al., (2016) Mol Cell 62, 943-957; Jurida, et al., Cell Rep 10, 726-739; Handschick, et al. (2014), Mol Cell 53, 193-208).

Your profile: You have successfully finished your university degree in medicine, biochemistry, biology or a related field. A specific interest in mechanistically oriented basic medical research, biochemistry, cell biology, molecular imaging and molecular biology is expected.

We seek a highly engaged and motivated person, who enjoys integrating into a life science research team and who is also willing to develop an independent research profile.

The Justus Liebig University, Giessen seeks to support women in scientific research. Therefore we strongly encourage women to apply for the available position. As a family friendly institution of higher education, the Justus-Liebig-University Giessen, welcomes applicants with children.

Please send your application (no e-mail please) stating the **application number 514/79809/11** with the usual documents until **17.08.2018** to **Prof. Dr. Michael Kracht, Rudolf Buchheim Institute of Pharmacology, Biomedical Research Center Seltersberg, Schubertstrasse 81, 35392 Giessen, Germany**. Applicants with disabilities but otherwise equal qualifications will be preferred. Please do not send originals documents as these will not be returned after end of the selection procedure.